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Review Article

Radiomics and Artificial Intelligence for Thyroid Cancer Diagnosis: Concepts, Challenges, and Solutions

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Abstract
Thyroid cancer is an increasing global health concern that requires advanced diagnostic methods. Ai-driven radiomics has shown great promise in improving diagnostic precision and predicting treatment outcomes. Therefore, this review examined the application of AI and radiomics to thyroid cancer diagnosis and treatment. Multiple databases, including PubMed, Medline, EMBASE, Scopus, and Web of Sciences, were reviewed until October 2024. A combination of keywords led to the discovery of an English academic publication on thyroid cancer and related subjects. Among the 42 investigated studies, radiomics analysis, incorporating ultrasound images, demonstrated its effectiveness in diagnosing thyroid cancer. Some studies presented new strategies that outperformed the status quo. The literature emphasized various challenges faced by AI models, including interpretability issues, dataset constraints, and operator dependence. The synthesized findings of the 42 included studies revealed the need for standardization efforts and prospective multicenter studies to address these concerns. Furthermore, several approaches to overcome these obstacles were identified, such as advances in explainable AI technology and personalized medicine techniques. Despite challenges, future research on multidisciplinary cooperation, clinical applicability validation, and algorithm improvement holds the potential to improve patient outcomes and diagnostic precision in the treatment of thyroid cancer.
Keywords: Artificial intelligence, Neoplasms, Machine learning, Radiomics, Thyroid cancer

Introduction
Thyroid cancer ranks seventh globally in incidence with 820,000 cases in 2022, and 24th in mortality with approximately 47,000 deaths. Strikingly, women face a tripled risk of this type of cancer, highlighting the need for research, specifically to overcome radioiodine therapy resistance.[1] Of all endocrine neoplasms, thyroid carcinoma is the most frequent. Its incidence is continuously rising globally, ranking it as the fifth most frequent solid tumor in women and the sixteenth most common in males.[1] Accordingly, an accurate diagnosis must be quickly made to effectively plan treatments and manage patients. Physicians mainly use imaging tests, such as computed tomography (CT), ultrasound (US), and magnetic resonance imaging (MRI), to figure out what kind of thyroid nodule a patient has. Experienced radiologists may find it challenging to interpret these imaging tests, though, as they must be able to identify subtle cancerous signs. The quantitative feature analysis of medical image data is the focus of the medical imaging

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subfield known as radiomics.[2] These features include textural, morphological, and intensity characteristics that are methodically extracted to disclose information that has been hidden in images obtained using modalities, such as computed CT, MRI, or positron emission tomography (PET).[3] Using advanced computational techniques, radiomics aims to convert conventional medical images into data that can be analyzed. Moreover, radiomics enables the detailed characterization of tissues, tumors, and other anatomical structures by extracting a multitude of quantitative features.[4] Additionally, it has a wide range of applications in healthcare, with a particular focus on situations involving cancer, and is important for the identification, formulation, and assessment of cancer treatments. To analyze the extracted features, spot complex patterns, and possibly find biomarkers for prognostic and diagnostic uses, artificial intelligence (AI) and machine-learning (ML) algorithms are essential.[5]

In addition, radiomics is particularly helpful in the field of tumor analysis when it comes to assessing the heterogeneity within tumors, forecasting treatment outcomes, and enabling personalized medicine by tailoring treatments based on distinct tumor characteristics.[6] The combination of intricate mathematical and computational methods with medical imaging not only improves our understanding of images, particularly health-related ones, but also presents opportunities for future advancements in the field. This progression demonstrates the continuous advancement and improvement of methods that link mathematical sciences, computational techniques, and medical imaging to enhance prognostic and diagnostic capabilities.[7]

In the contemporary landscape of thyroid cancer diagnosis, there has been a discernible surge in research endeavors, particularly those delving into the integration of radiomics and AI. The heightened interest in this specific intersection of technologies reflects a growing recognition of their potential to reshape and enhance diagnostic approaches.[8] As the number of studies exploring the application of radiomics and AI in thyroid cancer diagnosis continues to multiply, there emerges an imperative to conduct a thorough and exhaustive review. Therefore, this review aims not only to synthesize the current state of knowledge but also to identify gaps, challenges, and opportunities for further investigation. By systematically analyzing the existing body of literature, the study seeks to provide a comprehensive understanding of the progress made and the avenues yet to be explored, thereby laying the groundwork for continued advancements in the integration of radiomics and AI for thyroid cancer diagnosis.

Hence, recent advancements in the integration of radiomics and AI for thyroid cancer are explored in this review, with a specific focus on comprehensively examining AI, ML, and deep learning (DL) in the context of thyroid cancer and thoroughly delving into thyroid cancer, considering epidemiological and pathophysiological aspects. This review will also assess various techniques and methods employed in thyroid cancer diagnosis, focus on the development of radiomics and AI models in the field of radiomics, and compile and analyze studies reporting the outcomes of radiomics in thyroid cancer diagnosis through the application of AI techniques. The goal is to provide valuable insights for researchers in the AI domain, aiding them in the creation and enhancement of efficient, high-performance tools for diagnosing and treating thyroid cancer. Additionally, it is anticipated that this review will promote interdisciplinary collaboration, encouraging future experimental and theoretical works in healthcare, particularly in the realm of thyroid cancer diagnosis and treatment.

Literature Search Method

A thorough analysis of the body of research was conducted, involving searching various scholarly scientific databases, including PubMed, Medline, EMBASE, Scopus, and Web of Sciences. The investigation focused on academic publications published up until October 1, 2024, and was restricted to those available in the English language. In addition, supplementary articles were sourced by examining the reference sections of screened papers. An intricate search strategy was devised, incorporating a range of keyword combinations, such as “radiomics,” “artificial intelligence,” “deep learning,” “machine learning,” “thyroid cancer,” “thyroid neoplasm,” and “thyroid tumor.” These search strings were carefully constructed by combining keywords with their synonyms. Further, study selection involved initially identifying 368 research papers. Subsequently, 112 redundant documents were eliminated, and a review of titles and abstracts by authors [Sorrenti and Li] resulted in the exclusion of 176 articles that did not meet predetermined criteria. A comprehensive review of full-text articles was then conducted by two authors [Sorrenti and Li]. All review and conference studies were eliminated, leading to the exclusion of six additional studies. Afterward, titles and abstracts were screened to select relevant studies based on the inclusion and exclusion criteria, resulting in a final set of 42 studies.[6,9-50] Figure 1 presents a detailed flow chart of the study selection procedure.

Overview of Thyroid Cancers

Epidemiology

Based on the GLOBOCAN 2022 database of cancer incidence and mortality by the International Agency for Research on Cancer of the World Health Organization, thyroid cancer, a malignancy arising in the butterfly-shaped gland at our throat’s base, may not rank highest in mortality, but its global reach demands attention. The year 2022 witnessed it claim the unfortunate title of seventh most common incidence (820,000 cases) of cancer (Figure 2) and 24th most common in mortality (about 47000 deaths), with over 83,000 diagnosed cases (Figure 3).[51] While enhanced detection methods contribute to this number, a concerning shadow of overdiagnosis looms over specific regions, thereby urging

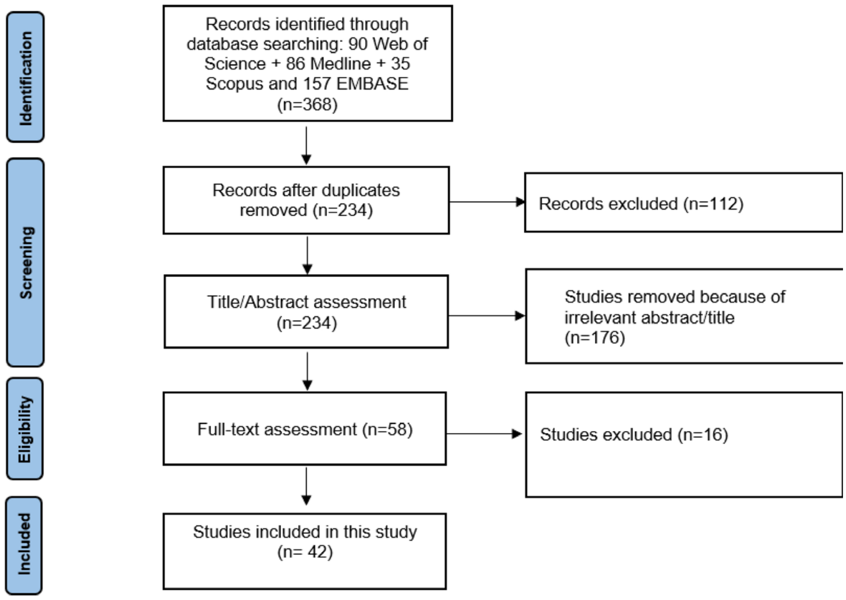

Figure 1. Review Process Flow Diagram

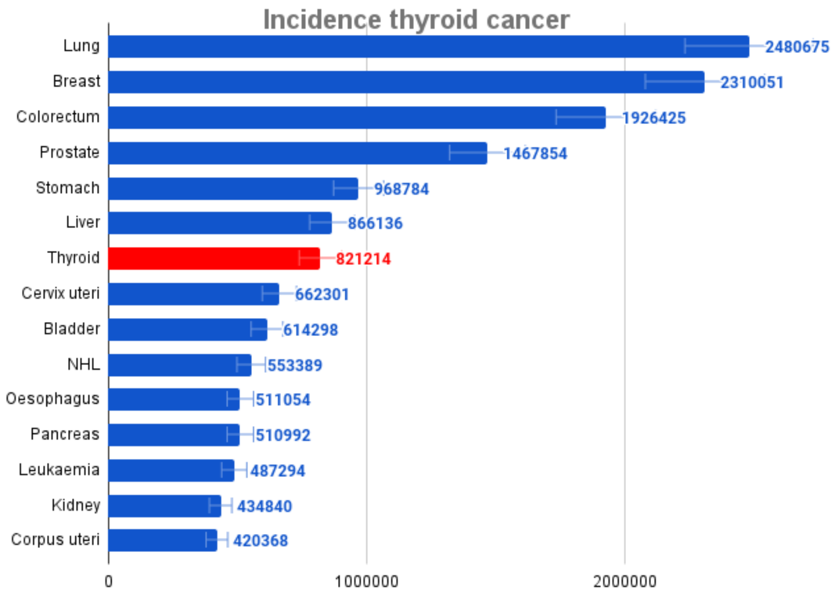

Figure 2. The Incidence Ranking of Thyroid Cancer Among the Other Types of Cancers According to GLOBOCAN Data From 2022
Note. NHL: Non-Hodgkin lymphoma; GLOBOCAN: The Global Cancer Observatory: CANCER TODAY

deeper understanding. This shadow falls unevenly, with women disproportionately bearing the burden. They are three times more likely to develop thyroid cancer, particularly the papillary and follicular types, which, thankfully, frequently boast favorable prognosis [52]

However, not all thyroid cancers share the same characteristics. Although less prevalent, medullary cancer introduces a unique challenge with its slow growth and limited treatment options. On the opposite end of the spectrum, anaplastic carcinoma emerges as an aggressive entity with a nearly 100% mortality rate. This stark contrast in outcomes highlights the intricate nature of this disease.[53] Moreover, both preclinical and clinical settings are buzzing with activity, providing a ray of light for patients grappling with this formidable diagnosis. Beyond mere statistics, a deeper examination reveals that the median age of diagnosis typically falls in the early 50s.[54] Nonetheless, this silent predator can strike at any stage of life, with the alarming distinction of being the most common malignancy among young adults aged 16–33. Unraveling the root causes remains crucial. Exposure to radiation, pre-existing thyroid conditions, environmental toxins, iodine deficiency, and even obesity all participate in the complex dance of risk factors. Thus, understanding these intricate relationships empowers preventive measures and early detection efforts.[55]

Pathophysiology

Thyroid abnormalities are divided into two benign and malignant groups. Nodular goiter (NG), stemming from iodine deficiency, exhibits distinct classifications as endemic (>10% prevalence) or sporadic (≤10%). While endemic cases result from absolute iodine deficiency, sporadic instances involve various factors,

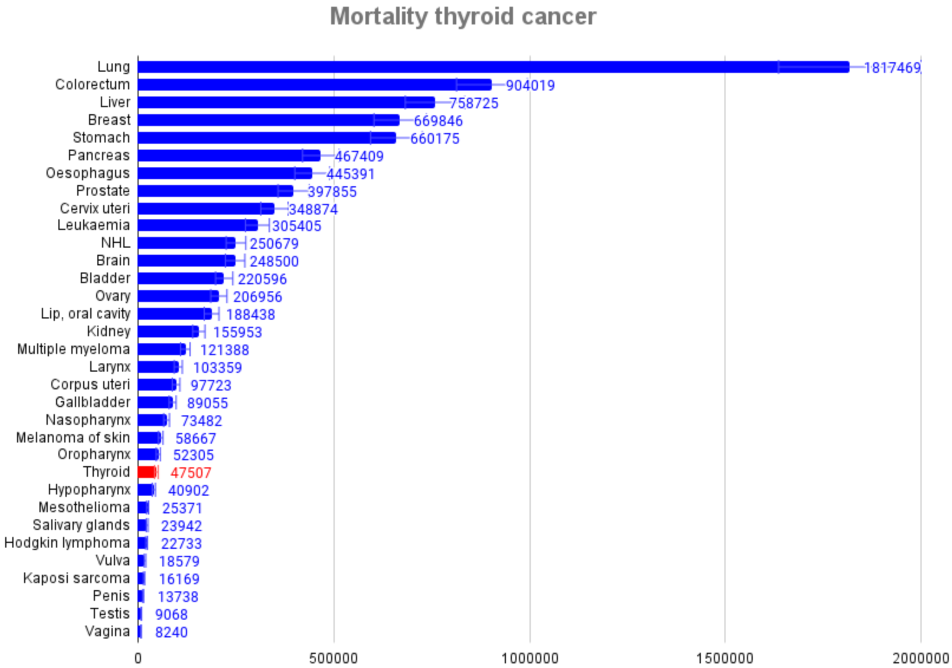

Figure 3. The Mortality Ranking of Thyroid Cancer Among the Other Types of Cancers Based on GLOBOCAN Data From 2022
Note. NHL: Non-Hodgkin lymphoma; GLOBOCAN: The Global Cancer Observatory: CANCER TODAY

such as increased thyroid hormone needs, dietary iodine insufficiency, goitrogen ingestion, and subclinical dyshormonogenesis.[56] Pathologically, NG manifests as a combination of hyperplastic and involutional changes, with challenges arising in distinguishing between follicular adenomas and hyperplastic nodules, particularly in the context of dominant nodules.[57] Beyond benign cases, encapsulated non-functioning nodules called follicular adenomas are common in people aged 30–50 and can seldom result in hyperthyroidism.[58] A thorough histological examination is necessary to distinguish between adenoma and carcinoma. Women in their fifth decade make up the majority of patients with follicular carcinomas.[59] Malignant cells that are not fully differentiated display behavior halfway between that of differentiated and undifferentiated carcinomas. More precisely, they are characterized as solid masses with a variety of histological features.[60] Anaplastic carcinomas are extremely malignant and have a poor prognosis. In addition, they are composed of spindle and epithelioid cells. *RET* gene mutation screening is required for medullary carcinomas, which can be sporadic or familial. The former typically presents in the 40–60 age range, while the latter is typically observed earlier and in both directions. In papillary carcinomas, BRAF and RET mutations activate the mitogen-activated protein (MAP) kinase signaling pathway; in follicular lesions, PAX8/PPARγ and Ras mutations have the same function. More precisely, these molecular pathways are responsible for the differences between papillary carcinomas and follicular lesions.[61] Germline mutations in the RET proto-oncogene are linked to medullary carcinoma, especially in multiple endocrine neoplasia type 2 syndromes.[62]

Thyroid Cancer Diagnosis

Palpation for thyroid gland nodules was a major diagnostic tool in the past, but it is now used only in 30–40% of cases to identify thyroid cancers. A multimodal approach involving laboratory testing, imaging modalities, and clinical assessment forms the basis of modern thyroid cancer diagnosis.[63] Currently, the detection of thyroid cancer can be achieved through a range of imaging modalities, such as neck and carotid USs, as well as scans of the chest, neck, and spine.[64] It is noteworthy that the ability to identify thyroid cancers even in the absence of palpable symptoms is improved by this extensive range of diagnostic techniques.[27]

One of the most important steps in the diagnosis of recently formed thyroid nodules is measuring serum thyroid-stimulating hormone (TSH) levels to assist in differentiating between nonfunctional.[65] Hyperfunctioning nodules, which are rarely malignant, are indicated by subnormal TSH levels; non-functioning nodules or those with Hashimoto's thyroiditis may be more susceptible to cancer. Although a diagnostic neck ultrasonography cannot definitively determine whether a nodule is malignant, it is recommended that the presence of nodules be confirmed and any suspicious features be assessed. Due to the elevated risk of malignancy, fine needle aspiration (FNA) is necessary, regardless of nodule size, especially for non-functioning nodules and if TSH is normal or elevated.[66] The outcomes of an FNA biopsy are categorized as benign, malignant, suspicious, indeterminate, or nondiagnostic concerning the diagnosis of thyroid cancer.[67] Distinct histological variants of thyroid cancer, including anaplastic, follicular, medullary, and papillary, are illustrated in Figure 4.[67,68]

The realm of thyroid cancer diagnosis and treatment has experienced enhanced efficacy with the escalating application of radiomics in recent years (Figure 5).[67,68]

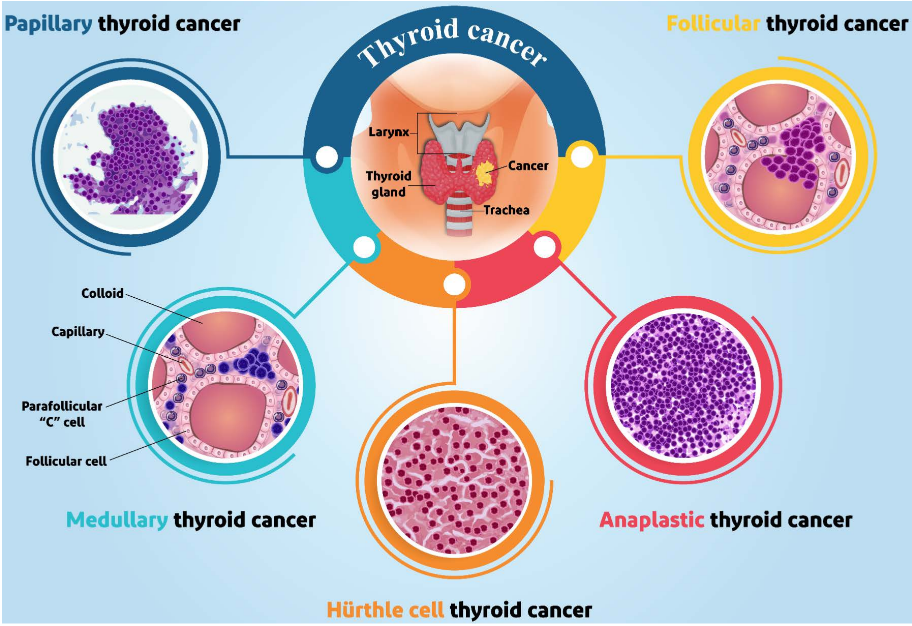

Figure 4. Different Types of Thyroid Cancer, Including Papillary Thyroid Cancer, Follicular Thyroid Cancer, Oncocytic Cell (Hurthle Cell) Thyroid Cancer, Medullary Thyroid Cancer, and Anaplastic Thyroid Cancer

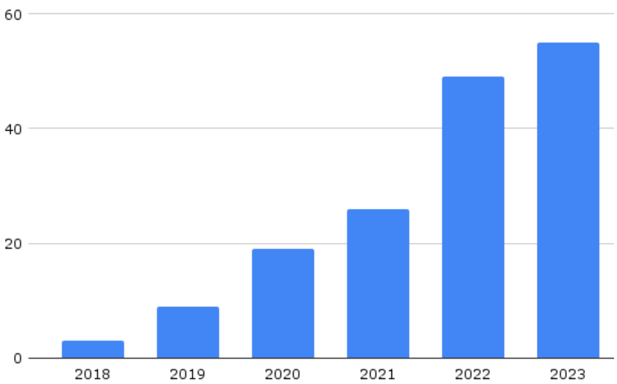

Figure 5. Increasing Investigations About Utilizing Radiomics and AI in Thyroid Cancer Diagnosis Over the Last 6 Years
Note. AI: Artificial intelligence

An Overview of Artificial Intelligence

The goal of AI, a fast-developing area of computer science, is to create machines that possess traits of human intelligence. AI encompasses a wide range of methodologies, including natural language processing (NLP), DL, and ML, which are the most well-known ones.[69] Notably, large language models (LLMs) constitute a unique class in the AI algorithmic framework that is capable of understanding, compressing, producing, and forecasting textual content by employing large-scale datasets and advanced DL methods. Given their inherent capacity for text generation, LLMs find versatile applications in various NLP tasks, including sentiment analysis, translation, summarization, rewriting, and classification.[70]

A branch of AI called NLP studies how human language is conceived, decoded, and understood. This broad field includes a variety of approaches, including sentiment analysis, speech recognition, machine translation, and text mining. The historical trajectory of AI has undergone notable shifts, moving from the first age of rule-based systems to the current era where ML and DL algorithms are the mainstays (Figure 6).[71-73]

Machine Learning

Within the field of AI, ML allows computers to grow without explicit programming by using experience as a learning tool. The primary objective is to develop algorithms that enable computers to identify patterns in data and extrapolate inferences or predictions.[74] Thus, a large amount of data (referred to as the training dataset) is fed into the system as part of standard ML procedures, and the algorithm is then allowed to search for patterns, relationships, and features in the data. By adjusting its internal parameters, the system gains experience and improves its ability to complete tasks. Artificial neural networks (ANNs), which resemble learning systems, are used in DL.[75] ML can be divided into three main categories (Figure 7):

Supervised Learning

In this approach, the algorithm is trained on a labeled dataset, where the input data are paired with the corresponding desired outputs. The goal is for the algorithm to learn a mapping function that can predict the output for new, unseen inputs.[76,77]

Semi-Supervised Learning

Semi-supervised learning occupies a middle ground between supervised and unsupervised learning methodologies within the realm of ML. This approach utilizes a limited set of labeled data in conjunction with a vast pool of unlabeled data for training purposes.[78] It is noteworthy that this hybrid training strategy proves advantageous when only a portion of the data has ground-truth labels available. Moreover, the amalgamation of labeled and unlabeled data has been observed to enhance the accuracy of classifying new instances. Restricted Boltzmann machines and deep belief networks are examples of semi-supervised learning algorithms.[79]

Unsupervised Learning

In this case, the algorithm is entrusted with identifying patterns or structures in the unlabeled data without the need for explicit guidance. This type of learning frequently involves tasks like clustering and dimensionality reduction.[80]

Reinforcement Learning

Systems can learn by interacting with real-world environments thanks to a subset of ML called reinforcement learning. The computer attempts to solve problems by making mistakes and testing different things. An entity referred to as the agent engages with the environment during this process, making observations, choosing actions, and getting rewarded or penalized in accordance with those decisions.[81] The agent's mainly aims to maximize cumulative rewards; the best course of action is known as the policy. Numerous fields (e.g., game theory, data science, and robotics) use reinforcement learning.[82]

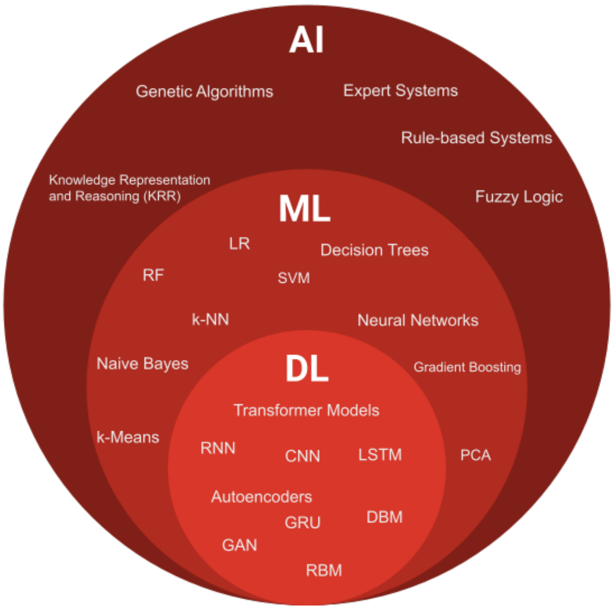

Figure 6. The Historical Trajectory of AI
Note. AI: Artificial intelligence; ML: Machine learning; DL: Deep learning; In ML algorithms: Linear regression (LR), random forest (RF), support vector machines (SVM), k-nearest neighbors (k-NN), principal component analysis (PCA), gradient boosting algorithms (e.g., XGBoost and LightGBM). In DL algorithms: Convolutional neural networks (CNN), recurrent neural networks (RNN), long short-term memory (LSTM), gated recurrent unit (GRU), generative adversarial networks (GAN), deep Boltzmann machines (DBM), restricted Boltzmann machines (RBM), and deep Q-networks (DQN).

ML applications are found in many different fields, such as recommendation systems, fraud detection, NLP, image and speech recognition, and autonomous cars. As technology develops, ML and DL models become particularly more and more popular because of their capacity to automatically extract hierarchical features from data, qualifying them for difficult tasks.[83]

Deep Learning

As mentioned earlier, fueled by advancements in computer processing, a subset of ML rooted in ANNs has emerged to address progressively intricate challenges autonomously. While early ANNs necessitated substantial human inputs for feature selection, the advent of DL applications has revolutionized this process by automatically extracting optimal features from raw data.[84] DL is predominantly deployed in pattern recognition systems, showcasing its efficacy in extracting crucial information from high-dimensional datasets. Notably, DL methods have exhibited promising outcomes, particularly in computer vision and image analysis, frequently rivaling or surpassing traditional ML approaches reliant on manually crafted features defined by human experts.[85] Moreover, DL can autonomously perform a designated task by extracting crucial features directly from unprocessed data. A DL method is characterized by its composition of multiple layers, forming a hierarchical structure of simple models. These models nonlinearly transform their input to generate output, thereby creating a complex mapping process.[86]

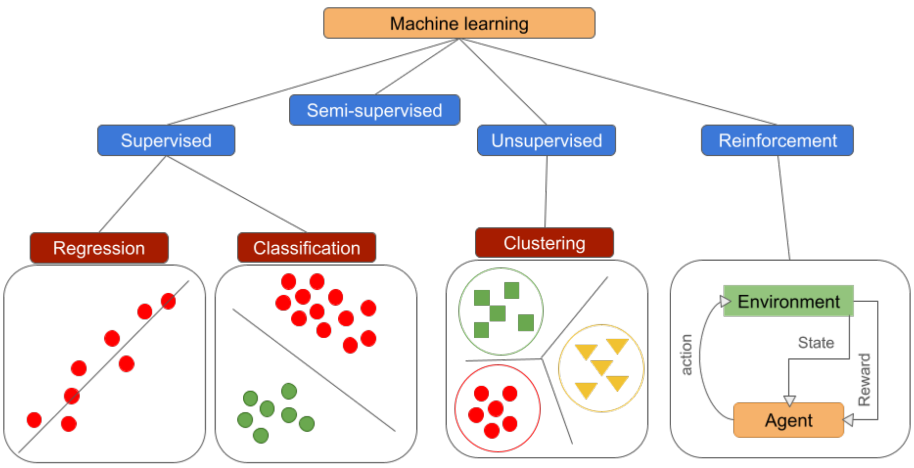

Figure 7. Three Learning Paradigms: Supervised, Unsupervised, And Reinforcement Learning
Note. Within the supervised category, the focus is on predicting outcomes through regression and classification. In the unsupervised realm, the emphasis is on revealing patterns by employing clustering techniques. Ultimately, the reinforcement learning section illustrates the dynamic process of decision-making, showcasing actions, states, and rewards

Each layer in this stack further refines the outputs from the previous layer, contributing to the enhancement of both selectivity and invariance within the representation. This iterative refinement process allows DL models to capture increasingly intricate patterns and features in the data. Overall, the multilayered architecture enables DL systems to achieve high levels of performance in various tasks, ranging from image recognition to NLP.[87] As an instance, Peng et al [88] introduced ThyNet, an AI model based on DL, to aid in the diagnosis and treatment of thyroid nodules. They used a dataset of 18,049 US images and involved 8,339 patients. The purpose of ThyNet is to differentiate between benign and malignant thyroid nodules in order to improve diagnostic precision while minimizing needless FNAs. In this study, radiologists employ ThyNet to assist in the diagnostic process. ThyNet achieved a significantly higher area under the receiver operating characteristic curve (AUROC) (0.922) than radiologists (0.839). Moreover, ThyNet assistance improved radiologists' AUROC from 0.837 to 0.875 in image reviews and from 0.862 to 0.873 in clinical tests. In simulations, this AI-based model reduced FNA from 61.9% to 35.2% and lowered missed malignancy rates from 18.9% to 17.0%. According to the study, ThyNet had much better accuracy and AUROC than radiologists alone. Both junior and senior radiologists performed better diagnoses with the help of ThyNet. Likewise, ThyNet showed promise in lowering needless FNAs, which may have an effect on clinical decision-making. Furthermore, ThyNet's efficacy in the real-world clinical setting is attributed to the particular DL architecture and methodology employed, including the training process on a large dataset and the integration of ThyNet with the ACR TIRADS classification.

Radiomics

In the realm of biology and medicine, many fields end in "-omics" to signify the analysis of massive datasets in order to uncover hidden insights. Radiomics is one such field, specifically focused on extracting valuable, measurable information from medical images, thereby helping us unlock secrets hidden within US images, CT, MRI, or PET/CT.[4] Using complex algorithms, radiomics analyzes medical images to extract a multitude of "radiomic features". Imagine being able to extract hidden information from a medical image, rather than just seeing shapes and shadows. That is what radiomics does.[89] Radiomics uses complex algorithms to mine medical images for a vast number of tiny details, revealing patterns and characteristics invisible to the naked eye. Additionally, this approach unlocks hidden insights about tumors, potentially predicting how they behave and respond to treatment.[90] Similarly, this emerging field, born from radiology and oncology, holds immense promise for personalized medicine, tailoring treatments based on the unique characteristics of each patient's disease.[91] While currently most advanced in these fields, its potential extends to any area where imaging unveils clues about disease processes. In recent years, a discernible integration of applied mathematics and statistical sciences has been witnessed across diverse domains, particularly in the development and optimization of AI and ML algorithms.[92] This interdisciplinary approach, heavily anchored in computer science and computational methods, has fortified the underpinnings of AI. Matrices, employed in image processing, have garnered significance, propelling the evolution of convolutional neural networks (CNNs). This evolution has significantly altered the landscape of image analysis, especially within fields such as medical imaging. It should be noted that the utilization of matrices in image description has concurrently given rise to innovative techniques, including radiomics.[91]

Data Acquisition

Image acquisition, the first crucial step in radiomics, acts as the gateway to unveiling hidden information within the patient. This intricate process involves capturing medical images that serve as the foundation for subsequent feature extraction and analysis.[93] Beyond CT, PET, and MRI, radiomics embraces the unique strengths and challenges of US. Its real-time visualization, lack of radiation, and cost-effectiveness make it ideal for dynamic assessments, monitoring, and point-of-care applications.[94] However, operator dependence, limited penetration, and speckle noise demand careful standardization, advanced techniques (e.g., elastography and ML), and tailored protocols. Despite these hurdles, US is unlocking its potential in radiomics for early cancer detection, assessing aggressiveness, monitoring treatment, and more, solidifying its role as a transformative force in personalized medicine.[95]

Region of Interest Segmentation

Within the burgeoning field of radiomics, the meticulous process of ROI segmentation occupies a pivotal role, particularly when unraveling the complexities of thyroid cancers. Akin to a sculptor carefully excavating a hidden masterpiece, this technique meticulously delineates the tumor region within medical images, thereby enabling the extraction of quantitative features crucial for diagnosis, prognosis, and treatment stratification. Let us delve deeper to illuminate the significance of ROI segmentation in this context.[4,96]

Fiduciary Accuracy: The Foundation of Feature Extraction

Envision setting out on a scientific quest to find valuable features that will reveal the mysteries of tumor biology, rather than buried treasure. Accurate ROI segmentation functions as the steadfast guide, ensuring that accurately extracted features capture the distinct qualities of the tumor, including its geometric structure, textural heterogeneity, and intensity distribution.[97] This precision is critical to building strong radiomics models, which are complex algorithms that analyze these features in-depth to distinguish between benign and malignant nodules, forecast aggressive behavior, and help choose the best course of treatment. Think of them as experienced detectives. Similar to a malfunctioning compass, inaccurate segmentation can result in dangerous misinterpretations that can misclassify a benign nodule as malignant or vice versa, with serious consequences for patient care.[98]

Converging on Standardized Segmentation to Close the Interobserver Gap

Consider a scenario in which two detectives are looking into the same crime scene while each having a different perspective on it. Radiologists may exhibit intrinsic subjectivity and interobserver variability when manually segmenting a tumor by visually tracing its outline; for instance, one radiologist may perceive a jagged boundary while another detects a smoother one.[99] This discrepancy can make it extremely difficult to create trustworthy radiomics models. Automated and semi-automated techniques are becoming valuable allies in closing this gap. More precisely, these techniques make use of advanced image processing algorithms to accurately and consistently identify the tumor, even when viewed by multiple observers and research projects. Envision a group of robotic investigators, outfitted with state-of-the-art equipment and unwavering accuracy, carefully examining the scene and removing any subjectivity that might skew human judgment.[62,96,100]

Revealing Latent Heterogeneity: Prospects for Personalized Medicine

Consider a tumor as a heterogenous terrain with hidden subregions, each characterized by unique biological characteristics, rather than as a single, monolithic structure. Sophisticated segmentation techniques that combine data from various imaging modalities (e.g., CT, PET, and US scans) are similar to making an intricate topographical map of this complex terrain. With unmatched granularity, these "multi-parametric" models can depict the tumor's heterogeneity and identify biologically distinct subregions. With this newfound understanding, a new era of personalized medicine may well be ushered in.[101] Medical practitioners may be able to tailor treatment regimens to target specific tumor regions by identifying these subregions, offering a more precise and effective method to treat the condition.

Pushing the Boundaries: Seeking Unrivaled Accuracy

The constant search for advancement is essential to the spirit of scientific inquiry. To improve ROI segmentation techniques, researchers are constantly looking for new approaches, especially in difficult situations where the tumor boundaries are hazy or overlap with adjacent structures.[63] Advanced image processing methods and DL algorithms are being used to achieve even more accuracy. Envision a novel type of detective, armed with state-of-the-art equipment and unparalleled analytical abilities, meticulously inspecting the crime scene and revealing every detail in their pursuit of the truth.[99,102]

Working Together and Using Open-Source Tools to Create a Shared Future

In addition to individual genius, the scientific community as a whole must contribute to the search for the best segmentation techniques. Researchers are actively cooperating to create open-source software tools and standardize segmentation protocols. Due to increased accessibility and reproducibility, researchers from all over the world can use these resources and add to the body of knowledge. Envision an international community of investigators, exchanging their knowledge, perspectives, and resources to advance their respective specialties and, finally, enhance patient results.[103]

ROI segmentation is the foundation of radiomics-based analysis for thyroid cancers. In addition, it enables researchers to extract useful features, build reliable models, and open the door to personalized medicine by precisely defining the tumor.[104] Future research is expected to yield even more advanced segmentation strategies, which will thoroughly manifest the potential of radiomics to transform the treatment of thyroid cancer. And who knows? Maybe these developments will motivate a new wave of medical sleuths to use knowledge and technology in order to solve medical mysteries and save countless patients' lives.[103,105]

Extraction of Features

In radiomics, feature extraction is essential for revealing patterns and data (from medical images) that are not immediately visible to the human eye. This is particularly true when analyzing thyroid cancer. To assist with diagnosis, prognosis, and treatment planning, feature extraction also extracts different aspects of images using complex algorithms and computational tools.[106] This process involves identifying and quantifying a wide variety of meaningful characteristics from the image data in order to obtain significant insights into the underlying tissue characteristics and potential abnormality indicators within the thyroid gland (Figure 8).[107]

Features of Shape

They include geometric attributes, such as the thyroid gland's size, area, roundness, and the eccentricity of its regions. By examining shape descriptors, researchers and radiologists can learn more about the spatial arrangement and structural traits of tissues, which may be suggestive of malignant growth or other anomalies.[103]

Features of Intensity

The distribution of pixel values throughout the image is the main focus of intensity features. By extracting information about variations in tissue density or contrast within the thyroid region, the analysis of intensity histograms can help identify lesions that may be cancerous.[105,107-109]

Textural Features

Some statistical metrics, such as gray-level co-occurrence matrix and gray-level run length matric, which reveal

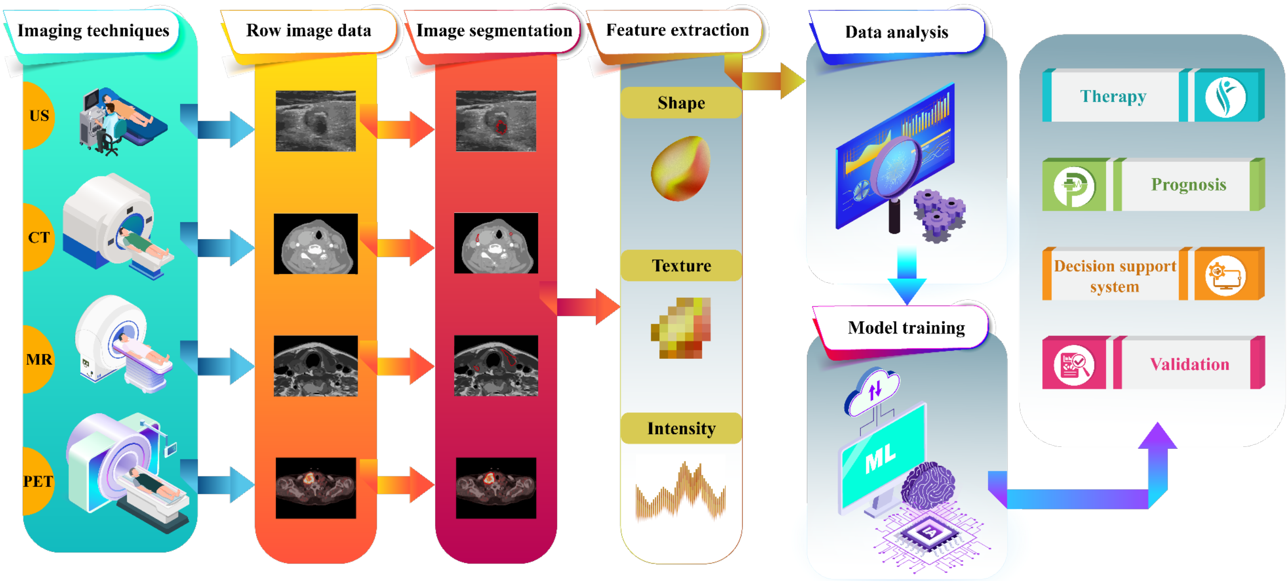

Figure 8. Radiomics Analysis Involving **(1)** Image Acquisition, **(2)** Image Preprocessing, **(3)** ROI Segmentation, **(4)** Feature Extraction, **(5)** Feature Selection, **(6)** Model Development, **(7)** Validation, **(8)** Interpretation and Reporting, and **(9)** Clinical Translation

Note. US: Ultrasound; CT: Computed tomography; MR: magnetic resonance imaging; PET: Positron emission tomography; ROI: Region of interest

spatial correlations between pixel intensities, are used in texture features. By evaluating texture features, radiomics can help differentiate between benign and malignant thyroid nodules by providing insight into tissue heterogeneity, smoothness, and coarseness.[110]

Wavelet Features

By breaking down the image data into distinct frequency components, wavelet analysis facilitates the extraction of spatial-frequency information. Wavelet features aid in capturing texture patterns at different scales, thereby providing a comprehensive analysis of the composition of thyroid tissue and possibly exposing minute alterations in texture linked to the development of thyroid cancer.[108,109]

To extract minute details from medical images, feature extraction in radiomics for thyroid cancer analysis entails a precise examination of shape, intensity, texture, and wavelet features. These characteristics act as quantitative biomarkers to help doctors make well-informed decisions regarding patient care, diagnosis, and treatment planning. Through the use of advanced computational methods, radiomics plays a significant role in providing personalized and data-driven approaches to thyroid cancer assessment, ultimately contributing to precision medicine initiatives.[108-110]

Feature Selection and Feature Dimension Reduction

Feature selection, which comes after radiomic feature extraction in radiomics, is a crucial step in enhancing the effectiveness of ML algorithms for thyroid cancer data analysis. Linked to high dimensionality model training, enabling quicker model training, and improving the repeatability of the acquired outcomes. Likewise, by choosing the most informative features from the pool of extracted characteristics, feature selection serves as a filtering mechanism to concentrate on the most pertinent characteristics that considerably aid in differentiating between various thyroid cancer phenotypes and obtaining accurate diagnostic outcomes.[111]

To optimize the selection process in the particular context of thyroid cancer analysis, a thorough investigation had six distinct feature selection techniques, including the analysis of variance (ANOVA), forward and backward elimination, Pearson correlation, ridge regression, and the least absolute shrinkage and selection operator (LASSO). By employing diverse feature selection methodologies, the investigators sought to capitalize on the advantages of each approach in pinpointing the most pivotal radiomic features that encapsulate critical details pertaining to tumor attributes, thereby facilitating a more precise and streamlined examination of thyroid cancer imaging data.[112]

Filter, wrapper, and embedded techniques are the three primary categories of feature selection techniques employed in this study. By using statistical tests to assess the relationship between features and tumor aggression, filters like Pearson correlation and ANOVA choose features according to their relative importance. By repeatedly modifying thresholds, wrapper techniques (e.g., forward and backward elimination) construct the subsets of features with the goal of assembling a set of variables with strong predictive ability. Feature selection is integrated into the model training process through embedded techniques, such as LASSO and ridge regression, which combine the elements of both filter and wrapper methods in order to balance model complexity and interpretability while optimizing predictive performance.[112,113]

The application of filter, wrapper, and embedded techniques in feature selection denotes a multimodal strategy for determining the most pertinent radiomic features for the analysis of thyroid cancer. While wrapper methods iteratively refine feature subsets to improve prediction accuracy, filter methods help with the initial screening of features based on their statistical significance.[107] In the context of thyroid cancer radiomics, embedded techniques seamlessly integrate feature selection into model training, by utilizing the advantages of both filter and wrapper methods, in order to achieve a balance between feature relevance, model interpretability, and predictive performance. Medical researchers are increasingly using DL to analyze medical images. By employing this method, they can directly collect a greater amount of data rather than having to go through the laborious process of manually extracting features from the images. In recent years, this has gained popularity as a trend.[114,115]

Model Development

Radiomics utilizes advanced image analysis techniques to extract valuable information hidden within medical scans. This information, known as radiomic features, goes beyond the visual capabilities of traditional diagnosis. These features capture the subtle characteristics of tissues, including their structure, texture, and intensity, similar to a unique fingerprint. By combining these features with powerful modeling techniques and extensive databases, radiomics empowers the development of classifiers. Similar to sophisticated detectives, these classifiers analyze new medical images and predict potential outcomes, ultimately shaping the field of personalized medicine.[105]

Currently, radiomics employs a diverse toolbox of ML algorithms for building these classifiers.[116] This toolbox includes established methods, such as linear regression (LR), random forest (RF), support vector machine (SVM), and decision tree (DT). Additionally, innovative techniques (e.g., k-nearest neighbors, ANNs, and Bayesian and clustering algorithms) are increasingly being explored. It is noteworthy that while most of these algorithms fall under the category of supervised learning, requiring pre-labeled data to train the models, some (e.g., clustering algorithms) operate under unsupervised learning, uncovering hidden patterns without prior labels.[117]

Building a robust classifier model involves the training and testing stages.[118] During the training phase, the model “learns” to distinguish between different outcomes based on the provided data. This data-set, which is crucial for successful learning, needs to be large and representative of the broader population being studied. Once trained, the model is put to the test in the testing phase. Here, the entirely new and unseen data are used to evaluate the model’s accuracy and ability to accurately predict outcomes. When possible, a third stage, known as validation, can further enhance the model’s performance. In this phase, the model parameters (e.g., the quantity and significance of the various features employed) are adjusted in light of the validation data.[118] Through the careful navigation of these phases, radiomics opens up new possibilities for medical images and ushers in a new era of customized healthcare.

Radiomics and Artificial Intelligence in Thyroid Cancer Diagnosis

The use of radiomics and AI models to improve thyroid cancer diagnosis and treatment has remarkably increased in the last few years. Numerous ML and DL techniques have been adopted in this rapidly developing field, demonstrating encouraging results. Various studies have examined the effectiveness of these approaches in assessing ML and DL models for the diagnosis and treatment of thyroid cancer, with varying degrees of accuracy.[119] These efforts represent a noteworthy progression in utilizing computational methods to enhance the comprehension and treatment of this type of cancer, with great promise for enhancing oncology patient outcomes and clinical procedures.[120] A selection of these studies is presented below based on the imaging type. It is worth mentioning that these studies pave the way for future developments in precision medicine by rigorously evaluating and comparing data, which helps validate and improve computational approaches for diagnosing and treating thyroid cancer.[121]

Among the selected studies (Table 1), the utilization of MRI images was relatively limited, with only three studies incorporating this modality into their analyses. MRI offers distinct advantages in capturing detailed anatomical information and soft tissue contrast, making it a valuable imaging tool in oncology. However, its application in thyroid cancer diagnosis and treatment remains less explored compared to other modalities, such as US or CT.[9] Nonetheless, studies that did incorporate MRI imaging demonstrated the potential for MRI-based radiomics to contribute to the understanding and management of thyroid cancer.

Radiomics and Artificial Intelligence Using Magnetic Resonance Imaging for Thyroid Cancer

Wei et al [10] used radiomics based on multiparametric MRI to predict extrathyroidal extension (ETE) in papillary thyroid carcinoma (PTC). Thirty-two patients made up the test cohort, and ninety-two patients made up the training cohort in their study. They created a radiomics predictive model that demonstrated the ability of MRI radiomics to stratify PTC patients based on ETE prior to surgery, achieving high area under the curves (AUCs) of 0.96 and 0.87 in the training and testing sets, respectively. A combination of high-performing features from DWI, T2 WI, and CE-T1WI images was employed in a retrospective trial that involved the manual segmentation of thyroid tumors for radiomic feature extraction. According to the findings, MRI-based radiomics may be able to predict ETE in PTC in a non-invasive manner, which would be helpful for preoperative evaluation and treatment planning. By combining features from contrast-enhanced T1-weighted, T2-weighted, and diffusion-weighted images, Dai et al [11] developed a multimodality MRI-based radiomics model for predicting aggressiveness in PTC, achieving a high accuracy of 0.917. Their research, which included 107 PTC patients, attempted to provide guidance

Table 1. Overview of Studies in the Field of Integration of Radiomics and Artificial Intelligence in Thyroid Cancers

Reference	Imaging	Sample Size	Tasks	Approaches	Performance
Hui Qin et al, 2021 [9]	MRI	MRI 109 patients with PTC	Classification (LNM or not)	MRI-texture (naked eye), MRI-radiomics (LR model), and combination model	MRI texture alone showed an AUC of 0.739, radiomics model AUCs of 0.805 (training) and 0.760 (validation), and a combined model AUC of 0.969, indicating high diagnostic efficiency for LNM in PTC.
Wei et al, 2021 [10]	MRI	MRI 132 patients with PTC	Binary classification (those with or without ETE)	DWI, T2 WI, and CE-T1WI	AUC = 0.87
Dai et al, 2022 [11]	MRI	MRI 107 patients with PTC	Classification (aggressiveness and non-aggressiveness)	Meta-analysis- sparse representation method	CE-T1WI, T2WI, and DWI combined 0.917
Lu et al, 2019 [12]	CT	CT images from 221 PTC patients	Classification (CLNM)	SVM and multivariate LR	AUCs of 0.795 and 0.822, respectively, for SVM and multivariate LR
Gu et al, 2019 [13]	CT	CT images 103 patients with suspected thyroid nodules	Classification (malignant or benign)	SVM	AUC = 0.87 Sensitivity = 0.93 Specificity = 0.73
Zhou et al, 2020, [14]	CT	CT images from 255 PTC patients	Classification (metastasis to CLN or not)	LR, radiomics signature model and combined model	Combined model displayed optimal performance in both training (AUC = 0.933) and validation set (AUC = 0.895)
de Koster et al, 2021 [15]	FDG-PET/CT	[18F] FDG-PET/CT thyroid nodule from 123 patients	Classification	SUV-elastic net regression classifiers	SUV-metrices revealed AUCs ranging from 0.705 to 0.729 in all, 0.708 to 0.757 in non-Hurthle, and 0.533 to 0.700 in Hurthle cell.
Li et al, 2021 [16]	CT	CT images of thyroid 678 patients with PTC	Binary classification (CLNM- and CLNM+)	KNN, LR, DT, L-SVM, Polynomial-SVM, and Gaussian SVM algorithm	L-SVM: Higher classification accuracy of 0.709 Internal and external validation c-index of 0.854
Zhou et al, 2022 [17]	CT	CT images from 346 patients with PTC	Classification (LNM and CLNM)	mRMR, RF, LASSO, LR, and decision curve analysis	Discrimination and calibration of training cohorts (AUC = 0.847; AUC = 0.837) Validation cohorts (AUC = 0.807; AUC = 0.795
Wu et al, 2022 [18]	CT	CT images from 412 patients with PTC	Classification (TCI + and TCI-)	KNN, LR, DT, L-SVM, polynomial-SVM, and SVM	Internal test cohort L-SVM, the AUC was 0.820 [95% CI: 0.758–0.888] External test cohort, the AUC was 0.776 (0.625–0.904)
Yu et al, 2022 [19]	CT	CT images from 153 patients with PTC	Classification (ETE)	LASSO, KNN, LR, DT, linear -SVM, gaussian-SVM, and polynomial-SVM	Best internal test cohort: L-SVM, AUC = 0.820 Best radiomics model (L-SVM, AUC = 0.733) Clinical model (AUC = 0.709 external test cohort, AUC = 0.776
Xu et al, 2022 [20]	CT	CT radiomics from 161 patients	Binary classification (malignant or benign)	LR	An AUC of 94.4%, an accuracy of 87.6% in the train, and 94.2%, and 86.8%, respectively, for the test group.
Xu et al, 2022 [21]	CT	CT radiomics from 280 patients	Predicting postsurgical recurrence of PTC	LR-, NN-, SVM-, and KNN-based radiomics models	The combined models based on the SVM, LR, KNN, and NN classifiers had AUCs of 0.754, 0.746, 0.669, and 0.711, respectively.
Huang et al, 2023 [22]	CT	CT from 376 patients	Classification (HT or thyroid cancer)	LASSO and mRMR	AUC, high accuracy, sensitivity, and specificity were measured at 0.911, 0.897, 0.889, and 0.862, respectively
Zhang et al, 2024 [23]	CT	CT radiomics and pathological data from 141 patients with TN	Classification (NG or malignant nodule)	Four different radiomics-based models: RF, RF hybrid feature, SVM hybrid feature, and LASSO	The RF hybrid feature model with an AUC of 0.87 for the validation cohort, outperforming the LASSO model, which had an AUC of 0.78.
Liu et al, 2019 [24]	US	US images from 450 PTC patients	Classification (presence of LNM or not)	SVM	AUORC = 0.727 Accuracy = 0.710
Zhou et al, 2020 [25]	US	US images from 1,734 patients	Binary classification (malignant or benign)	CNN, TL, and DLRT	AUCs of DLRT were 0.96, 0.95, 0.97, respectively, in the training, internal and external validation cohort.
Wang et al, 2020 [26]	US	US images from 1,040 patients	Binary classification (malignant or benign)	Radiomics model and DL	Accuracy of 66.81% in radiomics and 74.69% in DL
Kwon et al, 2020 [27]	US	US radiomics from 169 patients with FTC	Classification (distant metastasis or not)	SVM classifier radiomics and histological features	AUCs of 0.90 for SVM and 0.93 for radiomics and widely extensive histology feature
Yu et al, 2020 [28]	US	US images of 3,172 patients with PTC	Classification of patients into groups based on the risk of LNM in PTC	Transfer learning-based model	AUC main cohort = 0.90 Independent cohorts = 0.93
Kwon et al, 2020 [29]	US	Gray-scale US from 96 patients	Binary classification (presence or absence of BRAF mutation in PTC)	LR, SVM, and RF	An AUC of 0.651, accuracy of 64.3%, sensitivity of 66.8%, and specificity of 61.8%, on average, for the 3 models
Xia et al, 2021 [30]	US	Clinical and US data from 445 PTC patients	Classification (presence of LNM or not)	SVM and PNN	F1 score of 0.88 on the CLNM in PNN, F1 score of 0.93 on the lateral LNM in SVM

Table 1. Continued.

Reference	Imaging	Sample Size	Tasks	Approaches	Performance
Agyekum et al, 2022 [31]	US	Clinical and US data from 205 PTC patients	Classification (CLNM)	USR model, clinical model, and USR-clinical model	AUCs of 0.71, 0.74, and 0.63 in the USR-clinical, USR, and the clinical model, respectively.
Wang et al, 2022 [32]	US	US images from 138 patients with PTC	Binary classification (BRAF+and BRAF-)	LASSO-mRMR-	Elasticity US AUC of 0.952, grayscale US AUC of 0.792, and a combination AUC 0.914 in the training dataset, elasticity US AUC of 0.931, grayscale US AUC of 0. 725 and a combination AUC 0.938 in the test dataset
Yu et al, 2022 [33]	US	US images from 650 patients with PTC	Binary classification (RET/PTC and non-RET/PTC)	DLRN LR algorithm	AUCs of DLRN of 0.9545 and 0.9396 in the test cohort and training cohort, respectively
Zhou et al, 2022 [34]	US	US images of thyroid and central cervical lymph from 609 patients with PTC	Classification	LASSO regression model -multivariable LR radiomics signature and ultrasonography-reported LN	C-indices of 0.816 and 0.858 in the primary cohort and the validation cohort, respectively. AUC=0.858 In the validation cohort, the accuracy, sensitivity, specificity and AUC of this model were 0.812, 0.816, 0.810, and 0.858
Shi et al, 2022 [35]	US	US imaging, clinical data, and radiomics of 587 PTC patients	Classification (CCLNM)	Boruta algorithm and XGBoost model	AUC=91.53%
Zhu et al, 2022 [36]	US	US images from 306 PTC patients	Classification (large volume LNM)	ANN-based radiomics model	An AUROC and AUPR of 0.856 and 0.381 for the radiomic model, as well as an AUROC and an AUPR of 0.910 and 0.463 for the integrated model.
Keutgen et al, 2022 [6]	US	1,052 ultrasound images from 302 thyroid nodules	Binary classification (malignant or benign)	Two-class Bayesian ANN classifier	Achieved AUCs of 0.75 for MM vs. BB and 0.67 for IM vs. IB. On an independent test of 19 IM/IB cases, it reached an AUC of 0.88, outperforming a commercial molecular test (AUC=0.81).
Li et al, 2023 [37]	US	US images from 164 pediatric patients with PTC	Classification (extrathyroidal extension or not)	LightGBM, KNN, SVM, and RF	AUCs of 0.832, 0.720, 0.784, 0.728, respectively, for the four models.
Sharma et al, 2023 [38]	US	Two datasets: The US dataset (298 patients) and the histopathological dataset (156 thyroid tumors)	Classification (malignant or benign)	Transformation techniques (PCA, TSVD, FastICA, ISOMAP, LLE, and UMP, as well as LR, NB, SVC, KNN, and RF)	RF and PCA+FOX yielded the best performance: AUC of 99.13% and accuracies of 99.13% in the US, and 95.48%, and 90.65%, respectively, in the histopathological dataset.
Göreke et al, 2023 [39]	US	B-mode thyroid US images from 99 patients	Binary classification (malignant or benign)	ANN, CNN, LSTM, and RNN	AUC=1 Recall=0.99 for all of them
Zhu et al, 2023 [40]	US	US images from 371 PTC patients	Binary classification (with or without CLNM)	RF, LASSO, binary LR, KNN, SVM, and XGboost	An AUC of 0.812 for the RF-RF model validation group
Dai et al, 2023 [41]	US	US data from 498 PTC patients	Binary classification (CLNM or not)	AB, LDA, and SVM-based radiomics model	The multimodal-SVM model showed AUCs of 0.910, 0.851, 0.920, and 0.828 (95% CI: 0.769–0.887) in the validation, testing, cN0 subgroup-1, and cN0 subgroup-2, respectively.
Arabi et al, 2023 [42]	US	US data from 210 patients	Prediction (malignant or benign)	LASSO, mRMR, RF, and XGBoost	GLRLM-RLNU and GLZLM-GLNU demonstrated top AUCs of 0.67 in predicting nodule malignancy. On the test data, XGBoost with mRMR and LASSO selection achieved the highest performance with an AUC of 0.95.
Zhou et al, 2023 [43]	US	US data from 192 patients	Classification (malignant or benign)	KNN-based radiomics model, and other seven ML classifiers	The AUC, accuracy, sensitivity, and specificity of the KNN model were 0.909, 82.95%, 83.33%, and 89.90%, respectively.
Cozzi et al, 2023 [44]	US	476 US images from patients with intermediate nodules	Classification of intermediate nodules (final Dx: Benign or malignant)	Radiomics and DL-based models: Classifier combination model (SCM) and interpretability-driven combination model (ICM)	The models achieved mean AUCs of 0.75, 0.70, 0.77, and 0.76 for RM, DTLM, SCM, and ICM, respectively.
Gao et al, 2024 [45]	US	US and clinical data from 613 PTC patients	Classification (CLNM or non-CLNM)	Hand-crafted radiomics model, DL-based radiomics model, and integrated model	The integrated model achieved the highest AUC (0.841), surpassing both the radiomics (0.706) and DL (0.819) models.
Fan et al, 2023 [46]	US	US data from 211 DTC patients	Classification (CLNM or not)	ML-based radiomics model	The combined model achieved an AUC of 0.901, significantly outperforming the single ultrasound model (AUC=0.731) and the radiomics model alone (AUC=0.801).
Ni et al, 2024 [47]	US	US data from 854 PTC patients from three different center	Classification (large volume LNM or not)	LR-, KNN-, SVM-, MLP-, RF-, XGBoost-, and LightGBM-based radiomics model	The ExtraTrees model achieved an AUC of 0.787, while the DenseNet121 DL model reached an AUC of 0.766. The combined Thy-DL-radiomics model represented improved diagnostic accuracy, with AUCs of 0.839 and 0.789 in internal validation and external validation, respectively.
Fu et al, 2024 [48]	US	US data from 528 HT combined PTC patients	Classification (LNM or not)	RF, SVM, LightGBM, KNN, and XGBoost models	All five ML models performed well, with AUCs from 0.798 to 0.921. LightGBM and XGBoost achieved the highest performance, surpassing the other models.

Table 1. Continued.

Reference	Imaging	Sample Size	Tasks	Approaches	Performance
Du et al, 2024 [49]	US	US data 817 patients	Classification (malignant or benign)	Radiomics signature, DL signature, and clinical US semantic signature	The combined model achieved AUCs of 0.947, 0.917, and 0.929, with the comprehensive nomogram showing the best clinical utility. AUCs for differentiating benign and malignant thyroid nodules ranged from 0.714 to 0.752 for junior physicians from 0.891 to 0.908 for experts. With DL radiomics assistance, these improved to 0.858–0.923, 0.888–0.944, and 0.912–0.919, respectively.
Zhao et al, 2024 [50]	US	US data from 75 LNs	Classification (CLNM or non-CLNM)	SVM-, DT, and LDA-based radiomics model	The SVM model had the best diagnostic efficacy, with a sensitivity of 93.0%, a specificity of 93.8%, and an accuracy of 93.3%.

Note. CI: Confidence interval; US: Ultrasound; CT: Computed tomography; MRI: Magnetic resonance imaging; LN: Lymph bode; PTC: Papillary thyroid carcinoma; AUC: Area under the curve; LR: Logistic regression; RF: Random forest, KNN: K-nearest neighbor; SVM: Support vector machine; DT: Decision tree; NB: Naive Bayes; SVC: Support vector classifier; ETE: Extrathyroidal extension; LNM: Lymph node metastasis; CLNM: Central lymph node metastasis; FDG-PET: Fluorodeoxyglucose positron emission tomography; CNN: Convolutional neural network; TL: Transfer learning; DLRT: Deep learning radiomics technique; PNN: Probabilistic neural network; ANN: Artificial neural network; mRMR: Minimum redundancy maximum relevance; USR: Unsupervised representation learning; NG: Nodular goiter; TN: Thyroid nodule; XGBoost: Extreme gradient boosting machine; GLRLM-RLNU: Gray level run length matrix-run-length non-uniformity; GLZLM-GLNU: Gray-level zone length matrix-run-length non-uniformity; HT: Hashimoto's thyroiditis; LDA: Linear discriminant analysis; DTC: Differentiated thyroid carcinoma; AB: Adaptive boosting; LDA: Linear discriminant analysis; CCLNM: Central cervical lymph node metastasis; TCI: Thyroid capsule invasion; SUV: Standardized uptake value; DLRN: Deap-learning radiomics nomogram.

on prognosis and treatment options for severe cases. The study confirmed the potential of MRI-based radiomics in non-invasively assessing thyroid cancer aggressiveness by using a sparse representation method for feature selection and model establishment. Manual segmentation was performed for the region of interest delineation, and the study highlighted the possibility of exploring DL for automatic segmentation in future work. The model's high accuracy, supported by an AUC of 0.960, underscores the clinical relevance and utility of ML-based image analysis in rapid and informative cancer assessment. Likewise, Qin et al [9] examined preoperative MRI images from 109 PTC patients (77 with lymph node metastases and 32 without). They extracted radiomics signatures from fat-suppressed T2-weighted MRI images, identifying optimal features using Spearman correlation, hypothesis testing, and RF methods. The AUC for LN status based on visual diagnosis was 0.739 (sensitivity = 0.571, specificity = 0.906). The MRI radiomics model with five optimal signatures achieved AUCs of 0.805 and 0.760 in the training and validation groups, respectively. Moreover, the combined model of the best radiomics features and visual MRI assessment showed a high AUC of 0.969 (sensitivity = 0.938, specificity = 1.000), demonstrating superior diagnostic efficiency for LN metastases in PTC.

All three-research used different models and approaches to analyze and predict the progression of PTC. Specifically, the combined MRI radiomics model in the study by Qin et al [9] provided superior accuracy and specificity. These studies not only confirm the value of MRI-based radiomics in PTC, but also underline the importance of implementing personalized techniques that take into account individual clinical scenarios. Furthermore, this diversity of study ideas reflects radiomics' rising acceptance as a valuable tool in personalized medicine, with the ultimate goal of improving patient care and treatment outcomes in thyroid cancer.

Radiomics and Artificial Intelligence Using Computed Tomography Scan Imaging for Thyroid Cancer

Eleven studies employed CT images as part of their radiomics analyses in thyroid cancer research. CT imaging offers distinct advantages, including high spatial resolution and the ability to visualize anatomical structures in detail. Likewise, this modality provides valuable information on tumor size, shape, and density, thereby facilitating accurate diagnosis and staging of thyroid cancer. In these studies, CT-based radiomics approaches were utilized to extract quantitative imaging features from CT scans, enabling the development of predictive models for various aspects of thyroid cancer, such as LN metastasis (LNM), extrathyroidal extension, and cervical LNM (CLNM).

A CT-based radiomics model was created in a multicenter study directed by Li et al [16] to forecast CLNM in patients with PTC. By incorporating radiomic characteristics and clinical risk factors, the model displayed superior sensitivity and accuracy compared to a skilled radiologist, indicating its potential as a non-invasive preoperative instrument with practical applications. The model, which focused on the linear-SVM algorithm and included 4,227 extracted radiomic features, showed encouraging results and desirable agreement when predicting CLNM across a range of test sets. Additionally, the linear-SVM algorithm achieved the highest AUC of 0.709 in the internal test set, outperforming the other models (KNN, DT, LR, and Gaussian-SVM) with AUCs of 0.605. It also surpassed CT assessments by experienced radiologists in both sensitivity (0.702 vs. 0.477) and accuracy (0.670 vs. 0.642). The combined radiomics model using linear-SVM represented AUCs of 0.747 and 0.764 in the training set and external test set, respectively.

Similarly, Wu et al examined the use of a CT-based radiomics model for predicting thyroid capsule invasion (TCI) in PTC [18] CT scans were processed to extract radiomic features, and six supervised ML models were built accordingly. Due to its stable and clinically useful integration of optimal radiomics features and clinico-radiological risk factors, the combined-linear-SVM model performed better than the radiomics and clinical models in predicting TCI. In the internal test cohort, the combined-L-SVM model achieved the highest AUC of 0.820, outperforming both the best radiomics (AUC = 0.733) and clinical (AUC = 0.709) models. This combined model integrates 23 radiomics features with 1 clinico-radiological risk factor (CT-reported TCI). In the external test cohort, it showed stability with an AUC of 0.776. Notwithstanding the limitations of the study (e.g., the absence of a sizable sample size and the consideration of various factors), the ML-based methodology exhibited strong predictive capacity.

Likewise, Yu et al[19] created a radiomics nomogram that combines clinical risk factors with radiomics features taken from CT images to predict ETE in PTC patients. The AUCs ranged from 0.642 to 0.701, indicating the potential value of the nomogram in predicting ETE, although the study was retrospective in nature. Certain limitations were recognized, such as the possibility of selection bias and the requirement for prospective studies to account for confounding variables. The study sought to address the effects of ETE, which are linked to LNM and invade surrounding structures, which both have an impact on the outcomes. Using a variety of ML techniques, the radiomics nomogram yielded the potential to support preoperative ETE prediction in PTC. Overall, 153 patients were included in this study. Four radiomics features were selected, and six models demonstrated the value of radiomics, with AUCs ranging from 0.642 to 0.701. The nomogram combining the Rad-score and clinical risk factors (radiologists' interpretation) performed well, achieving AUCs of 0.750 and 0.797 in the internal and external test sets, respectively.

In another study, Xu et al[20] used an LR model to investigate the diagnostic potential of CT-based radiomics for differentiating between benign and malignant thyroid nodules. The research, which examined data from 161 patients, demonstrated how accurate the model was, with remarkable AUCs of 94.4% and 94.2% in the training and test groups, respectively. The model also had corresponding sensitivities of 89.7% and 89.4%, as well as specificities of 86.7% and 86.8%. The study's limitations, including its small sample size and dependence on single-center data, were acknowledged despite the obtained satisfactory results.

In the study performed by Gu et al,[13] a radiomics model was created for the noninvasive prediction of cytokeratin-19, galectin-3, and thyroperoxidase based on CT images. The study focused on the prediction of immunohistochemistry of suspected thyroid nodules in 103 patients using ML-based radiomics. The cytokeratin 19 model achieved accuracy of 80.0% in the validation cohort. Furthermore, the thyroperoxidase and galectin 3 models attained accuracies of 84.2% and 85.0% in validation. In contrast, the high-molecular-weight cytokeratin model underperformed at 65.7% accuracy and lacked validation Moreover, it was found that thyroperoxidase immunoexpression positivity is a separate risk factor for thyroid cancer.

In addition, Zhou et al[17] studied the radiomics analysis of iodine maps from dual-energy CT (DECT) to predict CLNM in PTC. Two radiomics nomograms were created and validated to predict CLNM. Nomogram 1 included LN rad-score, age (≥ 55), and CT-reported LN status, while Nomogram 2 incorporated CLN rad-score, capsule contact > 25%, and CT-reported CLN status. Both nomograms demonstrated strong performance with AUCs of 0.847 and 0.837 in the training cohort and 0.807 and 0.795 in the validation cohort. Additionally, significant improvements in AUC and other metrics confirmed the added predictive value of the rad-scores. Both nomograms also showed good efficacy in CT-reported LN or CLN negative subgroups, with AUCs of 0.766 and 0.744. These nomograms represented the promise of radiomics-based risk stratification in PTC, especially in CT-reported negative subgroups where they displayed favorable predictive efficacy. The study compared the predictive efficacy of radiomics nomograms and clinical models using DECT scanning with post-processing for radiomics analysis.

Furthermore, Lu et al[12] presented a radiomics-based approach to predict CLNM in 221 PTC patients prior to surgery. In their study, a radiomic signature with improved predictive performance was selected by extracting 546 radiomic features from CT images. The radiomic signature outperformed individual radiomic sub-signatures created by SVM. More precisely, adding the radiomic signature to the nomogram enhanced the predictive value, increasing the AUC from 0.807 to 0.867 in the training cohort, and confirmed it in the validation cohort, with an increase from 0.795 to 0.822. Further, de Koster et al[15] sought to improve radiomics and [18F] FDG-PET/CT assessment in the differentiation of indeterminate thyroid nodules. AUC values for various standardized uptake value (SUV) metrics ranged from 0.705 to 0.757. According to radiomic analysis, the PET model's AUC was 0.445. Although the study recommended higher SUV cut-offs for the best rule-out performance in Hürthle cell nodules, there were no specificity data for quantitative [18F] FDG-PET/CT evaluation. In another study by Zhou et al [14], of 255 lymph nodes (143 non-metastatic and 112 metastatic), radiomics features were extracted from iodine maps, and a radiomics signature was developed using LASSO logistic regression. Three models were created: model 1 (CT features), model 2 (radiomics signature), and model 3 (combined). The combined model (AUC = 0.933 training; AUC = 0.895 validation) outperformed both model 2 (AUC = 0.910 training; AUC = 0.847 validation) and model 1 in both sets. Additionally, Li et al[122] examined the effectiveness of a ML-based model in distinguishing NG from PTC using 3D arterial-phase contrast-enhanced CT features. Analyzing data from 407 patients and extracting 1,218 features, the radiomics model achieved an AUC of 0.877 in the validation group; this model outperformed clinical diagnosis, which had an AUC of 0.889 in the training group. With a classification accuracy of 80.49%, the results revealed that integrating advanced radiomics significantly enhances preoperative diagnostic accuracy for thyroid nodules. Similarly, Xu et al[21] investigated 280 patients with PTC. Recurrence was defined as confirmed disease or imaging evidence within 5 years post-surgery. Models were built for radiomics, clinical, and combined approaches using LR, SVM, KNN, and NN. Recurrence occurred in 89 patients, with 1,218 extracted radiomics features. Based on their results, five radiomics and six clinical features were linked to recurrence. The LR and SVM radiomics models outperformed the NN model. Among clinical models, only the AUC difference between LR and NN was significant. Combined models showed higher AUCs than individual models, with validation cohort AUCs of 0.746 (LR), 0.754 (SVM), 0.669 (KNN), and 0.711 (NN). Likewise, Zhang et al[23] collected CT imaging and pathology data from 141 patients with TN. From these, 1,316 radiomics features were extracted and refined using correlation testing, LASSO, or minimum redundancy maximum relevance selection. Four ML models (RF hybrid feature, RF, SVM hybrid feature, and LASSO) were developed and evaluated with ROC analysis. Their findings confirmed that the RF hybrid feature model performed best, achieving an AUC of 0.87, significantly improving over the LASSO model (AUC = 0.78) in reclassification and discrimination metrics.

In a retrospective study performed by Huang et al,[22] a total of 376 cases were collected and then divided into training and testing groups. Two radiologists identified ROI in the images and extracted 1,316 radiomic features. After feature screening, 11 optimal radiomic features were selected using minimum redundancy maximum relevance (mRMR) and LASSO to develop an automated tumor discrimination model. The model's performance, assessed via ROC curve analysis, achieved an AUC of 0.911 on the training set, with accuracy, sensitivity, and specificity of 0.897, 0.889, and 0.862, respectively.

In summary, the highest performing radiomics model in CT images based on AUC was the combined radiomics model developed by Zhou et al,[14] with AUCs of 0.933 and 0.895 in the training and validation sets, respectively, showcasing the effectiveness of integrating multiple features and methodologies in enhancing predictive accuracy for LNM in PTC. Overall, these studies collectively underline the growing recognition of radiomics as a powerful tool in personalized medicine for PTC, each contributing to advancing the understanding of tumor behavior and improving preoperative assessments.

Radiomics and Artificial Intelligence Using Ultrasound Data for Thyroid Cancer

The remaining studies in the review exclusively utilized US images as the primary imaging modality for radiomics analysis in thyroid cancer diagnosis and prognosis. Due to its non-invasive nature, accessibility, and ability to provide real-time imaging with high resolution, US imaging is widely employed in clinical practices.[119] Leveraging these images for radiomics analysis offers valuable insights into the morphological and textural features of thyroid nodules, facilitating the development of predictive models for risk stratification and treatment decision-making.

The DL radiomics of thyroid (DLRT) was investigated by Zhou et al[25] as a novel method for using US images to diagnose thyroid nodules. DLRT achieved the highest AUC and sensitivity across multiple validation cohorts, outperforming other DL models and even human observers in terms of accuracy. The AUCs of DLRT were 0.96, 0.95, and 0.97 in the training, internal, and external validation cohort, respectively. Further, DLRT performed significantly better than other DL models and human observers, Additionally, DLRT yielded the highest diagnostic accuracy for benign and malignant thyroid nodules. The sensitivities of DLRT reached 90.1, 89.3, and 89.5 in different cohorts. DLRT had higher accuracy compared to the TL and basic CNN models. This novel approach does away with the requirement for manual segmentation, makes use of TL to increase accuracy, and works well with a variety of US systems. The specificity of the model has not been stated in the study, and more research is needed to rule out any biases brought on by specimen collection and operator experience. Kwon et al,[29] evaluating the use of US in radiomics to predict the BRAF mutation in PTC, found that the technique was at most moderately successful. Even with an AUC of 0.65 and an average accuracy of 64.3%, it was not a highly desirable diagnostic tool. Several ML models were employed in the study, but none proved to be particularly beneficial. The researchers referred to several drawbacks, including a small sample size, the possibility of overfitting the models, and intrinsic difficulties in quantifying US data in comparison to other imaging modalities. They concluded that the current utility of radiomics using US to predict BRAF mutation is limited, and they advocate for more study with larger datasets and a wider range of diagnostic techniques to validate and improve the methodology.

Additionally, Zhu et al[36] described an US radiomics approach based on ANNs that predicts large-volume LNM in patients with clinical N0 PTC. They used deidentified data and a retrospective method and reported that utilizing the ANN-based integrated model enhanced performance with an AUROC of 0.910, while the ANN-based radiomic model achieved an AUROC of 0.856. With an accuracy of 91%, the integrated model outperformed the radiomic model, which had an accuracy of 86%. Nevertheless, the information that is currently available lacks specifics for both the integrated model and the ANN-based radiomic model.

Xia et al[30] reported a study utilizing an AI algorithm to predict LNM in patients with PTC prior to surgery. The AI algorithm used clinico-pathologic data to predict LNM by combining the probabilistic neural network (PNN) and SVM. With F1 scores of 0.88 and 0.93 for CLNM and lateral LNM, respectively, the study illustrated the utility of this combination. Before the surgery, the combination of AI algorithms and clinico-pathologic data was a useful tool for predicting LNM in PTC patients. AI algorithms in particular, which are predictive models, were useful for risk stratification.

Similarly, Agyekum et al[31] used a ML-based clinical-US radiomic (clinical-USR) model to assess CLNM in PTC cases. The clinical-USR model outperformed an experienced sonographer in terms of accuracy when predicting CLNM in PTC patients. The model considers PTC heterogeneity, a measurable characteristic linked to malignancy, which eliminates subjectivity in standard US imaging diagnosis. Overall, 205 patients were included in the retrospective study. Nine statistically significant variables were employed to build the clinical-USR model, with internal echo, shape, age, and mass being identified as the main predictors. The clinical-USR model distinguished PTC patients with CLNM, showing AUCs of 0.78 (training) and 0.71 (validation). It outperformed the clinical model, particularly in validation (0.71 vs. 0.63). The research noted certain difficulties, including the challenge of using ultrasonography to detect all metastatic lymph nodes, subjectivity in standard ultrasonography diagnosis, and limited visual measurement of PTC density and tissue heterogeneity.

In the study conducted by Wang et al,[26] thyroid nodule classification using US images was compared between radiomics and DL techniques. The study utilized a dataset consisting of 3,120 US images from 1,040 cases. Interestingly, DL performed better than radiomics, with an accuracy of 74.69% against radiomics' 66.81%. Their findings revealed that large datasets are essential for improving the performance of DL models. It was suggested that future work focuses on DL model optimization and multicenter data validation of efficacy.

Moreover, Yu et al[33] aimed to predict RET rearrangement in PTC by means of a novel method that combines DL and US radiomics. AUCs of 0.9545 in the test cohort and 0.9396 in the training cohort indicated the excellent performance of the DL radiomics nomogram, which was developed. The behavior of aggressive PTCs, RET rearrangement, was predicted by using ultrasonic radiomics and deep transfer learning. Among the clinical characteristics that separated patients with and without RET rearrangement were age, tumor size, and calcification.

In addition, Wang et al[32] attempted to predict BRAF V600E mutations in PTC using grayscale imaging and elasticity US. The development of radiomic models from US images showed high accuracy in mutation prediction, with AUCs ranging from 0.725 to 0.985. The model with the highest AUC was the combination of elasticity and grayscale. Overall, 138 PTC patients underwent preoperative ultrasonography, and radiomic features were taken out for model creation. The small sample size, the retrospective design, and the absence of outside validation were some of the limitations of their study.

By utilizing an US radiomics nomogram, Zhou et al[34] presented a novel method for the preoperative prediction of central neck LNM in papillary PTC. The study integrated radiomics features, US findings, and clinical factors to develop a predictive model in response to the suboptimal accuracy of US in diagnosing CCLNM in PTC. In the validation cohort, the SUC was 0.858.

An US-based radiomics XGBoost model was created by Shi et al [35] to predict CCLNM in PTC patients. The model used 11 radiomics features, including important variables, such as capsular invasion, radiomics score, diameter, age, and calcification, to calculate the radiomics score after retrospectively analyzing data from 587 PTC patients. When compared to radiologists, the XGBoost model performed better, displaying an astounding 44% increase in AUC. The AUC was 91.53% and 90.88% in the training and test sets, respectively. The stability of the XGBoost model was particularly noteworthy, as it demonstrated reliable performance on various kinds of US scanners. The study highlights the importance of CCLNM preoperative prediction in PTC and shows that US-based radiomics, XGBoost, and SHAP are effective tools for precise risk assessment and customized interpretation of predictive features in the diagnosis of thyroid cancer. The XGBoost model's positive and negative effects on each parameter were revealed by the SHAP plots, which enhances the model's interpretability and comprehension of its decision-making process. The extensive methodology emphasized the integration of cutting-edge techniques in thyroid cancer research and included image segmentation, feature extraction, normalization, LASSO logistic regression, and the creation of the XGBoost model.

Li et al [37] used a multi classifier US radiomics model to develop a ML technique for predicting ETE in pediatric PTC. Four supervised ML models were created, including LightGBM, k-nn, RF, SVM, and LightGBM. The LightGBM model performed exceptionally well in both the training and validation cohorts. In the training cohort, AUCs were 0.880, 0.873, 0.999, and 0.926 for SVM, KNN, RF, and LightGBM, respectively. In the validation cohort, the corresponding values were 0.784 (SVM), 0.720 (KNN), 0.728 (RF), and 0.832 (LightGBM). The amalgamated model, which fused ultrasonic radiomics and ML, demonstrated exceptional prognostic potential for ETE in pediatric PTC. Using a correlation coefficient screening method, ML models were developed, radiomics features were extracted from US images, and the SHAPley additive explanation SHAP framework was employed to explain the models.

Likewise, Kwon et al[27] utilized radiomics analysis based on gray-scale US to predict distant metastasis in FTC. The second most common thyroid cancer is called FTC, and distant metastasis is a major predictor of a poor prognosis. The researchers aimed to create an independent biomarker for distant metastasis in FTC using radiomics signatures. Radiomics analysis used the LASSO to create a radiomics signature by extracting features from US images. In addition, the radiomics signature was utilized to train an SVM classifier. The classifier showed an AUC of 0.90 on the test folds. With an AUC of 0.93, multivariate analysis represented the classifier's strong diagnostic performance. Distant metastasis was linked to clinical factors, such as size, age, widely invasive histology, LNM, and extrathyroidal extension. On the other hand, widely invasive histology and the radiomics signature were found to be independent variables related to distant metastasis. Using US and histological images, Sharma et al[38] provided a thorough framework for the detection of thyroid cancer that integrates DL, meta-heuristics, and multiple criteria decision making (MCDM) algorithms. The study evaluated five classifiers using three DL techniques and six feature transformation methods, and utilized MEREC-TOPSIS MCDM for model ranking. The PCA + FOX feature selection with RF achieved top performance, with a 99.13% accuracy, and 99.13% AUC-ROC on US data, and a 90.65% accuracy, as well as 95.48% AUC-ROC on histopathology data. By underlining early diagnosis, the framework seeks to reduce the workload for medical practitioners by offering enhanced diagnostic capabilities. The study pointed the significance of accurate CAD models for patient care by utilizing pre-trained DL models, dimensionality reduction techniques, and the FOX optimization algorithm for feature selection. The use of multiple imaging modalities (e.g., US) and the investigation of DL models (e.g., DeiT, Swin transformer, and mixer-MLP) for feature extraction were important components of their methodology. In addition, the novel FOX optimization algorithm for feature selection and ensemble learning was employed, along with dimensionality reduction techniques, such as PCA and ISOMAP. Though restricted by the availability of publicly available standard thyroid datasets, the framework showed promising results despite concentrating on two particular thyroid image datasets.

Liu et al [24] focused on the prediction of LNM in patients with PTC using a radiomics approach based on preoperative US images. After examining 450 US images, 50 features were found to have better accuracy in predicting the status of lymph nodes. With a 0.712 accuracy and a 0.782 AUROC, the proposed model appeared to be a promising noninvasive method for assessing metastasis risk. The method used a combined feature selection strategy, an SVM classifier for model building and validation, and 614 high-throughput features extracted from US images. The manual segmentation of tumors and a three-step feature selection method were applied to enhance the accuracy and reliability of the model. The study's findings contributed to the growing body of evidence, supporting the utility of radiomics in noninvasive cancer prediction and management, particularly in high-incidence cancers, including PTC.

In a retrospective study, Zhu et al[40] utilized ML techniques to create preoperative prediction models for evaluating LNM in thyroid cancer cases. The models combined clinical traits and ultrasonic radiomic features to help with diagnosis, predict recurrence, and guide treatment choices. With an accuracy of 0.7542 and an AUC of 0.812, the RF-RF model demonstrated the best predictive performance for CLNM among the five classifiers used in their study. Notably, age and a variety of radiomic features were the most important factors influencing the effectiveness of the RF-RF model. The superior performance of the RF-RF model was demonstrated by using Delong's test to compare its AUC with other models.

Additionally, Yu et al[28] presented a transfer learning radiomics model for predicting LNM in PTC patients, achieving a stable LNM prediction with an average AUC of 0.90 across three datasets totaling 3,172 patients. Decision curve analysis revealed that the transfer learning radiomics model performs better than other approaches, including DL models, such as VGG, ResNet, and inception ResNet, and benefits PTC patients more. Thus, it can be used to guide treatment decisions for PTC patients and improve diagnostic performance. Moreover, Keutgen et al [6] labeled US images from two institutions by FNA and surgical pathology as malignant (M), benign (B), or indeterminate (I), resulting in subgroups: 90 BB, 83 IB, 70 MM, and 59 IM thyroid nodules. Then, thyroid nodule margins were manually annotated, and radiomic texture analysis was performed within these contours. Using five-fold cross-validation and a two-class Bayesian neural network classifier with stepwise feature selection, the model was validated on a separate test set and compared to a commercial molecular testing platform. AUCs were 0.75 for MM vs. BB and 0.67 for IM vs. IB in the training/validation set of 263 nodules. For an independent test set of 19 IM/IB nodules, the algorithm achieved an AUC of 0.88, surpassing the commercial platform's AUC of 0.81. Furthermore, Gao et al[45] analyzed 613 PTC patients, developing a DL and radiomics model using primary lesion images, and integrating clinical and US features through multivariate analysis. Compared to junior and senior radiologists, the integrated model achieved the highest AUC (0.841), surpassing the radiomics (0.706) and DL (0.819) models. It lowered the missed CLNM rate and unnecessary CLND to 27.63% and 18.18%, respectively. Finally, SHAP analysis confirmed that DL features were central in diagnosing CLNM, with clinical and US features enhancing accuracy.

In a study by Fan et al,[46] a predictive model was developed for CLNM for 211 lymph nodes from postoperative differentiated thyroid carcinoma patients. Using data split into training ($n = 147$) and test ($n = 64$) cohorts, relevant radiomic features from US images were identified with the LASSO algorithm to build a radiomics model. The combined model, incorporating radiomics, US, and clinicopathological data, achieved an AUC of 0.901 in predicting CLNM in the test cohort, significantly outperforming the single US model (AUC = 0.731) and radiomics model alone (AUC = 0.801). Further, in a multicenter retrospective study of 854 PTC patients, Ni et al[47] built radiomics and DL models using multiple algorithms, including ExtraTrees, DenseNet121, and ResNet50. The ExtraTrees model achieved the highest AUC of 0.787 among radiomics models, while the DenseNet121 DL model reached 0.766. The combined Thy-DL-radiomics model, integrating radiomics and DL features, showed improved diagnostic performance with an AUC of 0.839 in internal validation and 0.789 in external validation. In addition, Arabi et al [42] investigated

210 patients with thyroid nodules and analyzed radiomics features from US images using LASSO, mRMR, and XGBoost for feature selection and classification. GLRLM-RLNU and GLZLM-GLNU achieved the top AUCs (0.67) in univariate analysis for malignancy prediction. In multivariate analysis, the XGBoost classifier combined with mRMR displayed the highest performance, achieving AUCs of 0.99 and 0.95 in training and testing, respectively. Similarly, Fu et al [48] examined 528 patients with Hashimoto's thyroiditis and PTC, and groups were formed based on the presence LNM. Three US specialists extracted radiomic features, which were combined with clinical data to build five ML models: RF, SVM, LightGBM, KNN, and XGBoost. Then, model performance was assessed with ROC curves, with LightGBM and XGBoost achieving the highest AUC scores (0.798–0.921) and outperforming others ($P < 0.05$). Models combining radiomic and clinical features depicted improved accuracy ($P < 0.05$). Moreover, SHAP analysis pointed features, such as anteroposterior and superoinferior diameters, voxel volume, and age as key predictors for both top models. Additionally, Du et al [49] included 1,076 thyroid nodules from 817 patients across three institutions. Radiomics and DL features were extracted from US images to create radiomics (Rad_sig) and deep-learning (DL_sig) signatures. A clinical US semantic signature (C_US_sig) was also developed, followed by building and evaluating a combined nomogram model. The model achieved AUCs of 0.947, 0.917, and 0.929, demonstrating superior clinical utility in decision curve analysis and good calibration. AUCs for distinguishing benign and malignant nodules ranged from 0.714 to 0.752 for junior physicians and from 0.891 to 0.908 for experts, improving to 0.858–0.923, 0.888–0.944, and 0.912–0.919 with DL radiomics assistance.

Furthermore, Zhou et al [43] analyzed 192 patients with 197 partially cystic thyroid nodules. Radiomics features were extracted from US images, and ML methods were used to build a classification model. Further, model performance was evaluated using AUC, accuracy, sensitivity, and specificity. Nineteen radiomics features were extracted for each nodule, and eight ML classifiers differentiated malignancy in partially cystic thyroid nodules. The k-NN model achieved an AUC of 0.909, with accuracy, sensitivity, and specificity of 82.95%, 83.33%, and 89.90%, respectively. The ML-based US radiomics system outperformed the ACR TI-RADS model and US features model in AUC. Likewise, Zhao et al [50] investigated the patients scheduled for surgical treatment due to thyroid cancer. Each patient underwent the US of CLNs suspected of metastasis, with a 2-minute imaging video recorded. Three ML models, including SVM, linear discriminant analysis, and DT, were developed after target tracking and feature extraction. A total of 75 lymph nodes were analyzed, with SVM showing the best diagnostic efficacy (93.0% sensitivity, 93.8% specificity, and 93.3% accuracy, calculated via leave-one-out cross-validation). In another study conducted by Dai et al,[41] 498 unifocal PTC cases with post-operative histopathology as the CLNM standard showing the best diagnostic efficacy. US images were segmented, and multimodal features were extracted using a 50-layer DNN. Features were then selected and fused, followed by classification using adaptive boosting, linear discriminant analysis, and SVM. Among the models, multimodal-SVM performed best ($P < 0.05$), achieving AUCs of 0.910 (validation) and 0.851 (testing), with the subgroup AUCs of 0.920 and 0.828 in cN0 subgroup-1 and cN0 subgroup-2, respectively.

In this review, most studies utilized US images as the primary modality for radiomics analysis in thyroid cancers, reflecting its widespread availability and effectiveness in clinical practices. The procedures included a wide range of DL techniques, such as CNNs and TL, which have shown remarkable promise in enhancing diagnostic accuracy. The TL model performed impressively across multiple cohorts, pointing its strength and potential for broad clinical applications.

Traditional ML models (e.g., SVM and RF) displayed more variable results, reflecting a variety of performance levels. This variation means that, while certain models may perform well in specific scenarios, they will be struggling to overcome the complexity of US data and the heterogeneity of thyroid cancers. Likewise, models that included clinical and radiomic features with imaging data provided better outcomes, indicating the need for a multimodal approach. This integration can combine quantitative data from radiomics with qualitative insights from clinical assessments to create a broader view of patient risk. However, some studies discovered lower accuracy, outlining the persistent problems in developing and validating radiomics models across patient groups and imaging conditions. These discrepancies raise important questions about the reproducibility and generalizability of current models in clinical settings. Although the findings underscore the promising role of AI and radiomics in improving diagnostic accuracy for thyroid cancer, they simultaneously point to the necessity for standardized methodologies and larger, more diverse datasets to enhance the reliability and applicability of these models in everyday clinical practices. Reviewing radiomics in thyroid cancers, especially when combined with AI applications, reveals a wide variety of results and approaches. On the other hand, a radiomics study with an average accuracy, sensitivity, and specificity of 64.3%, 66.8%, and 61.8%, respectively, demonstrated a moderate level of success in using US to predict the BRAF mutation in thyroid nodules. Notably, different feature-selection strategies did not considerably improve test performance in this particular study. Furthermore, different classifiers displayed varying performance in various studies, highlighting the variation in the results.[29]

In contrast, some studies introduced novel approaches that represented superior performance compared to existing literature. For instance, the application of a multi-layered classifier architecture, particularly utilizing RNN, exhibited high accuracy in comparison to traditional models.[39] Comparably, enhanced discrimination and clinical utility were demonstrated by the incorporation of ANN-based US radiomics for forecasting large-volume LNM in patients with PTC.[36,52] These results emphasize how customized AI applications can improve the precision of diagnoses in particular clinical situations.

The high F1 scores that the PNN and SVM classifiers achieved in different test sets [30] revealed how well AI algorithms combined with clinico-pathologic data could predict LNM in PTC cases. This was the subject of another study. To fully understand the potential of the technology, a collaborative approach was suggested by emphasizing the need for a supervisory framework for AI applications that include radiologists.[123] Moreover, given the variability of PTC, the clinical-USR model outperforms a skilled sonographer in assessing CLNM [31], underling the developing role of AI in improving diagnostic accuracy. Different results were also observed when comparing DL with radiomics-based methods. DL consistently outperformed radiomics-based methods in terms of accuracy and AUC in predicting different parameters, including BRAF V600E mutations [26] and RET rearrangement.[33] These findings imply that, for some diagnostic tasks, DL techniques may become more advantageous than traditional radiomics. Similarly, the literature pointed how radiomics is a flexible tool for predicting different aspects of thyroid cancers, including metastasis to central neck lymph nodes [35], distant metastasis in FTC [27], and ETE.[19] This versatile application demonstrates how radiomics can offer comprehensive insights into the features and prognosis of thyroid cancers.

In conclusion, there is a wide range of performance and utility levels in the literature on radiomics in thyroid cancers and AI applications. While some studies show encouraging outcomes and improvements in diagnostic accuracy, others draw attention to the necessity of precisely weighing the unique clinical context and cooperatively integrating AI into already-existing diagnostic frameworks.[124] The inconsistent results indicate the significance of individualized strategies and ongoing improvements in the use of AI and radiomics for thyroid cancer prognosis and diagnosis.

Staging

Based on publication of the eighth edition of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control in 2016, changes were made to the staging system for thyroid cancer.[125] Remarkably, age was taken into consideration, and the age cutoff was 55 instead of 45. Significant downstaging of tumor classifications resulted from the revisions. Overall, 38% of patients had their tumor classifications downstaged, and the percentage of patients classified as Stage I or II increased from 64% to 94%. These modifications provided a more accurate prognosis by better aligning staging with disease-specific survival. The American Thyroid Association's risk stratification system and AJCC staging together enhanced the prediction of disease-specific survival.[126] Detectable thyroid nodules are present in only 30–40% of thyroid cancer instances, rendering them a secondary diagnostic preference. Essential for identifying thyroid nodules are imaging techniques like cross-sectional and US imaging.[127] However, the concern of overdiagnosis underscores the importance of exercising prudence and adhering to evidence-based guidelines discouraging screening for asymptomatic individuals. US emerges as the favored imaging modality for evaluating nodule characteristics, though its application requires circumspection to prevent misdiagnoses. Presently, FNA remains a dependable diagnostic approach, particularly when coupled with risk assessment tools.[128] Molecular diagnostic methodologies, exemplified by ThyroSeq (version 3) and Afirma, have mitigated the necessity for diagnostic lobectomy in cases of indeterminate nodules. Striking a judicious balance between early detection and the risk of overdiagnosis persists as a formidable challenge confronting medical practitioners.[129,130]

Challenges, Limitations, and Future Directions

A persistent issue pertains to dependence on operator expertise and specimen gathering, which may introduce errors in production, highlighting the necessity of standardization and careful handling.[25] US-based radiomics has inherent limitations, especially in predicting the status of BRAF mutations, including operator dependence, difficulties with quantitative analysis, and the need for larger datasets to improve the efficacy of particular features.[29] To achieve more reliable and broadly applicable results, prospective multicenter approaches to validation are crucial, as evidenced by the retrospective nature of certain studies and the uneven distribution of data.[36] One major issue that arises is the interpretability of AI models, since classifiers are "black boxes," making it difficult to understand the causal relationships between them. Variations in tumor microenvironments and imaging protocols make generalizing models even more challenging, underscoring the necessity of fully comprehending the underlying concepts and incorporating clinical data.[34,110] Even with their promising performance, AI systems perform on par with or worse than experienced ultrasonography specialists, underlining the urgency of a supervisory structure for radiologists as of right now.[123] Problems with the dataset include small sample sizes, single-center designs, and low diversity, emphasizing the significance of using multi-modal, multi-center data for thorough validation.[18,27,32,33] Different imaging modalities, such as [18F]FDG-PET/CT, present difficulties for radiomics methodology due to limited specificity and difficult differentiation.[15] Similar challenges have been reported in medical image analysis, including the need for large annotated datasets, reduced performance in sequential data, computational inefficiency, and limited generalizability across imaging modalities.[130]

Based on difficulties in US radiomics, a lack of standardization is a common theme in radiomics models. It will take work to standardize the field, cut down on mistakes, and improve US radiomics' applicability in a variety of clinical contexts.[27] The necessity for additional validation in prospective datasets, with careful consideration of potential biases, is highlighted by retrospective study designs.[12] Difficulties in making clinical decisions, such as the erratic US physicians' rating skills and the lack of certainty in cytopathological diagnosis, reveal how difficult it is to incorporate these technologies into real-world medical settings. Additionally, limitations in the knowledge base for head and neck diseases, coupled with a scarcity of studies on radiomics in certain thyroid cancers, demonstrate the need for comprehensive research in these areas.[88] Accordingly, concerted efforts and innovative solutions will be required to overcome the challenges and limitations in the application of radiomics and AI for thyroid cancer detection and prognosis. Moreover, standardization efforts are essential for enhancing reliability and repeatability in a range of clinical settings, and multimodal data integration presents the possibility of developing comprehensive predictive models. Advancements in explainable AI technology have the potential to improve the interpretability of ML models, thereby simplifying their integration into clinical environments. Prospective multicenter studies with larger datasets are also necessary to validate the efficacy and generalizability of radiomics models, and personalized medicine approaches can customize treatment regimens to the specific features of individual tumors. Additionally, the creation of clinical decision support systems and funding for training and education programs for medical professionals are crucial for the widespread adoption and application of radiomics-based approaches. By embracing these new directions, the field will be able to advance and enhance patient outcomes in the treatment of thyroid cancer by facilitating more accurate diagnosis and customized treatment.

Conclusion

This review presented a landscape of changing approaches and results from a thorough analysis of the literature on the use of AI and radiomics in thyroid cancer diagnosis and prognosis. Due to its widespread availability and efficacy in clinical practice, US images have been the primary modality for radiomics analysis in the majority of studies in this domain. Notably, combining computational power with state-of-the-art imaging techniques has shown promise in improving accuracy, effectiveness, and customized patient care. Numerous approaches and methodologies have been used in the reviewed studies, producing a wide range of outcomes and results. While some studies introduced innovative techniques that outperform conventional approaches, other studies emphasized difficulties and restrictions that come with using AI and radiomics to diagnose thyroid cancer. Research employing multi-layered classifier architectures, specifically with RNN, has demonstrated superior accuracy in certain clinical situations. Furthermore, integrating ANN-based US radiomics has shown potential in predicting parameters like large-volume LNM in papillary thyroid cancer patients. However, problems like operator dependence, AI model interpretability problems, dataset limitations, and the ongoing need for standardization efforts still exist. Moreover, variations in performance and outcomes among studies highlight the necessity of additional methodology validation and improvement. Different results have been found when comparing radiomics-based methods, with DL consistently outperforming radiomics-based methods in some diagnostic tasks, implying that in some situations, DL techniques might be more advantageous than traditional radiomics. Despite the variability in results and performance levels observed in the literature, radiomics appears to be a flexible tool capable of predicting various aspects of thyroid cancers, including metastasis to central neck lymph nodes, distant metastasis in follicular thyroid cancer, and extrathyroidal extension. This adaptability emphasizes radiomics' potential to provide thorough insights into the characteristics and prognosis of thyroid cancers. In general, there is considerable potential for these technologies to transform thyroid cancer diagnosis and prognosis, even though the literature on radiomics in thyroid cancers and AI applications represents a wide range of performance and utility levels. Nonetheless, coordinated efforts in standardization, validation, and integration into clinical practice will be necessary to perceive this potential. Ultimately, the field can progress toward better patient outcomes and a more thorough comprehension of the pathophysiology of thyroid cancer by taking on obstacles and utilizing creative solutions.

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Competing Interests

The authors declare that there is no conflict of interests.

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Ethical Approval

This study was conducted under the principles outlined in the Declaration of Helsinki.

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