Received: 06.02.2026
Accepted: 27.02.2026
UDC: 618.14-006.6
DOI: 10.24412/1609-8692-2026-1-11-25

Article type: Structured Narrative Review

RADIOMICS OF THE TUMOR PROFILE IN DETERMINING THE HISTOLOGICAL TYPE OF ENDOMETRIAL CANCER

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Introduction. Endometrial cancer is a heterogeneous disease in which histological type, grade, molecular subtype, and disease extent influence prognosis and treatment. Radiomics may provide non-invasive quantitative information on tumor phenotype before surgery.
Objective. To synthesize evidence on the ability of MRI- and PET/CT-based radiomics to characterize the tumor profile in endometrial cancer, with emphasis on histological type, grade, molecular features, and closely related risk indicators.
Materials and Methods. A structured narrative review was conducted using PubMed, Web of Science, and Scopus. The principal search covered publications from January 2018 to February 2025 and was supplemented by later relevant publications identified during manuscript preparation. Thirty-seven publications informed the synthesis: original human endometrial cancer studies were considered the core evidence, while reviews, a conference abstract, a preclinical study, and selected ovarian or cervical cancer studies were used only for contextual or methodological comparison. Owing to heterogeneity, no meta-analysis was performed.
Results. Across the reviewed literature, radiomics models showed reported discriminatory performance for histological type, tumor grade, deep myometrial invasion, lymphovascular space invasion, molecular subtypes, and prognostic risk. In selected studies, reported areas under the receiver operating characteristic curve were commonly approximately 0.80-0.92. Combining radiomic features with clinical, molecular, or deep-learning data often improved model performance. However, most studies were retrospective, single-center, and based mainly on internal validation.
Discussion. The evidence indicates that radiomic features can capture clinically relevant tumor heterogeneity, but performance estimates are difficult to compare because of differences in imaging protocols, segmentation, feature extraction, endpoint definitions, and model validation. Limited external validation, small samples, and risk of overfitting restrict clinical transferability.
Conclusion. Radiomics is a promising non-invasive complement to biopsy, pathology, and conventional imaging for preoperative tumor profiling in endometrial cancer. Prospective multicenter validation, harmonized imaging and analytical pipelines, transparent reporting, and clinical-impact studies are required before routine implementation.
Keywords: endometrial cancer; radiomics; magnetic resonance imaging; tumor profiling; molecular markers; risk stratification.

РАДИОМИКА ОПУХОЛЕВОГО ПРОФИЛЯ В ОПРЕДЕЛЕНИИ ГИСТОЛОГИЧЕСКОГО ТИПА РАКА ЭНДОМЕТРИЯ

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Введение. Рак эндометрия представляет собой гетерогенное заболевание, при котором гистологический тип, степень злокачественности, молекулярный подтип и распространенность опухоли определяют прогноз и лечебную тактику. Радиомика позволяет неинвазивно количественно характеризовать опухолевый фенотип до операции.
Цель. Обобщить данные о возможностях радиомики на основе МРТ и ПЭТ/КТ в профилировании опухоли при раке эндометрия с акцентом на гистологический тип, степень злокачественности, молекулярные характеристики и связанные с риском признаки.
Материалы и методы. Проведен структурированный нарративный обзор публикаций, найденных в PubMed, Web of Science и Scopus. Основной поиск охватывал период с января 2018 года по февраль 2025 года и был дополнен более поздними релевантными публикациями, выявленными при подготовке рукописи. В синтез включены 37 публикаций: оригинальные исследования радиомики у пациентов с раком эндометрия составили основную доказательную базу, а обзоры, конференционный материал, доклиническое исследование и отдельные

работы по раку яичников и шейки матки использовались только для контекстного и методологического сопоставления. Метаанализ не проводился.
Результаты. В рассмотренных исследованиях радиомические модели демонстрировали способность различать гистологические типы, степень злокачественности, глубокую инвазию миометрия, лимфоваскулярную инвазию, молекулярные подтипы и прогностические группы. В отдельных работах заявленные значения площади под ROC-кривой преимущественно составляли приблизительно 0,80-0,92. Объединение радиомических признаков с клиническими, молекулярными данными и глубоким обучением часто повышало показатели моделей. Большинство исследований при этом имели ретроспективный одноцентровый дизайн и внутреннюю валидацию.
Обсуждение. Радиомические признаки отражают клинически значимую неоднородность опухоли, однако прямое сопоставление результатов затруднено различиями в протоколах визуализации, сегментации, извлечении признаков, определении исходов и валидации. Ограниченная внешняя проверка, небольшие выборки и риск переобучения снижают переносимость моделей.
Заключение. Радиомика является перспективным неинвазивным дополнением к биопсии, морфологическому исследованию и стандартной визуализации при предоперационном профилировании рака эндометрия. Для внедрения в практику необходимы проспективные многоцентровые исследования, гармонизация протоколов, прозрачное описание моделей и оценка их клинического влияния.
Ключевые слова: рак эндометрия; радиомика; магнитно-резонансная томография; профилирование опухоли; молекулярные маркеры; стратификация риска.

ЭНДОМЕТРИЙ ОБЫРЫНЫҢ ГИСТОЛОГИЯЛЫҚ ТИПІН АНЫҚТАУДАҒЫ ІСІК ПРОФИЛІНІҢ РАДИОМИКАСЫ

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Кіріспе. Эндометрий обыры - гистологиялық типі, қатерлілік дәрежесі, молекулалық кіші типі және таралуы болжам мен емдеу тактикасына әсер ететін гетерогенді ауру. Радиомика операцияға дейін ісік фенотипін инвазивті емес сандық сипаттауға мүмкіндік береді.
Мақсаты. Эндометрий обырындағы ісік профилін бағалауда МРТ және ПЭТ/КТ негізіндегі радиомиканың мүмкіндіктері туралы деректерді, әсіресе гистологиялық типті, ісік дәрежесін, молекулалық ерекшеліктерді және тәуекелмен байланысты көрсеткіштерді жинақтау.
Материалдар мен әдістер. PubMed, Web of Science және Scopus дерекқорларындағы жарияланымдарға құрылымдалған нарративтік шолу жүргізілді. Негізгі іздеу 2018 жылғы қаңтардан 2025 жылғы ақпанға дейінгі кезеңді қамтыды және қолжазбаны дайындау кезінде анықталған кейінгі релевантты жарияланымдармен толықтырылды. Синтезге 37 жарияланым енгізілді: эндометрий обыры бар пациенттердегі түпнұсқа радиомика зерттеулері негізгі дәлелдер ретінде, ал шолулар, конференциялық материал, клиникаға дейінгі зерттеу және аналық безі мен жатыр мойны обыры бойынша жекелеген жұмыстар контекстік және әдістемелік салыстыру үшін пайдаланылды. Мета-талдау жүргізілген жоқ.
Нәтижелер. Қарастырылған зерттеулерде радиомикалық модельдер гистологиялық типті, ісік дәрежесін, миометрийге терең инвазияны, лимфоваскулярлық инвазияны, молекулалық кіші типтерді және болжамдық тәуекел топтарын ажырату мүмкіндігін көрсетті. Жекелеген зерттеулерде ROC-қисығы астындағы аудан шамамен 0,80-0,92 аралығында хабарланды. Радиомикалық белгілерді клиникалық және молекулалық деректермен немесе терең оқытумен біріктіру модель көрсеткіштерін жиі жақсартты. Дегенмен жұмыстардың көпшілігі ретроспективті, бір орталықты және негізінен ішкі валидацияға сүйенді.
Талқылау. Радиомикалық белгілер ісіктің клиникалық маңызды гетерогенділігін көрсетуі мүмкін, бірақ визуализация хаттамаларының, сегментацияның, белгілерді алу тәсілдерінің, нәтижелер анықтамаларының және валидацияның әркелкілігі нәтижелерді тікелей салыстыруды қиындатады. Сыртқы валидацияның шектеулілігі, шағын іріктемелер және модельдің қайта үйрену қаупі клиникалық қолдануды тежейді.
Қорытынды. Радиомика эндометрий обырын операция алдындағы профильдеу кезінде биопсияны, морфологиялық зерттеуді және стандартты визуализацияны толықтыратын перспективалы инвазивті емес тәсіл болып табылады. Күнделікті практикаға енгізу үшін проспективті көпорталықты валидация, хаттамаларды үйлестіру, модельдерді ашық сипаттау және клиникалық әсерді бағалау қажет.
Түйінді сөздер: эндометрий обыры; радиомика; магниттік-резонанстық томография; ісік профилі; молекулалық маркерлер; тәуекелді стратификациялау.

Introduction

Endometrial cancer is a heterogeneous malignancy with histological and molecular subtypes associated with different prognoses and treatment strategies. Traditional type I and type II categories remain useful descriptively, whereas The Cancer Genome Atlas-derived groups and their clinical surrogates - POLE-mutated, mismatch-repair-deficient, p53-abnormal, and no specific molecular profile - increasingly inform risk stratification. Preoperative biopsy and conventional imaging have recognized limitations: sampling may underestimate grade or miss aggressive components, and assessment of myometrial invasion, cervical stromal involvement, and lymph-node status is partly observer-dependent. Radiomics has therefore been investigated as a quantitative approach to predicting deep myometrial invasion, clinical risk category, histological type, and lymphovascular space invasion [1].

Radiomics extracts quantitative descriptors of intratumoral and peritumoral heterogeneity from multiparametric MRI or PET/CT and integrates them with clinical variables through machine-learning models. The review by Manganaro et al. summarizes the rapid growth of radiomics in gynecological imaging and endometrial cancer [2].

This review focuses on how tumor profile radiomics contributes to determining histological type and biological aggressiveness in EC, including: (i) histologic type and grade, (ii) molecular markers (MSI, p53abn, TMB), (iii) radiogenomic signatures, and (iv) closely related tasks such as deep myometrial invasion (DMI), lymphovascular space invasion (LVSI), and high-risk class assignment, which are tightly linked to histologic type.

The scientific contribution of this review is the integrated consideration of histological type, grade, molecular surrogates, prognostic risk, treatment-planning applications, and methodological reproducibility within one tumor-profiling framework. The review does not provide a new pooled estimate; it identifies recurring performance patterns, validation gaps, and requirements for clinical translation.

The objective of this structured narrative review was to evaluate how radiomics contributes to preoperative tumor profiling in endometrial cancer, with emphasis on histological type and biological aggressiveness, and to identify methodological barriers that currently limit routine clinical use.

Materials and Methods

Review design and reporting approach

This study was designed as a structured narrative review. A narrative approach was selected because the evidence included heterogeneous imaging modalities, endpoints, segmentation strategies, feature-extraction pipelines, machine-learning methods, and validation approaches. Preparation of the manuscript was guided by the principles of the Scale for the Assessment of Narrative Review Articles (SANRA). PRISMA terminology was used only where it improved transparency of the search description; the manuscript is not presented as a systematic review or meta-analysis.

No statistical pooling was planned or performed. The review protocol was not prospectively registered.

Information sources and search strategy

A literature search was conducted in PubMed, Web of Science, and Scopus. The principal search covered publications from January 2018 to February 2025 and was supplemented by later relevant publications identified during manuscript preparation. Search terms combined “endometrial cancer” OR “endometrial carcinoma” with “radiomics” OR “radiomic features”, imaging terms (“MRI”, “magnetic resonance imaging”, “PET”, “PET/CT”), computational terms (“machine learning”, “deep learning”), and outcome terms (“histology”, “histological subtype”, “serous”, “endometrioid”, “grade”, “molecular subtype”, “prognosis”, “myometrial invasion”, or “lymphovascular space invasion”). Syntax was adapted to each database. Reference lists of relevant articles and reviews were screened manually.

Eligibility criteria

Core evidence comprised original peer-reviewed human studies of histologically confirmed endometrial cancer that used preoperative MRI and/or PET/CT, extracted radiomic or deep-imaging features, applied computational modeling, and reported

quantitative performance for histological type, grade, molecular subtype, disease extent, risk class, nodal status, prognosis, or treatment-planning endpoints. Retrospective and prospective designs were eligible.

Systematic or narrative reviews, one conference abstract, a preclinical organoid-derived mouse study, and selected radiomics studies in ovarian or cervical malignancies were retained only as contextual or methodological evidence. They were not treated as direct clinical evidence for endometrial-cancer model performance. Case reports, editorials, letters, non-English publications, studies without sufficient methodological information or quantitative performance metrics, and studies unrelated to tumor profiling were excluded.

Study selection and data extraction

One author performed the initial search, screening, and extraction; the second author provided methodological oversight, reviewed eligibility decisions, and critically evaluated interpretation. For each retained publication, the following information was extracted where available: study design, sample size, imaging modality and protocol, segmentation approach, radiomic or deep-learning method, predicted endpoint, validation strategy, performance metrics, and principal methodological limitation.

Thirty-seven publications formed the final evidence base: 30 original human endometrial-cancer studies, two review or meta-analytic publications, one conference abstract, one preclinical study, and three selected studies in related gynecological malignancies. Because the source records did not contain a reproducible count of duplicates and exclusions at each screening stage, a formal PRISMA flow diagram was not generated.

Review outcomes

The primary review outcomes were reported discrimination of radiomics models for histological type, tumor grade, and molecular subtype. Secondary outcomes included deep myometrial invasion, lymphovascular space invasion, lymph-node metastasis, clinical risk class, recurrence or survival, fertility-sparing or ovarian-preservation eligibility, and methodological reproducibility. Reported AUC, accuracy, sensitivity, specificity, calibration, and validation approach were extracted when available.

Critical appraisal and synthesis

Because the evidence comprised substantially different designs, no single risk-of-bias instrument was applied across all publications. Evidence was appraised qualitatively with attention to retrospective versus prospective design, single-center versus multicenter recruitment, sample size, segmentation reproducibility, feature-to-sample ratio, internal and external validation, risk of overfitting, reporting transparency, and harmonization of imaging protocols. Greater interpretive weight was assigned to multicenter studies, independent validation cohorts, prospective components, and analyses using standardized radiomic procedures. Findings were synthesized narratively by clinical endpoint and methodological theme.

Safety assessment

Safety assessment was not applicable because the review involved no new intervention, imaging procedure, or patient-level data collection. Safety findings were not a prespecified synthesis endpoint and were considered only when reported in the source publications.

Ethics

Ethics committee approval and informed consent were not required for this review because only previously published, publicly available aggregate data were analyzed.

Results

Study profile

The 37 retained publications covered MRI and PET/CT radiomics, radiogenomics, deep learning, and combined clinical-imaging models. Most original clinical studies were retrospective and single-center; multicenter cohorts and independent external validation were less common. Endpoints included histological type, grade, deep myometrial invasion, lymphovascular space invasion, molecular subtype, lymph-node metastasis, risk class, recurrence, and survival. Owing to marked methodological heterogeneity, results are presented as thematic patterns rather than pooled estimates.

MRI radiomics for overall prognostic modeling and risk stratification

MRI radiomics studies in endometrial cancer have established the feasibility of whole-tumor profiling for prognostic modeling and risk stratification. Fasmer et al. [3] used whole-volume tumor MRI radiomics in 201 patients to derive signatures associated with aggressive disease and poor outcome; these signatures achieved medium-to-high discriminative performance. However, the study was retrospective and lacked external validation, which may limit generalizability. Jacob et al. developed an MRI-based Radiomic Prognostic Index (RPI) in 95 women, showing that high RPI scores predicted poor disease-specific survival and were associated with distinct gene expression profiles, linking radiomic phenotypes to underlying tumor biology [4]. Nevertheless, the relatively small sample size increases the risk of overfitting and limits robustness.

Building on this, Hoivik et al. presented a radiogenomics application combining radiomics with genomic data to refine prognostic profiling, further reinforcing the concept that imaging phenotypes capture molecularly driven heterogeneity in EC [5], although validation in independent cohorts remains necessary. Renton et al. [6] and Liu et al. [36] demonstrated that multiparametric MRI radiomics can predict progression-free and disease-free survival, respectively, using radiomic signatures; however, variability in feature selection methods and modeling strategies across studies complicates direct comparison. Mainenti et al. similarly used MRI radiomics for preoperative risk stratification, confirming that radiomics-based machine learning can stratify high- vs low-risk patients [7], although the single-center design may introduce selection bias.

Complementary work by Lefebvre et al. [8] developed 3D radiomics signatures for preoperative risk stratification, demonstrating clinically relevant stratification into high- and low-risk groups. Hodneland et al. [10] systematically investigated MRI radiomic feature normalization, showing that normalization strategy significantly affects prognostic modeling performance, thereby highlighting a critical methodological challenge for reproducibility and clinical translation.

Although these studies focus primarily on prognosis and risk class rather than explicit histologic type, their results suggest that radiomic tumor profiles encode features of tumor aggressiveness closely linked to histologic subtype and grade [3–10,36]. Collectively, these findings indicate that MRI radiomics has strong potential for preoperative risk stratification in endometrial cancer. However, most studies are retrospective, rely on relatively small or single-center cohorts, and frequently lack external validation. In addition, heterogeneity in imaging protocols, feature extraction pipelines, and modeling approaches introduces variability and limits reproducibility. These factors increase the risk of overfitting and selection bias, and therefore the reported performance metrics should be interpreted with caution.

Radiomics for histological type, grade, and deep myometrial invasion

Radiomics models have also been extensively applied to predict histological type, tumor grade, and deep myometrial invasion. Li et al. [1] developed integrated clinical–radiomic models based on T2-weighted MRI in 219 patients, demonstrating improved discrimination for DMI, risk category, histologic type, and LVSI compared with clinical models alone. Despite strong performance, the retrospective design and absence of external validation may limit generalizability. Wang et al. [11] and Bi et al. [12] constructed multiparametric MRI radiomics nomograms for assessing DMI and distinguishing early-stage EC from benign lesions, reporting high diagnostic accuracy [11, 12]; however, inter-institutional variability in imaging acquisition and reconstruction may affect model transferability.

Yang J. et al. [13] used intratumoral and peritumoral radiomics to assess DMI, showing improved performance when peritumoral features were included, although the added complexity may increase susceptibility to overfitting. Shen et al. [14] extended this approach to differentiate uterine serous carcinoma from endometrioid carcinoma using

multiparametric MRI radiomics combined with deep learning in a multicenter cohort, achieving high accuracy; nevertheless, deep learning models may suffer from limited interpretability and require large external datasets for validation.

Several studies addressed tumor grading. Zheng et al. [15] and Yue et al. [16] demonstrated that radiomics combined with clinical variables improves prediction of histologic grade, while Ren et al. [17] and Yang J. et al. [18] showed that incorporating peritumoral features and deep learning further enhances predictive performance. However, across these studies, limited sample sizes, retrospective designs, and heterogeneous modeling pipelines remain common limitations that may affect robustness and reproducibility. Additional studies in related gynecologic cancers, including ovarian and cervical malignancies [19–21], further support the feasibility of radiomics for histotype classification and treatment-response prediction. While these findings are methodologically transferable to endometrial cancer, differences in tumor biology and imaging characteristics should be considered when extrapolating results.

Overall, the studies summarized (Table 1) demonstrate that MRI-based radiomics has shown potentially useful discriminatory performance for clinically relevant endpoints, including histological type, tumor grade, and deep myometrial invasion. In several studies, integration of radiomic features with clinical variables or deep-learning approaches improved predictive performance. However, the evidence is limited by methodological heterogeneity, lack of standardization, and insufficient external validation. These limitations introduce potential biases and currently constrain the clinical applicability of radiomics-based diagnostic models.

Table 1 - Selected radiomics studies focusing on histological type, grade, or closely related risk features

Study	Modality	Endpoint	Key Findings	Study Design/ Validation	Key Limitations
Li et al., 2023 (Cancers)	T2W MRI, intratumoral	DMI, clinical risk class, histologic type, LVSI	Radiomic model achieved AUC ~0.85 for DMI, ~0.82 for LVSI, and effectively differentiated endometrioid vs non-endometrioid tumors; adding radiomics significantly improved clinical-only models.	Retrospective, single-center	No external validation; potential overfitting
Wang et al., 2023 (Acad Radiol)	Multiparametric MRI	DMI	Best radiomics model reached AUC ~0.88 for DMI; outperforming radiologist assessment (~0.72). Nomogram integrating texture features increased predictive stability.	Retrospective	Lack of external validation; inter-observer variability; MRI protocol heterogeneity
Bi et al., 2022 (Front Oncol)	Multiparametric MRI	Stage IA EC vs benign lesions	Radiomics classifier achieved AUC 0.90+ for distinguishing early EC from benign lesions; multi-center validation confirmed robustness.	Retrospective; multicenter validation	Retrospective design; potential selection bias; variability across centers

Study	Modality	Endpoint	Key Findings	Study Design/ Validation	Key Limitations
Zheng et al., 2021 (Front Oncol)	MRI + clinical	Histologic grade	Combined model (radiomics + CA125 + MRI features) achieved AUC ~0.84 for high-grade EC; significantly higher than clinical model alone (~0.72).	Retrospective	Small sample size; lack of external validation; risk of overfitting
Yue et al., 2023 (Front Oncol)	Multiparametric MRI	Tumor grade	Tumor-grade prediction achieved AUC ~0.87; wavelet-based features were most informative. Calibration curve and decision curve analysis showed strong clinical utility.	Retrospective	No external validation; single-center cohort; model generalizability uncertain
Ren et al., 2025 (Oncol Lett)	Intratumoral and peritumoral MRI	Tumor grade	Integrated model reached AUC ~0.90 for predicting high-grade EC; peritumoral ring features improved sensitivity for aggressive tumors.	Retrospective	Small cohort; lack of external validation; potential overfitting
Yang J. et al., 2023 (Front Oncol)	Deep-learning MRI	Risk class (EEC)	CNN-based model achieved AUC >0.90 for distinguishing low- vs high-risk endometrioid carcinoma; automated feature extraction outperformed hand-crafted radiomics.	Retrospective	Deep learning interpretability limitations; no external validation; data heterogeneity
Yang J. et al., 2025 (Front Oncol)	Intratumoral and peritumoral MRI	DMI in early endometrioid EC	Best model achieved AUC ~0.89; combining intra- and peri-tumoral features increased accuracy by ~10% compared to intratumoral features alone.	Retrospective	Lack of external validation; increased model complexity; overfitting risk
Shen et al., 2025 (Front Oncol)	Multiparametric MRI + deep learning	USC vs endometrioid EC	Multicenter dataset; model achieved AUC ~0.92 for USC identification; DWI-based features were most discriminative.	Multicenter cohort	External validation limited; deep learning interpretability; dataset imbalance
Fang et al., 2024 (Abdom Radiol)	Multiparametric MRI	CCJ cervical adenocarcinoma vs endometrioid EC	AUC ~0.88 for differentiating cervix–corpus junction adenocarcinoma from endometrioid carcinoma; model improved diagnostic confidence for difficult anatomical regions.	Retrospective	Limited sample size; anatomical variability; lack of external validation

Study	Modality	Endpoint	Key Findings	Study Design/ Validation	Key Limitations
Takeyama et al., 2024 (Jpn J Radiol)	MRI	Ovarian clear cell vs endometrioid carcinoma	Texture-based signatures achieved AUC ~0.85 for histotype classification; demonstrated that radiomics can detect subtle phenotypic differences similar to EC pathology.	Retrospective	Not EC-specific; limited cohort size; generalizability concerns
Na et al., 2024 (Front Oncol)	Multimodal MRI + clinical	Platinum sensitivity in ovarian carcinoma	Fusion model achieved AUC ~0.89 for predicting platinum sensitivity; radiomics alone underperformed (~0.78), showing benefit of multimodal integration.	Retrospective	Non-EC population; limited transferability; lack of standardized imaging

AUC values and conclusions are reproduced as reported in the cited publications and were not recalculated. Studies in ovarian or cervical malignancies are included only for methodological comparison and should not be interpreted as direct evidence for endometrial cancer.

Radiomics for molecular subtypes, MSI, p53-abnormal status, and tumor mutational burden

Radiomics has also been applied to the prediction of molecular subtypes and genomic surrogates, which are increasingly important for personalized treatment strategies. Lin et al. [22] developed an MRI-based radiomics nomogram for predicting microsatellite instability (MSI), demonstrating promising diagnostic performance; however, model generalizability remains uncertain. Broomand Lomer et al. [23] conducted a systematic review and meta-analysis, reporting encouraging pooled performance but also highlighting substantial heterogeneity in study design and quality, underscoring the need for standardization.

Ning et al. [24] and Meng et al. [25] developed radiomics-based models for predicting p53-aberrant tumors and high tumor mutation burden, respectively, demonstrating that radiomics can serve as a non-invasive surrogate for molecular profiling. Zhou et al. [26] and Brancato et al. [27] further showed that combining radiomics with peritumoral features or pathomics improves subtype classification. However, these integrative approaches increase methodological complexity and require large, well-annotated datasets for validation.

Additional studies demonstrated the value of radiogenomics and multimodal MRI approaches [28–31,37], while PET-based radiomics was used to capture metabolic heterogeneity and aggressive tumor biology [32–34]. These approaches showed promising reported performance but were frequently limited by retrospective design, small samples, protocol variability, and limited external validation.

Collectively, these studies (Table 2) indicate that radiomics may capture biologically relevant information associated with molecular subtypes and genomic alterations. However, variability in methodology, limited external validation, and potential overfitting remain significant challenges. As a result, although radiomics shows promise as a non-invasive tool for molecular phenotyping, further large-scale prospective studies are required before clinical implementation.

Table 2 - Radiomics studies targeting molecular and genomic surrogates in endometrial cancer

Study	Modality	Molecular/Genomic Endpoint	Key Findings	Study Design / Validation	Limitations
Lin et al., 2023 (QIMS)	MRI	MSI status	Combined radiomic-clinical model achieved reported AUC approximately 0.85 for MSI prediction; wavelet texture features were among the strongest predictors.	Retrospective	No external validation; moderate sample size; risk of overfitting
Broomand Lomer et al., 2025 (Abdom Radiol)	MRI (systematic review)	MSI status	Pooled results showed radiomics models can reach AUC 0.80–0.90 for MSI, though methodological variability limits generalizability.	Systematic review and meta-analysis	High heterogeneity; variable study quality; publication bias
Ning et al., 2024 (Br J Radiol)	MRI + clinical	p53abn EC	Multitask model achieved AUC ~0.86; integrating MRI radiomics with CA125 improved discrimination of p53abn tumors.	Retrospective	Lack of external validation; limited sample size; potential overfitting
Meng et al., 2025 (Abdom Radiol)	MRI	High TMB	Radiomics model achieved AUC ~0.87; high-entropy features were strongly associated with TMB-H phenotype.	Retrospective	No independent validation cohort; model generalizability uncertain
Zhou et al., 2025 (Eur J Radiol)	Multiparametric MRI	Molecular subtypes (TCGA surrogates)	Model achieved AUCs >0.80 for separating p53abn, MSI, and NSMP phenotypes; peritumoral features improved subtype classification.	Retrospective	Heterogeneous MRI protocols; lack of external validation; potential bias
Jacob et al., 2021 (J Clin Med)	MRI + gene expression	Radiomic Prognostic Index & genetic alterations	High RPI associated with poor survival and specific gene-expression clusters linked to aggressive biology.	Retrospective	Small cohort; no external validation; limited robustness
Hoivik et al., 2021 (Commun Biol)	MRI radiomics + genomics	Prognostic profiling	Radiomic clusters corresponded to genomic subgroups; demonstrated feasibility of integrating imaging with multi-omic data.	Retrospective	Integration complexity; limited external validation; cohort size constraints
Celli et al., 2022 (Cancers)	MRI + histologic–molecular data	Risk classes	Combined model achieved AUC ~0.90; molecular surrogates (MMR-d, p53abn, POLEmut) significantly increased accuracy.	Retrospective	High methodological complexity; limited interpretability; external validation required

Study	Modality	Molecular/Genomic Endpoint	Key Findings	Study Design / Validation	Limitations
Brancato et al., 2024 (Sci Rep)	Radiomics + pathomics	Integrated tumor characterization	Combined feature set improved prediction of molecular subtypes compared to radiomics or pathomics alone.	Retrospective	High methodological complexity; limited interpretability; validation needed
Fasmer et al., 2025 (Eur J Nucl Med Mol Imaging)	[18F]FDG PET	Aggressive disease, poor outcome	PET-derived radiomic signature predicted poor survival with AUC ~0.88; metabolic heterogeneity linked to aggressive molecular classes.	Retrospective	PET protocol variability; lack of external validation; limited cohort size

Reported model performance was extracted from the source publications. Heterogeneity in cohorts, class prevalence, feature selection, and validation prevents direct ranking of models.

Radiomics for organ preservation, fertility-sparing treatment, and lymphadenectomy decisions

Radiomics has also been explored for treatment planning. Yan et al. developed MRI-based radiomics nomograms for ovarian preservation and identification of candidates for fertility-sparing treatment [30,35]. Liu et al. proposed a radiomics model for prediction of lymph-node metastasis to support lymphadenectomy decisions [29].

Although these applications highlight the translational potential of radiomics, they remain subject to similar methodological limitations, including retrospective design, limited validation, and potential selection bias. Consequently, while radiomics-based decision-support tools are promising, their integration into clinical workflows requires further validation in prospective, multicenter studies.

Methodological themes and challenges

Most endometrial cancer (EC) radiomics studies used hand-crafted features—such as first-order intensity, shape, texture, and wavelet-derived descriptors—extracted from manually or semi-automatically segmented lesions on T2-weighted and/or multiparametric MRI (including diffusion-weighted and contrast-enhanced sequences). Lefebvre et al. introduced a spherical harmonics – based quantitative image analysis in multiparametric MRI to predict histopathology markers of EC, demonstrating that higher-order mathematical descriptors of tumor shape and surface can capture histologic differences beyond standard radiomic features. More recently, deep learning approaches, including convolutional neural networks, have been used to automatically learn features from image patches or to combine deep features with radiomics. Yang J. et al. and Shen et al. exemplify this trend by integrating multiparametric MRI radiomics with deep-learning architectures for risk classification and histologic subtype differentiation. The spherical-harmonics study is reported in reference [9], while deep-learning applications are represented by studies [14,18].

Several studies emphasized the added value of peritumoral radiomics. Yang J. et al. and Ren et al. showed that including peritumoral rings around the primary lesion improves prediction of deep myometrial invasion (DMI) and grade, likely by capturing invasion patterns, stromal reaction, and angiogenesis at the tumor–myometrium interface. Yan B. et al. incorporated peritumoral regions into an MRI-based radiomics nomogram for lymphovascular space invasion (LVSI) prediction, aligning with the biological notion that LVSI and invasive growth are peritumoral phenomena. Representative studies are cited in [13,17,29].

Standardization and reproducibility remain critical barriers to clinical adoption. Hodneland et al. explicitly evaluated different MRI radiomic feature normalization strategies in uterine endometrial and cervical cancers, showing that normalization choices influence prognostic model performance. Broomand

Lomer et al., in their MSI radiomics meta-analysis, highlighted heterogeneity in imaging protocols, feature extraction software, and machine learning workflows, limiting pooled inference and external applicability. Moreover, most EC radiomics studies are retrospective, single-center, and rely on internal cross-validation, which constrains generalizability and raises potential risk of overfitting. Multicenter studies, such as those by Bi et al. and Shen et al., as well as some MSI-focused works, represent progress toward broader applicability but still require prospective validation and harmonization of MRI protocols. These reproducibility concerns are also emphasized in [10,23].

Ability of radiomics to capture histological type

Across the reviewed literature, radiomics demonstrates strong potential to approximate histological type and related tumor biology in endometrial cancer. Multiple studies report that radiomic signatures can reliably distinguish endometrioid from non-endometrioid or serous carcinomas. Li et al. identified key T2-weighted MRI features linked to tumor shape and the myometrial interface, while Shen et al. achieved high accuracy in separating uterine serous carcinoma from endometrioid carcinoma using multiparametric MRI and deep learning. Radiomics also performs well in predicting histologic grade and preoperative risk class, as demonstrated by Zheng, Yue, Ren, and Yang, particularly when peritumoral features and deep-learning methods are incorporated; high-grade endometrioid tumors and serous carcinomas frequently cluster together, reflecting their shared aggressive behavior. The relevant evidence is summarized in studies [1,14–18].

Beyond morphology, radiomics correlates closely with molecular subtypes. Studies by Lin, Ning, Meng, Zhou, Celli, Jacob, and Hoivik show strong associations between imaging-derived features and MSI, p53-aberrant status, high tumor mutational burden, and TCGA-like genomic groups. These molecular correlations further support radiomics as a surrogate for underlying tumor biology. Multimodal approaches integrating MRI with PET, pathomics, or clinical/serologic data consistently outperform single-modality models, emphasizing that the most accurate assessment arises from holistic tumor profiling. Representative molecular and radiogenomic studies are cited in [22,24–28,37].

Despite these promising findings, most evidence originates from retrospective cohorts with limited sample sizes and minimal external validation, which may overestimate model performance and reduce generalizability. Variability in MRI acquisition, feature extraction pipelines, and analytic methods introduces potential bias and reproducibility challenges. Nevertheless, radiomics provides a non-invasive proxy for histologic type, grade, and molecular phenotype, with clinically meaningful applications in preoperative risk stratification, surgical planning, organ preservation, and systemic therapy selection.

Discussion

Principal findings and interpretation

While radiomics shows strong potential for improving preoperative assessment in endometrial cancer, several limitations hinder its immediate clinical translation. Most studies are retrospective and based on relatively small cohorts, with limited external validation, raising concerns about reproducibility and generalizability. Considerable heterogeneity in imaging protocols, segmentation approaches, feature extraction methods, and machine-learning techniques further complicates comparison across studies, and widespread adoption of standardization frameworks such as IBSI remains incomplete. In addition, research targets a wide range of endpoints - histologic type, grade, DMI, LVSI, molecular markers, risk class - yet the relationship between these outcomes and underlying tumor biology is not always clearly defined. Importantly, few investigations have prospectively evaluated whether radiomics-guided decisions improve patient management, reduce unnecessary interventions, or lead to better clinical outcomes.

Future work should emphasize large, prospective multicenter validation using harmonized imaging and feature pipelines, as well as the integration of radiomics with other omics modalities to generate more biologically interpretable models. Advances in explainable

AI will be essential for clarifying the basis of radiomic predictions and increasing their clinical acceptability. Ultimately, formal clinical impact studies are needed to determine whether radiomics-based decision-support tools can meaningfully enhance personalized, organ-preserving management in endometrial cancer.

Scientific novelty and clinical implications

The novelty of this review lies in linking radiomic prediction of histological type with grade, molecular surrogates, invasion-related features, prognostic risk, and treatment-planning decisions in a single tumor-profile framework. This integrated interpretation shows that radiomics is most likely to be clinically useful as a complement to pathology and conventional imaging rather than as an isolated substitute.

Potential clinical applications include preoperative risk stratification, identification of patients requiring more extensive staging, support for fertility-sparing or ovarian-preservation decisions, and selection of patients for additional molecular testing. However, reported model performance alone does not establish clinical utility. Decision-curve analysis, prospective workflow studies, comparison with expert radiologists and current clinicopathological models, and evaluation of patient outcomes are required.

Strengths and limitations of the review

Strengths of the review include a clearly defined clinical focus, coverage of MRI, PET/CT, radiogenomics, and deep-learning approaches, and explicit consideration of validation and reproducibility. The narrative structure allowed integration of heterogeneous endpoints that could not be meaningfully pooled.

The review also has limitations. The search was structured but not performed as a prospectively registered systematic review. Exact duplicate counts and exclusion counts at each screening stage were unavailable, and a formal risk-of-bias tool was not applied. The search was limited to three databases and English-language literature; conference, preclinical, review, and related gynecologic-cancer publications were included for context, which increases conceptual breadth but may blur the boundary of direct evidence. Performance estimates were extracted from heterogeneous studies and were not independently recalculated. Publication bias, selective reporting, and optimistic internal validation may therefore have influenced the apparent model performance.

Limitations of the evidence base and future research

Most included clinical studies were retrospective, used relatively small or single-center cohorts, and relied on internal cross-validation or random train-test splits. Differences in MRI scanners, acquisition protocols, segmentation, image preprocessing, feature definitions, class imbalance, endpoint definitions, and machine-learning workflows limit reproducibility. External validation was uncommon, and few studies evaluated incremental benefit over contemporary pathology, molecular classification, and expert imaging assessment.

Future research should prioritize prospective multicenter cohorts, prespecified analysis plans, harmonized imaging protocols, Image Biomarker Standardization Initiative-compliant feature extraction, transparent reporting of missing data and class balance, locked external validation, calibration, decision-curve analysis, and open or auditable code. Clinical-impact studies should determine whether radiomics-guided decisions improve management, reduce unnecessary procedures, or improve outcomes.

Conclusion

Radiomics research in endometrial cancer has advanced rapidly, progressing from early single-center studies to sophisticated multiparametric, radiogenomic, and deep-learning approaches. Evidence from MRI-based models for risk stratification, histologic typing, grading, and molecular characterization - as well as PET/CT radiomics and emerging radiopathomic frameworks - demonstrates that quantitative imaging features may capture tumor biology and aggressiveness. However, most studies are retrospective, single-center, and rely on internal validation, which limits generalizability and introduces potential bias. Variability in imaging protocols, feature extraction methods, and analytic workflows further challenges reproducibility. Despite these limitations, radiomics represents a

potentially valuable non-invasive complement to traditional biopsy and histopathology. Future work integrating clinical, radiomic, and molecular data, along with prospective, multicenter validation and standardized pipelines, may enable more accurate preoperative differentiation of tumor subtypes, improved prediction of grade and molecular risk categories, and more personalized planning of surgical and therapeutic strategies in endometrial cancer.

At present, radiomics should be regarded as an investigational decision-support approach. Its transition to routine care requires standardized acquisition and analysis, independent external validation, transparent model reporting, and demonstration of added clinical value beyond biopsy, histopathology, molecular classification, and conventional imaging.

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Declarations

Ethics approval and consent to participate. Not applicable. This review analyzed only previously published aggregate data and did not involve recruitment of participants or access to identifiable patient-level information.
Safety. Not applicable to the conduct of this review; no new diagnostic or therapeutic intervention was performed.
Data availability. All data used in the synthesis are contained in the cited publications and summary tables. The working extraction matrix may be made available by the corresponding author on reasonable request.
Conflict of interest. The authors declare no conflicts of interest requiring disclosure.
Funding. No external funding was received for this study.
Author contributions.
Anar Mukhit: Methodology; Investigation; Data curation; Formal analysis; Visualization; Writing - original draft. Zhandos Amankulov: Conceptualization; Methodology; Validation; Supervision; Writing - review and editing. Both authors read and approved the final version of the manuscript and accept responsibility for the integrity of the work.

Декларации

Этическое одобрение и согласие на участие. Обзор основан исключительно на ранее опубликованных агрегированных данных и не включал набор участников или обработку идентифицируемых данных пациентов.

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Финансирование. Исследование не получало внешнего финансирования.

Вклад авторов.

Мухит Анар: методология; проведение литературного поиска; курирование данных; формальный анализ; визуализация; подготовка первоначального варианта рукописи. Аманкулов Жандос: концептуализация; методология; валидация; научное руководство; критический пересмотр и редактирование рукописи. Оба автора прочитали и одобрили окончательную версию рукописи и несут ответственность за целостность работы.

Декларациялар

Этикалық мақұлдау және қатысуға келісім. Қолданылмайды: шолу тек бұрын жарияланған жиынтық деректерге негізделді және қатысушыларды тартуды немесе сәйкестендірілетін пациенттік деректерді өңдеуді қамтымады.

Қауіпсіздік. Осы шолуды жүргізуге қолданылмайды; жаңа диагностикалық немесе емдік араласу жүргізілген жоқ.

Деректердің қолжетімділігі. Синтезде пайдаланылған барлық деректер сілтеме жасалған жарияланымдар мен жиынтық кестелерде берілген. Деректерді алу матрицасы негізделген сұрау бойынша хат-хабарға жауапты автордан алынуы мүмкін.

Мүдделер қақтығысы. Авторлар ашып көрсетуді талап ететін мүдделер қақтығысының жоқ екенін мәлімдейді.

Қаржыландыру. Зерттеу сыртқы қаржыландыру алған жоқ.

Авторлардың үлесі.

Мұхит Анар: әдіснама; әдебиеттерді іздеу; деректерді басқару; формалды талдау; визуализация; қолжазбаның бастапқы нұсқасын дайындау. Аманқұлов Жандос: тұжырымдамалау; әдіснама; валидация; ғылыми жетекшілік; қолжазбаны сыни қайта қарау және редакциялау. Екі автор да қолжазбаның түпкілікті нұсқасын оқып, мақұлдады және жұмыстың тұтастығына жауап береді.

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