



“A Review of RCC Centred Radiomics in The Context of Benign And Malignant Renal masses”

Mohammad Omar Faruk^{1*}, Saiful Islam², Syeda Sadia Ssafa³

MBBS, MD, MBA, Radiology And Nuclear Medicine, NXMU.

*Corresponding Author Mohammad Omar Faruk

MBBS, MD, MBA, Radiology And
Nuclear Medicine, NXMU.

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Abstract: Due to radiologists' subjective interpretation, radiomics texture analysis offers objective image information that would not otherwise be available. In this paper I examined the implications of radiomics for the evaluation of kidney tumors and produced a thorough research. I looked up English-language research on radiomics applications in renal tumor assessment in the PubMed-MEDLINE database till 2023. 52 papers total are included in the analysis, which is divided into four categories: patient outcome prediction, nuclear grade prediction, renal mass differentiation, and gene expression-based molecular markers. The research's main goal is to accurately differentiate benign from malignant renal masses, with a particular emphasis on renal cell carcinoma (RCC) subtypes, angiomyolipoma without visible fat, and oncocytomas. Nuclear grade prediction may help in more appropriate patient selection for risk-stratified treatment. Individualized treatment regimens may be made easier by predicting patient responses and outcomes from targeted drugs, and gene mutations predicted by radiomics may serve as stand-in biomarkers for high-risk disorders. Studies have generally demonstrated that radiomics is better than expert radiological interpretation. Compared to subjective visual interpretation, radiomics provides a more objective way to diagnose kidney cancers. Adding more clinical and imaging data to radiomics algorithms will improve tailored therapy and boost the accuracy of tumor prediction.

Keywords: Renal Cell Carcinoma (RCC), Radiomics, Renal masses, Benign, Malignant, Kidney cancer, Imaging, Tumor characterization, Machine learning, Precision medicine.

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INTRODUCTION

Renal cell carcinoma (RCC) resulted in more than 400,000 newly diagnosed cancer cases and more than 175,000 deaths worldwide in 2018 [1,70]. In the United States alone, RCC represents 5% and 3% of all newly diagnosed cases annually, ranking it as the sixth most frequent cancer in men and the eighth most common cancer in women [2,71]. A rise in the inadvertent detection of renal masses by means of cross-sectional imaging led to the diagnosis of more asymptomatic, small, and clinically localized renal masses. With a diameter of less than 4 cm, small renal masses (SRMs) account for about 55% of all renal masses. About 10% to 15% of these have benign histology [3,72,73]. Patients who are diagnosed with SRMs face the risk of overtreating lesions and enduring unnecessary procedures.

Tissue sampling is made possible by renal tumor biopsy (RTB), which aids in the histology and subtype identification of tumors for risk-stratified therapy [4, 74-83]. Despite its high diagnostic accuracy for RCC, RTB is an intrusive process that has drawn criticism for its failure to differentiate between tumor histologic

subtypes and nuclear grade, as well as for sampling tumors at several locations [5]. Magnetic resonance imaging (MRI) is superior to computed tomography (CT) in the assessment of ambiguous renal masses [6, 65-70], local invasion, and intravascular extension [7], owing to its enhanced soft-tissue contrast. Oncocytoma and angiomyolipoma without visible fat (AMLwvf) are two examples of benign lesions that might be difficult to distinguish from RCC because of subjective radiological image interpretation [8]. The word "radiomics" refers to a group of methods for quantitatively identifying aspects in medical pictures in order to increase the accuracy of image interpretation for prognostic, predictive, and diagnostic purposes. In essence, it is the process of transforming pictures into information so that it may be further mined to enhance clinical decision-making systems [9]. By applying artificial intelligence (AI) techniques, it helps doctors recognize intricate visual patterns that are invisible to the human eye [10]. Advances in AI, particularly in machine and deep learning, have sped up the use of radiomics in medical imaging as a new clinical decision-guiding tool.

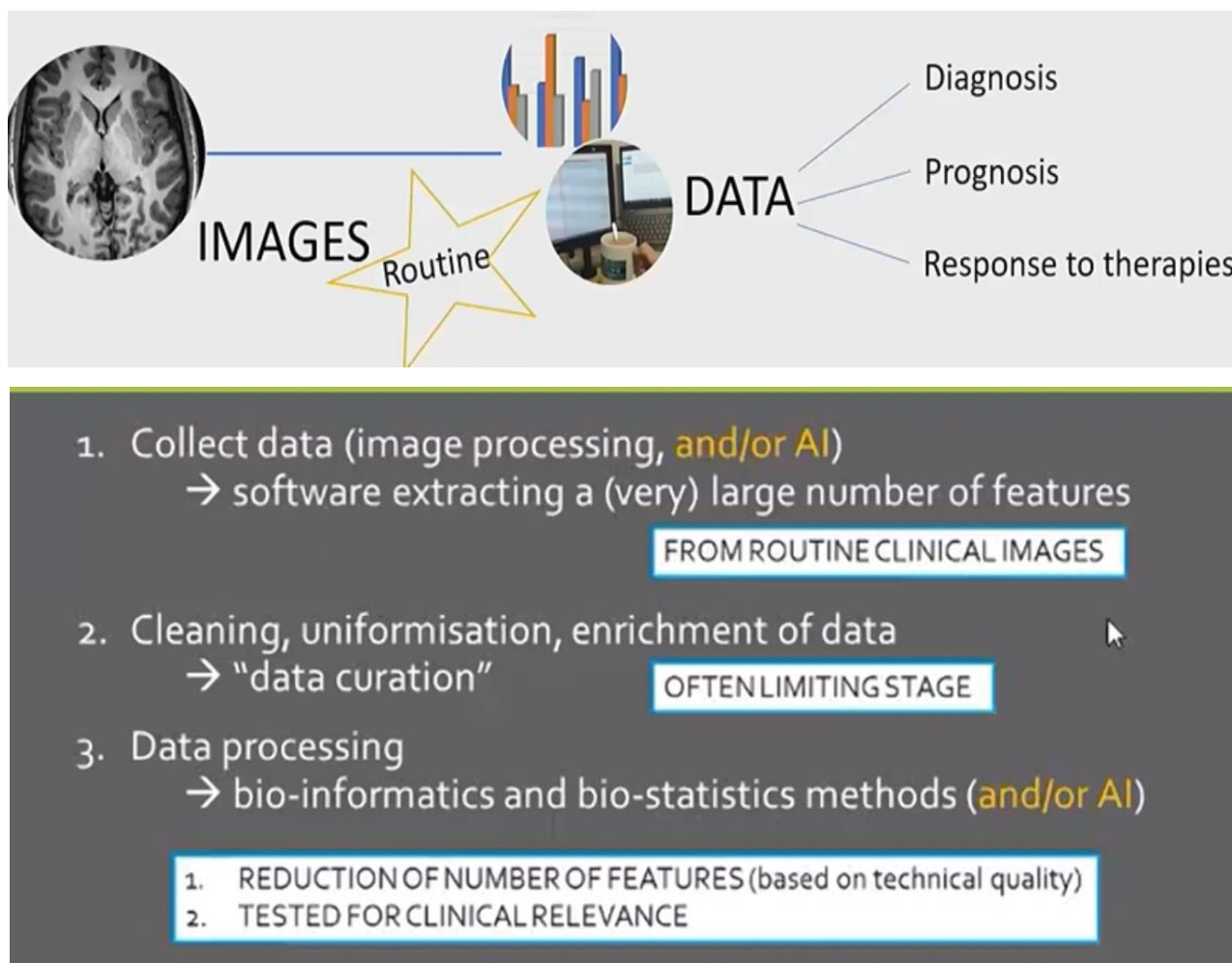


Figure 1: simplification of radiomics

Radiomics Approach

The radiomics workflow typically consists of several intricate stages. Image acquisition and registration are fundamental steps that demand careful attention to ensure the reliability and spatial alignment of the images across different modalities or time points. Subsequently, preprocessing techniques are employed to normalize imaging data, correct for potential noise or artefacts, and harmonize images for consistent analysis. Segmentation of regions of interest (ROIs) then follows, involving the precise delineation of anatomical structures or lesions to focus analysis on specific areas of interest. Feature extraction is a pivotal stage in the radiomics pipeline, encompassing the computation of an extensive range of quantitative features to characterize the spatial relationships, intensity distributions, and texture patterns within the segmented ROI. These features can encompass first-order statistical measures, texture features, shape descriptors, and higher-order statistical metrics, providing a comprehensive representation of the underlying tissue morphology and heterogeneity. Subsequent to feature extraction, sophisticated algorithms for feature selection are employed to identify the most relevant and discriminative features that are predictive of the clinical outcome or biological characteristics of interest. The selected features are then leveraged to construct predictive models through machine learning techniques, such as support vector machines, random forests, or deep learning architectures, tailored to the specific clinical task at hand. These models can be utilized for tasks ranging from disease diagnosis and prognosis to treatment response prediction and patient stratification. Through this comprehensive and data-driven approach, radiomics holds immense potential in unlocking hidden patterns within medical images, facilitating enhanced decision-making in clinical practice, and ultimately paving the way for personalized and precision medicine initiatives.

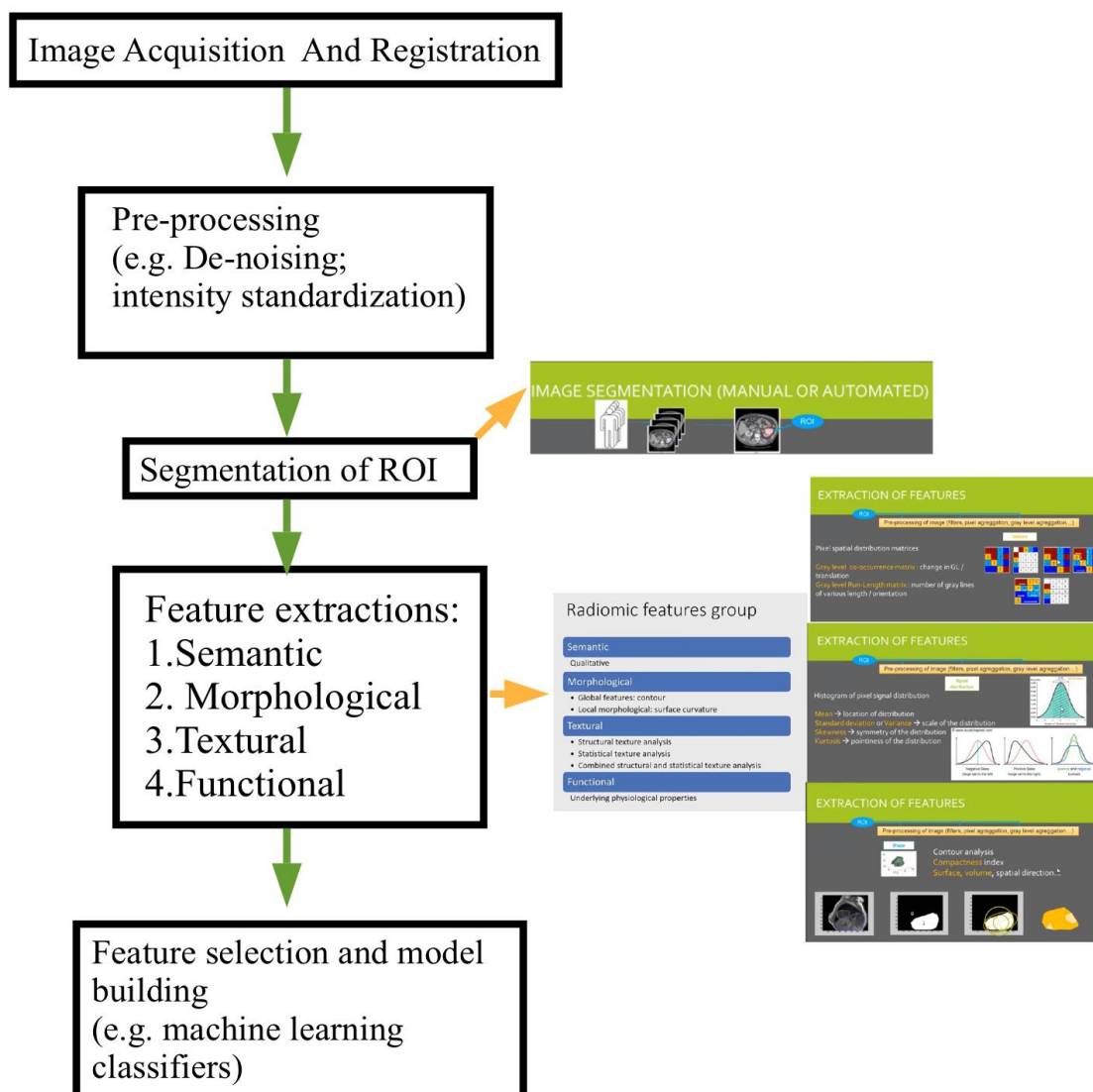


Figure 2: radiomics process

Materials & Methods

Objectives: The main goal was to conduct a thorough literature evaluation on the state of the art radiomics applications in renal mass assessment. A synthesis of publications assessing radiomics precision in identifying benign and malignant tumors, estimating nuclear grade, identifying gene expression-based biomarkers, and prognosticating RCC patients was the secondary target.

Review of The Literature: Using the PubMed-MEDLINE database, a thorough search of English-language literature was carried out till 2023. The search was mainly conducted to publications released in the previous eight years in order to include current trends in radiomics applications. The following broad phrases, either alone or in combination, were part of the search strategy: "radiomics," "deep learning," "machine learning," "renal cell carcinoma," and "kidney cancer." Until no more important articles could be located, I conducted repeated searches and independently reviewed potentially suitable papers against the study selection criteria on all of the recently discovered articles. Articles found using the keyword search had their titles and abstracts collected for full-text analysis.

Criteria for Inclusion & Exclusion: Every article that was retrieved in full text was individually decided to be included or excluded, and any disagreements were settled using disagreements tools. I have Included the studies that fulfilled the following requirements: Radiomics-based analysis of Renal tumors (a); English papers (b); peer-reviewed (c); approach with reproducibility, detailed and consistent documentation (d); related to RCC (e). Following the selection of publications based on eligibility requirements, the following categories of research were disqualified: articles unrelated to renal malignancies; articles not written in English; review articles; editorials; and author comments, inconsistent documentation, not related to RCC. Figure 3 was provided to outline the article selection procedure based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. Following the full-text assessment, I have extracted data to further evaluate the synthesis of both qualitative and quantitative evidence.

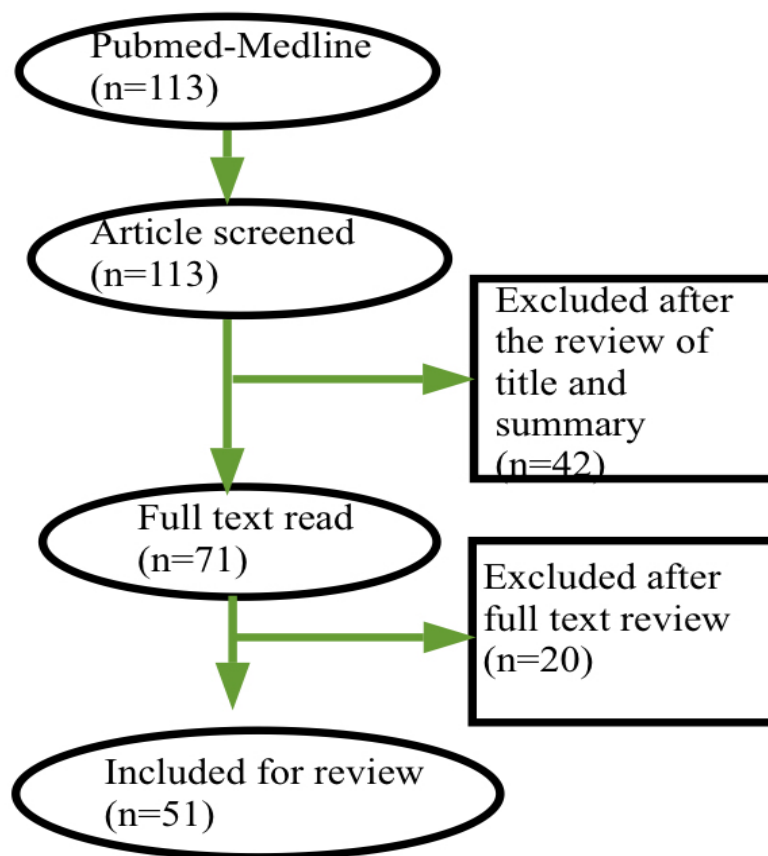


Fig 3: summary of study selection process

Extracting Data and Evaluating Quality: Each study's data extraction was carried out by me. I specified the eligibility criteria using the population, intervention, comparator, outcomes, and research design approach, as recommended by the PRISMA guidelines. The studies were deemed eligible if the population of patients with renal masses underwent evaluation using CT/MRI/positron-emission tomography (PET)-based radiomics data (intervention), in comparison to the subjective image assessment of radiologists (comparator), or as a single-arm study group, to explore the precision of differentiating benign and malignant tumors, predict nuclear grade, find molecular biomarkers, and ascertain patient outcomes. Following the full-text assessment, I separately extracted data to further evaluate the synthesis of both qualitative and quantitative evidence. Every study's imaging technique, number of patients, mean age, mean lesion diameter, radiomics approach, extracted texture characteristics, and accuracy of outcome prediction were considered.

Results

Features of the Included Research: 113 articles in all were found relevant using the search phrase. Following title and abstract evaluation, around 62 papers were ultimately disqualified for the following reasons: Fifteen unrelated urology papers, fourteen unrelated renal cell carcinoma articles, seven reviews, four non-English articles, and two author replies. Twenty papers were eliminated following full-text review on the grounds that they

failed to satisfy the study's goals. Lastly, carefully went over each of the 51 items that were still included in the review in its entirety. Figure 3 displays the flow chart for the study selection procedure. Based on the study aims, the 51 included studies were categorized into four primary areas: 20 for tumor differentiation, 15 for nuclear grade prediction, 10 for gene expression-based molecular biomarkers, and 6 for patient outcome prediction. Subclassifications were identified in tumor differentiation: six for diagnosis of malignant vs benign renal masses, five for RCC against angiomyolipoma without apparent fat, five for RCC versus oncocytoma, and four for RCC subtypes.

Differentiation of Renal Masses: The prevalence and implementation of cross-sectional imaging led to a rise in the number of renal masses detected [24-29, 11]. Though many accidental renal masses are unlikely to grow and provide a long-term hazard to patients, the diagnostic shift toward early disease stages did not transfer into better cancer-specific mortality for localized RCC [12, 67-70]. The overdiagnosis and overtreatment of these malignancies have come to light as a result of these findings. It is common practice to decide whether to treat individuals with renal masses without obtaining a conclusive histologic diagnosis. Clinical imaging is therefore crucial to the decision-making and management of treatment. While RTB has the potential to distinguish between benign and malignant histology, its use in differentiating between aggressive and indolent illness is restricted and selective. Numerous research investigations have demonstrated an inverse relationship between the size of the renal mass on

radiography and the likelihood that surgical specimens would include benign or low-grade disease [13, 30-32, 63]. Current imaging techniques and subjective radiological image interpretation are unable to effectively identify malignant tumors from some benign tumors, such as oncocytomas and AMLwvf, despite the fact that the chance of malignancy rises with mass size [14, 19-23, 66]. Research findings indicate that various renal masses, such as RCC subtypes, AMLwvf, and oncocytomas, may be seen through unique gray-level imaging patterns that can be identified using radiomic analysis [15].

Numerous methods are included in radiomics that are intended to transform medical pictures into high-dimensional, quantitative, and minable data [3]. Histogram, texture, and shape information that may not be visible to the human eye are automatically extracted and analyzed from image data using machine learning (ML) and deep learning (DL) techniques. There is growing interest in using radiomics in oncological imaging as a technique to extract diagnostic, prognostic, and predictive data from regular clinical imaging, given the shortcomings of traditional medical imaging [16, 64]. But routine clinical application of radiomics remains to be observed, even with its broad research use and positive results relating CT/MRI texture characteristics to renal mass characterisation. In order for imaging markers, such as texture-based metrics, to fill the gap between an experimental research tool and a diagnostic algorithm that can be used in clinical settings, it is first necessary to establish the imaging markers' biological validity, technical validity, qualification, and cost-effectiveness [3, 65].

Differentiation of Benign vs. Malignant Renal Masses: To create a clinical decision support (CDS) tool for the classification of renal masses, Kunapuli et al. examined eleven machine learning (ML) techniques. From four-phasic contrast enhanced computed tomography (CECT) scans of 150 patients with a range of benign and malignant lesions, features representative of pertinent metrics were identified. Their relational functional grading boosting (RFGB) model was found to be a potential CDS tool for renal mass diagnosis, with the greatest prediction accuracy and area under the curve (AUC) (0.83) of all 11 techniques [17, 18, 32]. In a similar vein, Erdim et al. built a prediction model for renal mass identification based on CECT imaging from benign and malignant lesions by comparing eight machine learning methods. In nine-tenths of patients, the random forest model had the best accuracy (90.5%) and AUC (0.92), making it a useful technique for differentiating between benign and solid renal tumors [33]. Sun et al. evaluated the ability of expert-level radiologists and radiologic radiomic machine learning models to distinguish benign from malignant solid kidney masses using CECT tests. For the purpose of distinguishing clear cell renal cell carcinoma (ccRCC) from papillary RCC (pRCC) and chromophobe RCC (chRCC), ccRCC from AMLwvf and oncocytoma, and pRCC and chRCC from AMLwvf and oncocytoma, the radiomic ML model produced overall higher performance values in terms of sensitivity and specificity [31]. Likewise, Xi et al. used MRI data to create a DL model, which they then tested against the opinions of four radiologists with extensive training to differentiate between benign and RCC renal tumors. The DL model was equivalent to professional

diagnostic opinion and had generally greater accuracy, sensitivity, and specificity [34].

Angiomyolipoma (AMLwvf) vs. Subtypes of RCC: The most prevalent benign solid kidney tumor, angiomyolipoma (AML), is made up of different proportions of mature adipose tissue, smooth muscle components, and dysmorphic blood vessels [35]. The identification of macroscopic fat, which is often easily visible by CECT or MRI, is essential to the diagnosis. But although AML without visible fat (AMLwvf) accounts for up to 5% of cases, it is difficult to distinguish AMLs from RCC using standard imaging techniques [36, 66, 67,]. AMLwvf is strongly suggested by a number of imaging characteristics that have been published in several investigations and examined using radiomics models [20–23,25,26, 68, 69, 70]. Using three-phase CECT scan pictures, Yan et al. demonstrated that texture analysis (TA) may be a dependable quantitative method to distinguish between AMLwvf, ccRCC, and pRCC with an accuracy in the range of 90.7–100% by using artificial neural network (ANN) classifiers [20]. Similar methodologies were used in other research, however they used ML-based TA from CECT pictures, and the results showed greater accuracy (93.9%) and AUC (0.955) [21, 24, 35]. Furthermore, Cui et al. suggested an automatic computer identification method that uses an over-sampling approach to enhance the sample volume of AMLwvf in order to distinguish AMLwvf from all RCC subtypes from whole-tumor CECT pictures [36, 23]. They demonstrated that radiologists' overall ability in distinguishing AMLwvf from all RCC subtypes was poorer when interpreting morphological data. While some studies looked into improving texture features to further enhance the distinction between AMLwvf and RCC through deep feature classification using ML and ANN-based classifiers [22], others constructed radiomics nomograms from these texture features and demonstrated their superiority over other models that rely solely on clinical factors [36]. Fascinatingly, Ma et al. demonstrated that the unenhanced phase had a higher AUC than the corticomedullary phase (CMP) and nephrographic phase (NP), in addition to demonstrating the superiority of whole-tumor radiomics-based CECT analysis over traditional CECT analysis [37]. These results are promising for the collection of imaging investigations in the future that do not require contrast agents, sparing patients with renal masses from the radiation load associated with multi-phasic CECT.

Oncocytoma vs. Subtypes of RCC: Renal oncocytoma represents around 3-8% of all renal tumors and is a benign kidney tumor [38]. While a central stellate scar is commonly thought to be the primary feature, studies have shown that it is present in around 50% of patients and may also arise in about 25% of chRCC [38]. Furthermore, it might be difficult to distinguish between ccRCC and oncocytoma due to similar imaging characteristics [39, 40]. Thus, a trustworthy radiomics technique that does not depend on the existence of a central scar to identify oncocytomas would be a priceless diagnostic aid. The usefulness of TA in differentiating between RCC subtypes and oncocytomas was assessed by Yu et al. ccRCC and pRCC were both well-distinguished from oncocytoma by the ML model, with AUC values of

0.93 and 0.99, respectively [41]. In order to distinguish oncocytoma from chRCC, Li et al. investigated the clinical use of radiomics-based techniques by combining TA with five ML-based models. They discovered that, with AUC values more than 0.85, all five classifiers did a good job of distinguishing between the two and came to the important conclusion that their method offers useful preoperative diagnostic accuracy [29, 42]. In contrast to final pathology results, several investigations achieved almost total sensitivity in successfully classifying chRCC and oncocytoma using deep learning techniques such as convolutional neural networks (CNN) [30, 42]. In a study including 179 patients who underwent standard four-phasic CECT and had pathologically proven renal masses, Coy et al. examined the diagnostic utility and practicability of a DL-based renal lesion classifier to distinguish between ccRCC and oncocytoma [43, 44]. The excretory phase had the best accuracy of classification with 74.4% accuracy, 85.8% sensitivity, and an 82.5% positive predictive value when the full tumor volume and tumor mid-slices were used.

Differentiation of RCC Subtypes: RCCs may be broadly classified into three primary subtypes based on cell appearance: ccRCC, pRCC, and chRCC, which together account for over 90% of all RCCs [40]. While the pRCC and chRCC subtypes have higher survival rates, the clear cell variation is the most deadly subtype and is more prone to spread [41]. Therefore, because the use of innovative molecular targeted treatment drugs has risen, RCC subtyping has become therapeutically significant. Kocak and colleagues created models utilizing machine learning-based quantitative CECT TA to differentiate between the three main RCC subtypes. While textural characteristics obtained from the enhanced phase outperformed those from the unenhanced phase, the total accuracy of 69.2% achieved by ML-based TA was very low in differentiating between the three main RCC subtypes. Nevertheless, accuracy increased to 84.6% when an ANN boosting technique was used with CMP pictures [32, 54]. In a similar vein, Han et al. used CECT pictures and a DL framework to differentiate between RCC subtypes. An ANN was trained using three-phasic input pictures, and its results, regardless of subtypes, demonstrated an AUC of 0.90 on a dataset of 169 biopsy-proven cases [45]. Li et al. created machine learning (ML)-based radiomics models using CECT pictures to distinguish ccRCC from non-clear-cell variations. They also looked into a possible radiogenomics connection between imaging characteristics and the von Hippel-Lindau gene mutation. A machine learning-based model was constructed using the eight most pertinent CMP characteristics, and it was able to achieve 92.5% accuracy and a validation AUC of 0.95. The von Hippel-Lindau gene mutation was substantially correlated with five of the eight all-important traits [43]. In patients with primary ccRCC, Yin et al. used a combination of positron-emission tomography (PET) and magnetic resonance imaging (MRI)-based radiomics as a surrogate biomarker for intratumoral disease risk of genetic subtypes ccA and ccB [33, 46]. The approach of discriminant analysis using sparse partial least squares was utilized on 168 radiomics characteristics that were chosen from 23 specimens belonging to eight patients. The accurate

classification rate for molecular subtype categorization using only radiomics characteristics was 86.96%. The best classification rate was 95.65% when clinical characteristics, mRNA, and microvascular density from each sample were combined with radiomics features.

Prediction of Nuclear Grades: Based on clinical findings, the International Society of Urological Pathology (ISUP) and the Fuhrman grading system classify patients' risk into high- and low-risk tumors, which are correlated with prognosis. When deciding between nephron-sparing and radical procedures, the heterogeneity of tumor pictures quantitatively evaluated by radiomics may improve appropriate patient selection for monitoring avoiding RTB. Because there is a chance of invasiveness and sample bias with RTB, it is sense to look for non-invasive, safe, and accurate alternatives. Additionally, 16% of nuclear grade upstaging on surgical pathology was recorded, yielding a 51.5% to 75.9% accuracy for grade discrimination [13]. A number of retrospective investigations assessed the accuracy of radiomics in predicting RCC nuclear grade and found that it performed satisfactorily. The ability of non-enhanced CT scan pictures to distinguish between low-grade and high-grade cancers was evaluated in two trials. ML-based TA was shown to have an accuracy of 85.1%, which is comparable to the 81.5% accuracy reported with ANN algorithms [42, 43]. Furthermore, the majority of research constructed models using texture characteristics that were obtained from various CECT scan stages. Models that included texture characteristics from many phases fared better than those that relied just on TA in one phase. Lin et al. extracted textural characteristics from each phase of the CT scan (pre-contrast phase, CMP, and NP) using ML classifiers, and then compared each phase to three-phase CT images. The model that included all stages produced the highest results in terms of AUC (0.87), accuracy (74%), positive predictive value (91%), and negative predictive value (59%). Using ANN-based radiomics, He et al. revealed the top-ranked models, with a predicted mean value of $92.5\% \pm 1.83\%$. Combining textural characteristics from conventional images, such as mean attenuation, parenchyma attenuation, absolute enhance attenuation, and CMP, which were computed from manually chosen areas of interest (ROI), resulted in the greatest accuracy ($94.1\% \pm 1.14\%$) [45-47, 48-51]. The benefit of MRI is that it can characterize soft tissues finely without exposing patients to radiation; As a result, Goyal et al. used a small cohort of patients ($n = 29$) in order to extract textural characteristics from multiphasic MRI. They discovered numerous features that performed exceptionally well in radiomics, with the top three features having AUCs >0.82 [50].

Similar to this, Cui et al. conducted TA from multiphasic MRIs ($n = 93$) and CECTs ($n = 347$), validating the results externally on 20 patients who received both modalities. Interestingly, there were notable improvements in accuracy for machine learning classifiers based on all-sequence MRI pictures (71% to 73% in internal validation and 64% to 74% in external validation) and all-phase CT images (77% to 79% in internal validation and 61% to 69% in external validation) [51]. With the addition of TA-based ratings that might increase prediction accuracy, radiomics is a step forward in the promising field of risk assessment scores for customized medication. Ding et al. developed a prediction score that included ML-based texture and non-texture data, going beyond textures features. In general, a round shape performed comparably to TA features as a good discriminator of high-grade tumors (AUC: 0.723 (0.632–0.803)); nevertheless, the accuracy of a model that included

both texture and non-texture characteristics was not higher than that of the TA-based model [44]. Gill et al. looked into image TA outside of the tumor in a similar manner. They discovered that most characteristics were substantially different between low- and high-grade tumors based on TA from juxtatumoral perinephric fat, with the gray-level co-occurrence matrix having the greatest accuracy (AUC 0.746 (0.63–0.86)). [52]. The therapeutic usefulness of radiomics to differentiate between low- and high-grade cancers has shown significant accuracy rates, particularly with multi-phase pictures. The evidence against MRI being superior for discriminating was limited to small patient populations. Additionally, using additional quantitative data based on the widely used standard radiological characteristics and incorporating textural feature analysis from tissues other than the tumor may enhance radiomics performance. Using clinical characteristics and even genetic data to integrate radiomics with customized medicine algorithms might lead to the development of more durable prediction scores.

Molecular Biomarkers Based on Gene Expression: Radiomics-based molecular biomarker prediction has potential therapeutic use as TA-derived scores may be surrogate biomarkers and reach adequate accuracy. According to genome-wide association studies, BRCA1-associated protein (BAP1) gene mutations are present in around 15% of ccRCC and are linked to high-grade malignancies and a poor prognosis. In order to predict the BAP1 mutation status on ccRCC, Ghosh et al. examined radiomics and discovered that characteristics obtained from the NP phase of CECT scans had an AUC of 0.71. Similar to this, Kocak et al. used CMP pictures to create an ANN algorithm and ML-based TA in order to predict the existence of gene PBRM1 mutations. They discovered that the former performed better than the latter, maintaining 0.987 AUC and 95% accuracy for the PBRM1 mutation status. A mutation in this tumor suppressor gene has been linked to higher grade and advanced-stage colorectal cancer (ccRCC), and it may also affect how well immune checkpoint medicines work [53, 54]. Since angiogenesis is a well-understood process in the pathophysiology of RCC, several targeted medications for the condition try to stop it from developing. Thus, in a small cohort (n = 9), Yin et al. investigated the viability of predicting tumor vascularity using radiomics parameters from PET and MRI. Fresh frozen tissue specimens were used to assess tumor vascularity, microvascular density, and vascular endothelial growth factor (VEGF) expression. The microvascular density was associated with radiomic characteristics, and the combination of image datasets from both modalities, PET/MRI, showed the best association ($r = 0.639$, $p = 0.044$). A link between VEGF expression and radiomic features was not identified ($p = 0.539$). This proof-of-concept work emphasizes the potential for radiomics to predict pathological findings alone, which is extremely useful when such results may act as biomarkers [55]. The creation of nomograms that impact clinical decision-making can be facilitated by these data. By using quantitative genomics data as predictors, several writers so cleared the way for individualized therapy. Park et al. used a model based on deep neural network methods and data from FOXC2, PBRM1, and BAP1 gene and protein expression to predict T1 ccRCC aggressiveness with 85% accuracy (AUC: 0.796) [56]. Similar to this, Li et al. created a gene panel of 15 genes and created an expression-based prediction score that correctly distinguished between ccRCCs at low and high risk and predicted overall survival for three years (AUC: 0.784). Actually, the authors

developed a nomogram that comprised biochemical and clinical data, and once more validation is received, it could prove to be an invaluable clinical tool [57]. To distinguish between ccRCC samples and normal tissue, Azuaje et al. studied data from proteomics, gene expression, and DL-based TA of histology samples. It is noteworthy that there was a correlation between the proteomics data and the image-based data, and that the immune response and extracellular organization activities were associated with the biological processes and pathways of the proteins involved. Additionally, there was a good correlation ($r = 0.76$) between the expression of genes and complementary RNA (cRNA) and image-based data. Even though these investigations didn't do any radiological TA, the pertinent data gathered can be used to further create prediction scores made up of quantitative image data [58].

Disease Development and Patient Prognosis Forecasting:

Making clinical treatment decisions requires prompt identification of individuals who might have worse outcomes. Additionally, anticipating resistance profiles or responses to targeted therapies would result in customized medical algorithms, saving time and money while preventing the negative consequences of ineffective medications. This would increase survival rates and the quality of life for RCC patients. These options have recently been investigated. A pilot research on forecasting the response to sunitinib therapy in two patients with metastatic RCC was published by Antunes et al. With the use of fluorothymidine as a radiotracer, the authors aimed to assess feature variations between test and retest images obtained from multiphasic MRI and PET scans at baseline and three weeks following sunitinib administration. ROIs from tumor and normal tissue pictures were used to investigate the changes in texture aspects of the images in order to determine whether either had changed. Overall, for both modalities, there was little variation between test and retest photos. Furthermore, following three weeks of sunitinib treatment, there was a 63% change in the top-ranked textural characteristics of the tumor regions compared to pretreatment photos, but only a 17% difference in the normal tissue regions. The scientists came to the conclusion that early structural and functional changes in treatment response can be detected using MRI and PET texture characteristics. Of course, more research with a bigger sample size is necessary [59]. Singh et al. used machine learning (ML) techniques to evaluate and categorize data derived from RNA sequencing (RNA-seq) and gene expression profiles. This allowed them to distinguish between patients with early stages (I–II) and late stages (III–IV) of pRCC. Between normal and malignant samples, as well as between early and late stages, the principal component analysis that was only based on gene expression distinguished them with accuracy. Additionally, the various algorithms used to the majority of the characteristics that were chosen produced acceptable accuracy rates, ranging from 82.5 to 82.5 percent, as well as an AUC for precision and recall of 0.69 to 0.79 and a correlation value of 0.60 to 0.68. Following the biological pathways and interactions between proteins, it was discovered that the majority of expression variations were found in microtubule, chromosomal, and cell cycle-related activities. It's interesting to note that kinetochore and centromere protein expression was elevated in late stages of pRCC, which are well-known changes and characteristic neoplastic traits that cause chromosomal instability [59, 60]. Tabibu et al. used a risk assessment based on tumor and nucleus shape characteristics on

histopathological slices created by a CNN to classify a TCGA (The Cancer Genome Atlas) dataset into high- and low-risk ccRCC. When survival probability was assessed following grade discrimination, the high-grade group had a reduced survival rate [61]. It is obvious that radiomics-based progression prediction in RCC is still in its infancy, but if this objective is accomplished, it can represent a significant advancement in RCC treatment.

Current Limitations and Difficulties in Radiomics: Despite the fact that radiomics is becoming more and more popular in medicine and oncology in general, there are still challenges with its practical application in the clinical setting. Primarily, the heterogeneity in research design, utilized radiomic techniques, extracted texture characteristics, and documented outcomes provide challenges for doing quantitative analysis and comparing different methodologies. Second, as the majority of the ML and DL algorithms used in these research were verified using their own dataset, results cannot be generalized or replicated to other datasets and populations in the absence of external validation [62]. Thirdly, future research must continue to take into account the critical elements of repeatability, reproducibility, sample size, statistical power, and standardization [63]. Fourthly, variations in genes can lead to markedly distinct radiomics properties that are inconsistent over all imaging stages [64]. Consequently, a statistical association between radiomics and genetic footprints or prognosis should be established, correlation does not indicate causation, and the relationship between image tumor characteristics and tumor biology is not clear [65].

Incorporating radiomics into clinical workflows also presents practical challenges that need to be addressed. Seamless integration with existing imaging systems and platforms is essential for smooth adoption. Furthermore, the role of radiomics in guiding treatment selection, response assessment, and treatment monitoring requires further exploration through prospective clinical trials. In addition to radiomics, the field of radiogenomics has the potential to provide valuable insights into cancer biology, prognostic markers, and optimize management in RCC patients using imaging data. Many studies have focused on correlating imaging changes and response kinetics with outcomes in advanced/metastatic disease, but there is a need to investigate the specific radiogenomic correlates associated with biological behavior. Ongoing studies aim to correlate response patterns with underlying genetics. While most published studies have focused on qualitative data, the correlation of quantitative imaging data with genomic analysis could provide additional valuable information. Conversely, genomic data have predominantly relied on microarray data, and there is a lack of studies investigating the prognostic significance of micro-RNAs, which can serve as gene regulators. CT and MR-based texture analysis, a quantitative technique for assessing tumor heterogeneity, has shown promising results as a non-invasive imaging biomarker for prognosis and treatment response. Finally, it will be difficult to bridge the translational gap from an experimental research tool to a crucial clinically usable diagnostic and predictive instrument if dataset heterogeneity is not taken into consideration for the conduct of future investigations [3, 64].

Prospects for The Future: To improve the accuracy of radiomics approaches, future research should concentrate on building larger unified medical registries and databases. Better algorithms should be used everywhere—not just at huge computer analysis facilities, but also on mobile devices and through cloud services that secure

users' private information. Customized AI-based software will require specific international regulatory permissions in order to work with robotic platforms in operating rooms all over the world and make intraoperative choices in real time. Furthermore, the validity of diagnoses derived from algorithms and the influence of programming biases on patient care are significant areas of concern. It is obvious that human intelligence will remain the primary influence on the development of more advanced AI in the future, helping to guarantee that patient care is given top priority in these systems and to provide safeguards against unwanted usage. While the field of RCC radiomics shows promise, it is important to acknowledge the limitations of the studies reviewed. Addressing challenges related to standardization, validation, and integration will be crucial for the successful implementation of radiomics in clinical practice. Further research, including large-scale multi-institutional and big institutional studies and prospective clinical trials, is needed to fully elucidate the potential of radiomics in the management of RCC. There are also need for prediction studies based on latest developed gradings, for example need more research on CT Radiomic Analysis of clear cell and papillary RCC subtypes to predict the latest WHO/ISUP Grading in bigger datasets.

Conclusion

Personalized medicine will continue to benefit from radiomics' prediction precision by adding additional data and strengthening models. Large semi-automated patient datasets and electronic medical records can yield instant predictive analytics that can be utilized to provide insights into a variety of disease processes. On the other hand, the quality of the data and its effective integration with other sources to generalize it greatly influence the diagnostic accuracy. These techniques won't replace shared decision-making, but they could be a useful addition to the knowledge patients get from conventional medical treatment. Without a question, a new age in medicine is dawning, with countless potential uses for radiomics in the future. With continued advancements and collaborations, radiomics has the potential to enhance personalized medicine and improve patient outcomes in RCC.

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