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Challenges and benefits of using texture analysis of computed tomography and magnetic resonance imaging scans in diagnosis of bladder cancer

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ABSTRACT

Radiomics and texture analysis is a new step in the evaluation of digital medical images using specialized software and quantitative assessment of signs invisible to the eye. The textural parameters obtained through mathematical transformations correlate with morphological, molecular, and genotypic characteristics of the examined area.

This article reviews scientific studies on challenges and benefits of using texture analysis in diagnosis of bladder cancer. The authors describe the practical value of this approach, and consider the challenges and potential of using it. Forty publications published between 2016 and 2024 were selected using keywords from PubMed and Google Scholar.

Multiple studies demonstrate high accuracy of radiomics in local staging of bladder cancer, morphologic assessment of the tumor, and prediction of long-term clinical outcomes.

Therefore, texture analysis of medical images can provide additional information to diagnose bladder cancer in uncertain cases. Standardization of the method is currently one of the key issues to accelerate implementation of radiomics analysis in clinical practice.

Keywords: radiomics; texture analysis; bladder cancer; magnetic resonance imaging; computed tomography.

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Трудности и перспективы применения текстурного анализа компьютерно-томографических и магнитно-резонансных изображений в диагностике рака мочевого пузыря

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АННОТАЦИЯ

Радиомика и текстурный анализ — новый шаг в изучении цифровых медицинских изображений, основанный на использовании специализированного программного обеспечения и количественной оценки невидимых глазу показателей. Извлекаемые путём математических преобразований текстурные показатели коррелируют с морфологическими, молекулярными и генотипическими характеристиками исследуемой области.

В настоящей статье проведён обзор научных исследований, посвящённых возможностям и трудностям применения текстурного анализа в диагностике рака мочевого пузыря. Авторами описана практическая значимость данного метода, рассмотрены сложности и перспективы его использования. С помощью поисковых систем PubMed и Google Scholar по ключевым словам отобраны 40 публикаций, изданных за период с 2016 по 2024 гг.

Результаты многочисленных исследований демонстрируют высокую точность радиомики в местном стадировании рака мочевого пузыря, оценке морфологической картины опухоли и прогнозировании отдалённых клинических исходов.

Таким образом, текстурный анализ медицинских изображений способен предоставить дополнительную информацию в диагностике рака мочевого пузыря в неоднозначных клинических случаях. Сегодня стандартизация метода является одной из ключевых задач для ускорения внедрения радиомического анализа в клиническую практику.

Ключевые слова: радиомика; текстурный анализ; рак мочевого пузыря; магнитно-резонансная томография; компьютерная томография.

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计算机断层扫描和磁共振图像纹理分析在膀胱癌诊断中的应用困难与前景

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摘要

放射组学和纹理分析是基于专用软件和对肉眼不可见指标定量评估的数字医学图像研究的一个新阶段。通过数学变换提取的纹理指数与所研究区域的形态、分子和基因型特征相关。

本文对纹理分析在膀胱癌诊断中的可能性和困难的科学研究进行了概述。作者描述了该方法的实际意义，分析了其使用的困难和前景。利用PubMed和Google Scholar搜索引擎，使用关键词筛选出从2016年至2024年期间发表的40篇文章。

大量研究结果显示，放射组学在膀胱癌的局部分期、肿瘤形态学图像评估和远期临床结果预测方面具有很高的准确性。

由此可见，医学图像的纹理分析能在不明确的临床病例中为膀胱癌的诊断提供额外的信息。如今，方法的标准化是放射组学分析加速推广到临床实践中的关键任务之一。

关键词：放射组学；纹理分析；膀胱癌；磁共振成像；计算机断层扫描。

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DIFFICULTIES IN DIAGNOSING BLADDER CANCER WITH CONVENTIONAL IMAGING AND THE ROLE OF RADIOMICS

Accurately *predicting muscle invasion* is essential for determining an appropriate treatment approach. Magnetic resonance imaging (MRI) with intravenous contrast serves a critical role in the noninvasive diagnosis and staging of bladder cancer. The Vesical Imaging-Reporting and Data System (VI-RADS) is a standardized framework widely applied for interpreting MRI findings during local staging of bladder cancer [1].

Despite advances in multiparameter imaging and enhanced imaging techniques, assessing the extent of local disease remains difficult. Staging tumors based on MRI findings is particularly challenging when the lesion is located in the bladder trigone, urethral neck, or urethral orifice due to the complex anatomy of these regions. Patients classified as VI-RADS 3 present the greatest uncertainty regarding tumor grade. For instance, morphological assessments in this group revealed absence of muscle invasion in 53% of cases and presence of muscle invasion in 47% [2].

The reliability of morphological evaluations obtained through invasive diagnostic procedures heavily depends on the quality of transurethral resection (TUR) of the tumor. Incomplete resection and coagulation-related tissue damage during TUR contribute to the risk of understanding. A systematic review reported that up to 32% of patients experienced disease upstaging and were subsequently diagnosed with muscle invasion following repeat [3]. Furthermore, up to 50% of specimens collected after an initial TUR lacked a muscle layer [2].

The tumor risk category, which partially relies on tumor grade, guides the selection of adjuvant chemotherapy regimens for non-muscle-invasive bladder cancer.

Texture analysis (TA) has emerged as a promising method to enhance the accuracy of bladder cancer staging and address limitations associated with conventional invasive and noninvasive diagnostic approaches.

PROCEDURE AND PRACTICAL ASPECTS OF TEXTURE ANALYSIS

TA is a technique for postprocessing digital medical images that utilizes specialized software to extract texture features (TFs). Several TA software programs have been developed, including *PyRadiomics*, *MaZda*, *MATLAB*, *3D Slicer*, and *LIFEx*.

TA involves a sequence of stages:

- Stage 1: acquisition of medical images and storage in the Digital Imaging and Communications in Medicine format
- Stage 2: selection of the region of interest (ROI) and image segmentation
- Stage 3: extraction of TFs
- Stage 4: statistical analysis using predictive models followed by model testing [4]

Segmentation may be performed manually, semi-automatically, or automatically and can involve either a single slice (2D ROI) or the entire region of interest (3D ROI). The extracted TFs and study outcomes are closely influenced by image quality and segmentation accuracy. The presence of artifacts or specific morphological features (such as calcifications, hemorrhages, or coagulation areas) within the ROI, or analysis extending beyond the ROI, can affect the results [5].

Image preprocessing is an intermediate step between segmentation and TF extraction. This optional process is intended to homogenize images, which is particularly important when dealing with heterogeneous datasets resulting from the use of different imaging equipment and parameters. A wide range of image preprocessing techniques is available. The most commonly used methods include the following [5]:

- Interpolation to achieve isotropic voxels
- Intensity level filtering
- Sampling of cell (bin) number and width
- Application of various filters (such as Laplace–Gaussian and wavelet filters)

Image preprocessing plays a crucial role in standardizing and enhancing the reproducibility of TFs [6–8].

The extracted TFs are generally categorized into several groups. *First-order features* refer to histogram-based characteristics that describe the distribution of voxel intensities within an image. These include kurtosis, entropy, skewness, intensity, skewness ratio, and uniformity. *Second-order features* are derived from the relationships between voxels within the ROI and describe the spatial distribution of gray-level intensities, using matrices such as the Gray-Level Run Length Matrix, Gray-Level Zone Length Matrix, Gray-Level Co-Occurrence Matrix, and Neighborhood Gray-Level Difference Matrix. *Higher-order features* are based on specific mathematical transformations, such as wavelet filtering and Fourier transforms [4].

In clinical practice, TA is applied across various imaging modalities, including computed tomography (CT), PET/CT, X-ray, MRI, and ultrasound. Most studies have investigated the role of radiomics in cancer management for the following objectives [5]:

- Identifying the type of neoplasm (benign or malignant)
- Evaluating the tumor's morphological and biological characteristics (grade, invasiveness)
- Comparing the tumor's texture profile with its genetic profile (radiogenomics)
- Monitoring the response to treatment

Most researchers agree that TA can enhance the effectiveness of localization diagnosis in cancer. Combined predictive models that incorporate TFs along with clinical, laboratory, genetic, and histological data can support personalized patient assessments [9, 10].

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TA, similar to a virtual biopsy, is used to assess tissue heterogeneity [11, 12]. However, traditional biopsy assesses heterogeneity in a specific anatomical site, which may offer limited diagnostic value due to the low number of sampled cells. In contrast, radiomics enables noninvasive analysis of the entire tumor. Additionally, radiomics can help predict overall survival and treatment response [13–16].

TEXTURE ANALYSIS OF MRI IMAGES FOR BLADDER CANCER DIAGNOSIS

In recent years, radiomics has been increasingly applied to the interpretation of MRI findings and the identification of new characteristics and clinically relevant data in bladder cancer. Most published studies on radiomics in bladder cancer focus on identifying TFs that can predict muscle invasion and tumor grade. A three-dimensional ROI (3D ROI) is the preferred segmentation approach among most researchers. The findings of key studies on the TA of MRI images in bladder cancer are summarized in Appendix 1.

Radiomics shows greater effectiveness in bladder cancer diagnosis when combined models incorporating TFs, clinical (morphological) variables, and data from multiple MRI sequences are used [17–19]. For instance, Xu et al. conducted TA on three MRI sequences: T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) maps. Their analysis demonstrated that a model integrating T2WI and DWI TFs was the most effective in distinguishing muscle-invasive from non-muscle-invasive bladder cancer, achieving an area under the curve (AUC) of 0.98, accuracy of 96.3%, sensitivity of 92.6%, and specificity of 100% [18]. Subsequently, Xu et al. reported that combining TUR results with TFs further increased the sensitivity for predicting muscle invasion to 0.96 [17].

Published data indicate that final predictive models capable of differentiating muscle invasion and tumor grade generally incorporate both first- and second-order TFs [20, 21]. However, some studies have concentrated exclusively on histogram features as key TFs [22–24].

Razik et al. reported that only two first-order features—the mean value of positive pixels and kurtosis—extracted from non-preprocessed images were effective in distinguishing high-grade from low-grade tumors. Contrary to expectations, no predictive features were identified when using Laplace–Gaussian filters. Additionally, the study did not identify any TFs capable of differentiating muscle-invasive from non-muscle-invasive bladder cancer. Possible explanations include the use of two-dimensional (2D) segmentation, analysis limited to ADC images, a small sample size (40 observations), standardized machine learning classifiers, and variability in MRI scanners and study protocols [24].

Segmentation can be performed using various methods. Zheng et al. were the first to segment both the tumor and its base. A 3D analysis of T2WI identified 23 discriminative features distinguishing muscle-invasive from non-muscle-invasive bladder cancer, with 10 (43%) of these features in the tumor base. The AUC for the training and test samples was 0.913 and 0.874, respectively. When tumor size (a morphological parameter) was added to the TFs, the AUC slightly improved to 0.922 and 0.876, respectively [21].

Lim et al. assessed data from 36 patients to compare the effectiveness of T2WI and ADC TA for local disease staging. Notably, the study employed two 2D segmentation approaches: the tumor and the adjacent paravesical fat [23]. Multivariate regression analysis showed that entropy was the only feature with significant differences between ⩽T2 and ⩾T3 tumors, as well as between T1 and ⩾T2 tumors. Unlike the findings of Razik et al., the agreement rates for TFs in this study were not influenced by the use of Laplace–Gaussian filters. The authors concluded that entropy correlates directly with tumor heterogeneity and aggressiveness and that TA can be applied for local staging of bladder cancer. Limitations of the study included MRI scans performed on all patients after TUR, as well as variations in magnetic field strength between the scanners (1.5 and 3 T) [23].

TEXTURE ANALYSIS OF CT IMAGES FOR BLADDER CANCER DIAGNOSIS

The role of CT in assessing the extent of tumor spread beyond the bladder is limited. CT scans remain primarily used for detecting distant metastases. However, some recent large studies have explored the application of TA in diagnosing bladder cancer.

Cui et al. used TFs from the venous phase as prognostic markers for muscle-invasive bladder cancer. The study included data from 188 patients, divided into training and test samples. The accuracy of the model was 0.98 [25].

Similarly, Zhang et al. assessed 196 CT scans during the nephrographic phase. The authors used axial scans for 3D segmentation, selecting the largest tumor for analysis when multiple tumors were present. A total of 851 TFs were extracted for each tumor. Ultimately, 12 first-order (*original_shape_Sphe-ricity, original_shape_Elongation, original_shape_Least-AxisLength*) and second-order TFs were chosen for the models. The authors concluded that the risk of muscle invasion was higher in spherical tumors. Three models were developed: clinical, radiomics, and combined. The combined model was the most accurate for predicting muscle invasion, with an AUC of 0.89, whereas the radiomics model also performed well, with an AUC of 0.85. The combined model incorporated radiomic attributes (RadScore) and tumor grade (high-grade/low-grade) [26].

In contrast to previous studies, Ren et al. investigated the potential of radiomics analysis of CT urograms, alongside excretory phase evaluation. The authors analyzed 296 images after preprocessing with a fixed voxel size ($1 \times 1 \times 1$ mm^3) and pixel size scaling to 0.1. The artificial neutral network-based model showed a sensitivity of 0.89 and specificity of 0.93 in diagnosing muscle-invasive bladder cancer [27].

Jing et al. conducted multiphase TA of 204 thick-slice CT scans. The authors used 54 features from the native, corticomedullary, and nephrographic phases (8 first-order features, 3 shape features, and 43 second-order features) to differentiate between low-grade and high-grade bladder cancer, achieving an AUC of 0.79, accuracy of 0.71, sensitivity of 0.68, and specificity of 0.73. Additionally, three models were developed based on the analysis of each phase individually, with the following results: AUCs of 0.70, 0.74, and 0.75 for the native, corticomedullary, and nephrographic phases, respectively. To enhance efficacy, the authors created a combined clinical and radiomics model, which outperformed the radiomics-only model (AUC 0.90, accuracy 0.79, sensitivity 0.81, specificity 0.77). Based on logistic regression, the combined model included two independent predictors of bladder cancer grade: the patient's age and RadScore. Limitations of the study included the use of thick CT slices (5–6 mm) and the absence of image preprocessing, which could have led to lower AUC values in models based solely on TFs [28].

TEXTURE ANALYSIS FOR PREDICTING RESPONSE TO TREATMENT AND LONG-TERM OUTCOMES IN PATIENTS WITH BLADDER CANCER

Despite advancements in endoscopic imaging (such as photodynamic diagnosis and narrow-band imaging) and improved surgical methods, the prognosis for patients following cystectomy remains poor, with an overall 5-year survival rate of about 60% [29].

Two models are commonly used to assess the risk of relapse and progression in non-muscle-invasive bladder cancer after a macroscopically complete TUR. These are the European Organization for Research and Treatment of Cancer and Club Urologico Español de Tratamiento Oncologico (CUETO) [30, 31] classifications. However, these models, which rely on clinical and histological parameters, have limitations, such as low discriminative ability for predicting relapses and a tendency to overestimate risk.

Currently, there is no reliable method for predicting the response to neoadjuvant chemotherapy (NACT) before or during treatment.

These issues highlight the need for research into radiomics as a novel approach for assessing clinical outcomes in bladder cancer. Identifying up-to-date prognostic markers is crucial for more accurately selecting patients likely to respond to NACT, particularly due to the high toxicity of *cisplatin*, a chemotherapy drug recommended for treatment.

Several studies have explored the potential of TA in monitoring therapy [32, 33]. Cha et al. were the first to investigate the use of radiomics to predict the response to NACT in bladder cancer. The authors analyzed CT scans from 82 patients before and after three chemotherapy cycles, with the model achieving an accuracy of 0.7. Although the analysis was based on follow-up CT scans after three chemotherapy cycles, the authors suggest that trained models could be applied at any clinically significant time point to facilitate timely treatment adjustments or discontinuation, before toxic effects occur [34].

Cai et al. developed a nomogram to predict relapse-free survival in patients after partial or complete cystectomy. The study included data from 80 MRI scans, analyzing four MRI sequences (T2WI, DWI, ADC, and post-contrast images) [35].

LIMITATIONS, CHALLENGES, AND PROSPECTS FOR RADIOMICS

The absence of a standardized and unified workflow hinders the broader clinical application of TA [34, 36]. A study assessing the reproducibility of MRI TFs found that the preprocessing settings needed for reliable feature extraction may vary depending on the MRI sequence [37].

Segmentation is a crucial and debated aspect of radiomics. Semi-automatic segmentation is generally preferred over manual segmentation due to its better reproducibility of TFs and faster analysis time. The reproducibility of segmentation is mainly influenced by the tumor type and location [38].

The reproducibility of specific TFs or groups of TFs can differ based on the image standardization method used [39].

TF agreement rates can vary by software, which limits the interchangeability of software tools. Specialized software packages may be designed to analyze specific pixel ranges or tissue types; therefore, images outside the defined analysis framework may not accurately reflect the tissue texture [40].

CONCLUSION

Radiomics is an emerging noninvasive diagnostic tool. In urologic oncology, it shows promise for local disease staging, tumor grade assessment, and long-term prognosis. However, before routine clinical implementation, multicenter randomized studies are necessary.

ADDITIONAL INFORMATION

Appendix 1. Generalized the largest studies based on texture analysis of MRI in bladder cancer. doi: 10.17816/DD633363-4221933

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