Review

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CT-based radiomics in ovarian and endometrial cancers: toward predictive biomarkers for targeted therapy

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Abstract: Ovarian and endometrial malignancies provide significant therapeutic hurdles owing to their molecular variability and inconsistent treatment responses. Identifying non-invasive predictive biomarkers is essential for tailoring treatment and improving patient care. Radiomics has emerged as a promising methodology, facilitating the systematic extraction of quantitative features from computed tomography (CT) images to assess tumor heterogeneity, genetic changes, and microenvironmental properties that may affect prognosis and therapy response. Nonetheless, the evidence substantiating radiomics as a validated prognostic biomarker for targeted therapy is still limited. Most contemporary models should be regarded as prognostic or hypothesis-generating tools, rather than as instruments intended to guide therapeutic decision-making. Recent studies integrating CT-derived radiomic characteristics with clinical and genetic data have demonstrated improved predictive accuracy, especially in stratifying patients likely to benefit from targeted therapies, including poly-ADP-ribose polymerase (PARP) inhibitors and immunotherapy. In gynecologic oncology, the application of diverse methodologies indicates that radiomics holds promise for enhancing existing biomarkers and propelling precision oncology forward. The primary obstacles to widespread implementation encompass variations in feature extraction and analysis techniques, the utilization of different imaging modalities, and the absence of comprehensive validation across diverse patient populations. To enable clinical adoption, these issues must be addressed through extensive, multi-institutional studies and the establishment of standardized methodologies. This review examines the current status of CT-based radiomics in ovarian and endometrial cancers, evaluating its role as a prognostic biomarker and its potential to guide customized therapy approaches. Further investigation to integrate radiomics into treatment protocols, with the aim of improving prognoses for women diagnosed with gynecologic cancers is needed.

Keywords: radiomics; computed tomography (CT) imaging; ovarian cancer; endometrial cancer; targeted therapy; predictive biomarkers

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Introduction

Ovarian and endometrial cancer are recognized worldwide as the most aggressive gynecologic malignancies, attributed to late-stage detection and elevated recurrence rates [1]. In high-income countries, the 5-year survival rate for high-grade epithelial ovarian cancer is approximately 50 % across all stages, despite slight advancements in targeted therapies such as poly-ADP-ribose polymerase (PARP) inhibitors, anti-angiogenic agents, and antibody–drug conjugates [2]. Although ovarian and endometrial cancers differ substantially in incidence, mortality, and stage at diagnosis, both diseases share a common clinical challenge: marked

biological heterogeneity that complicates treatment selection [1]. Endometrial cancer is the most frequently diagnosed gynecologic cancer in developed countries, and its global incidence is increasing with an age-standardized incidence rate in 2022 of approximately 8.4 per 100,000 women [3], and an estimated 420,000 new cases and nearly 97,700 fatalities worldwide [4, 5]. Patients with features including p53-abnormal tumors, serous histology, or advanced-stage disease have a high mortality risk [6, 7].

Although the incidence and stage distribution of ovarian and endometrial cancers differ at the time of diagnosis, both malignancies are distinguished by significant biological heterogeneity, making therapeutic choice more challenging. In contrast to endometrial cancer, which is often diagnosed early but includes aggressive molecular types linked to worse outcomes, ovarian cancer is frequently diagnosed at a later stage and has a high rate of recurrence [8, 9].

A major challenge in both diseases is the absence of reliable, non-invasive biomarkers capable of predicting treatment efficacy before starting therapy [10].

Although targeted therapies and immunotherapies have enhanced outcomes in specific patient populations, therapeutic responses remain highly variable [11]. The Cancer Genome Atlas (TCGA) has improved the ability to predict immunotherapy efficacy by classifying endometrial cancer at the molecular level. This classification encompasses four main subtypes: POLE-ultramutated, mismatch repair-deficient (microsatellite instability-high [MSI-H]), copy number-high, and copy number-low [12].

In ovarian cancer, biomarkers such as BRCA1/2 mutations and homologous recombination deficiency (HRD) can guide the use of PARP inhibitors. Despite advancements in molecular classification, clinically relevant non-invasive biomarkers, capable of predicting treatment efficacy before initiation remain scarce. This highlights the need to investigate imaging methods like radiomics, which can enhance tissue-based profiling and detect spatial variations within a tumor [13].

Moreover, patient outcomes within each molecular class still exhibit considerable heterogeneity [14]. Alongside molecular approaches, like the use of circulating miRNA panels for early diagnosis [15], tissue biopsies are still considered the standard method. However, they have limitations due to their invasiveness, potential sampling bias, and their inability to fully capture the spatial and temporal heterogeneity of tumors, especially in cases of recurrence or metastasis [16]. Radiomics could offer a non-invasive tool to extract clinically relevant information from routine clinical imaging [17].

It is important to distinguish between prognostic and predictive biomarkers [18]. Prognostic biomarkers are associated with overall outcomes irrespective of treatment, whereas predictive biomarkers identify differential benefits from a specific therapy [19]. Most radiomics studies in ovarian and endometrial cancers focus on associations with survival or recurrence and are therefore predominantly prognostic, while evidence supporting their role as true predictive biomarkers for guiding targeted therapy remains limited [20].

This review critically evaluates current research on using CT-based radiomics to predict the effectiveness of targeted therapies in ovarian and endometrial cancers. Key challenges and new directions for future research are also highlighted.

Radiomics: current status in oncology

Radiomics involves the extraction of large numbers of quantitative features from medical images (such as CT, magnetic resonance imaging [MRI], and positron emission tomography [PET]) that describe tumor characteristics, including shape, intensity, texture, and spatial relationships beyond what the human eye can perceive [21]. The concept emerged on the premise that imaging-derived features could serve as surrogates for the tumor characteristics, heterogeneity, and even molecular alterations [22]. Since then, radiomics has been applied across many cancer types for diagnosis, risk stratification, treatment response prediction, and prognosis [23]. In gynecologic malignancies (cervical, ovarian, endometrial), early studies suggest that radiomics models correlate with histologic grade, molecular subtype, risk of recurrence, and survival rates [24]. However, many of these studies are retrospective, single-institution, and based on modest sample sizes with limited external validation [25].

CT radiomics

CT radiomics seeks to quantify imaging features that reflect the biological heterogeneity within tumors [26]. Table 1 delineates the key types of radiomics parameters derived from CT images, linking these quantitative features with the fundamental tumor biology and relevant clinical or genetic markers. Variability in voxel intensity, texture, and shape, as well as factors such as necrosis, fibrosis, angiogenesis, and variations in cellular density, affect CT attenuation and contributes in quantifiable radiomics signatures [27]. In high-grade serous ovarian carcinoma (HGSOC), differences in tumor areas, evidenced by patterns of contrast enhancement or regions with varying enhancement, may indicate regions of low oxygenation or poor blood flow [28].

Table 1: Key radiomics features and their biological/clinical associations in gynecologic cancers.

Radiomics feature type	Examples	Biological basis	Associated clinical/molecular markers
First-order statistics	Mean, variance, skewness	Tumor intensity and heterogeneity	BRCA mutation status (moderate link)
Texture features (GLCM, RLM)	Entropy, correlation, homogeneity	Intratumoral texture variation	Immune markers (CXCL9, CCR5), recurrence risk
Shape features	Sphericity, volume, surface area	Tumor morphology	Tumor grade, histological subtype
Wavelet/transformed features	High-pass/low-pass filtered texture	Multiscale texture analysis	Deep learning-derived classifiers
Deep learning based features	CNN-derived representations	High-level feature extraction form initial data	BRCA, survival, platinum sensitivity (combined models)

GLCM, gray-level co-occurrence matrix; RLM, (gray-level) run-length matrix; BRCA, breast cancer gene (BRCA1/BRCA2), CNN: Convolutional Neural Network.

Figure 1 provides a practical illustration of a CT-based radiomics workflow applied to ovarian cancer, encompassing tumor segmentation and representative feature extraction steps critical for model development.

Radiomics features derived from texture-based matrices (e.g., gray level co-occurrence matrix, run-length features), and first-order statistics heterogeneity have been shown to unveil biologic complexity not captured by qualitative imaging alone (Figure 2) [29].

Correlation with histopathology and molecular subtypes

Some studies tried to correlate CT radiomics features with molecular and histopathologic markers in ovarian cancer [30, 31]. A recent multicenter study found that the predictive value of radiomics and deep-learning features for BRCA status or early recurrence in HGSOC was limited when considered independently. Nevertheless, the model's performance was moderately improved when integrating these features with clinical parameters [32]. The expression of immunomodulatory chemokines, such as CXCL9 and CCR5, as well as survival outcomes, were correlated with radiomics features, suggesting that they have the potential to reflect the underlying tumor immunophenotypes [33]. Furthermore, a multicenter investigation demonstrated that radiomic features extracted from contrast-enhanced CT scans could differentiate between different histological subtypes of epithelial ovarian cancer, specifically high-grade serous, endometrioid, clear cell, and mucinous carcinomas; this distinction holds clinical significance, influencing both prognostic assessments and therapeutic approaches [34].

Correlation with molecular profiles

Radiogenomics involves correlating imaging features with genomic or transcriptomic data. The goal is to noninvasively determine the molecular characteristics of tumors [35]. In ovarian cancer, several studies have used TCGA/TCIA datasets to investigate gene expression stratification based on radiomics risk models [36]. Although CT-based features alone could provide low independent predictive value, their integration with clinical or molecular data improves the accuracy of these models, particularly with BRCA mutational status and survival forecasting [34]. These results endorse a hybrid modeling methodology that integrates imaging, clinical, and molecular data [37, 38]. The existing body of research in gynecologic radiomics is primarily characterized by retrospective studies conducted at single institutions, often involving relatively small sample populations and lacking extensive external validation [39]. Although associations with histopathology, molecular classifications, and patient outcomes are documented [40], the majority of these models are exploratory in nature. As a result, there is a significant need for robust prospective validation and compelling evidence of their clinical applicability.

Applications of CT-based radiomics in ovarian cancer

Neoadjuvant chemotherapy followed by interval debulking has become an accepted strategy in advanced-stage ovarian cancer due to favorable survival and morbidity profiles [39]. In this context, CT-based radiomics may offer a valuable non-invasive tool for pre-treatment stratification and prediction of chemotherapy response [40]. Radiomics obtained from CT scans proved effective in differentiating benign tumors from early-stage cancers [41]. A retrospective investigation of over 200 cases revealed that a radiomics nomogram derived from contrast-enhanced CT had effective diagnostic capability in distinguishing benign from early-stage (FIGO I/II) malignant ovarian tumors [42], underscoring also the importance to report quantitative performance measures when evaluating

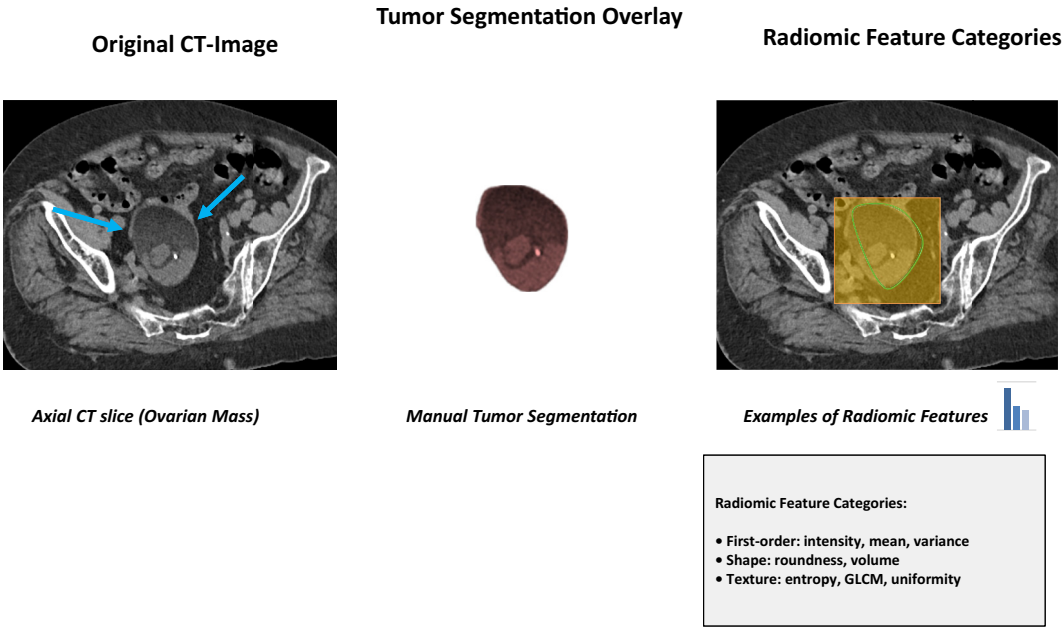

Figure 1: Example of computed tomography (CT)-based radiomics workflow in ovarian cancer. Left image: axial CT image of a left ovarian teratoma (O-RADS 4, intermediate risk) (arrows). Middle: tumor segmentation with manual delineation of the lesion. Right: illustration of representative radiomics features extractable from the segmented tumor, including first-order intensity features, shape descriptors, and texture metrics (e.g., entropy, gray level co-occurrence matrix [GLCM]-based parameters). Accurate segmentation is essential for reproducible radiomics analysis and predictive modeling.

radiomics models. Furthermore, CT radiomics is promising in noninvasive prediction of the histological subtypes of epithelial ovarian cancer across large, multicenter studies, thereby supporting its potential use in preoperative risk assessment [43].

Although most radiomics investigations in ovarian cancer focused on sensitivity to platinum-based chemotherapy, research evaluating its predictive ability regarding responses to targeted therapies, such as PARP inhibitors and antiangiogenic agents, is lacking [44]. Radiomics and deep learning models were used to predict BRCA status and early recurrence in HGSOC; despite their somewhat limited individual performance, the accuracy of these models is improved when combined with clinical data. However, there is still limited evidence supporting their ability to predict therapeutic responses to targeted treatments [32].

Despite numerous studies investigated the correlations between radiomics features and BRCA status or homologous recombination deficiency [34, 45], direct evidence substantiating the prediction of responses to PARP inhibitors, anti-angiogenic agents, or immunotherapy is currently limited[44].

Therefore, current CT-based radiomics models cannot yet be considered treatment-directing tools for targeted therapies.

Radiomics offers significant potential in prognostic modeling and risk classification [45]. A study including patients with high-grade serous ovarian cancer revealed that a predictive model integrating CT-based radiomics characteristics with clinicopathological data exhibited moderate concordance with progression-free survival results in both development and validation cohorts[46]. Other studies demonstrated that radiomics characteristics correlate with immune-related gene expression profiles, including CXCL9 and CCR5, and were linked to differences in patient survival, hence underscoring the prospective function of radiomics in holistic outcome prediction models models [47, 48].

In epithelial ovarian carcinoma, a radiomics model, constructed from contrast-enhanced CT scans, showcased considerable precision in forecasting response to platinum-based chemotherapy, demonstrating strong efficacy in both internal and external validation cohorts [33, 49]. Moreover, a machine learning study centered on advanced ovarian cancer indicated that particular radiomic characteristics could consistently predict three-year recurrence-free survival across diverse datasets, thus highlighting their value in individualized prognostic assessments [44, 50].

Applications of CT-based radiomics in endometrial cancer

Compared to ovarian cancer, the application of radiomics in endometrial cancer has been mostly focused on MRI, with a

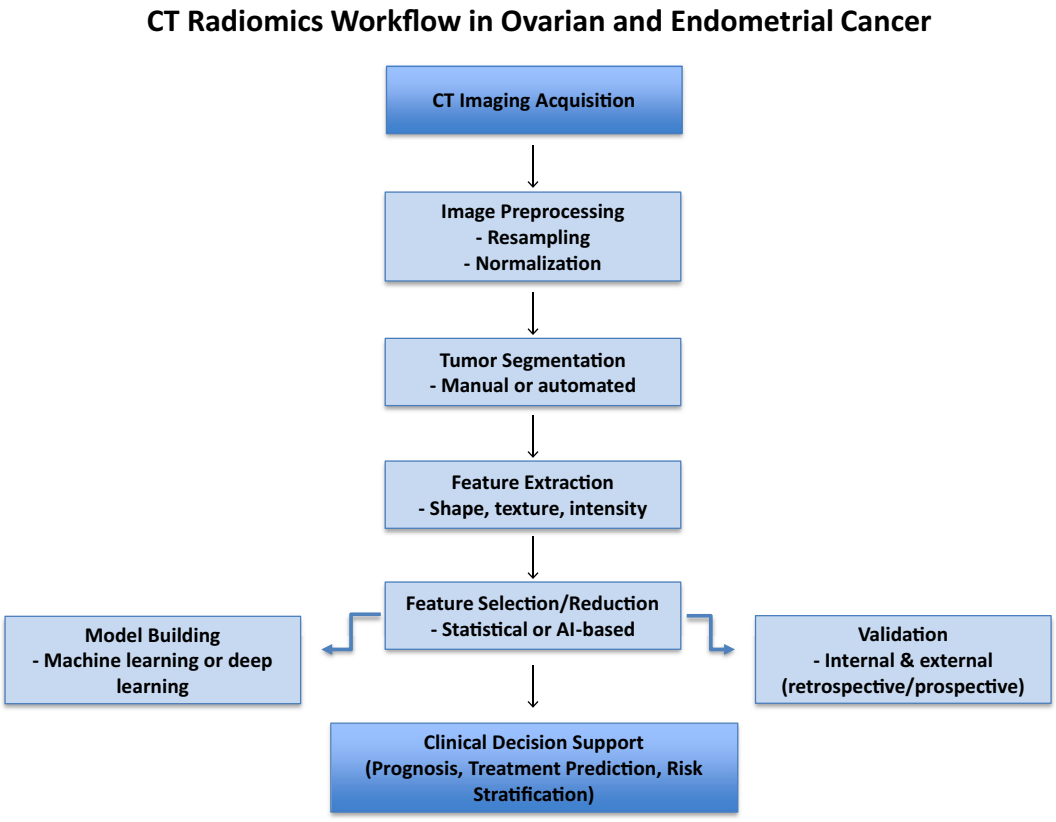

Figure 2: Conceptual workflow for computed tomography (CT)-based radiomics in gynecologic oncology. Each step, from acquisition to clinical integration, requires standardization to ensure reproducibility, particularly in multi-institutional settings.

limited number of studies investigating CT-based methodologies (Table 2) [51].

While MRI is the referral imaging technique for local staging in endometrial cancer [52], CT continues to be extensively employed for assessing nodal and distant metastatic disease, especially in advanced-stage cases. CT-based radiomics is still clinically relevant for systemic risk evaluation and treatment planning, even though MRI-based radiomics currently presents more robust evidence for local prognostic stratification [53, 54]. Most

Table 2: Overview of computed tomography (CT)-based radiomics research in ovarian and endometrial cancers.

Category	Ovarian cancer	Endometrial cancer
Primary imaging modality	CT (widespread use, especially in advanced disease)	MRI preferred; CT used less frequently
Common applications	Staging, histological subtyping, platinum sensitivity, BRCA prediction, prognosis	Recurrence prediction, risk stratification
Integration with molecular data	Moderate (BRCA, HRD, immune markers)	Limited (few studies integrating with TCGA or MMR status)
Mature models	Several externally validated models (e.g., recurrence, platinum sensitivity)	Mostly pilot studies; few robust models
Predictive value for targeted therapies	Limited but evolving (mostly PARP inhibitors and anti-angiogenics)	Currently lacking (especially for hormonal and immunotherapies)
Limitations	Heterogeneous protocols, limited deep learning interpretability	Small sample sizes, lack of CT-based molecular classification tools
Research priority areas	Deep learning integration, prospective validation, multi-omics fusion	Developing CT-based molecular subtype classifiers, expanding datasets

BRCA, breast cancer; HRD, homologous recombination deficiency; MRI, magnetic resonance imaging. TCGA, the cancer genome Atlas; MMR, mismatch repair.

current research focuses on MRI-derived features and their ability to predict risk based on factors such as tumor grade, lymphovascular invasion, and depth of myometrial invasion [55]. There is currently no validated CT-based radiomics model that reliably predicts response to hormonal agents or immune checkpoint inhibitors, even in the context of mismatch repair deficiency or PD-L1 status [56].

TCGA-based molecular classification is now considered a critical component of endometrial cancer management [56]. While some recent studies have combined PET/CT radiomics with deep learning segmentation to predict molecular subtypes such as mismatch repair (MMR) deficiency and TP53 mutations, standalone CT radiomics has yet to demonstrate consistent predictive value for these molecular profiles [57]. Further work is needed to ascertain whether non-hybrid CT-based approaches can contribute meaningfully to molecular characterization [58].

In contrast, MRI-based provided large amounts of evidence with significant prognostic accuracy achieved in multicenter studies for the identification of nodal metastasis and differentiation between Type I and Type II disease [59]. CT radiomics primarily reflects tissue density, necrosis, and blood vessel characteristics through X-ray absorption and contrast enhancement, while MRI radiomics, using various imaging sequences, provides a more detailed analysis of cell density, substance movement, and vascularization [60, 61]. Emerging data suggests that the biology of endometrial tumors is significantly shaped by epigenetic mechanisms, such as chromatin remodeling and DNA methylation; these processes contribute to transcriptional dysregulation and variability in therapeutic outcomes [62]. This molecular intricacy offers a biological basis for radiomics features that characterize variations in texture and intensity, potentially mirroring underlying chromatin and microenvironmental changes [62]. Transvaginal ultrasound and other standard imaging methods are still the primary tools for assessing endometrial cancer before surgery, especially for evaluating how far the cancer has spread into the muscle of the uterus and the cervix [63], their accuracy is heavily dependent on the operator's expertise. This has led to growing interest in objective imaging methods like CT radiomics. However, CT-based radiomics has advanced more in ovarian cancer than in endometrial cancer, due to the greater use of CT in advanced ovarian cases and the predominance of MRI in endometrial cancer research. Therefore, CT radiomics findings in endometrial cancer should be interpreted with caution.

Clinical translation: challenges and future directions

Radiomics showed great potential in gynecologic oncology by identifying high-risk characteristics before surgery, improving immunotherapy, guiding adjuvant treatments, and personalizing surgical approaches [64]. Numerous models that integrate radiomics with clinical data demonstrated high accuracy in risk stratification [65]. There are no clinical guidelines for CT-based radiomics biomarkers in ovarian or endometrial cancers, due to the retrospective nature and lack of external validation in most studies, with challenges including regulatory approval, model interpretability, imaging standardization, and integration into clinical workflows [66–68]. Nomogram-based approaches, such as the ultrasound and laboratory–integrated model by Pino et al. [68], demonstrated that non-invasive, data-driven prediction of nodal involvement is clinically feasible in endometrial cancer. Radiomics extends this concept by incorporating quantitative imaging biomarkers into similar predictive frameworks, potentially improving individualized risk stratification.

Notwithstanding its potential, radiomics research in ovarian and endometrial malignancies encounters significant limitations, primarily due to methodological inconsistencies [69]. Reproducibility is a perpetual issue due to the heterogeneity in segmentation methods and feature extraction software, as well as the variability in CT imaging processes, such as discrepancies in slice thickness, contrast timing, and reconstruction approaches [70]. The risk of overfitting is increased, and the generalizability of the results is restricted by the fact that a significant number of existing studies are retrospective and based on small, single-center cohorts [70, 71]. Moreover, relatively few models undergo external validation or prospective testing, both of which are essential steps for clinical translation [23].

Prospective, multi-institutional studies that adhere to established reporting guidelines, such as the METhodological RadiomICs Score (METRICS), Radiomics Quality Score (RQS), and Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines, are urgently required to advance the field [72–75].

However, many studies, especially in endometrial and ovarian carcinomas, still lack prospective validation, calibration, and impact analysis, hindering their clinical implementation [76, 77]. Methodological variability across studies is being addressed through the implementation of standardization initiatives [78]. The Imaging Biomarker

Standardization Initiative (IBSI) has proposed consensus definitions and validation tools for feature extraction, while the Quantitative Imaging Network (QIN), which is supported by the National Cancer Institute, is in the process of developing reproducible and clinically applicable quantitative imaging methodologies [79, 80]. Recently, the European Society of Medical Imaging Informatics (EuSoMII) Radiomics Auditing Group has introduced comprehensive resources such as the METRICS and its elaborated version METRICS-E3, as well as the CheckList for EvaluAtion of Radiomics research (CLEAR) and its explanation CLEAR-E3, to improve transparency, reproducibility, and methodological rigor in radiomics research [81–84]. Future advancements will likely depend on combining different types of data. Integrating radiomics with genomic, transcriptomic, methylation, and circulating tumor DNA data could lead to the creation of combined and, hopefully more effective biomarkers.

Conclusions

Radiomics offers a non-invasive, compelling avenue for the advancement of personalized care in gynecologic oncology. While its application in ovarian and endometrial cancers is still in the early phases, studies are showing promising results for the patient management. Future research must prioritize consistent methodological standards, broader multicentric collaboration, and robust technical validation in order to improve the consistency of the current evidence. Radiomics has the potential to become a fundamental component of personalized cancer treatment in the future when combined with molecular profiling, artificial intelligence, and clinical background.

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