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Research progress of multimodal ultrasound radiomics and deep learning in predicting lymph node metastasis of papillary thyroid carcinoma

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Abstract. Papillary Thyroid Carcinoma (PTC) accounts for more than 80% of thyroid cancers, and cervical Central Lymph Node Metastasis (CLNM) is a critical risk factor affecting patient prognosis. Conventional ultrasound is the first-line method for preoperative evaluation of PTC, but it is restricted by operator subjectivity, image quality interference, and limited diagnostic accuracy for CLNM. Multimodal ultrasound radiomics and deep learning have emerged as innovative technical approaches to address these limitations. This paper reviews the research progress of multimodal ultrasound radiomics and deep learning in predicting CLNM in PTC, covering modality composition, feature extraction, multimodal fusion strategies, model efficacy, and clinical application value. Current studies confirm that multimodal ultrasound radiomics integrating B-mode, contrast-enhanced ultrasound, elastography and microflow imaging achieves an Area Under the Curve (AUC) of 0.78–0.97 for CLNM prediction, significantly outperforming single-modal ultrasound. Deep learning models based on convolutional neural networks and Transformer architectures realize end-to-end automatic prediction with high efficiency. However, most studies are retrospective single-center designs, resulting in insufficient model generalization; the "black box" problem of artificial intelligence and the shallow application of Explainable Artificial Intelligence (XAI) also restrict clinical translation. In conclusion, multimodal ultrasound radiomics and deep learning break through the bottlenecks of conventional ultrasound and provide reliable support for preoperative non-invasive risk assessment of PTC. Future research should focus on prospective multicenter trials, unified imaging standards, optimized XAI methods and multi-omics integration to promote clinical application.

Keywords: papillary thyroid carcinoma, central lymph node metastasis, multimodal ultrasound, radiomics, deep learning

1. Introduction

Thyroid cancer is one of the most common malignant tumors in endocrinology, and Papillary Thyroid Carcinoma (PTC) is the predominant pathological subtype, accounting for more than 80% of cases [1, 2]. In particular, Papillary Thyroid Microcarcinoma (PTMC), despite its slow disease progression and favorable prognosis, still develops regional lymph node metastasis in approximately 30% of patients at an early stage [3]. Central Lymph Node Metastasis (CLNM) in the neck is a critical risk factor in the clinical diagnosis and treatment of PTC patients. Preoperative non-invasive and accurate assessment of CLNM status is key to achieving individualized treatment, improving prognosis, and preventing recurrence [4]. Ultrasound is the first-line examination for preoperative evaluation of PTC; however, its diagnosis relies on operator experience and is susceptible to interference from acoustic shadowing, image resolution, and other factors, leading to limitations in the sensitivity and specificity for CLNM [5]. In recent years, multimodal ultrasound radiomics and deep learning technologies have demonstrated significant application value in predicting PTC Lymph Node Metastasis (LNM) [1, 6-10]. Radiomics high-throughput extracts thousands of quantitative features from images and combines machine learning algorithms to deeply mine tumor heterogeneity, enabling objective quantification of tumors. With its powerful autonomous feature learning capability, deep learning algorithms outperform traditional statistical models in medical image analysis [9]. Although multimodal ultrasonic radiomics and deep learning have demonstrated promising potential in predicting Papillary Thyroid Carcinoma (PTC) lymph node metastasis, existing research still confronts multiple limitations including insufficient model generalizability, inadequate interpretability, and a lack of multi-center evidence. Furthermore, there is an absence of systematic sorting of different technical pathways, fusion strategies and clinical transformation bottlenecks in this field. Therefore, this systematic review aims to comprehensively review the research progress of multimodal ultrasonic radiomics and deep learning in PTC Central Lymph Node Metastasis (CLNM) prediction, summarize the application patterns, performance advantages and core bottlenecks of existing technologies, and discuss future development directions, so as to provide references for clinical transformation and research design in this field..

2. Application of multimodal ultrasound radiomics in predicting PTC CLNM

Multimodal ultrasound radiomics integrates the advantages of multiple ultrasound imaging modalities and realizes quantitative prediction of PTC CLNM through a standardized workflow, which is the core technical direction of current clinical transformation.

2.1. Construction of modalities

Multimodal ultrasound is based on core imaging modalities including conventional ultrasound (B-mode), Contrast-Enhanced Ultrasound (CEUS), and elastography (Shear Wave Elastography/Super Microvascular Imaging, SWE/SMI), which has greatly elevated the role of ultrasound in the early diagnosis, precise differentiation, and interventional guidance of PTC. The emergence of radiomics has further broken through the core bottleneck of conventional ultrasound that only relies on visual qualitative interpretation. By high-throughput extracting quantitative features such as morphology, texture, and gray level in images that are unrecognizable to the naked eye, it achieves objective quantitative characterization of tumor heterogeneity, effectively compensating for the inherent defects of traditional ultrasound such as strong subjectivity, poor reproducibility, and susceptibility to image quality interference. This builds a key quantitative analysis bridge for the preoperative non-invasive and precise prediction of PTC lymph node metastasis.

The workflow of ultrasound radiomics for predicting PTC lymph node metastasis generally includes four core steps: image segmentation, feature extraction, feature selection, and model construction and validation. Feature extraction requires precise delineation of the Region of Interest (ROI), with dual regions of intratumoral and peritumoral areas routinely selected to reflect the heterogeneous characteristics of the tumor itself and its invasive microenvironment. Among them, radiomic features combining intratumoral and 3 mm peritumoral regions have high predictive importance [11]. For multimodal ultrasound, quantitative features can be directionally extracted from grayscale ultrasound, elastography, and microflow images; a single study extracted up to 1561 high-throughput features, and 16 key features were retained after screening [12]. Commonly used feature selection methods include Least Absolute Shrinkage and Selection Operator (LASSO) and Boruta algorithm [12-14] to eliminate redundant features and improve model stability and generalizability.

2.2. Predictive efficacy and clinical value

Multimodal ultrasound fusion can enhance model performance, with predictive effects superior to single-modal ultrasound. Intratumoral and peritumoral models constructed by ultrasound combined with elastography capture both morphological and stiffness features of tumors, and their Area Under the Curve (AUC) is higher than that of single-modal models [14]. On this basis, the introduction of microflow imaging enables more accurate assessment of tumor microvascular status. The model based on multilayer perceptron achieves AUCs of 0.886 and 0.873 in the training and test sets, respectively, confirming the unique value of microflow imaging [12]. The multimodal ultrasound radiomics model combined with CEUS achieves AUCs of 0.957 and 0.932 in the training and validation sets, respectively, showing excellent predictive ability [15]. In the diagnosis of PTC cervical lymph node metastasis, the accuracy of the radiomics model combined with CEUS reaches 92.22%, which is significantly higher than 73.33% to 81.11% of single examination methods [6]. At present, the AUC of multimodal ultrasound radiomics models for predicting PTC CLNM ranges from 0.78 to 0.97, and the AUC of the large-sample CLNM prediction model in the training set reaches 0.935 [13]. The training and validation set AUCs of the joint model based on random forest are as high as 0.9726 and 0.9694, respectively [16]. In clinical practice, such models can significantly improve physicians' diagnostic efficiency, increasing the sensitivity of junior and senior radiologists by 19.7% and 18.3%, respectively [14]. Independent predictors of the model cover multi-dimensional indicators, including clinical features, laboratory parameters, microvessel density, elastic contrast index, etc. [11, 12, 14, 16, 17]. B-mode can clearly display basic indicators for judging malignant risk such as nodule morphology, boundary, internal echo, calcification foci, and aspect ratio [18]; CEUS can dynamically observe the microvascular perfusion inside the nodule in real time [19]; SWE/SMI can quantify tissue stiffness by measuring the degree of deformation after external force application [20].

Multimodal ultrasound radiomics provides a powerful tool for the preoperative non-invasive prediction of PTC lymph node metastasis by constructing a joint model integrating radiomics scores and clinical risk factors, improving diagnostic efficacy [21]. In the future, combining molecular markers such as gene detection may be the key direction to further improve model accuracy and screen highly invasive PTC.

2.3. Innovative expansion of multimodal fusion strategies

Current fusion strategies have expanded from the integration of internal ultrasound modalities to cross-imaging and cross-omics directions, becoming a new research hotspot. Feng et al. fused ultrasound and Computed Tomography (CT), screened 4 ultrasound features and 11 CT features via LASSO, and modeled using Gradient Boosting Machine (GBM), achieving excellent performances with AUCs of 0.973, 0.803, and 0.975 in the training set, internal validation set, and external validation set, respectively [22]. In more cutting-edge fusion explorations, a joint model combining ultrasound radiomics and proteomics features achieved an AUC of 0.84 in the validation set, significantly superior to the single radiomics model (0.75) or proteomics model (0.75) [23]. Multicenter studies confirmed that the 3 mm peritumoral region model (AUC = 0.909) is superior to the pure intratumoral model (AUC = 0.891), and the AUC is further increased to 0.928 after combining clinical features, clarifying the core predictive value of the peritumoral microenvironment [24].

3. Application of deep learning models in predicting PTC CLNM

With the advantage of autonomous learning of deep imaging features, deep learning has achieved end-to-end prediction of PTC CLNM, becoming a cutting-edge technical direction in this field.

3.1. Core model architecture design

Mainstream deep learning architectures are divided into two categories: classic Convolutional Neural Networks (CNN) and Transformer architectures, both showing excellent predictive capabilities. The ResNet-50 integrated model fuses clinical variables and ultrasound images, achieving AUCs of 0.86 and 0.77 in the internal and external test sets [25]. ResNet-34 combined with Bayesian strategy realizes automatic tumor segmentation and metastasis diagnosis, with AUCs of 0.83 in both internal and external test sets [26]. For more complex multimodal data, researchers proposed the DualSwinThyroid model, which is based on the Swin Transformer architecture and achieves an AUC of 0.924 and an accuracy of 96.3% in the test set by processing multimodal ultrasound imaging data [27]. In addition, classic networks such as DenseNet and GoogLeNet also perform well in ultrasound image-based metastasis prediction systems. Among them, DenseNet-121 shows an AUC of 0.766 in the Thy-DL-Radiomics model integrating radiomics and deep learning features [28, 29]. In more cutting-edge attempts, Pyramid Vision Transformer v2 (PVTv2) combined with Second Harmonic Generation (SHG) imaging technology achieves an AUC of 0.99 for lymph node metastasis classification [30].

3.2. Model efficacy evaluation

Efficacy evaluation is the core of verifying model practicability. Deep learning models have good predictive capabilities for lymph node metastasis in different regions. The Deep Learning-based Automatic Pipeline System (DLAPS) model achieves an accuracy of 80%, sensitivity of 76%, specificity of 83%, and AUC of 0.794 in the test set [31]. For more extensive lateral cervical lymph node metastasis, the cervical lymph node ultrasound network model achieves sensitivity and specificity of 86.14% and 78.67%, respectively, with an accuracy of 88.49% [32]. In terms of multimodal fusion, the multimodal model combining ultrasound and cytological images achieves AUCs of 0.891 and 0.875 in the internal and external validation sets, respectively, significantly superior to single-modal models [33].

3.3. Application limitations

Although deep learning has excellent efficacy, there are core bottlenecks in clinical transformation, which are caused by multiple complex factors, mainly including data privacy and security, insufficient model generalizability, and lack of interpretability [34]. At present, most studies are retrospective single-center or dual-center designs, lacking prospective large-scale multicenter external validation [34]. A prospective multicenter study showed that the Multimodal Deep Learning (MMD-DL) model based on ultrasound videos achieves an AUC of 0.81 in the external validation cohort, which is accurate and reliable but still needs further optimization [35].

4. Preliminary application of Explainable Artificial Intelligence (XAI) in radiomics prediction

The "black box" problem of artificial intelligence is a core obstacle restricting clinical transformation. Explainable Artificial Intelligence (XAI) provides a direction to solve this problem, and is mainly used for the visualization and quantitative explanation of PTC CLNM risk before and during surgery [36].

SHapley Additive exPlanations (SHAP) can explain the feature contribution of multilayer perceptron models, but it has problems such as strong model dependence and inconsistent feature independence assumptions, resulting in insufficient interpretation reliability [37]. Gradient-weighted Class Activation Mapping (Grad-CAM) is used for visual interpretation of deep CNN, which can locate the model's attention region, but still has problems such as inaccurate positioning, sensitivity to parameters, and mismatched interpretation granularity, failing to meet the needs of high-risk clinical decision-making [38].

5. Conclusion

In summary, multimodal ultrasound radiomics and deep learning technologies have completely broken through the bottlenecks of conventional ultrasound such as strong subjectivity, single dimension, and limited diagnostic efficacy, realizing three leaps in PTC CLNM prediction: from "empirical judgment" to "quantitative analysis", from "single modality" to "multimodal fusion", and from "manual extraction" to "autonomous learning". These technologies can provide precise decision support for clinical preoperative non-invasive assessment of metastasis risk, formulation of individualized surgical plans, and avoidance of unnecessary invasive procedures. The technical route has evolved from single two-dimensional ultrasound to multimodal ultrasound combining grayscale, CEUS, SWE, and SMI, and further expanded to the fusion of ultrasound with CT and proteomics; in analysis, it has advanced from manual radiomics to end-to-end deep learning modeling; in region, it has expanded from pure intratumoral analysis to comprehensive evaluation of the peritumoral microenvironment. However, most studies are retrospective single-center studies in China, and model performance generally decreases after external validation, lacking high-quality prospective multicenter evidence. The application of XAI technology is superficial, and the "black box" problem has not been fundamentally solved, leading to low recognition by clinicians. Multimodal and multi-omics fusion is still in the primary superposition stage, and a deeply integrated prediction network has not been formed. In the future, it is necessary to promote prospective, multicenter, and large-sample studies, unify image acquisition and analysis standards, improve model generalizability and stability, develop precise and stable interpretable methods, establish an integrated "prediction + explanation" model, and enhance clinical acceptance; integrate multi-dimensional data such as imaging, clinical, gene, and protein to achieve precise screening of highly invasive PTC.

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