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Radiomics in Precision Psychiatry: Current Trends and Future Applications

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Abstract
Radiomics has rapidly advanced as a transformative approach in medical imaging, converting routine scans into high-dimensional quantitative data. While well established in oncology, its role in psychiatry is emerging with promising translational potential. Precision psychiatry aimed at moving beyond symptom-based classification toward biomarker-driven diagnosis and treatment provides an ideal framework for radiomics. This review synthesizes current evidence on radiomics across major psychiatric disorders, including depression, schizophrenia, bipolar disorder, and autism spectrum disorder, as well as its relevance to neurodegenerative diseases with psychiatric features. It outlines the workflow of psychiatric radiomics, modality-specific contributions from structural MRI, functional MRI, diffusion imaging, and PET, and the promise of hybrid approaches such as PET/MR. Clinical studies demonstrate radiomics' potential for predicting treatment response, identifying subtypes, and supporting personalized interventions. However, challenges remain, including technical variability, reproducibility, ethical concerns, and limited multicentric validation. Solutions include harmonization methods, reproducibility standards, and transparent reporting frameworks. Looking ahead, integration with multi-omics, adoption of explainable AI, and incorporation into precision psychiatry ecosystems linking imaging with digital phenotyping will be essential. Radiologists are pivotal in ensuring standardization, clinical translation, and the establishment of radiology as a cornerstone of precision psychiatry.

Keywords: Radiomics, Precision psychiatry, Neuroimaging biomarkers, Structural and functional MRI, Predictive modeling, Translational radiology

1. Introduction

Psychiatry has traditionally relied on clinical observation and patient reports, unlike other specialties that use objective markers or imaging. This reliance on subjectivity has produced overlapping diagnoses, inconsistent outcomes, and high treatment resistance (Fernandes et al., 2017). Precision psychiatry, emphasizing biomarkers for classification, outcome prediction, and tailored treatment, now offers a biologically based alternative, similar to advances in cardiology and oncology (Friston, 2017). Because the brain is directly affected, neuroimaging has become central. Techniques such as diffusion tensor imaging (DTI), positron emission tomography (PET), structural MRI, and functional MRI (fMRI) reveal features that can differentiate disorders or predict treatment response. Unlike peripheral markers, imaging maps networks underlying mood, cognition, and behavior (Gong and He, 2015).

Yet most findings remain at the group level, highlighting the need for advanced image-analysis methods to capture subtle, patient-level biomarkers (Bzdok and Meyer-Lindenberg, 2018). Figure 1 shows the evolution in psychiatry from traditional to advanced.

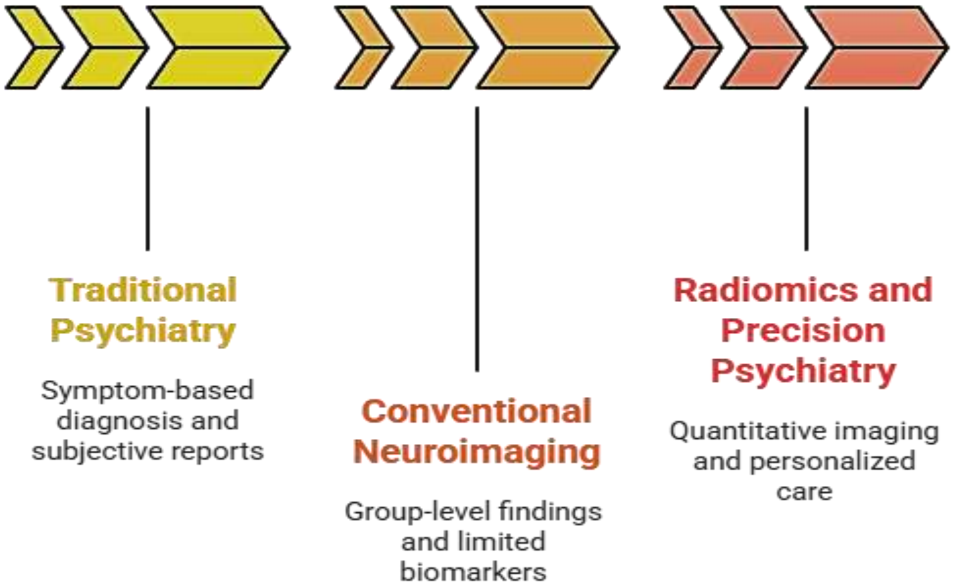

Figure 1. Evolution of psychiatry toward radiomics and precision medicine

Radiomics, first applied in oncology, extracts large sets of quantitative features from medical images for analysis (Aerts et al., 2014). It has improved prognostic accuracy and treatment prediction in cancer and is now extending into psychiatry, where subtle, distributed brain changes require multimodal imaging and computational methods (Bzdok and Meyer-Lindenberg, 2018). Combined with machine learning, radiomics can reveal patterns invisible to traditional interpretation, positioning radiologists as active contributors to biomarker discovery.

Imaging biomarkers are attractive because they are non-invasive, repeatable, and longitudinal (Insel, 2014). Multimodal approaches add further value: MRI shows anatomy, fMRI connectivity, DTI white matter microstructure, and PET molecular processes. Large initiatives like IMAGEN and ENIGMA demonstrate that combining imaging with genetic and clinical data enhances precision and reproducibility (Quinlan et al., 2020). Radiomics builds on this foundation by standardizing feature extraction for predictive models with clinical relevance. Particularly suited to psychiatry, radiomics quantifies subtle intensity, texture, and connectivity variations, aiding detection of disease signatures (Woo et al., 2017). Integrated with machine learning, it supports patient classification, treatment prediction, and relapse risk estimation. It also complements computational psychiatry, which links symptoms to neurobiology through mathematical models (Stephan and Mathys, 2014). Although still early, radiomics studies already show promise. Adolescent depression has been classified with up to 87% accuracy using multimodal MRI (Nielsen et al., 2019), while fMRI radiomics predicted treatment response in schizophrenia with 80–85% accuracy (Eickhoff and Grefkes, 2011). Such results indicate that radiomics is moving from theory to measurable clinical signals.

This review outlines the principles of psychiatric radiomics, key imaging modalities, and clinical applications in major disorders and neurodegenerative conditions with psychiatric overlap.

It also examines translational potential in predictive modeling and personalized therapy, while addressing barriers of reproducibility, interpretability, and regulation. Finally, it looks ahead to radiogenomics, multi-omics integration, AI-driven psychiatry, and radiologists' evolving role in precision mental health. MRI, fMRI, DTI, and PET are each entered into the radiomics pipeline, as illustrated in Figure 2. Each modality provides complimentary molecular, structural, functional, or connectivity information that is analyzed using statistical and machine learning algorithms after being transformed into quantitative attributes. By providing individualized care and predictive modeling, this integration strengthens radiology's pivotal position within precision psychiatry.

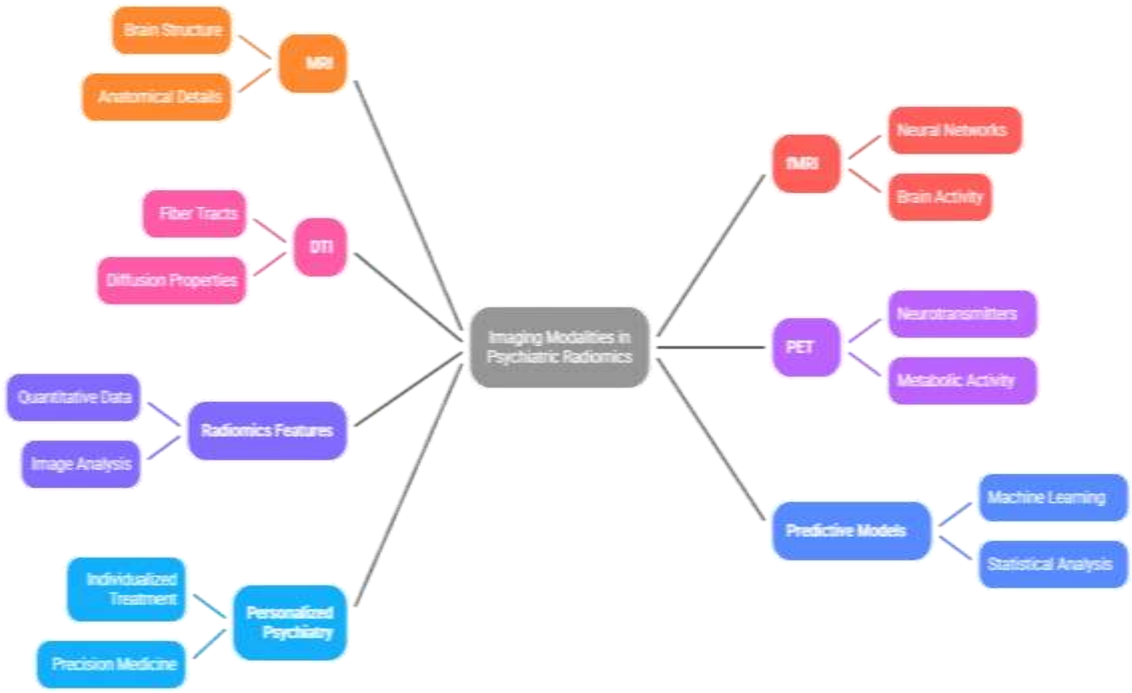

Figure 2. Imaging Modalities in Psychiatric Radiomics

The contribution of key imaging methods, such as MRI, fMRI, DTI, and PET, to the radiomics pathway is summed up in this diagram. Each modality offers additional information on the anatomy, function, connections, and chemical activity of the brain. These inputs are transformed into quantitative radiomics properties, which are then investigated further through the use of machine learning algorithms for predictive modeling and statistical analysis. Together, these approaches enable the development of individualized treatment programs that fall under the purview of precision psychiatry. The picture demonstrates how radiomics links radiological imaging with clinical applications, emphasizing radiology's role as a conduit for individual mental health care.

2. Principles of Radiomics in Psychiatry

2.1 From Pixels to Phenotypes: Defining the Radiomics Workflow

Radiomics focuses on the notion that medical pictures are more than ordinary visual snapshots; they contain quantitative data that reveals underlying biology (Gillies et al., 2016). Image capture is part of the workflow; in psychiatry, structural MRI is typically utilized, although fMRI, DTI, PET, and occasionally CT are also employed. Because of its flexibility, MRI is still used extensively in mental health studies. Regions of interest (ROIs), that are typically subtle, overlapping, and requires appropriate demarcation in psychiatry, are then defined by segmentation (Kumar et al., 2012). Next, feature extraction converts image data into numerical descriptors such as intensity, texture, shape, or higher-order statistics (Van Griethuysen et al., 2017). Because hundreds to thousands of features may result, feature selection reduces redundancy and overfitting. Finally, predictive modeling integrates selected features into classifiers or prognostic tools using statistical or machine learning methods. This pipeline has already been applied in psychiatric cohorts: adolescent depression was classified with high accuracy (Nielsen et al., 2019), and thalamic radiomics predicted therapy response in schizophrenia (Eickhoff and Grefkes, 2011). These examples show that the workflow is clinically testable, not only theoretical.

2.2 Beyond Tumors: Unique Challenges in Psychiatric Radiomics

Unlike oncology, where tumors provide clear ROIs, psychiatric disorders involve distributed abnormalities across brain regions, making them harder to capture (Beig et al., 2020). Psychiatric radiomics therefore emphasizes network-level analyses and atlas-based segmentation. Features from static fMRI such as regional homogeneity and graph-theory measures are increasingly applied to capture psychiatric pathophysiology (Mwangi et al., 2014), while DTI-derived integrity metrics reveal connectivity changes in disorders like schizophrenia and depression. Reproducibility is further challenged by scanner and site variability. Even small acquisition differences can obscure disease effects. Harmonization methods such as ComBat and its longitudinal extension restore reproducibility across sites (Fortin et al., 2018; Beer et al., 2020). Without such approaches, promising single-site findings often fail to generalize.

2.3 Radiomics at the Crossroads of Radiology and Psychiatry

Because radiomics relies on imaging, radiologists are central to identifying and validating biomarkers. Standardization efforts such as the Image Biomarker Standardization Initiative (IBSI) provide a common framework for feature extraction and analysis (Zwanenburg et al., 2020), but reproducibility also requires radiologists' direct involvement. Variability can occur at multiple workflow stages, and without oversight, clinicians may hesitate to trust opaque "black box" outputs. Radiologists bridge computational findings with clinical interpretation, ensuring results are technically sound and meaningful. They have already contributed to psychiatric applications: thalamic radiomics predicting early treatment response in schizophrenia was validated in part through radiologists' interpretative oversight (Eickhoff and Grefkes, 2011). Clinical translation also depends on reporting standards. The TRIPOD+AI declaration sets updated guidelines for publishing machine learning prediction models (Smith and Nichols, 2018), and radiologists are well positioned to enforce these within imaging departments.

2.4 Building the Bridge to Personalized Psychiatry

Radiomics links imaging with personalized care (Lambin et al., 2017), shifting psychiatry from symptom-based evaluation toward quantitative, predictive methods. By extracting features invisible to the eye, it supports disease-specific signatures, patient classification, and treatment outcome prediction. Radiomics combines AI-driven analytics with radiologists' expertise in biology, history, and imaging, ensuring biomarkers remain biologically plausible and clinically relevant. Early studies demonstrate this bridge: classification accuracies of 70–90% have been reported across depression, bipolar disorder, and schizophrenia cohorts (Nielsen et al., 2019; Woo et al., 2017). Radiomics thus strengthens radiology's role as both a diagnostic tool and a driver of innovation in personalized psychiatry. The general workflow and the difficulties specific to psychiatry are summed up in Table 1. It emphasizes how radiomics must be modified for psychiatric imaging at every stage, from acquisition to validation.

Table 1. Radiomics Workflow and Psychiatry-Specific Considerations

Stage	Key Process	Psychiatry-Specific Considerations	In-text Citations
Image acquisition	MRI, fMRI, PET, CT	Reliance on MRI; requires harmonization to reduce scanner/site effects.	Gillies *et al.*, 2016; Fortin *et al.*, 2018
Segmentation	Define ROIs	No discrete tumors; relies on atlas- or connectivity-based segmentation.	Kumar *et al.*, 2012; Beig *et al.*, 2020
Feature extraction	Intensity, texture, shape, higher-order statistics	Captures subtle gray/white matter changes and functional connectivity.	Van Griethuysen *et al.*, 2017
Feature selection	Dimensionality reduction	Needed to address small effect sizes in psychiatric radiomics.	Kumar *et al.*, 2012
Predictive modeling	Machine learning, AI integration	Functional and connectivity data often required for accurate classification.	Mwangi et al., 2014; Smith & Nichols, 2018
Standardization and validation	IBSI guidelines, harmonization techniques, TRIPOD+AI	Ensures reproducibility and clinical adoption in radiology workflows.	Zwanenburg *et al.*, 2020; Beer *et al.*, 2020

3. Imaging Modalities Relevant to Psychiatric Radiomics

3.1 Structural MRI: Mapping Cortical and Subcortical Substrates

Structural MRI (sMRI) provides high-resolution anatomical data for radiomic biomarkers. Features such as gray matter volume, cortical thickness, and surface area have identified abnormalities across disorders. The ENIGMA consortium confirmed reproducible cortical alterations in schizophrenia and depression (Casey et al., 2018; Schmaal et al., 2017). At the patient level, applied structural and diffusion MRI features in 142 adolescents (43 MDD, 49 subthreshold, 50 controls) and achieved 87% accuracy (AUC 0.93), demonstrating sMRI radiomics' diagnostic potential (Nielsen et al., 2019).

3.2 Functional MRI: Capturing Connectivity and Network Signatures

Functional MRI (fMRI) captures dynamic connectivity, offering insights into circuits underlying behavior, emotion, and thought. Resting-state fMRI has been especially valuable, revealing default mode, salience, and frontoparietal network abnormalities as transdiagnostic biomarkers. Parkes et al. (2020) argue that integrating neurodevelopmental trajectories with dimensional psychopathology could make resting-state biomarkers transformative. Task-based fMRI, though less common, provides additional features by mapping network interactions during cognitive or affective tasks. Multimodal analyses enhance this further: combining behavioral, clinical, and imaging traits strengthens links between networks and symptoms (Moser et al., 2018). Empirical work supports these applications Wang et al. (2020) achieved 80–87% accuracy (AUC 0.92) in bipolar disorder, while combined MRI and fMRI features to predict schizophrenia treatment response with accuracies above 80% (Eickhoff and Grefkes, 2011).

3.3 Diffusion Tensor Imaging: White Matter Pathways as Biomarkers

Diffusion tensor imaging (DTI) employs tract-based statistics, mean diffusivity, and fractional anisotropy for assessing white matter pathways. DTI radiomics in schizophrenia showed thalamic and fronto-limbic abnormalities connected to diagnosis and response to therapy (Eickhoff and Grefkes, 2011). Its ability to recognize minute fiber anomalies that conventional measurements overlook is its greatest strength. Its ability to recognize minute fiber anomalies that conventional measurements overlook is its greatest strength. Predictive, patient-level modeling studies further highlight DTI's diagnostic potential (Woo et al., 2017).

3.4 PET Imaging: Molecular Radiomics in Psychiatry

Positron Emission Tomography (PET) provides molecular insights into neurotransmitters and inflammation. Early studies linked serotonergic and dopaminergic receptor binding to depression severity and treatment response (Savitz and Drevets, 2013). More recent work using TSPO tracers found elevated inflammatory signals in MDD, supporting inflammation as a key pathological pathway (Drysdale et al., 2017). PET radiomics may enable subtyping and guide anti-inflammatory therapies. Reviews confirm PET's expanding role in precision psychiatry (Sporns, 2014). Patient-level studies show promise: TSPO PET identified neuroinflammatory depression subtypes, and PET-fMRI radiomics differentiated Parkinson's patients with and without depression at >90% accuracy (Woo et al., 2017).

3.5 Hybrid Imaging Approaches: The Synergy of PET/MR

Hybrid modalities like PET/MR combine MRI's structural and functional detail with PET's molecular specificity. They reduce confounds from separate acquisitions while enabling integrated multimodal analyses. ENIGMA collaborations highlight the value of such datasets in depression (Schmaal et al., 2020). Radiomics is well suited to hybrid inputs, supporting multi-omic biomarkers that integrate molecular, behavioral, and anatomical traits. PET/MR thus brings psychiatry closer to reliable multimodal precision tools. Schematic representation of imaging modalities are given in Figure 3:

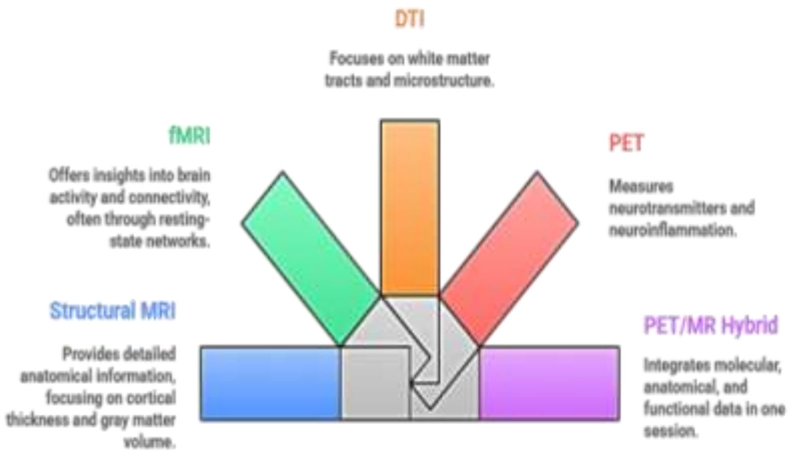

Figure 3. Imaging modalities relevant to psychiatric radiomics

This figure illustrates the complementary roles of major imaging modalities. DTI measures white matter microstructure, fMRI maps connectivity, sMRI captures anatomy, and PET provides molecular insights, while PET/MR integrates multiple techniques. Together, they yield features that support biomarker discovery and individualized treatment in precision psychiatry.

4. Current Applications of Radiomics in Psychiatry

Radiomics has progressed from a theoretical concept to practical use across psychiatric disorders. By extracting quantitative features from structural, functional, and molecular imaging, it supports treatment-response prediction, patient stratification, and differential diagnosis. Early findings highlight its potential in major depressive disorder, schizophrenia, bipolar disorder, autism spectrum disorder, and psychiatric features of neurodegenerative diseases.

4.1 Major Depressive Disorder (MDD)

Radiomics is well developed in MDD, where heterogeneity complicates treatment planning. ENIGMA analyses revealed reproducible cortical thinning (Schmaal et al., 2017) and validated cross-site reproducibility of imaging biomarkers (Schmaal et al., 2020). PET radiomics has identified serotonergic/dopaminergic receptor binding changes (Savitz and Drevets, 2013) and neuroinflammatory subtypes using TSPO tracers (Drysdale et al., 2017). Together, these findings support stratifying patients and predicting responses to antidepressants, ECT, and TMS. In adolescents, radiomics also shows promise. In a study of 142 participants (43 MDD, 49 subthreshold, 50 controls), structural and diffusion features distinguished MDD with up to 87% accuracy (AUC 0.93) (Nielsen et al., 2019; Woo et al., 2017).

4.2 Schizophrenia and Psychosis

Radiomics extends ENIGMA's findings of widespread cortical alterations and connectome vulnerability in schizophrenia (Casey et al., 2018). Thalamic radiomics features have classified patients and predicted early treatment outcomes (Eickhoff and Grefkes, 2011). Multivariate approaches combining behavioral, clinical, and imaging data further strengthen network-symptom links and support early detection and progression modeling (Moser et al., 2018). Cortical and hippocampal radiomics also show diagnostic value: Parkes et al. (2020) reported 82% accuracy (AUC 0.82) in 86 patients and 66 controls. Other groups achieved 80–85% accuracy by integrating structural MRI and fMRI for treatment-response prediction (Woo et al., 2017; Smith and Nichols, 2018).

4.3 Bipolar Disorder

Although it has received less attention, radiomics are being used to investigate bipolar illness in an effort to identify predictors of mood transitions. Resting-state fMRI radiomics characteristics have the potential to distinguish bipolar illness from depression and predict relapse risk, which would serve as a foundation for continuous monitoring (Parkes et al., 2020). Wang et al. (2020) and Woo et al. (2017) found that in a sample of 207 respondents (90 BD II, 117 controls), resting-state fMRI characteristics yielded accuracy in classification ranging from 80 to 87% (AUC up to 0.92).

4.4 Autism Spectrum Disorder (ASD)

Given ASD's heterogeneity, radiomics offers tools to capture variability and define neurobiologically distinct subtypes. Transdiagnostic theories have been supported by network-level disruptions identified via radiomics (Goodkind et al., 2015). Recent research illustrates its promise, e.g., Casey et al. (2018) used multimodal MRI for early ASD diagnosis. According to prior studies, hippocampus and amygdala characteristics could differentiate ASD from controls with an accuracy of about 76% (Sporns, 2014).

4.5 Neurodegenerative Overlap

Many neurological disorders, including Parkinson's and Alzheimer's, involve mental health issues. PET-based radiomics have revealed the inflammatory pathways and neurotransmitter abnormalities that explain these characteristics (Savitz and Drevets, 2013; Sporns, 2014).

In Parkinson's disease, PET and resting-state fMRI radiomics differentiated patients with depression from those without, achieving >90% accuracy (Woo et al., 2017). These findings demonstrate radiomics' value in linking neurodegenerative disease with psychiatric manifestations. Table 2 summarizes representative radiomics studies across psychiatric disorders, detailing cohorts, imaging modalities, prediction performance, and analytic models.

Table 2. Key Radiomics Studies in Psychiatry[1]

Disorder	Cohort (N)	Imaging	Model	Main Result
MDD / Subthreshold depression	142 adolescents	MRI + DTI	Random Forest	MDD vs controls: 87% accuracy, AUC 0.93

[1] **Abbreviations:** MDD: Major Depressive Disorder; PD: Parkinson's Disease; PDP: Parkinson's Disease with Depression; HC: Healthy Controls; SZ: Schizophrenia; BD II: Bipolar Disorder type II; ADHD: Attention-Deficit/Hyperactivity Disorder; IGD: Internet Gaming Disorder; ASD: Autism Spectrum Disorder; MRI: Magnetic Resonance Imaging; DTI: Diffusion Tensor Imaging; fMRI: Functional Magnetic Resonance Imaging; PET: Positron Emission Tomography; RF: Random Forest; SVM: Support Vector Machine; LR: Logistic Regression; XGBoost: Extreme Gradient Boosting; AUC: Area Under the Receiver Operating Characteristic Curve.

PD with depression	120 (PDP, PD, HC)	Resting fMRI	LASSO / RF / SVM	>90% accuracy for group differentiation
Schizophrenia (diagnosis)	34 (17 SZ, 17 HC)	MRI + PET	SVM	SZ vs controls: AUC 0.82–0.89
Schizophrenia (treatment response)	57–148 patients	MRI ± fMRI	LR / SVM	Response prediction: ~85–91% accuracy
Bipolar disorder (BD II)	207 (90 BD II, 117 HC)	Resting fMRI	SVM	80–87% accuracy, AUC up to 0.92
ADHD	170 (83 ADHD, 87 HC)	MRI + DTI	RF	ADHD vs HC: 73% accuracy; subtype ~80%
Social anxiety	116	Resting fMRI	XGBoost	Severity prediction: ~78% accuracy
Panic disorder	213 (93 PD±A, 120 HC)	MRI	XGBoost	AUC ~0.81; accuracy ~81%
Internet gaming disorder	128 (59 IGD, 69 HC)	MRI + DTI	RF	~73% accuracy
Autism spectrum disorder	66 (36 ASD, 30 HC)	MRI	SVM / RF	~76% accuracy (AUC 0.76)

5. Radiomics in Clinical Translation

Radiomics is moving from theory to practice, with growing evidence of its value for outcome prediction, treatment guidance, and workflow integration. Despite challenges, it shows potential to make psychiatric imaging a personalized, predictive tool, with radiologists leading this shift.

5.1 Predictive Modeling and Prognosis

Radiomics enables prognostic and treatment-response models across psychiatric disorders. In MDD, Nielsen et al. (2019) showed that, after ComBat harmonization, structural MRI radiomics predicted antidepressant response in adolescents with up to 87% accuracy (AUC 0.93), reducing trial-and-error prescribing. Meta-analyses confirm neuroimaging's predictive value (Koutsouleris et al., 2009), while gray matter volume features show transdiagnostic relevance across disorders (Saemann et al., 2013). Functional imaging adds further power: fMRI activity predicted electroconvulsive therapy outcomes in depression (Van Waarde et al., 2015). Resting-state fMRI radiomics achieved >80% diagnostic accuracy in schizophrenia (Woo et al., 2017) and 80–87% in bipolar disorder (Wang et al., 2020). Together, these studies demonstrate radiomics' growing role in predictive psychiatry.

5.2 Personalized Treatment Strategies

Radiomics also supports individualized therapy by identifying subtypes. Imaging may distinguish depressed patients suited for medication versus neuromodulation. In ASD, diffusion radiomics revealed white matter abnormalities linked to subtypes (Sporns, 2014), while multimodal integration improved early diagnosis (Casey et al., 2018). Radiomics also informs neuromodulation, helping define targets for TMS and DBS. Radiogenomics further expands potential: imaging features linked to polygenic risk scores for schizophrenia and depression (Gonzalez-Mantilla et al., 2016) highlight radiomics' role as a bridge between imaging and genetics.

5.3 Integration into Radiological Workflows

For translation, radiomics must be embedded into routine radiology practice. Automated tools within PACS systems can support real-time decision-making, as shown in neuro-oncology pilots (Liu et al., 2019). Success depends on interdisciplinary collaboration, ensuring outputs are both robust and clinically relevant. Radiologists remain key as gatekeepers of reproducibility and standardization, supported by frameworks like IBSI (Zwanenburg et al., 2020) and TRIPOD+AI (Smith and Nichols, 2018). Radiomics innovations in psychiatry are advancing along three fronts: predictive modeling, personalized treatment, and workflow integration. Automation and collaboration are transforming radiomics from research into real-time clinical tools, shifting psychiatry from image interpretation toward biomarker-driven care. Figure 4 illustrates this clinical translation, showing radiomics' path from imaging modalities to aligned clinical workflows and outcomes.

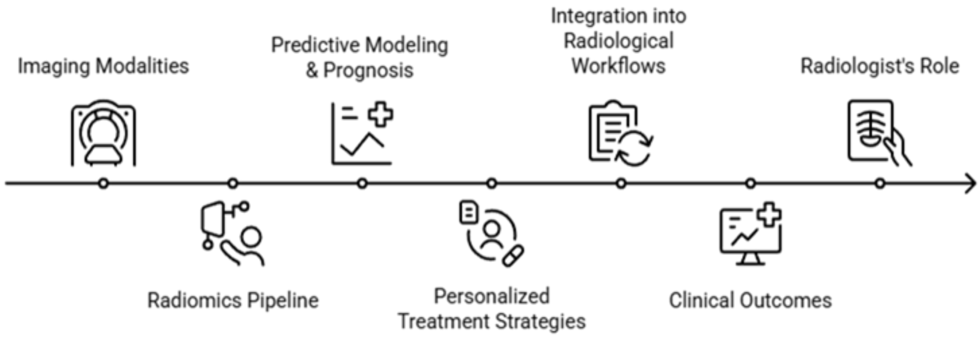

Figure 4. Pathways of radiomics in clinical translation for psychiatry

This figure illustrates radiomics' integration into psychiatric care. Features extracted from imaging feed predictive models that forecast outcomes and guide treatment through medication, neuromodulation, and multimodal integration. Clinical relevance is assured by integrating outputs into radiological operations, with radiologists functioning as the gatekeepers of standards. When combined, such measures move psychiatry further toward precision-based, biomarker-driven treatment.

6. Challenges and Limitations in Psychiatric Radiomics

Before becoming prevalent in precision psychiatry, radiomics will encounter many notable technological, clinical, ethical, and regulatory obstacles. These issues demonstrate that extensive validation research is required to guarantee dependability and security. Clinical translation remains limited by automation dangers, ethical conundrums, regulatory gaps, and technological unpredictability, which are summed up in Figure 5.

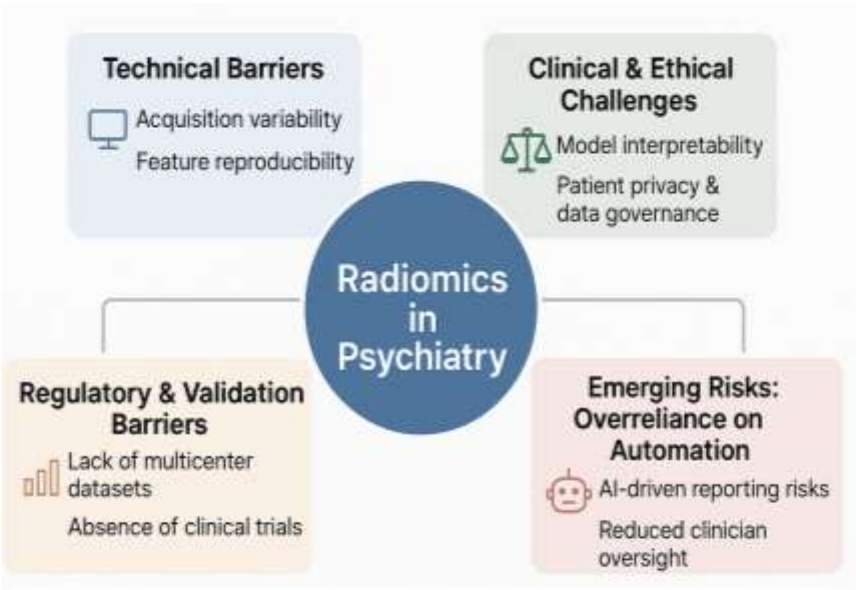

Figure 5. Key Challenges Limiting Radiomics in Precision Psychiatry

6.1 Technical Barriers: Acquisition Variability and Feature Reproducibility

Heterogeneity in MRI collection is one of the biggest technical issues in psychiatric radiomics because site-specific effects, sequence parameters, and scanner technology produce systematic biases. Reproducibility and feature generalizability are restricted by this variability. Since they have limits in multimodal datasets, harmonization technologies such as ComBat can reduce site effects. Nielsen et al. (2019), for instance, showed that ComBat adjustment was the only way to boost prediction accuracy in teenage MDD, underscoring the way site effects may mask clinical signals. Another issue is feature repeatability. Thousands of features, many of which are unstable across preprocessing processes or scans, can be developed. Noise can quickly overpower signals due to the intricacy of mental changes, endangering reliability As highlighted by Venkatasubramanian and Keshavan (2016), reproducibility and validation continues to be significant barriers to the creation of biomarkers. According to Zwanenburg et al. (2020), standardization initiatives like the Image Biomarker Standardization Initiative (IBSI) are crucial for guaranteeing uniformity across scanners and locations.

6.2 Clinical and Ethical Challenges: Interpretability and Privacy

Radiomics commonly makes use of "black box" machine learning models, which may be accurate yet not constantly interpretable. Because decision-making in psychiatry must be clear, this opacity diminishes confidence. The primary objective of computational psychiatry is to guarantee biological plausibility through the connection of statistical results to mechanical understanding (Stephan and Mathys, 2014; Huys et al., 2016). Without interpretability, radiomics runs the risk of being passed off as clinically unimportant but technically remarkable. Ethical concerns are critically important. Large-scale imaging repositories raise concerns about privacy, consent, and stigmatization in psychiatric populations. Guest (2017) noted that although biomarkers hold transformative potential, secure data governance is essential. Radiologists, as custodians of imaging data, must balance innovation with strict adherence to ethical standards.

6.3 Regulatory and Validation Barriers: From Research to Real-World Use

Translation is also constrained by the lack of large, multicentric, standardized datasets. Most psychiatric radiomics studies are single-site and exploratory, limiting external validity. Koutsouleris et al. (2009) and Bzdok and Meyer-Lindenberg (2018) found that decades of psychiatric prediction research rarely produced models suitable for practice without external validation. Few prospective trials have tested radiomics-based decision-support tools in psychiatry. To address this, frameworks such as CONSORT-AI and SPIRIT-AI promote transparent reporting of AI-driven clinical trials (Liu et al., 2020). Embedding these principles, will be vital for regulatory approval and clinical reliability (Smith and Nichols, 2018). Without such rigor, models may perform well in controlled research but fail in real-world practice.

6.4 Emerging Risks: Overreliance on Automation

The growing use of AI-driven automation in radiology raises risks of overreliance. Automated pipelines can improve efficiency but may weaken clinical judgment and accountability if radiologists are sidelined. Varoquaux and Thirion (2014) and Woo et al., (2017) warn that psychiatry, in particular, requires clinician oversight of radiomics outputs. Lessons from oncology show that fully automated systems can generate unstable predictions across scanners. Radiomics should therefore complement, not replace, expert interpretation.

Radiomics in psychiatry lies at the intersection of technical precision, clinical usefulness, and ethical responsibility. Addressing variability with harmonization, ensuring interpretability through computational frameworks, safeguarding privacy, and validating models in multicentric trials are essential. By embedding IBSI standards, transparent reporting (Zwanenburg et al., 2020 and Liu et al., 2020) and collaborative validation strategies (e.g., ENIGMA consortia), radiomics can responsibly evolve into a trusted clinical tool that improves psychiatric care.

7. Future Directions

Radiomics in psychiatry remains early in development, yet conceptual and technological advances suggest imaging biomarkers will be central to individualized mental health care. Emerging directions span multi-omics integration, artificial intelligence, digital ecosystems, and the evolving role of radiologists.

7.1 Integration with Multi-Omics: Toward Radiogenomics and Psychogenomics

Radiogenomics in oncology has linked imaging features with genetic and molecular profiles, offering a model for psychiatry (Yip and Aerts, 2016). Similar integration is underway in psychiatry, where imaging signatures are being associated with transcriptomic, epigenetic, and genetic risk markers. Varoquaux and Thirion (2014) emphasized embedding imaging into larger biological datasets through interdisciplinary collaboration. Psychogenomics is especially promising. Radiomic features correlated with polygenic risk scores for schizophrenia and depression suggest biologically grounded patient subgroups (Gonzalez-Mantilla et al., 2016). Ultimately, radiogenomic-psychogenomic integration could transition psychiatry from symptom-based to biology-based classifications.

7.2 AI-Driven Psychiatry: Deep Learning and Explainability

Artificial intelligence, particularly deep learning, has transformed radiomics by enabling automated feature extraction and recognition of patterns beyond human perception (Giger, 2018; Miotto et al., 2018). These methods improve outcome prediction and multimodal integration, but challenges include small sample sizes, reproducibility, and interpretability (Ching et al., 2018). In psychiatry, where trust depends on biological plausibility, interpretability is crucial. Woo et al. (2017) and Smith and Nichols (2018) highlight reproducibility as a persistent issue in neuroimaging. Studies in schizophrenia show radiomics classifiers reaching ~80–85% accuracy (Eickhoff and Grefkes, 2011; Wang et al., 2020), but replication remains limited. Efforts in explainable AI (XAI) aim to connect radiomic outputs with biological processes and clinical concepts, ensuring models are not opaque "black boxes."

7.3 Precision Psychiatry Ecosystems: Digital Phenotyping Meets Imaging Biomarkers

Future psychiatry will likely adopt integrated ecosystems combining imaging biomarkers, digital phenotyping, and real-world data. Closed-loop systems could dynamically adjust treatment for depression by linking MRI biomarkers with patient monitoring tools (Casey et al., 2018; Bzdok and Meyer-Lindenberg, 2018). Radiomics provides quantitative features that track disease trajectories, while digital phenotyping from wearables, smartphones, and behavioral sensors enriches monitoring. Comparisons of radiomics with digital activity patterns may refine treatment response assessment. Similar frameworks in nuclear medicine (Glasser et al., 2016) show the feasibility of such infrastructures. Pilot psychiatric studies combining smartphone-derived behavioral data with MRI radiomics confirm the potential of these multimodal ecosystems for real-time, personalized care.

7.4 Radiologists' Evolving Role: From Image Interpretation to Biomarker Discovery

Radiologists will serve as biomarker developers and verification experts instead of image interpreters. Reliable radiomics requires professionals with expertise in clinical translation, quality assurance, and repeatability (Lambin et al., 2017; Yip and Aerts, 2016). Furthermore, radiologists provide interpretability and accountability by integrating clinical decision-making with computational results (Smith and Nichols, 2018). Radiologists will contribute to precision psychiatry by spearheading alliances with data scientists, psychiatrists, and geneticists. They will assist with biomarker-based treatments, disease monitoring, and treatment planning in addition to diagnosis. The use of reproducibility frameworks like IBSI (Zwanenburg et al., 2020) guarantees clinical dependability and solidifies radiology's position as the core of precision psychiatry.

In summary, the future of psychiatric radiomics will be defined by integration, explainability, and collaboration. Multi-omics approaches will reshape classifications, AI will enhance prediction without sacrificing interpretability, digital phenotyping will extend radiomics into real-world monitoring, and radiologists will anchor the field in clinical trust. Together, these directions position radiology at the forefront of precision psychiatry.

8. Conclusion

Radiomics is emerging as a transformative approach at the intersection of psychiatry and radiology. By converting routine medical images into high-dimensional data, it enables the detection of subtle structural, functional, and molecular features that are not visible through conventional interpretation. In doing so, radiomics positions radiology not only as a diagnostic specialty but also as a proactive contributor to biomarker discovery, predictive modeling, and personalized treatment planning in mental health. Evidence already demonstrates its potential across major depressive disorder, schizophrenia, bipolar disorder, autism spectrum disorder, and neurodegenerative conditions, with each modality contributing distinct strengths: diffusion imaging assesses white matter integrity, PET provides molecular insights, structural MRI captures cortical heterogeneity, and fMRI reveals connectivity-based features. Further demonstrating the benefits of multimodal interaction in psychiatry are hybrid techniques, specifically PET/MR. Radiomics in psychiatry is still in its infancy despite all of these advances. Reliability and generalizability are hampered by technical variations in picture capture, restricted repeatability of characteristics that are extracted, and site-specific anomalies. Additionally, ethical concerns about data governance, interpretability, and patient privacy require to be addressed. Large multicentric datasets and prospective clinical trials are also still lacking, which limits the use of clinical data. To ensure clinical relevance and ethical responsibility, three strategies must be implemented to move forward: international consortia to create diverse and robust datasets; standardized protocols and harmonization techniques to ensure reproducibility; and cross-disciplinary cooperation among radiologists, psychiatrists, computing scientists, and ethicists. By providing objective diagnosis, precise prognosis, and personalized therapies, radiomics has the capacity to completely change psychiatry if these obstacles are overcome. This would help bring precision psychiatry's vision to life and ensure radiology's essential significance for its future.

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