https://doi.org/10.62587/AFRJMS.3.1.2026.66-83 ISSN: 3006-7421

African Research Journal of Medical Sciences

Journal homepage: https://www.afrjms.com

Research Paper Open Access

Machine learning and radiomics in the preoperative differentiation of testicular germ cell tumor subtypes: Current landscape and future directions

Rabeya Akbarbasha[1*], Sudhakar Pachiappan[2], Sabarinath Chandrasekar[3] and Sasirekha Arangannan[4]

[1]Assistant Professor, Department of Pharmacology, Swamy Vivekananda College of Pharmacy, Elayampalaym-637205, Tamil Nadu, India. E-mail: rabeyapharma85@gmail.com

[2]Professor and Head, Department of Pharmacology, Swamy Vivekananda College of Pharmacy, Elayampalayam-637205, Namakkal, Tamil Nadu, India. E-mail: sudhakar00pharma@gmail.com

[3]Professor, Department of Pharmacology, Swamy Vivekananda College of Pharmacy, Elayampalayam-637205, Namakkal, Tamil Nadu, India. E-mail: revathisabari@gmail.com

[4]Department of Pharmacology, Swamy Vivekananda College of Pharmacy, Elayampalayam-637205, Namakkal, Tamil Nadu, India. E-mail: sasiarangannan@gmail.com

Article Info

Volume 3, Issue 1, January 2026
Received : 02 July 2025
Accepted : 30 December 2025
Published : 25 January 2026
doi: 10.62587/AFRJMS.3.1.2026.66-83

Abstract

Testicular Germ Cell Tumors (TGCTs) are rare but the most common solid cancer in young men, and distinguishing seminomas from Non Seminomatous Germcell Tumors (NSGCTs) preoperatively is essential because therapies and prognoses diverge. Conventional tools serum markers, scrotal ultrasound, and cross sectional imaging often fail to reliably separate subtypes, leading to diagnostic orchidectomy. Radiomics extracts high-dimensional quantitative features from imaging, offering a "digital biopsy" that, when paired with machine learning algorithms, can differentiate TGCT subtypes more accurately than standard methods. Early ultrasound and MRI based radiomics studies show promising results, though reproducibility, standardization, and external validation remain hurdles. This review outlines the current diagnostic landscape, introduces the radiomics ML pipeline, and summarizes early evidence, while highlighting barriers and future directions such as multi institutional collaboration, multi omics integration, deep learning, explainable AI, and prospective trials. Radiomics and ML promise a non-invasive shift toward precision oncology for TGCTs.

Keywords: *Testicular germ cell tumors, Seminoma, Non-seminomatous germ cell tumors, Radiomics, Machine learning, Digital biopsy, Precision oncology*

1. Introduction

Testicular Germ Cell Tumors (TGCTs) represent the most common solid malignancy affecting young adult men, typically between the ages of 15 and 40 years, despite accounting for only about 1% of all male cancers

* *Corresponding author: Rabeya Akbarbasha, Assistant Professor, Department of Pharmacology, Swamy Vivekananda College of Pharmacy, Elayampalaym-637205, Tamil Nadu, India. E-mail: rabeyapharma85@gmail.com*

worldwide. Over the past several decades, their incidence has steadily risen, particularly in Western countries, underscoring the growing clinical relevance of this disease (Batool *et al.*, 2019). From an epidemiological standpoint, TGCTs are broadly divided into two major histological subtypes: seminomas and Non-Seminomatous Germ Cell Tumors (NSGCTs) (Katabathina *et al.*, 2021). Seminomas generally exhibit a more indolent biological course, with high radiosensitivity and a favorable prognosis, whereas NSGCTs are more heterogeneous, often presenting with aggressive features and requiring multimodal therapy. The distinction between these two groups is crucial, as it informs therapeutic decision-making, follow-up strategies, and ultimately, patient outcomes. Pathophysiologically, TGCTs arise from primordial germ cells or gonocytes that undergo abnormal maturation and malignant transformation (Elendu *et al.*, 2024). This aberrant development results in distinct tumor phenotypes: seminomas tend to retain features of undifferentiated germ cells, while NSGCTs encompass multiple subtypes, including embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma, each with unique biological behaviors. These differences in origin and differentiation pathways explain the divergent clinical courses and therapeutic responses observed between seminomas and NSGCTs (Yang *et al.*, 2025). Consequently, accurate preoperative differentiation is not only academically significant but also directly impacts patient management and prognosis. Current diagnostic approaches, however, remain limited in their ability to achieve reliable non-invasive subtype differentiation. Serum tumor markers—alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-hCG), and lactate dehydrogenase (LDH)—are routinely employed in clinical practice (Naryzhny and Legina, 2025). While elevated marker levels may suggest NSGCTs, sensitivity and specificity are suboptimal, and a substantial proportion of patients present with normal marker profiles. High-frequency scrotal ultrasonography remains the imaging modality of choice for the initial evaluation of testicular masses. Although capable of detecting lesions with high sensitivity, ultrasound interpretation is largely qualitative, highly operator-dependent, and limited in distinguishing histological subtypes. Cross-sectional imaging modalities such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are predominantly utilized for staging and assessment of metastatic spread rather than histopathological characterization of primary tumors (Murali *et al.*, 2025). The global epidemiological profile of TGCTs is summarized in Table 1. As a result, the definitive diagnosis of TGCT subtype still relies on radical inguinal orchidectomy, which, while curative in many cases, imposes psychological stress, fertility concerns, and delays in tailoring patient-specific therapeutic strategies.

Table 1: Epidemiology of Testicular Germ Cell Tumors (TGCTs)

Parameter	Details	Notes
Global incidence	1% of male cancers; ~70,000 cases annually worldwide	The most common solid malignancy in young men
Peak age	15-40 years	Bimodal distribution is occasionally reported
Geographic variation	Higher incidence in Northern & Western Europe	Lower incidence in Asia & Africa
Trends	Rising incidence over decades	Likely due to environmental and genetic factors

These diagnostic limitations create an urgent need for novel, non-invasive tools capable of providing more accurate preoperative insights into TGCT biology. Radiomics, an emerging imaging science, has the potential to address this gap by converting routine medical images into high-dimensional, quantitative datasets that capture tumor heterogeneity beyond human visual assessment (Sharafaddini *et al.*, 2025). Features related to texture, shape, and intensity can be systematically extracted and analyzed, effectively creating a "digital biopsy" of the entire tumor volume. When integrated with advanced Machine Learning (ML) algorithms, radiomics enables the development of predictive models that may outperform conventional radiological assessments in differentiating between seminomatous and non-seminomatous tumors (Feng *et al.*, 2023). Early studies have shown promising results, suggesting that these approaches could transform preoperative decision-making and usher in a new era of precision oncology in testicular cancer. Thus, the exploration of radiomics and ML represents not merely a technological advancement but a paradigm shift in TGCT management (Zhang *et al.*, 2025). This review will first outline the limitations of existing diagnostic modalities, then introduce

the principles of the radiomics pipeline and machine learning integration, and finally discuss current evidence, challenges, and future directions for the clinical translation of this innovative approach.

2. Current diagnostic landscape

The accurate preoperative characterization of Testicular Germ Cell Tumors (TGCTs) remains a central challenge in clinical oncology. While significant advances have been made in the management and survival outcomes of TGCT patients, existing diagnostic tools often fall short when tasked with reliably distinguishing seminomas from Non-Seminomatous Germ Cell Tumors (NSGCTs) (Beccari *et al.*, 2023). This limitation has direct implications for patient care, as treatment strategies, intensity of surveillance, and overall prognoses differ considerably between the two subtypes (Deng *et al.*, 2025). Below is an overview of the key diagnostic modalities currently employed in clinical practice.

2.1. Serum tumor markers

Serum tumor markers are widely used in the initial evaluation and management of TGCTs. The three most clinically relevant markers are alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-hCG), and lactate dehydrogenase (LDH) (Rojas-Cadena *et al.*, 2025).

- **AFP:** Elevated in most yolk sac tumors and some mixed NSGCTs, but never in pure seminomas.
- **β-hCG:** May be elevated in choriocarcinoma and in a subset of seminomas, though at lower levels compared to NSGCTs.
- **LDH:** A nonspecific marker, reflecting tumor burden rather than histology.

While helpful, these markers are limited by poor sensitivity and specificity. Up to 30-40% of patients may present with normal marker levels, and marker elevation alone is insufficient for definitive subtype differentiation. Furthermore, serum markers may fluctuate during disease progression or treatment, complicating interpretation (Figure 1).

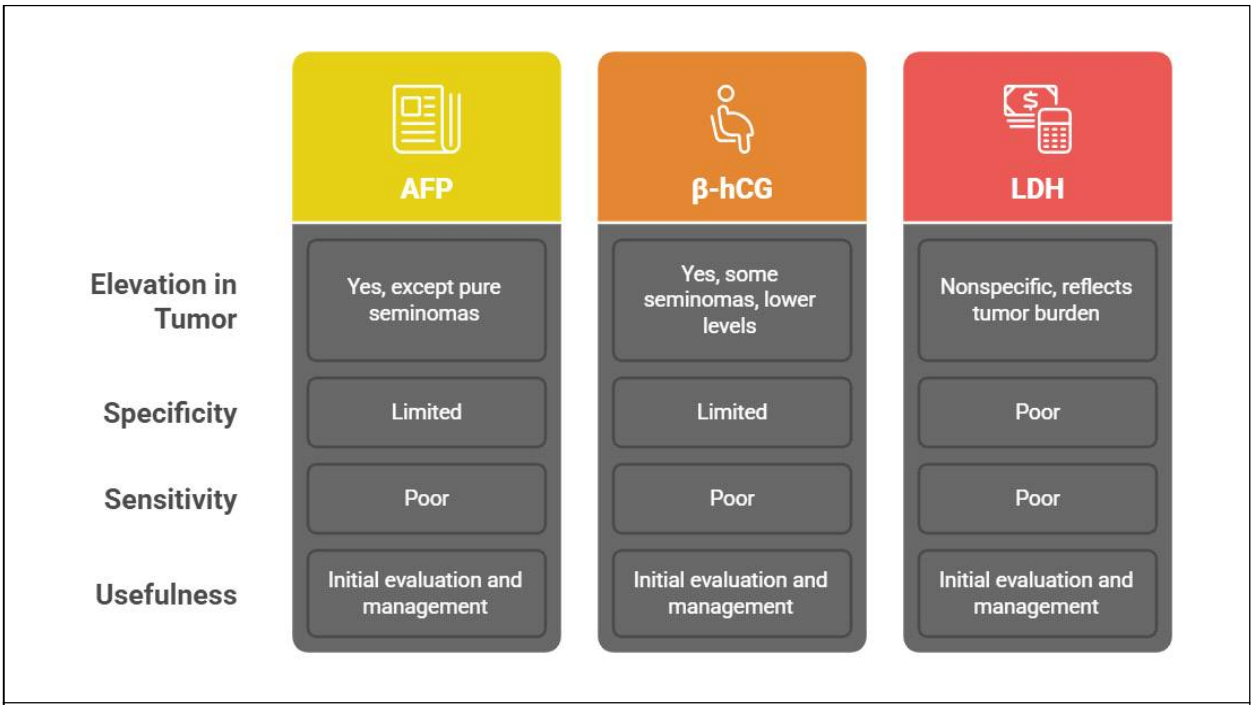

Figure 1: Comparison of serum tumor makers in TGCTs

2.2. Ultrasonography

High-frequency scrotal ultrasonography remains the first-line imaging modality for evaluating testicular masses (Sidhu *et al.*, 2025). Ultrasound offers several advantages: it is widely available, cost-effective, non-invasive, and highly sensitive in detecting intratesticular lesions. Seminomas typically appear as homogenous,

hypoechoic masses with well-defined margins, while NSGCTs often present as heterogeneous lesions with cystic, calcified, or necrotic components (Gillingham and Shanbhogue, 2025). Despite these general patterns, significant overlap exists between subtypes, limiting diagnostic accuracy (Figure 2). Operator dependence further complicates interpretation, as subtle imaging distinctions may be subjectively assessed. Although advanced ultrasound techniques, such as elastography and contrast-enhanced ultrasonography, are being explored, their role in routine preoperative differentiation remains investigational (Solomon *et al.*, 2025).

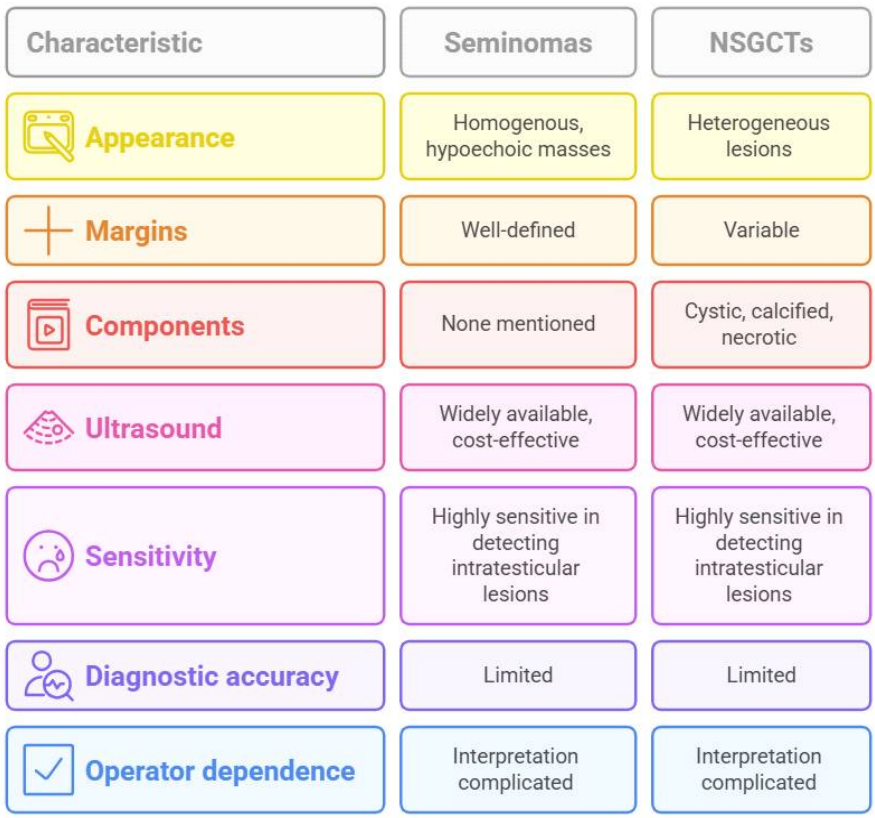

Figure 2: Testicular masses: Ultrasound characteristics

2.3. Cross-sectional imaging

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are typically reserved for staging purposes rather than primary tumor characterization. CT is the gold standard for evaluating retroperitoneal lymph node involvement and metastatic spread. However, it provides little insight into the histological subtype of the primary tumor (Gupta *et al.*, 2025). MRI, with its superior soft-tissue contrast, has been investigated for better tumor delineation and detection of local invasion. Certain studies suggest that diffusion-weighted MRI may aid in differentiating seminomas from NSGCTs by analyzing Apparent Diffusion Coefficient (ADC) values (Kim *et al.*, 2023), but findings remain inconclusive and require validation in larger cohorts. Overall, while CT and MRI play an indispensable role in staging and treatment planning (Figure 3), their contribution to histological differentiation is limited.

2.4. Histopathological confirmation

Given the limitations of markers and imaging, histopathology following radical inguinal orchidectomy remains the gold standard for definitive diagnosis (Skopelidou *et al.*, 2023). Surgical excision provides tissue for microscopic evaluation, immunohistochemistry, and genetic studies, thereby ensuring accurate subtype classification. However, this reliance on surgical intervention comes at a cost. Orchidectomy, though often curative, carries physical, psychological, and reproductive implications (Boulware *et al.*, 2022). Moreover, patients must endure uncertainty until postoperative results confirm the diagnosis, potentially delaying the initiation of optimal therapy (Table 2).

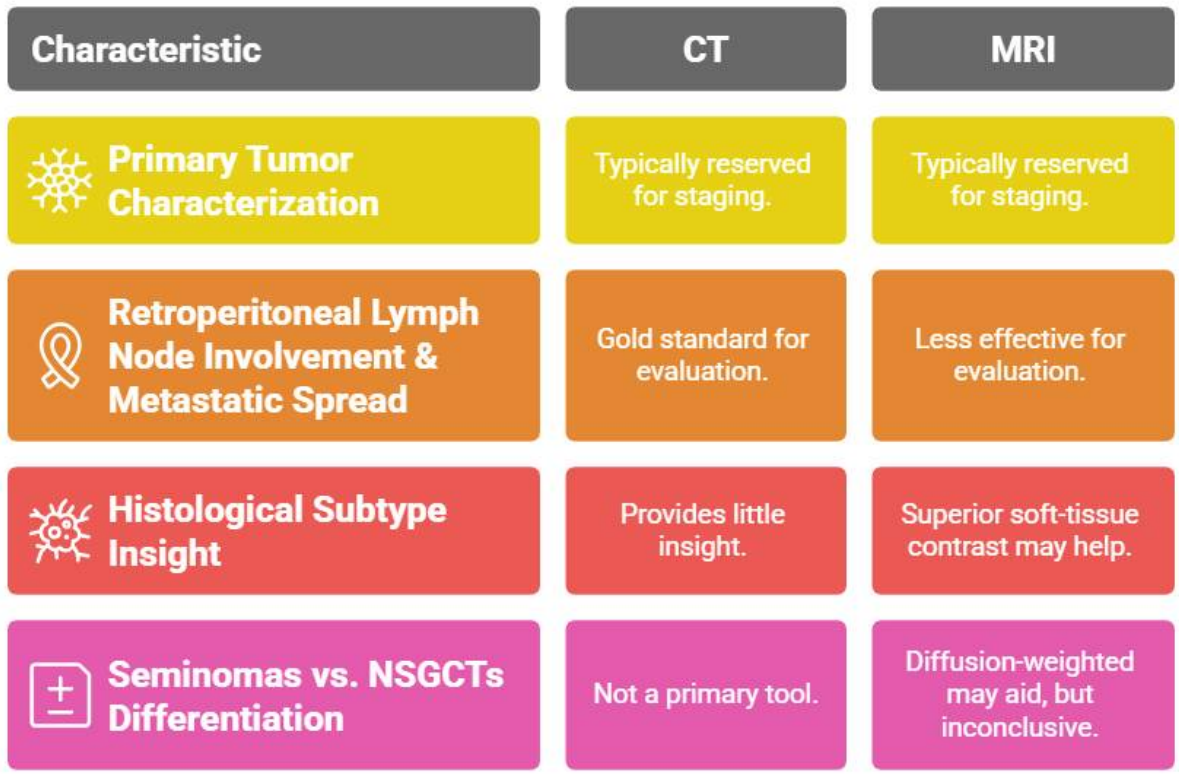

Figure 3: CT vs MRI in tumor characterization

Table 2: Current diagnostic tools for TGCTs: Strengths and limitations

Modality	Clinical role	Strengths	Limitations
Serum markers (AFP, β-hCG, LDH)	Initial evaluation	Minimally invasive, inexpensive	Limited sensitivity/specificity; not elevated in all cases
Ultrasound	First-line imaging	Accessible, sensitive	Operator-dependent; limited subtype differentiation
CT	Staging/metastasis assessment	Widely available, reliable for nodal disease	Limited role in histological classification
MRI	Problem-solving, soft-tissue characterization	Excellent soft-tissue contrast; multiparametric imaging	Costly; limited TGCT evidence base
Histopathology (orchidectomy)	Definitive diagnosis	Gold standard, subtype classification	Invasive; delays tailored therapy

2.5. Limitations of current approaches

The current diagnostic landscape for TGCTs highlights several key gaps:

1. Inadequate sensitivity and specificity of tumor markers, leading to false negatives or inconclusive results.
2. Operator dependence in ultrasonography, introducing variability and reducing reliability.
3. Restricted role of CT and MRI, which primarily inform staging but not histological differentiation.
4. Dependence on invasive surgery for definitive diagnosis, which may delay personalized treatment planning and impose unnecessary psychological burden.

These limitations underscore the pressing need for advanced, non-invasive diagnostic strategies that can reliably characterize tumor subtypes preoperatively.

2.6. Transition to emerging technologies

In this context, radiomics and Machine Learning (ML) offer a promising alternative. By extracting high-dimensional quantitative features from routine medical imaging and applying predictive algorithms, these approaches may overcome the subjectivity and limitations of current methods (Mansouri, 2023). Radiomics, when integrated with ML, holds the potential to provide a "virtual biopsy," enabling accurate, reproducible, and non-invasive tumor classification.

3. Radiomics: Concept and workflow

Radiomics is an emerging field in medical imaging that seeks to transform standard radiological data into mineable, quantitative information (Guiot *et al.*, 2022). By extracting a large number of mathematical features from medical images—features that are often imperceptible to the human eye—radiomics enables a deeper analysis of tumor biology and heterogeneity. Unlike conventional imaging interpretation, which relies on subjective visual assessment, radiomics provides an objective, reproducible, and data-rich "digital biopsy" of the entire tumor volume (Panayides *et al.*, 2020). This approach is particularly relevant in Testicular Germ Cell Tumors (TGCTs), where accurate, non-invasive differentiation between seminomas and Non-Seminomatous Germ Cell Tumors (NSGCTs) remains elusive. The radiomics process can be conceptualized as a multistep pipeline, typically comprising image acquisition, segmentation, feature extraction, feature selection and reduction, and model development (Lekkas *et al.*, 2025). Each stage is critical to ensure reproducibility, robustness, and clinical applicability of the resulting predictive models.

3.1. Image acquisition and preprocessing

The first step in radiomics involves acquiring high-quality medical images, most commonly from CT, MRI, or ultrasound. Consistency at this stage is crucial, as variations in imaging parameters, scanner hardware, or patient positioning can significantly impact the stability of extracted features. For TGCTs, scrotal ultrasound remains the frontline modality, but the growing interest in MRI and multiparametric imaging makes these platforms promising candidates for radiomic analysis (Lin *et al.*, 2025). Preprocessing techniques are often employed to standardize images before further analysis. These may include normalization of intensity values, noise reduction, resampling to uniform voxel sizes, and harmonization across scanners. Such steps aim to minimize technical variability and highlight biological differences, thereby improving feature reproducibility.

3.2. Tumor segmentation

Segmentation defines the Region of Interest (ROI) from which radiomic features are extracted. In TGCTs, segmentation typically involves delineating the primary intratesticular lesion (Hu *et al.*, 2024).

- Manual segmentation, performed by expert radiologists, is considered the gold standard but is time-consuming and subject to inter-observer variability.
- Semi-automatic and fully automated segmentation methods, often driven by machine learning algorithms, are being developed to reduce variability and improve efficiency.
- Accurate segmentation is essential because errors in defining tumor boundaries can propagate downstream, undermining the reliability of extracted features and predictive models.

3.3. Feature extraction

Radiomics features are broadly categorized into four groups:

1. **First-order features:** Describe the distribution of voxel intensities within the ROI, such as mean, median, skewness, and kurtosis.
2. **Shape features:** Quantify tumor geometry, including volume, surface area, sphericity, and compactness.
3. **Texture features:** Capture spatial relationships among voxel intensities, providing insight into intra-tumoral heterogeneity. Examples include Gray-Level Co-occurrence Matrix (GLCM), Gray-Level Run-Length Matrix (GLRLM), and Gray-Level Size Zone Matrix (GLSZM) features (Doniselli *et al.*, 2023).

4. **Higher-order features:** Derived through mathematical transformations such as wavelet filtering, Laplacian of Gaussian, or Fourier transforms, which highlight specific image patterns or frequency domains. By combining these feature classes, radiomics provides a high-dimensional description of tumors, often generating hundreds to thousands of variables per case.

3.4. Feature selection and reduction

The abundance of extracted features creates challenges related to redundancy, collinearity, and overfitting. Feature selection and dimensionality reduction techniques are, therefore, critical.

- Statistical methods, such as correlation analysis, univariate testing, and Principal Component Analysis (PCA), help eliminate redundant or irrelevant features.
- Regularization techniques, including Least Absolute Shrinkage and Selection Operator (LASSO), are commonly used to retain only the most predictive variables.
- Cross-validation strategies ensure that the selected features maintain robustness across different datasets. Effective feature reduction ensures that only the most biologically meaningful and statistically stable parameters are carried forward for model building (Tukhtaev *et al.*, 2024).

3.5. Model development and validation

The final stage of the radiomics pipeline integrates the selected features into predictive models using statistical or machine learning algorithms (Stüber *et al.*, 2023). Commonly employed methods include logistic regression, Support Vector Machines (SVM), random forests, and, increasingly, deep learning networks. For TGCT differentiation, these models can be trained to classify tumors into seminomatous or non-seminomatous categories based on extracted features (Panayides *et al.*, 2020). Importantly, rigorous validation is essential to avoid overfitting and ensure generalizability (Table 3). This typically involves: Internal validation: Techniques such as k-fold cross-validation within the same dataset. External validation: Testing on independent datasets from different institutions or imaging platforms, which is considered the gold standard for clinical translation.

Table 3: Radiomics pipeline in TGCTs: Steps, challenges, and solutions

Step	Purpose	Challenges	Solutions/Advances
Image acquisition	Collect diagnostic scans	Scanner variability; protocol differences	Harmonization, IBSI guidelines
Segmentation	Define tumor ROI	Manual variability, time-consuming	AI-based auto-segmentation
Feature extraction	Quantify tumor heterogeneity	Instability of some features	Standardized extraction software
Feature selection	Dimensionality reduction	Overfitting risk	LASSO, PCA, cross-validation
Model building	Train predictive algorithms	Data scarcity	Federated learning, multi-center validation

3.6. Radiomics as a "digital biopsy"

A defining strength of radiomics lies in its ability to capture spatial and biological heterogeneity across the entire tumor volume, in contrast to conventional biopsy, which samples only a small portion of tissue. This concept of a "digital biopsy" is particularly attractive in TGCTs, where tumor subtypes may coexist within mixed lesions and heterogeneity often dictates clinical behavior (Tukhtaev *et al.*, 2024). By providing a comprehensive, non-invasive characterization, radiomics may facilitate earlier, more accurate treatment decisions without relying solely on invasive procedures.

3.7. Integration with clinical and molecular data

Radiomics does not exist in isolation. Its predictive power can be enhanced by integrating imaging features

with clinical variables (e.g., age, tumor markers) and molecular or genomic data. This multi-omics approach, termed radiogenomics, has already shown promise in other cancers such as glioblastoma and lung cancer (Kumar *et al.*, 2025). In TGCTs, such integration could further refine subtype classification and even predict treatment response or resistance patterns. Radiomics represents a paradigm shift in oncologic imaging by transforming standard medical scans into quantitative data capable of revealing underlying tumor biology. Through a structured pipeline of acquisition, segmentation, feature extraction, and model building, radiomics offers a reproducible and objective method for tumor characterization (Perniciano *et al.*, 2025). When combined with machine learning, radiomics has the potential to non-invasively differentiate seminomas from NSGCTs, offering an attractive complement—or even an alternative—to traditional diagnostic tools.

4. Machine learning in oncologic imaging

Machine Learning (ML), a subset of Artificial Intelligence (AI), refers to computational techniques that allow systems to learn patterns from data and improve predictions without being explicitly programmed. In medical imaging, ML has emerged as a transformative tool capable of analyzing complex, high-dimensional datasets such as those generated in radiomics. By identifying subtle imaging features imperceptible to the human eye, ML can assist in classification, prognosis, and treatment-response prediction across multiple cancer types (Galic *et al.*, 2023). For Testicular Germ Cell Tumors (TGCTs), ML holds particular promise in addressing the unmet need for accurate, non-invasive preoperative subtype differentiation.

4.1. Principles of machine learning in imaging

The fundamental premise of ML in imaging lies in its ability to map input data (radiomic features) to an output (diagnosis or classification). This process involves three key stages:

1. **Training:** Algorithms learn from labeled datasets, where outcomes (e.g., seminoma vs. NSGCT) are known.
2. **Validation:** Performance is tested on unseen data within the same cohort to adjust hyperparameters and prevent overfitting.
3. **Testing:** Final model evaluation is performed on external datasets to assess generalizability. Robust performance at each stage is essential for clinical translation, as models must demonstrate consistent reliability across diverse populations and imaging platforms.

4.2. Categories of machine learning algorithms

ML algorithms commonly applied in oncologic imaging include:

- **Supervised learning:** Algorithms are trained using labeled data. Examples include:
  - **Logistic regression:** Simple yet effective for binary classification tasks.
  - **Support Vector Machines (SVM):** Useful for handling high-dimensional radiomic datasets with clear margins of separation (Ghaddar and Naoum-Sawaya, 2018).
  - **Random forests:** Ensemble models that reduce overfitting by combining multiple decision trees.
- **Unsupervised learning:** Used for clustering unlabeled data to uncover hidden patterns, such as grouping tumors based on imaging similarity.
- **Deep learning:** A subset of ML based on artificial neural networks. Convolutional Neural Networks (CNNs), in particular, can learn hierarchical image features directly from raw data, bypassing the need for handcrafted feature extraction. Deep learning has demonstrated state-of-the-art performance in tasks like lesion detection and classification.

4.3. Applications of ML in oncologic imaging

ML has already shown substantial impact in several cancers, paving the way for applications in TGCTs:

- **Lung cancer:** Radiomic signatures combined with ML have been used to distinguish benign from malignant nodules and to predict EGFR mutation status (Zhang *et al.*, 2021).

- **Glioblastoma:** ML-driven radiomics has been applied to predict survival and treatment response, highlighting the value of imaging biomarkers in heterogeneous tumors.
- **Prostate cancer:** ML algorithms integrated with multiparametric MRI have improved risk stratification and tumor grading.

These successes provide a strong foundation for extending ML approaches to testicular cancer, where imaging heterogeneity between seminomas and NSGCTs may similarly be quantified and exploited for subtype differentiation.

4.4. Challenges in model development

While promising, ML applications in oncologic imaging face several challenges:

- **Small sample sizes:** Rare tumors like TGCTs often lack large, publicly available datasets, increasing the risk of overfitting.
- **Feature redundancy:** High-dimensional radiomic datasets may contain many correlated features, complicating model training.
- **Data heterogeneity:** Variability in imaging protocols, scanner types, and preprocessing methods can reduce reproducibility.
- **Interpretability:** Black-box models, particularly deep learning, may lack transparency, making clinical adoption more difficult.

Addressing these challenges requires robust feature selection, multi-institutional collaborations, and the development of explainable AI (XAI) models that clinicians can trust.

4.5. ML in TGCT differentiation

Although research is still in its infancy, early studies suggest that ML models can classify seminomas and NSGCTs with encouraging accuracy. Radiomic features extracted from ultrasound or MRI images, when combined with supervised learning algorithms, have demonstrated predictive performance superior to traditional imaging interpretation. For example, Seminomas tend to exhibit more homogeneous texture features, whereas NSGCTs display greater heterogeneity, captured effectively by radiomic texture metrics (Ahmed, 2025). Shape and volumetric features may further distinguish subtypes, as NSGCTs are often more irregular and heterogeneous in morphology. By integrating these features, ML algorithms can provide objective, reproducible classifications, potentially reducing reliance on invasive histopathology for initial treatment planning.

4.6. Toward clinical translation

The integration of ML into routine TGCT diagnostics requires:

- **Standardized imaging protocols:** To ensure reproducibility across institutions.
- **External validation:** Multi-center studies testing model performance on independent datasets.
- **Integration with clinical data:** Combining radiomics with serum markers, epidemiological variables, and genomic information could yield comprehensive decision-support tools (Lei *et al.*, 2023).
- **Regulatory approval and clinical workflow adaptation:** Ensuring compliance with medical device regulations and seamless incorporation into radiology practice. Machine learning has emerged as a cornerstone of modern oncologic imaging, offering the ability to extract clinically meaningful insights from complex radiomic datasets. For TGCTs, ML-driven models show potential in differentiating seminomas from NSGCTs, addressing a long-standing diagnostic gap. While challenges remain in data standardization, validation, and interpretability, the trajectory of ML in oncology suggests that these tools will soon play a central role in precision diagnostics and personalized treatment strategies.

5. Radiomics and ML in TGCT differentiation

The preoperative distinction between seminomas and Non-Seminomatous Germ Cell Tumors (NSGCTs) is of

paramount importance, as treatment regimens, surveillance protocols, and prognoses differ significantly between these subtypes (Scalia *et al.*, 2024). Traditional diagnostic modalities, while indispensable, often fall short in reliably differentiating these histologies before surgery. Radiomics and Machine Learning (ML), by contrast, provide an innovative, non-invasive strategy that leverages high-dimensional imaging features and advanced algorithms to improve diagnostic precision. Although research in Testicular Germ Cell Tumors (TGCTs) remains nascent compared to other malignancies, early studies and translational insights highlight their promising potential.

5.1. Rationale for radiomics in TGCTs

Seminomas and NSGCTs exhibit distinct biological and morphological characteristics that may not be visually discernible but are encoded in imaging data. Seminomas typically present as homogeneous, well-defined masses, while NSGCTs are often heterogeneous with necrotic, cystic, or calcified components (Hashemi *et al.*, 2024). These subtle differences can be captured through radiomic texture, shape, and intensity features. When integrated into ML algorithms, these features can generate predictive models capable of distinguishing histological subtypes preoperatively with greater accuracy than conventional radiology alone.

5.2. Early evidence from ultrasound-based radiomics

Ultrasound (US) is the first-line imaging modality for evaluating testicular masses, making it a logical platform for radiomic analysis. Several exploratory studies have investigated whether radiomic features extracted from scrotal US can aid in TGCT differentiation (Batool *et al.*, 2019).

- **Texture analysis:** Seminomas often demonstrate lower entropy and higher uniformity on Gray-Level Co-occurrence Matrix (GLCM) metrics compared to NSGCTs, reflecting their relative homogeneity.
- **Shape features:** NSGCTs tend to be more irregular, a trait quantifiable through parameters like compactness and sphericity.
- **Preliminary ML models:** Trained on these features (e.g., support vector machines and random forests) have reported classification accuracies ranging from 70-85%, suggesting a clear improvement over subjective human interpretation. These findings highlight the potential of radiomics-enhanced US to act as a decision-support tool, though broader validation remains necessary.

5.3. MRI and multiparametric imaging studies

MRI, with its superior soft-tissue contrast and functional imaging capabilities, offers another promising platform for TGCT radiomics. Diffusion-Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC) maps, in particular, have been explored for their ability to capture microstructural differences between seminomas and NSGCTs (Feliciani *et al.*, 2021).

- **Radiomic ADC features:** Seminomas often exhibit more uniform diffusion characteristics, while NSGCTs display greater heterogeneity in ADC values.
- **ML integration:** Models incorporating ADC radiomics have achieved predictive accuracies upwards of 80% in small pilot studies.
- **Multiparametric MRI:** Combining T2-weighted, DWI, and contrast-enhanced sequences has further enriched radiomic datasets, allowing ML models to integrate complementary biological signals. Although sample sizes remain limited, these studies underscore the potential of MRI-based radiomics as a robust platform for non-invasive TGCT characterization.

5.4. CT and cross-sectional imaging applications

CT remains the gold standard for staging TGCTs, but its role in primary tumor characterization has been underexplored. Radiomic analysis of CT images could theoretically capture differences in tumor density, texture, and morphology (Laino, 2025). While direct evidence in TGCTs is sparse, lessons from other cancers (e.g., lung and renal tumors) suggest CT radiomics may eventually contribute to subtype classification, especially when combined with ML approaches.

5.5. Comparative performance against conventional methods

Early radiomics-ML models have shown performance metrics that rival—and in some cases exceed—traditional diagnostic tools. For instance:

- Tumor markers (AFP, β-hCG, LDH) have limited discriminatory power, especially in marker-negative cases.
- Conventional US interpretation is subjective and operator-dependent.
- Radiomics-ML models, however, provide objective, reproducible classification with higher diagnostic accuracy, often in the 75-85% range in initial studies (Wu *et al.*, 2025). This suggests that radiomics may serve as a valuable adjunct to existing diagnostic pathways, potentially reducing reliance on invasive procedures.

5.6. Limitations of current evidence

Despite encouraging results, several limitations must be acknowledged:

1. Small, single-center studies dominate the field, limiting generalizability.
2. Heterogeneity in imaging protocols (e.g., different scanners, acquisition settings) introduces variability in feature reproducibility.
3. Lack of external validation: Most studies rely on internal cross-validation rather than independent datasets.
4. Limited integration with clinical data: Few models incorporate tumor markers, patient demographics, or genetic information alongside radiomics (Anagnostopoulos *et al.*, 2022). These gaps underscore the need for large, multi-institutional efforts to establish standardized workflows and externally validated models.

5.7. Future directions in TGCT radiomics

To realize clinical utility, radiomics and ML approaches in TGCT differentiation must evolve beyond proof-of-concept studies. Future efforts should focus on:

- Multi-omics integration: Combining radiomics with genomics, proteomics, and serum biomarkers for comprehensive tumor characterization.
- Prospective trials: Incorporating radiomics into clinical workflows to assess real-world performance.
- Automated segmentation: Leveraging deep learning to standardize tumor delineation and reduce observer variability.
- Federated learning: Collaborative AI frameworks enabling multi-center model training without sharing raw patient data, thus overcoming privacy and data scarcity challenges. Radiomics and ML have shown early promise in differentiating seminomas from NSGCTs using ultrasound and MRI platforms. By quantifying subtle imaging features that escape conventional radiology, these approaches provide objective, reproducible classification with accuracies surpassing traditional methods.
- Although current evidence is limited by small sample sizes, heterogeneity in methods, and lack of validation, the trajectory of research strongly suggests that radiomics-ML integration could transform preoperative TGCT diagnostics.
- With continued development, these tools may enable clinicians to make faster, more precise, and less invasive treatment decisions, heralding a new era of personalized oncology for testicular cancer patients.

6. Challenges in clinical translation

Radiomics and Machine Learning (ML) hold substantial promise for transforming the preoperative differentiation of Testicular Germ Cell Tumors (TGCTs). However, despite encouraging preliminary findings, significant barriers remain before these approaches can be reliably integrated into routine clinical practice (Vollmer *et al.*, 2018). Translating radiomics from research settings to patient care requires addressing challenges related to reproducibility, standardization, validation, clinical integration, and ethical considerations.

6.1. Reproducibility and feature robustness

One of the most pressing challenges in radiomics is the reproducibility of extracted features. Radiomic parameters can be influenced by several technical factors, including image acquisition protocols, scanner hardware, reconstruction algorithms, and preprocessing techniques (Chaddad and Liang, 2024). For example, the same testicular lesion imaged on two different ultrasound machines or MRI scanners may yield different feature values, reducing reliability. To address this, harmonization strategies—such as image normalization, resampling, and feature standardization—are essential. The Image Biomarker Standardization Initiative (IBSI) has proposed guidelines to improve reproducibility, but adherence remains inconsistent across studies. Without robust and reproducible features, predictive models cannot achieve the consistency required for clinical translation.

6.2. Data scarcity and limited cohorts

Unlike lung, prostate, or brain cancers, TGCTs are relatively rare, which restricts the availability of large, annotated imaging datasets. Most published studies to date are single-center with small cohorts, often fewer than 100 patients (Casiraghi *et al.*, 2011). Such small datasets increase the risk of overfitting—where models perform well on training data but fail to generalize to external populations. Collaborative, multi-institutional studies are needed to overcome this barrier. The development of federated learning approaches (Darzidehkalani *et al.*, 2022), where models are trained across multiple centers without requiring direct data sharing, may offer a solution to data scarcity while maintaining patient privacy.

6.3. Standardization of imaging protocols

Variability in imaging protocols represents another obstacle. For example, differences in ultrasound transducer frequency, MRI sequence parameters, or CT reconstruction techniques can introduce systematic biases in radiomic features. Without standardized acquisition protocols, results may not be comparable across institutions. Standardization efforts must extend to segmentation methods as well (Libling *et al.*, 2023). Manual segmentation is still widely used in TGCT radiomics, but it is labor-intensive and subject to inter-observer variability. Automated or semi-automated segmentation using deep learning offers a path forward, though these tools require validation and regulatory approval before routine deployment.

6.4. Validation and generalizability

Most radiomics-ML models for TGCT differentiation have relied on internal validation techniques, such as cross-validation or bootstrapping, within a single dataset. While these methods help prevent overfitting, they do not guarantee external validity. External validation on independent datasets, ideally from multiple institutions with heterogeneous patient populations and imaging protocols, is essential to demonstrate generalizability. Without external validation, even the most promising models risk failing when applied in real-world clinical scenarios (van der *et al.*, 2019). This limitation has historically slowed the adoption of AI in oncology and remains a critical barrier for TGCT applications.

6.5. Integration with clinical workflows

For radiomics and ML to be clinically impactful, they must integrate seamlessly into existing diagnostic pathways. Radiologists and oncologists require tools that are user-friendly, time-efficient, and compatible with hospital information systems. Models that demand complex preprocessing, extensive computational resources, or manual feature selection may struggle to gain traction in busy clinical settings (Khan *et al.*, 2020). Moreover, radiomics outputs must provide actionable insights. For instance, a probability score distinguishing seminoma from NSGCT must translate into clear clinical recommendations. Integration with other diagnostic data, such as serum tumor markers and patient demographics, could improve usability and adoption.

6.6. Interpretability and trust

Many ML models, particularly deep learning algorithms, function as “black boxes,” producing predictions without clear explanations. This lack of transparency poses a challenge for clinicians, who are unlikely to adopt tools they cannot interpret or trust. Explainable AI (XAI) approaches, such as feature importance ranking,

saliency maps, or decision trees, can enhance interpretability by clarifying why a model reached a particular decision (Vilone and Longo, 2021). Trust also extends to regulatory and medicolegal domains. Clinicians must be confident that AI-driven tools meet rigorous safety, ethical, and accountability standards before incorporating them into patient care.

6.7. Ethical and regulatory considerations

AI applications in healthcare raise ethical concerns regarding data privacy, informed consent, and algorithmic bias. For rare cancers like TGCTs, small datasets may inadvertently reflect population biases, leading to models that underperform in underrepresented groups. Additionally, regulatory pathways for AI-based diagnostic tools are still evolving. Agencies such as the FDA and EMA require rigorous validation, quality assurance, and post-market surveillance before approval. Ensuring patient privacy is another concern, particularly as multi-institutional collaborations and federated learning approaches expand. Robust frameworks for data governance and ethical oversight will be necessary for clinical implementation (Moses, 2019). The translation of radiomics and ML into clinical practice for TGCT differentiation faces significant challenges. These include technical issues such as reproducibility and standardization, methodological limitations such as small sample sizes and lack of external validation, and broader concerns related to workflow integration, interpretability, and ethics. Overcoming these barriers will require multi-institutional collaboration, standardized imaging protocols, the development of explainable AI models, and robust regulatory frameworks. While obstacles remain, addressing these challenges is essential to unlock the full potential of radiomics and ML as reliable, non-invasive diagnostic tools for TGCTs (Hussain *et al.*, 2024).

7. Future Directions

Radiomics and Machine Learning (ML) are still in the early stages of application to Testicular Germ Cell Tumors (TGCTs), yet their trajectory mirrors the rapid progress seen in other malignancies such as lung, brain, and prostate cancers. To unlock their full clinical potential, future research and development must focus on expanding datasets, integrating multi-modal information, standardizing workflows, and moving toward clinical adoption through prospective trials and regulatory approval. The following directions are likely to shape the next phase of innovation in this field.

7.1. Multi-institutional collaboration and data sharing

The rarity of TGCTs poses a significant barrier to building large, diverse datasets necessary for robust model development. Future progress depends on multi-institutional collaborations that pool imaging, clinical, and molecular data across geographic regions. Initiatives such as international testicular cancer consortia could help establish centralized radiomics repositories. To overcome data privacy concerns, federated learning frameworksmay play an important role. In federated learning, algorithms are trained collaboratively across institutions without requiring raw data to be exchanged (Myakala *et al.*, 2024). This approach preserves patient confidentiality while ensuring that models learn from diverse populations, thereby improving generalizability.

7.2. Standardization of imaging and radiomics workflows

For radiomics to gain clinical acceptance, standardization of imaging acquisition, preprocessing, and feature extraction is critical. Future work should focus on:

- **Protocol harmonization:** Establishing consensus on optimal ultrasound, MRI, and CT acquisition parameters for TGCT imaging (Woznicki *et al.*, 2023).
- **Automated segmentation tools:** Leveraging deep learning to standardize tumor delineation, reduce inter-observer variability, and improve reproducibility.
- **Feature standardization:** Adhering to guidelines from the Image Biomarker Standardization Initiative (IBSI) to ensure consistent feature definitions and calculation methods. Such efforts will facilitate reproducibility across studies and accelerate the integration of radiomics into multicenter clinical trials.

7.3. Integration of radiomics with multi-omics data

The future of TGCT diagnostics will likely involve integrated models that combine radiomics with genomics, transcriptomics, proteomics, and clinical biomarkers. This "multi-omics" strategy could yield more comprehensive models of tumor biology. For example:

- Radiogenomics could reveal associations between radiomic features and genetic alterations, offering insights into tumor aggressiveness and therapeutic vulnerabilities.
- Integration with serum tumor markers (AFP, β-hCG, LDH) may improve diagnostic accuracy, especially in marker-negative patients (Ilcus *et al.*, 2021).
- Clinical variables such as age, fertility status, and comorbidities can be incorporated to personalize predictions further. By unifying imaging and molecular data, future predictive models could evolve from simple subtype classification to guiding individualized treatment planning and predicting therapeutic response.

7.4. Deep learning and end-to-end models

While most current TGCT radiomics studies rely on handcrafted features, the future may see broader adoption of deep learning approaches, particularly Convolutional Neural Networks (CNNs). These models can learn hierarchical imaging representations directly from raw data, potentially bypassing traditional feature extraction and selection steps (Deng, 2012). End-to-end deep learning models could automatically segment tumors, extract relevant features, and provide subtype predictions in a single pipeline. Although challenges remain regarding interpretability and data requirements, advances in explainable AI (XAI) and transfer learning may enhance their clinical applicability.

7.5. Prospective clinical trials and real-world validation

To move beyond proof-of-concept, future studies must be prospective and multicenter, assessing the performance of radiomics-ML models in real-world clinical workflows (Xie and Chen, 2025). These trials should evaluate not only diagnostic accuracy but also impact on clinical decision-making, treatment planning, and patient outcomes. Potential endpoints could include:

- Reduction in unnecessary orchidectomies.
- Shorter time to treatment initiation.
- Improved risk stratification and surveillance strategies.
- Cost-effectiveness of integrating radiomics into diagnostic pathways. Demonstrating tangible clinical benefits will be key to securing regulatory approval and adoption.

7.6. Clinical decision-support systems

The ultimate goal is the development of user-friendly decision-support tools that integrate seamlessly into radiology and oncology workflows. Such systems could provide probability scores or risk stratifications directly within Picture Archiving and Communication Systems (PACS) or electronic health records. For clinicians, this would mean actionable, interpretable outputs rather than raw data or complex feature sets. User interfaces should emphasize explainability, enabling radiologists and oncologists to understand why a model produced a particular prediction (Prince, 2025). This transparency will be essential to building trust and encouraging adoption.

7.7. Ethical, regulatory, and educational considerations

As radiomics and ML evolve, attention must also be given to ethical and regulatory frameworks. Future directions should include:

- **Bias mitigation:** Ensuring that models perform equitably across diverse populations.
- **Data privacy safeguards:** Expanding the use of anonymization techniques and federated learning.

- **Regulatory approval pathways:** Establishing clear standards for AI-based diagnostic tools through bodies such as the FDA and EMA.
- **Clinician education:** Training radiologists, oncologists, and pathologists in AI literacy to ensure informed use of these technologies.

These measures will help ensure that the deployment of AI in TGCTs aligns with patient safety, ethical standards, and professional practice. The future of radiomics and ML in TGCT differentiation lies in collaboration, standardization, and integration. Large, diverse datasets enabled by multi-institutional cooperation and federated learning will improve model robustness (Yang *et al.*, 2022). Advances in deep learning, multi-omics integration, and prospective validation will enhance diagnostic precision and clinical impact. Finally, regulatory frameworks, explainable AI, and clinician engagement will ensure safe and effective translation into practice (Waqas, 2024). By pursuing these directions, radiomics and ML could transform TGCT management, enabling non-invasive, personalized diagnostics that reduce reliance on invasive procedures and accelerate tailored treatment strategies.

8. Conclusion

Testicular Germ Cell Tumors (TGCTs), though relatively rare, remain the most common solid malignancy in young men and pose unique diagnostic challenges. The accurate preoperative differentiation between seminomas and Non-Seminomatous Germ Cell Tumors (NSGCTs) is critical, as management strategies and prognoses diverge sharply between these subtypes. Conventional tools—including serum tumor markers, ultrasound, and cross-sectional imaging—are indispensable but fall short of providing reliable histological classification before surgery. As a result, definitive diagnosis still depends on radical inguinal orchidectomy, which, while curative in many cases, introduces psychological, reproductive, and clinical burdens. Radiomics and Machine Learning (ML) offer an innovative, non-invasive approach to addressing this diagnostic gap. By extracting high-dimensional features from medical images and integrating them with predictive algorithms, radiomics provides a "digital biopsy" of the entire tumor volume, capturing heterogeneity that eludes conventional interpretation. Early studies employing ultrasound and MRI-based radiomics have demonstrated encouraging performance in differentiating seminomas from NSGCTs, often exceeding the accuracy of traditional methods. Nevertheless, the clinical translation of radiomics and ML in TGCTs faces significant challenges. Issues of reproducibility, small dataset sizes, variability in imaging protocols, lack of external validation, and limited integration into clinical workflows remain pressing concerns. Furthermore, ethical considerations, interpretability of AI models, and regulatory pathways must be carefully addressed before widespread adoption. Looking ahead, the future of this field lies in multi-institutional collaboration, standardized imaging protocols, integration with multi-omics data, and prospective clinical trials. Advances in explainable AI, deep learning, and decision-support tools will be essential to build clinician trust and ensure practical utility. If these challenges are met, radiomics and ML have the potential to fundamentally reshape the preoperative management of TGCTs, advancing precision oncology and improving outcomes for patients worldwide.

References

Ahmed, M.I. (2025). Evaluating and enhancing semi-supervised learning algorithms for pancreatic cancer segmentation in ct images. Vilniaus Universitetas.

Anagnostopoulos, A.K., Gaitanis, A., Gkiozos, I., Athanasiadis, E.I., Chatziioannou, S.N., Syrigos, K.N., ... and Papanikolaou, N. (2022). Radiomics / radiogenomics in lung cancer: Basic principles and initial clinical results. *Cancers,* 14(7): 1657.

Batool, A., Karimi, N., Wu, X.-N., Chen, S.-R. and Liu, Y.-X. (2019). Testicular germ cell tumor: A comprehensive review. *Cellular and Molecular Life Sciences,* 76(9): 1713-1727.

Beccari, T., Albi, E., Chiurazzi, P. and Ceccarini, M.R. (2023). Omics sciences in the personalization of diagnosis and therapy. *Clin Ter.,* 174(2): 6.

Boulware, S., Kamody, R., Kuper, L., McNamara, M., Olezeski, C., Szilagyi, N. and Alstott, A. (2022). Biased science: The Texas and Alabama measures criminalizing medical treatment for transgender children and

adolescents rely on inaccurate and misleading scientific claims. *Yale Law School, Public Law Research Paper Forthcoming*.

Casiraghi, M., De Pas, T., Maisonneuve, P., Brambilla, D., Ciprandi, B., Galetta, D., ... and Tessitore, A. (2011). A 10-year single-center experience on 708 lung metastasectomies: The evidence of the "international registry of lung metastases". *Journal of Thoracic Oncology*, 6(8): 1373-1378.

Chaddad, A. and Liang, X. (2024). Stability of radiomic models and strategies to enhance reproducibility. *IEEE Transactions on Radiation and Plasma Medical Sciences*, 8(5): 540-555.

Darzidehkalani, E., Ghasemi-Rad, M. and Van Ooijen, P. (2022). Federated learning in medical imaging: Part I: toward multicentral health care ecosystems. *Journal of the American College of Radiology*, 19(8): 969-974.

Deng, L. (2012). Three classes of deep learning architectures and their applications: A tutorial survey. *APSIPA Transactions on Signal and Information Processing*, 57: 58.

Deng, X., Mehta, A., Xiao, B., Chaudhuri, K.R., Tan, E.-K. and Tan, L.C. (2025). Parkinson's disease subtypes: Approaches and clinical implications. *Parkinsonism & Related Disorders*, 130: 107208.

Doniselli, F.M., Pascuzzo, R., Agrò, M., Aquino, D., Anghileri, E., Farinotti, M., ... and Moscatelli, M. (2023). Development of a radiomic model for MGMT promoter methylation detection in glioblastoma using conventional MRI. *International Journal of Molecular Sciences*, 25(1): 138.

Elendu, C., Amaechi, D.C., Elendu, T.C., Fiemotonghan, B.-E., Okoye, O. K., Agu-Ben, C.M., ... and Asekhauno, M. (2024). A comprehensive review of heart failure: Unraveling the etiology, decoding pathophysiological mechanisms, navigating diagnostic modalities, exploring pharmacological interventions, advocating lifestyle modifications, and charting the horizon of emerging therapies in the complex landscape of chronic cardiac dysfunction. *Medicine*, 103(3): e36895.

Feliciani, G., Mellini, L., Carnevale, A., Sarnelli, A., Menghi, E., Piccinini, F., ... Giganti, M. (2021). The potential role of MR based radiomic biomarkers in the characterization of focal testicular lesions. *Scientific Reports*, 11(1): 3456.

Feng, Y., Feng, Z., Wang, L., Lv, W., Liu, Z., Min, X., ... and Zhang, J. (2023). Comparison and analysis of multiple machine learning models for discriminating benign and malignant testicular lesions based on magnetic resonance imaging radiomics. *Frontiers in Medicine*, 10: 1279622.

Galic, I., Habijan, M., Leventiæ, H. and Romic, K. (2023). Machine learning empowering personalized medicine: A comprehensive review of medical image analysis methods. *Electronics*, 12(21): 4411.

Ghaddar, B. and Naoum-Sawaya, J. (2018). High dimensional data classification and feature selection using support vector machines. *European Journal of Operational Research*, 265(3): 993-1004.

Gillingham, N. and Shanbhogue, K. (2025). MR imaging evaluation of the testes and scrotum. *Radiologic Clinics*.

Guiot, J., Vaidyanathan, A., Deprez, L., Zerka, F., Danthine, D., Frix, A.N., ... and Miraglio, B. (2022). A review in radiomics: Making personalized medicine a reality via routine imaging. *Medicinal Research Reviews*, 42(1): 426-440.

Gupta, S., Chandola, S., Goel, D., Khandelwal, Y., Haria, P., Ray, M. and Das, C.J. (2025). Imaging of peritoneal surface malignancies: Diagnosis and clinical implications. *Abdominal Radiology*, 1-20.

Hashemi Gheinani, A., Kim, J., You, S. and Adam, R.M. (2024). Bioinformatics in urology—molecular characterization of pathophysiology and response to treatment. *Nature Reviews Urology*, 21(4): 214-242.

Hu, C., Qiao, X., Xu, Z., Zhang, Z. and Zhang, X. (2024). Machine learning-based CT texture analysis in the differentiation of testicular masses. *Frontiers in Oncology*, 13: 1284040.

Hussain, D., Abbas, N. and Khan, J. (2024). Recent breakthroughs in pet-ct multimodality imaging: Innovations and clinical impact. *Bioengineering*, 11(12): 1213.

Ilcus, C., Silaghi, H., Georgescu, C.E., Georgiu, C., Ciurea, A.I., Nicoara, S.D. and Silaghi, C.A. (2021). Molecular pathology and targeted therapies for personalized management of central nervous system germinoma. *Journal of Personalized Medicine*, 11(7): 661.

Katabathina, V.S., Vargas-Zapata, D., Monge, R.A., Nazarullah, A., Ganeshan, D., Tammisetti, V. and Prasad, S.R. (2021). Testicular germ cell tumors: Classification, pathologic features, imaging findings, and management. *Radiographics,* 41(6): 1698-1716.

Khan, S., Parkinson, S., Grant, L., Liu, N. and Mcguire, S. (2020). Biometric systems utilising health data from wearable devices: Applications and future challenges in computer security. *ACM Computing Surveys (CSUR),* 53(4): 1-29.

Kim, J.H., Choe, J., Kim, H.K. and Lee, H.Y. (2023). MRI-based stepwise approach to anterior mediastinal cystic lesions for diagnosis and further management. *Korean Journal of Radiology,* 24(1): 62.

Kumar, R., Sporn, K., Khanna, A., Paladugu, P., Gowda, C., Ngo, A., ... and Tavakkoli, A. (2025). Integrating radiogenomics and machine learning in musculoskeletal oncology care. *Diagnostics,* 15(11): 1377.

Laino, M.E. (2025). Combination of CT-based radiomics features and clinical data for predicting tumor genetic profile in patients with intrahepatic cholangiocarcinoma.

Lei, P., Hu, N., Wu, Y., Tang, M., Lin, C., Kong, L., ... Chan, L.W.C. (2023). Radiobioinformatics: A novel bridge between basic research and clinical practice for clinical decision support in diffuse liver diseases. *iRADIOLOGY,* 1(2): 167-189.

Lekkas, G., Vrochidou, E. and Papakostas, G.A. (2025). Advancements in radiomics-based AI for pancreatic ductal adenocarcinoma. *Bioengineering,* 12(8): 849.

Libling, W.A., Korn, R. and Weiss, G.J. (2023). Review of the use of radiomics to assess the risk of recurrence in early-stage non-small cell lung cancer. *Translational Lung Cancer Research,* 12(7): 1575.

Lin, T., Chen, S. and Miao, S. (2025). Development of an ultrasound based clinical radiomic nomogram for predicting histologic subtypes in focal testicular tumors. *Journal of Ultrasound in Medicine*.

Mansouri, N. (2023). Simultaneous multimodal imaging of metabolic and functional parameters of tumors; tumor heterogeneity, prediction of precision medicine effectiveness by radiomic analysis and machine learning algorithms. Université Paris Cité.

Moses, J. (2019). Federated learning for privacy-preserving hepatocellular carcinoma prediction in multi-institutional hcv patient cohorts.

Murali, S., Lee, W.S.-Y., Wei-En, L., Samuel, C.Y., Tan, J.A., Wei, B.J., ... and Okoli, O. (2025). Exploring the accuracy of whole-body MRI in assessing treatment response in metastatic breast cancer: A narrative review. *Radiography*, 103099.

Myakala, P.K., Jonnalagadda, A.K. and Bura, C. (2024). Federated learning and data privacy: A review of challenges and opportunities. *International Journal of Research Publication and Reviews,* 5(12): 10.55248.

Naryzhny, S. and Legina, O. (2025). Selection of optimal protein sets as serological tumor marker signatures. *Biomeditsinskaya Khimiya,* 71(3): 163-194.

Panayides, A.S., Amini, A., Filipovic, N.D., Sharma, A., Tsaftaris, S.A., Young, A., ... and Kurc, T. (2020). AI in medical imaging informatics: Current challenges and future directions. *IEEE Journal of Biomedical and Health Informatics,* 24(7): 1837-1857.

Perniciano, A., Loddo, A., Di Ruberto, C. and Pes, B. (2025). Insights into radiomics: impact of feature selection and classification. *Multimedia Tools and Applications,* 84(26): 31695-31721.

Prince, E.W. (2025). User-centered artificial intelligence to support clinical interpretation of preoperative MRI for pediatric patients with Central Nervous System Tumors. University of Colorado Anschutz Medical Campus.

Rojas-Cadena, M., Rodríguez-Arcentales, F., Lata, W., Sacoto, K.M., Guerrero, L., Narváez Inca, K., ... and Izquierdo-Condoy, J.S. (2025). Unusual presentation of metastatic testicular mixed-germ cell tumor with intracardiac extension: A case report. *Journal of Clinical Medicine,* 14(10): 3564.

Scalia, G., Ferini, G., Shams, Z., Graziano, F., Ponzo, G., Giurato, E., ... and Galvano, G. (2024). Spinal metastases in non-seminomatous germ cell testicular tumors: Prognosis and integrated therapeutic approaches—A systematic review with an institutional case illustration. *Current Oncology,* 31(12): 7459.

Sharafaddini, A.M., Esfahani, K.K. and Mansouri, N. (2025). Deep learning approaches to detect breast cancer: A comprehensive review. *Multimedia Tools and Applications,* 84(21): 24079-24190.

Sidhu, P.S., Yusuf, G.T., Sellars, M.E., Deganello, A., Fang, C. and Huang, D.Y. (2025). A review of multiparametric ultrasound imaging in the clinical setting: Scrotal contents. *Abdominal Radiology,* 50(3): 1363-1375.

Skopelidou, V., Hurník, P., Židlík, V., Tulinský, L., Lenz, J., Balner, T., ... and Škripková, M. (2023). Unnecessary orchiectomy due to atypical sarcoidosis manifesting as a unilateral scrotal mass: A case report and literature review. *Frontiers in Immunology,* 14: 1253120.

Solomon, C., Petea-Balea, D.-R., Dudea, S.M., Bene, I., Silaghi, C.A. and Lenghel, M.L. (2025). Role of ultrasound elastography and Contrast-Enhanced Ultrasound (CEUS) in diagnosis and management of malignant thyroid nodules—An update. *Diagnostics,* 15(5): 599.

Stüber, A.T., Coors, S., Schachtner, B., Weber, T., Rügamer, D., Bender, A., ... and Ricke, J. (2023). A comprehensive machine learning benchmark study for radiomics-based survival analysis of CT imaging data in patients with hepatic metastases of CRC. *Investigative Radiology,* 58(12): 874-881.

Tukhtaev, A., Turimov, D., Kim, J. and Kim, W. (2024). Feature selection and machine learning approaches for detecting sarcopenia through predictive modeling. *Mathematics,* 13(1): 98.

van der Voort, S.R., Incekara, F., Wijnenga, M.M., Kapas, G., Gardeniers, M., Schouten, J.W., ... and French, P.J. (2019). Predicting the 1p / 19q codeletion status of presumed low-grade glioma with an externally validated machine learning algorithm. *Clinical Cancer Research,* 25(24): 7455-7462.

Vilone, G. and Longo, L. (2021). Classification of explainable artificial intelligence methods through their output formats. *Machine Learning and Knowledge Extraction,* 3(3): 615-661.

Vollmer, S., Mateen, B.A., Bohner, G., Király, F.J., Ghani, R., Jonsson, P., ... and Myles, P. (2018). Machine learning and AI research for patient benefit: 20 critical questions on transparency, replicability, ethics and effectiveness. *arXiv preprint arXiv:1812.10404.*

Waqas, A. (2024). From graph theory for robust deep networks to graph learning for multimodal cancer analysis. University of South Florida.

Woznicki, P., Laqua, F.C., Al-Haj, A., Bley, T. and Baeßler, B. (2023). Addressing challenges in radiomics research: systematic review and repository of open-access cancer imaging datasets. *Insights into Imaging,* 14(1): 216.

Wu, C., Andaloussi, M.A., Hormuth, D.A., Lima, E.A., Lorenzo, G., Stowers, C.E., ... and Tamir, J.I. (2025). A critical assessment of artificial intelligence in magnetic resonance imaging of cancer. *NPJ Imaging,* 3(1): 15.

Xie, X.-Y. and Chen, R. (2025). Research progress of MRI-based radiomics in hepatocellular carcinoma. *Frontiers in Oncology,* 15: 1420599.

Yang, W., Contente, S. and Rahman, S. (2025). Virus-positive merkel cell carcinoma model supports unified cancer origin. *bioRxiv*, 2025.2005: 2006.652325.

Yang, Z., Xia, W., Lu, Z., Chen, Y., Li, X. and Zhang, Y. (2022). Hypernetwork-based personalized federated learning for multi-institutional CT imaging. *arXiv preprint arXiv:2206.03709.*

Zhang, B., Qi, S., Pan, X., Li, C., Yao, Y., Qian, W. and Guan, Y. (2021). Deep CNN model using CT radiomics feature mapping recognizes EGFR gene mutation status of lung adenocarcinoma. *Frontiers in Oncology,* 10: 598721.

Zhang, J., Li, R., Tan, X. and Wang, C. (2025). Targeting glypican-3 for liver cancer therapy: Clinical applications and detection methods. *Journal of Clinical and Translational Hepatology,* 13(8): 665.

Cite this article as: Rabeya Akbarbasha, Sudhakar Pachiappan, Sabarinath Chandrasekar and Sasirekha Arangannan (2026). Machine learning and radiomics in the preoperative differentiation of testicular germ cell tumor subtypes: Current landscape and future directions. *African Research Journal of Medical Sciences.* 3(1), 66-83. doi: 10.62587 / AFRJMS.3.1.2026.66-83.