BMC Medical Imaging

RESEARCH Open Access

Predictive impact of T2-MRI radiomics model on initial diagnosis of bone metastasis in prostate cancer patients

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Abstract

Objective The purpose of this study was to examine the potential predictive impact of the T2-MRI radiomics model on the initial diagnosis of bone metastasis in patients with prostate cancer (PCa).

Methods We retrospectively analyzed a total of 141 patients with confirmed PCa from clinical pathology records. Among them, 52 cases had bone metastasis and 89 cases did not. By employing a computer, the patients were randomly assigned to either a training group or a test group. Using ITK-SNAP software, we manually outlined T2WI images for all patients and performed radiomic analysis using Analysis Kit (AK) software. A total of 396 tumor texture features were extracted. In the training group, a single-variable t-test was conducted to identify features strongly associated with PCa bone metastasis. Statistical significance was defined as $P < 0.05$. After dimensionality reduction, the Lasso model was employed to select the best subset, and a random forest model was established. To evaluate the performance of the radiomics model in predicting PCa bone metastasis in the test group, receiver operating characteristic (ROC) curves and confusion matrices were utilized.

Results The selected imaging features exhibited a significant correlation with the differential diagnosis of prostate cancer presence or absence of metastasis. The radiomic model demonstrated high predictive efficiency for PCa bone metastasis, achieving accuracy rates of 0.81% and 0.85% in the training and test groups, respectively. The sensitivities were 92% and 93%, and the specificities were 85% and 81%. The area under the curve values were 0.88 and 0.80 for the training and test groups, respectively.

Conclusion The MRI radiomics method based onT2WI images shows promise in accurately predicting PCa bone metastasis and can serve as a valuable tool for developing clinical treatment plans.

Keywords Prostate cancer, Bone metastasis, Radiomics model, Magnetic resonance imaging, T2WI images

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Introduction

Prostate cancer (PCa) is a prevalent form of cancer among middle-aged and elderly men in China. In the United States [1], it ranks first in terms of incidence and second in terms of mortality among male tumors. While the incidence of PCa in China is lower than in European and American countries, it has been rapidly increasing in recent years [2, 3]. Bone metastasis (BM) is the primary form of metastasis for PCa, with the pelvis and spine being the most commonly affected areas. These metastases occur in 65-90% of cases [4]. Managing bone metastases and related symptoms is crucial for PCa patients, as it greatly impacts their quality of life [5]. Once bone metastases are present, patients are no longer eligible for surgery and must rely on hormonal and/or chemotherapy, palliative care, and radiation therapy [6]. Early detection of bone metastasis in PCa patients is essential for determining the most appropriate treatment plan and predicting prognosis [7].

Previous studies have shown that symptoms and PSA levels are not reliable indicators of metastasis in prostate cancer patients [8]. Computed tomography (CT) is.

more effective in detecting bone lesions and assessing bone destruction and osteogenic changes. However, it is challenging to differentiate small osteoblastic metastases from bone islands. Additionally, CT has limitations in evaluating the activity of metastatic bone tumors and the effectiveness of treatment. Currently, bone scanning, positron emission tomography - X-ray computed tomography (PET-CT), and other imaging techniques are commonly used for diagnosing bone metastases in prostate cancer patients [9]. However, these methods involve ionizing radiation and can be economically burdensome for patients. Magnetic resonance imaging, particularly diffusion-weighted imaging (DWI), has emerged as a valuable tool for detecting bone metastasis with higher sensitivity, specificity, and accuracy than radionuclide bone scan. However, interpreting DWI images can be complex due to the diverse manifestations of bone metastases, which may result in false-positive or false-negative findings. To address these challenges, the use of the Prostate Imaging Reporting and Data Development System (PI-RADS) and radiomics based on big data and artificial intelligence have been proposed as powerful tools for improving diagnosis. Radiomics involves extracting and analyzing quantitative imaging features from medical images to support clinical decision-making [10, 11]. Multiparametric magnetic resonance imaging (mpMRI) is a promising tool in the field of prostate cancer (PCa) diagnosis and treatment. It offers the ability to integrate information about tissue structure and function, making it a valuable diagnostic tool [12]. Over the years, there has been significant advancement in utilizing mpMRI for studying PCa, with a particular focus on its application in the areas of diagnosis, differential diagnosis, and prognosis assessment [13–15].

This study aimed to investigate the potential of using texture features from MRI images to predict the occurrence of bone metastases in prostate cancer patients. Previous studies have shown that radiomics based on T2-MRI sequences can effectively differentiate between benign and malignant prostatic nodules. However, there is a lack of research in the field of radiomics for the prediction and diagnosis of bone metastases in prostate cancer patients. Consequently, this study seeks to bridge this gap by examining whether the combination of texture features extracted from MRI images can accurately predict the development of bone metastases in prostate cancer patients.

Materials and methods

Clinical data

A retrospective analysis was performed on the clinical and imaging records of 141 patients diagnosed with bone metastases from PCa at Jiangxi Provincial People's Hospital. In a 7:3 ratio, these patients were divided into two groups: a training group consisting of 100 cases, and a testing group consisting of 41 cases. This study was approved by the hospital ethics committee, and all patients provided informed consent. Diagnostic procedures involved either Transrectal ultra-sonography (TRUS)-guided biopsy or radical prostatectomy, and both clinical and pathological data were collected. Basic data of the patients, including symptoms such as dysuria, increased urinary frequency and urgency, Gleason's score from pathology report, pathological grade, levels of prostate-specific antigen (PSA) (> 4ng/mL).

The inclusion criteria specified that patients had to undergo MRI examination followed by ultrasound-guided biopsy or surgical pathology to confirm the diagnosis of PCa, without receiving any prior treatment, and that all patients had to undergo multi-parameter MRI using the same scanning type and imaging parameters. Bone metastases were diagnosed using positron emission tomography (PET)-CT. The patients were randomly assigned to either the training or testing group based on the presence or absence of bone metastases.

Exclusion criteria included patients with a history of previous malignancies or related diseases, patients who had undergone prostate surgery, radiotherapy, chemotherapy, endocrine therapy, or particle implantation before the MRI examination, patients with metal objects, claustrophobia, or an inability to cooperate with the examination, patients with poor image quality or artifacts that affected the diagnostic image, and patients with lesions too small to accurately delineate the volume of interest (VOI) during image post-processing. Clinical data, such as age and serum levels of total

prostate-specific antigen (T-PSA), Gleason's score were recorded.

Pathology assessment procedure

To obtain the pathology of the prostate, TRUS was utilized. Sonographers performed punctures, while pathologists read and diagnosed the pathological sections. PET-CT (18 F-FDG) was utilized to examine all cases for the presence of bone metastasis. Osteoblastic lesions with a negative PET-CT and no change in size or density within 6 months of follow-up were included in the bone metastasis negative group (nBS), while osteoblastic lesions with a positive PET-CT or change in size or density within 6 months of follow-up were included in the bone metastasis positive group(pBS).

Influence on omics analysis and image acquisition

Bone metastatic lesions were delineated on standardized T2-weighted imaging (T2WI) based on pathological findings. Two radiologists with 5 years of experience in prostate cancer diagnosis (Doctors A and B) manually segmented areas of interest on T2WI and blinded them to pathological results. First, the two doctors analyzed 20 random images to assess repeatability between groups. Doctor A then repeated the same procedure. ICC greater than 0.8 indicated good consistency of feature extraction, and the rest of the image segmentation was performed by Doctor A. When drawing the T2 image of each tumor, we should select the largest section of the lesion and delineate the ROI along the lesion boundary. ROI should be drawn as close to the edge of the tumor as possible and exclude edema, necrosis, and calcification. For each lesion, the maximum cross-section was selected, and the region of interest (ROI) was outlined along the lesion's boundary. the ROI was manually sketched across all layers of the lesion. Ultimately, these were combined into a three-dimensional (3D) ROI diagram, ensuring that the diameter of the area of interest was no less than 3 mm.

The original image and the corresponding file containing the segmented ROI were imported into the AK software (Artificial Intelligence Kit V3.0.0.R, GE Healthcare) at the same time. A total of 396 quantitative parameters pertaining to image characteristics were extracted. These included metrics such as texture, histogram, form factor, gray scale co-occurrence matrix (GLCM), gray scale run matrix (RLM) and gray scale area size matrix (GLZSM). To address variability in the scale of extraction values, Z-score normalization was applied to the values of each feature. The processes of feature selection and model development occurred within the training group. Initially, Spearman's method was employed to evaluate redundancy among the features, retaining only those with a correlation greater than 0.9. Following this, the maximum-relevance minimum-redundancy (mRMR) algorithm was applied to select features, with the objective of amplifying the relationship between the selected features and their ability to differentiate between benign and malignant cases while reducing redundancy. The calculation of the radiomic signature (Radscore) for each case involved a linear combination of selected features, each weighted according to its respective coefficient. Independent predictors of nBS and pBS were determined using multivariate logistic regression analysis, taking into account possible predictors, including imaging features and clinical risk factors. The least absolute shrinkage and selection operator (LASSO) method was utilized to identify the most relevant features, utilizing a penalty parameter, denoted as λ. The optimal λ value was determined based on the minimum criteria derived from tenfold cross-validation.

In order to equip clinicians with a quantitative tool that differentiates between nBS and pBS, we created a radiomic nomogram, which incorporates both radiomic and clinical features derived from a multiple logistic regression model. We evaluated the discriminative performance of the radiomic nomogram and computed the Radscore for each patient in the testing dataset through formulas established in the training dataset. The methods used for data processing were similar to those described in our previous studies [16].

Results

Characteristics of the patients

In the training group, there were 37 patients with prostate cancer who tested positive for bone metastasis and 63 patients who tested negative. In the testing group, there were 15 patients who tested positive and 26 patients who tested negative for bone metastasis.

In terms of clinical factors, the univariate logistic analysis showed that PSA was a significant factor in predicting PCa. Multivariate Logistic regression analysis showed that PSA and the radiomic signature were significantly different (all $p < 0.05$) (Table 1).

Construction of Normo diagram and evaluation of performance

To construct an image-omics Normo graph, two independent predictors, namely Rad-score and PSA level, were utilized. The chosen features were employed for the calculation of the radscore utilizing formulas disclosed in the Supplementary Data. In the training and testing groups, the accuracy rates were 81% and 85% respectively, with specificities of 85% and 81%, and sensitivities of 92% and 93%. The area under ROC curve (AUC) for the training set was 0.88, and for the testing set, it was 0.80 (Table 2 and Figs. 1, 2, 3 and 4).

Univariate logistic regression was used to find independent predictors of bone metastasis in prostate cancer.

Table 1 Demographic characteristics in the training and testing set

	Training set (*n* = 100)		*P*	Testing set (*n* = 41)		*P*
	Bone metastases	Nonbone metastases		Bone metastases	Nonbone metastases	
Number	37	63		15	26	
Age (yr)	72 ± 5.2	56.3 ± 4.8	0.6253	59.6 ± 1.9	75.9 ± 10.1	0.379
Psa	75.4 ± 15.7	45.7 ± 14.2	< 0.001	69.7 ± 21.6	46.9 ± 11.9	0.0001
RM[iqr]	0.19 [-2.6, 1.7]	-1.24 [-3.9, 0.75]	< 0.0001	-0.35 [-0.46, 2.9]	-0.162 [-3.7, 1.5]	0.0001
GS	0.98 [0.13, 7.26]	0.86 [0.32, 7.95]	0.981	0.87 [0.45, 6.98]	0.81 [0.67, 7.23]	0.69

PCa: prostate cancer; BM: Bone metastasis; NBM: nonbone metastases; GS: Gleaso; RM: Radscore median

Table 2 Diagnostic efficacy of the radiomics model in the training and testing set

Group	Accuracy	AUC (95% CI)	Sensitivity	Specificity
Training set	0.81	0.88 [0.81;0.95]	92%	85%
Testing set	0.85	0.8 [0.64;0.96]	93%	81%

Multivariate logistic regression is used to combine these single predictors (Rad-score and PSA) to develop more robust predictive models for bone metastasis in prostate cancer (Fig. 3). The calibration curves exhibited a strong concordance between the predicted and actual pathology for both groups of patients in the radiomics model.

Discussion

Based on the MP MRI radiomics method, this study personalized analysis and prediction of BM in PCa patients, which provides a new diagnostic method and idea for Bone metastases in PCa patients to facilitate clinical decision-making.

In recent years, some studies based on single sequence or multi-sequence MRI imaging methods to predict the aggressiveness of prostate cancer patients have achieved certain results, but there is no clear consensus on the most effective imaging biomarkers to distinguish the aggressiveness of prostate cancer. Wang et al. [17] established a model based on dynamic contrasts-enhanced MRI (DCE-MRI) combined with T2WI radiomics. Zhang et al. [18] combined DCE-MRI, T2WI and DWI to establish an AUC of 0.86 for predicting bone metastases of newly diagnosed prostate cancer. Based on T2WI combined with ADC images, 11 optimal radiomics features including morphology, Glrlm and Glszm were selected to construct the radiomics model. The AUC of this model was 0.82 for bone metastases of newly diagnosed prostate cancer. Previous studies used T2WI, T1, DWI and other sequences to distinguish the presence of bone metastasis in the imaging diagnosis. We selected all T2 sequences to sketch the images, and we mentioned the reason for this in the previous study. In clinical practice, we find that DWI images are often strongly affected by device performance and often suffer from artifacts. Therefore, DWI images are not reliable in delineating lesions. In addition, due to the high cost of enhanced scans, some patients will give priority to conventional plain scans, which would make the number of enhanced scans in our subjects too small, resulting in a certain degree of selection bias. which provides a theoretical basis for why we choose the T2 sequence, the most versatile and stable image quality, as the research sequence. In this study, the radiomics tags constructed based onT2-MRI extraction and screening features have very good diagnostic performance (AUC = 0. 88), the independent Certification Unit also showed that (AUC = 0. 8). This result is consistent with the previous results of Wang et al. [17]. Radiomics methods can be used through the existing free T2-MRI images can noninvasively quantify tumor heterogeneity, which also validates the central hypothesis of radiomics research, that describing tumor microenvironment based on radiomics method can assist tumor evaluation.

Radiomics is a high-throughput approach for extracting quantitative features from medical imaging images. A total of 396 candidate radiomic features are condensed into 13 potential predictors, including morphology, Glrlm, and Glszm, which are then combined with clinical inquiries to assess the biological behavior of tumors. This methodology has been referenced in various studies focusing on radiomic-based cancer research [15, 19–21].

The composition of each tumor is not absolutely uniform, there may be bleeding, necrosis, calcification, etc. But because the image is three-dimensional, we analyze the tumor through three-dimensional map, although it is difficult to avoid the appearance of some uneven components [22], but also relatively representative of the whole tumor, so that the analysis of the tumor is relatively accurate and reliable [23].

In this study, univariate and multivariate logistic analysis was conducted to examine common clinical factors. The results revealed that prostate-specific antigen (PSA) is an independent clinically relevant risk factor for bone metastasis in primary prostate cancer, which aligns with the findings of Previous researcher [24, 25]. Prostate cancer can disrupt the blood-epithelial barrier, leading to direct release of PSA into the bloodstream and subsequent elevation of PSA levels. The severity of tissue destruction and the risk of bone metastasis are positively correlated with higher levels of PSA. Changes in PSA levels can serve as indicators for evaluating bone alterations,

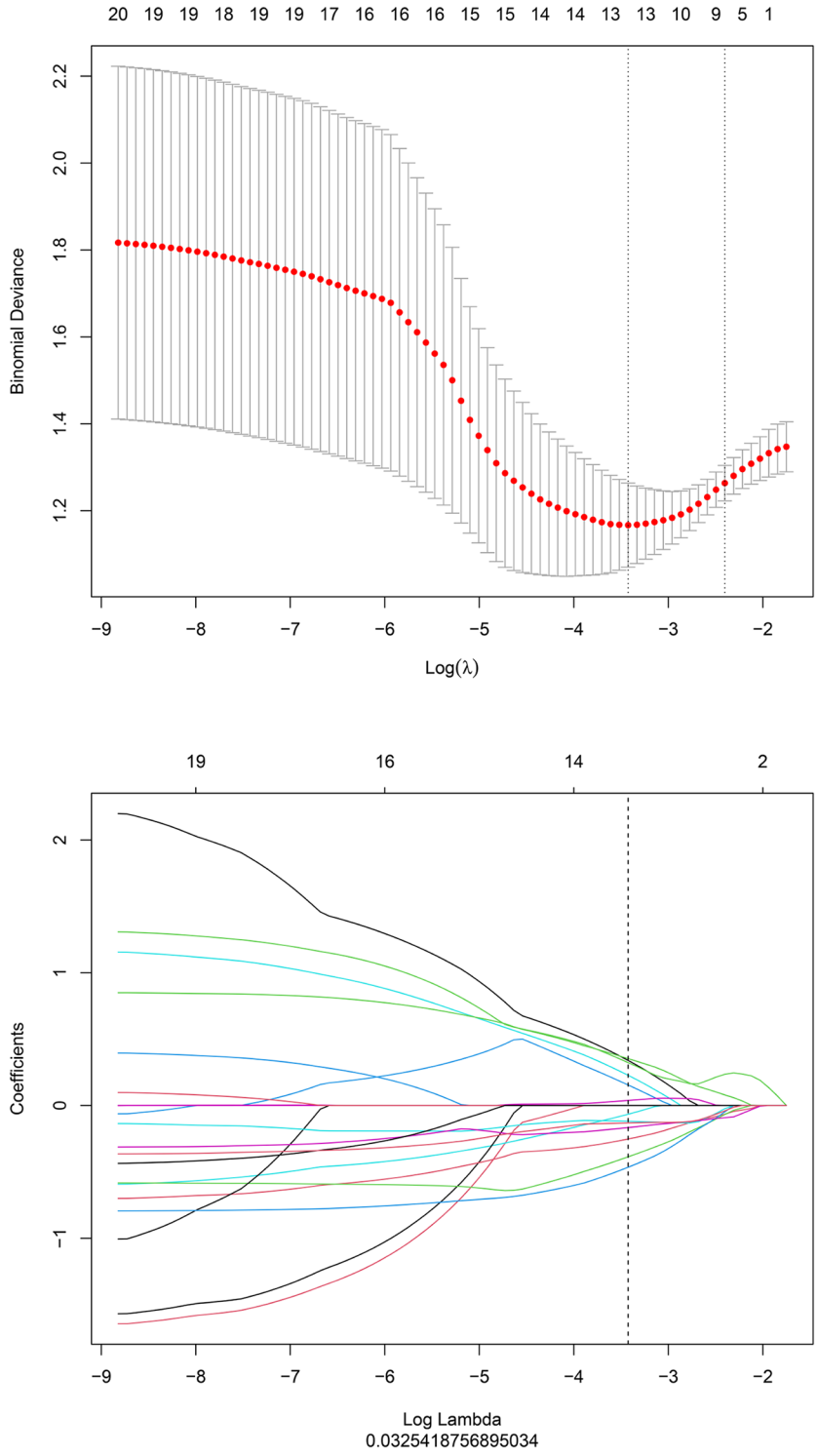

Fig. 1 The establishment of LASSO regression model. (**A**) Curve of binomial deviation of MR radiomics model varying with parameter λ. Adjust the λ parameter to filter out the best feature set. The vertical dotted line on the left indicates the log (λ) value corresponding to the optimal λ value. (**B**) The image shows that the coefficients of 20 texture parameters change with λ. Vertical lines correspond to 9 non-zero coefficient features selected using LASSO cross-validation

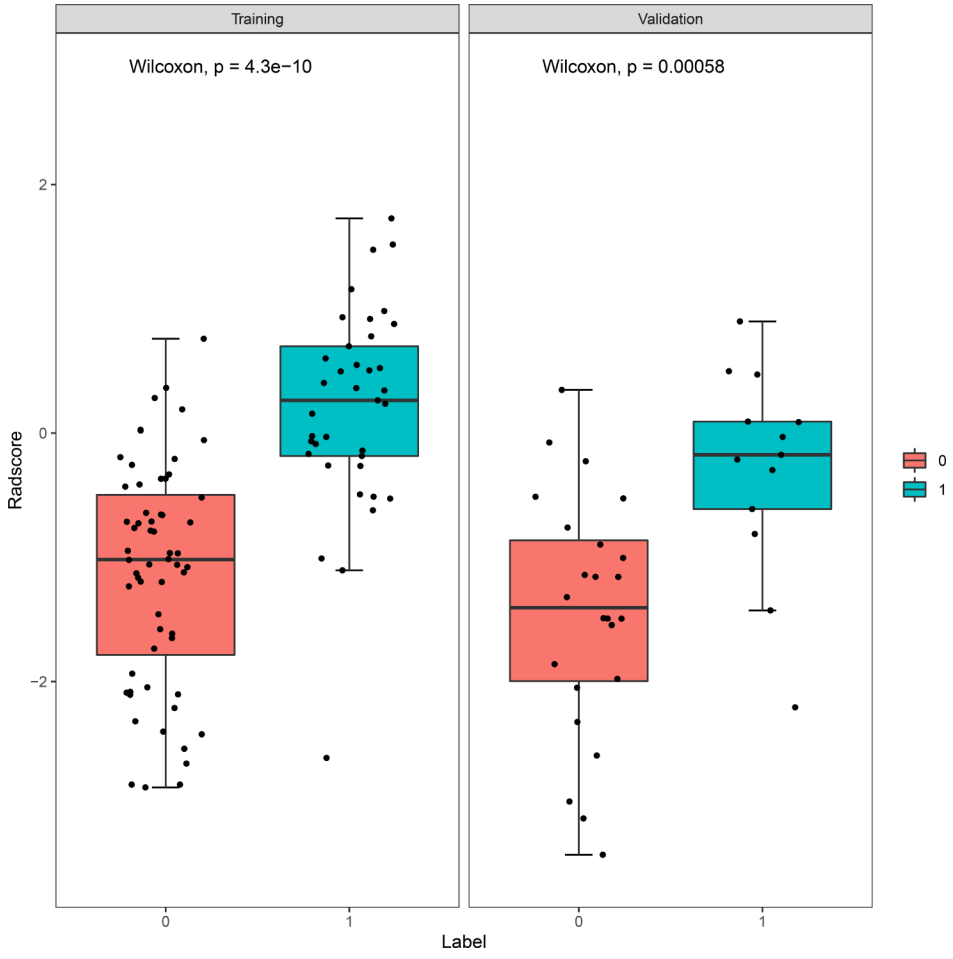

Fig. 2 Radiomic labels used in the group model. Comparison of imaging score between MR model training set (left) and testing set (right). The red label is nonbone metastases of the prostate cancer and the blue label is bone metastases of the prostate cancer

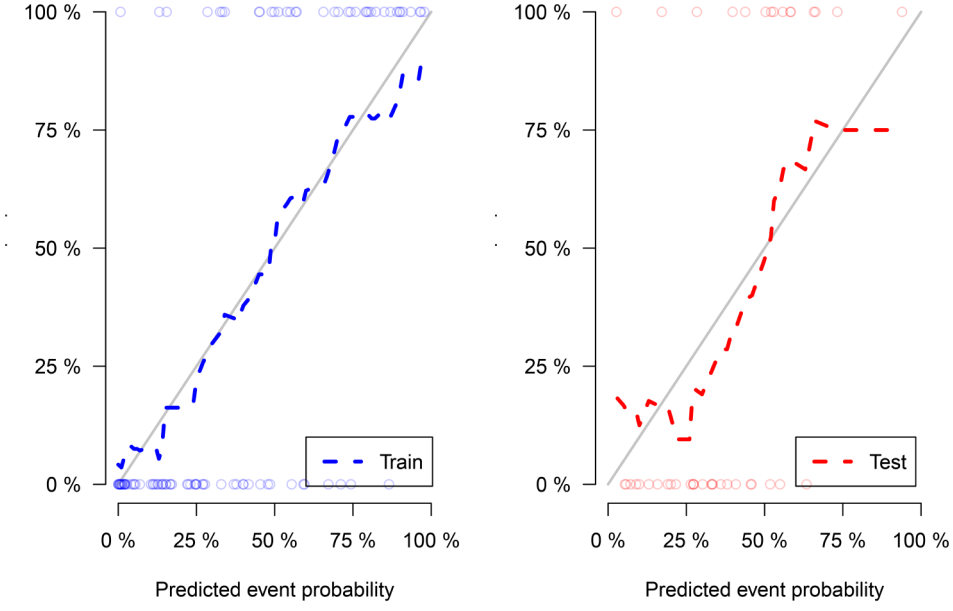

Fig. 3 Correction curves of the training group and the testing group. The left is the train group, the right is the test group

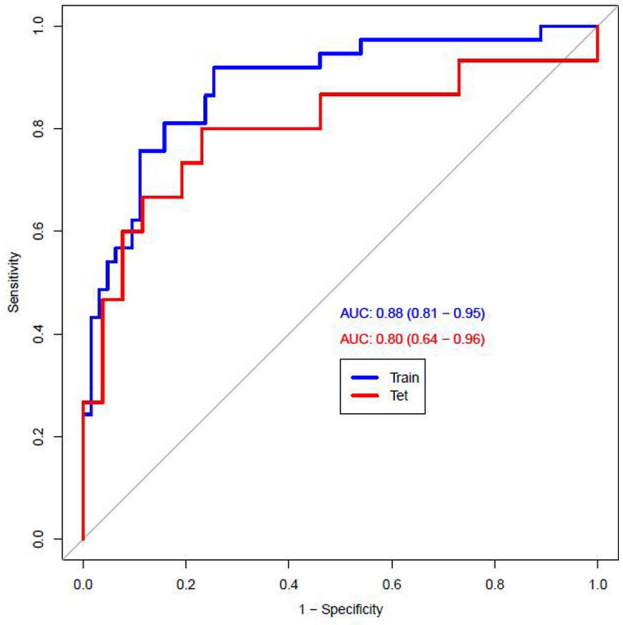

Fig. 4 Evaluation of the prediction model based on T2WI images using ROI in the training group, where the AUC is 0.88(Blue). where the AUC in the testing group is 0.8(Red)

osteoblast activity, and prostate cancer-related bone metastasis.

Some previous studies have suggested that GS may be a predictor of bone metastasis in prostate cancer, but this is not the case in our study. Of course, there are many reasons for this similar result. In my opinion, the possible reasons include: the level of experts who make GS score is inconsistent, and the number of biopsies may also make the postoperative score inaccurate [26].

All of our current case selection is retrospective, so selection bias is inevitable. In the future, we can conduct prospective studies, including diagnosis at admission and follow-up after treatment. For example, regular detection of magnetic resonance images and clinically relevant indicators such as PSA value will guide the clinical treatment effect.

This study has several limitations: (1) The sample size collected is relatively small, and there are fewer BM cases, so the reliability of the study results may be affected after they are divided into the training group and the validation group. (2) We are currently manually sketching all the images, which inevitably causes manual errors. (3) All of our current case selection is retrospective, so it is inevitable that there will be selection bias. (4) At present, we only use T2 images. Although we have made a thoughtful choice about this, we still have to try to explore more diagnostic approaches for the diagnosis of prostate bone metastases by using new technologies, such as automatic image segmentation and deep learning. (5) At present, imaging genomics is developing, and in the future, we can also combine the radiomic characteristics of prostate cancer bone metastases with PTEN, PSMA and other genes to analyze [27, 28]. While this may be an interesting endeavor, it is unclear whether imaging genomics analysis is a more direct representation of tumor heterogeneity than predictive models constructed using radiomics alone. (6) The images before and after treatment of bone metastasis patients were compared with clinical indicators to see if the efficacy could be evaluated, so as to reduce additional PET-CT imaging after treatment of bone metastasis patients with prostate cancer.

In conclusion, the good predictive performance based on T2WI images has certain guiding value for the treatment of prostate cancer.

Acknowledgements
The first and second author (Si Nie, Bing Fan) contributed equally to this study and share the first authorship.

Author contributions
The authors made the following contributions: Si Nie made the conception for this research. Data collection and analysis were performed by Shaogao Gui and Bing Fan, Bing Fan and Hua Chun Zou analyzed the data and drafted the article. Si Nie, Min Lan reviewed/ edited the manuscript. All the authors critically revised the article for important intellectual content. The authors read and approved the final manuscript.

Funding
No funding was obtained for this study.

Data availability
All the data will be available upon reasonable request to the corresponding author of the present paper.

Declarations

Ethics approval and consent to participate
This study was approved by the ethics committee of the Jiangxi Provincial People's Hospital, (The First Affiliated Hospital of Nanchang Medical College). All procedures performed in this study involving human participants were in accordance with the bioethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments. the volunteer involved in the study consent to participate in the study, and the written consent has been obtained from the volunteer.

Consent for publication
All individual person's data consent to publish.

Competing interests
The authors declare no competing interests.

Received: 20 November 2024 / Accepted: 17 March 2025
Published online: 31 March 2025

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49.
2. Hassanipour AS, Mohammadian HA, Ghoncheh M, et al. Incidence and mortality of prostate cancer and their relationship with the Human Development Index worldwide. Prostate Int. 2016;4:118–24.
3. Cao W, Chen HD, Yu YW, et al. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. Chin Med J (Engl). 2021;134(07):783–91.

4. D`Oronzo S, Coleman R, Brown J et al. Metastatic bone disease: pathogenesis and therapeutic options: up-date on bone metastasis management. J Bine Oncol. 2019;15:e004.2018.10.004.
5. Expert consensus on multidisciplinary diagnosis and treatment of prostate cancer bone metastases. (2020 edition). Cancer research, 2020,47(7):479–486.
6. Filograna L, Lenkowicz J, Cellini F, et al. Identification of the most significant magnetic resonance imaging (MRI) radiomic features in oncological patients with vertebral bone marrow metastatic disease: a feasibility study. Radiologia Med. 2019;124:50–7.
7. Chen S, Wang L, Qian K, et al. Establishing a prediction model for prostate cancer bone metastasis. Int J Biol Sci. 2019;15(1):208.
8. Gillessen S, Attard G, Beer TM et al. Management of patients with advanced prostate cancer: the report of the Advanced Prostate Cancer Consensus Conference APCCC 2017. Eur Uro1. 2018;73(2):178–211.
9. Ghafoor S, Burger IA, Vargas AH. Multimodality imaging of prostate cancer. J Nucl Med. 2019;60:1350–8.
10. Aerts HJ, Velazquez ER, Leijenaar RT, et al. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. Nat Commun. 2014;5:400614.
11. Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images are more than pictures, they are data. Radiology. 2016;278:563–77.
12. Mottet N, Van Den Bergh RC, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer—2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol. 2021;79(2):243–62.
13. Sidhu HS, Benigno S, Ganeshan B, et al. Textural analysis of multiparametric MRI detects transition zone prostate cancer. Eur Radiol. 2017;27:2348–58.
14. Ginsburg SB, Algohary A, Pahwa S, et al. Radiomic features for prostate cancer detection on MRI differ between the transition and peripheral zones: Preliminary findings from a multi-institutional study. Magn Reson Imaging. 2017;46:184–93.
15. Algohary A, Viswanath S, Shiradkar R et al. Radiomic features on MRI enable risk categorization of prostate cancer patients on active surveillance: Preliminary findings. J Magn Reson Imaging. 2018;10:1002.
16. Gui S, Lan M, Wang C, Nie S, Fan B. Application Value of Radiomic Nomogram in the Differential Diagnosis of Prostate Cancer and Hyperplasia. Front Oncol. 2022;12:859625.
17. Wang Y, Yu B, hong F, et al. MRI-based texture analysis of the primary tumor for pre-treatment prediction of bone metastases in prostate cancer. Magn Reson Imaging. 2019;60:76–84.
18. Zhang W, Mao N, Wang Y, et al. A Radiomics nomogram for predicting bone metastasis in newly diagnosed prostate cancer patients. Eur J Radiol. 2020;128:109020.
19. Wu S, Zheng J, Li Y, et al. A Radiomics Nomogram for the Preoperative Prediction of Lymph Node Metastasis in Bladder Cancer. Clin Cancer Res. 2017;23:6904–11.
20. Ren S, Qian LC, Cao YY, et al. Computed tomography-based radiomics diagnostic approach for differential diagnosis between early- and late-stage pancreatic ductal adenocarcinoma. World J Gastrointest Oncol. 2024;16(4):1256–67.
21. Ren S, Zhao R, Cui W, et al. Computed Tomography-Based Radiomics Signature for the Preoperative Differentiation of Pancreatic Adenosquamous Carcinoma From Pancreatic Ductal Adenocarcinoma. Front Oncol. 2020;10:1618.
22. Christian MS, Rasche L, Frauenfeld L, et al. A review on tumor heterogeneity and evolution in multiple myeloma: pathological, radiological, molecular genetics, and clinical integration. Virchows Arch. 2020;476(3):337–51.
23. Falagario UG, Ratnani P, Lantz A, et al. Staging Accuracy of Multiparametric Magnetic Resonance Imaging in Caucasian and African American Men Undergoing Radical Prostatectomy. J Urol. 2020;204(1):82–90.
24. Chaoying L, Chao M, Xiangrui Y, et al. Risk factors of bone metastasis in patients with newly diagnosed prostate cancer. Eur Rev Med Pharmacol Sci. 2022;26(2):391–8.
25. Liu W-C, Li M-X, Qian W-X, et al. Application of Machine Learning Techniques to Predict Bone Metastasis in Patients with Prostate Cancer. Cancer Manag Res. 2021;13:8723.
26. Rapiti E, Schaffar R, Iselin C, et al. Importance and determinants of Gleason score undergrading on biopsy sample of prostate cancer in a population-based study. BMC Urol. 2013;13:19.
27. Mc Cann SM, Jiang Y, Fan X, et al. Quantitative multiparametric MRI features and PTEN expression of peripheral zone prostate cancer: a pilot study. AJR Am J Roentgenol. 2016;206:559–65.
28. Heidenreich A, Aus G, Bolla M, et al. EAU guidelines on prostate cancer. Eur Urol. 2008;53:68–80.

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