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APPLICATIONS OF RADIOMICS AND ARTIFICIAL INTELLIGENCE IN PEDIATRIC NEURO-ONCOLOGY IMAGING: BALANCING INNOVATION WITH CLINICAL REALITY – A NARRATIVE REVIEW

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ABSTRACT

Background: Pediatric brain tumors are the most common solid tumors in children, and they continue to have an important impact on cancer-related morbidity and mortality. Radiomics imaging and artificial intelligence are transforming disease diagnosis and treatment by enhancing precision and reducing the need for invasive procedures.

Aim: The aim of this study is to provide a comprehensive analysis of the current applications, challenges, and prospective advancements of radiomics and artificial intelligence in pediatric neuro-oncology.

Methods: Recent peer-reviewed studies in pediatric radiology, oncology, and data science were utilized to conduct a narrative review. The primary subjects were the basics of radiomics, prognosis modeling, treatment response evaluation, molecular subtyping, explainability, and regulatory issues.

Results: Radiomics allows for the extraction of quantitative features from standard imaging, leading to the creation of reproducible biomarkers for molecular profiling, diagnosis, and prognosis. AI-driven models have been demonstrated to be highly efficient for tumor delineation, mutation prediction, and distinguishing between true progression and pseudoprogression. Federated learning enables joint model development without exposing data, and multi omics integration deepens biological understanding. However, several essential issues continue to persist.

Conclusions: Radiomics and artificial intelligence have the potential to create a digital revolution in pediatric neuro-oncology by allowing for non-invasive diagnosis, personalized patient-centered treatment, and extended follow-up. To achieve therapeutic integration it is essential to establish common standards, ensure explainable AI and create fair global strategies. We anticipate that these technologies will significantly impact precision imaging in the field of pediatric oncology.

Keywords: pediatric neuro-oncology, radiomics, artificial intelligence, multi-omics integration, explainable ai, precision medicine

INTRODUCTION

Pediatric brain tumors are the most prevalent solid malignancies in childhood and continue to be the primary cause of cancer-related mortality among children and adolescents [1-6]. While less common than adult brain tumors, they pose a formidable threat to global health given the complexity of their biology, the severity of symptoms they cause, and their long-term impact on neurocognitive development and on quality of life. Such significant differences between pediatric malignancies of the brain and those in adults - with respect to molecular pathogenesis and developmental context - point to the unique environment of the developing brain. Both developmental anatomy and tumor genetics are main components of the pediatric-specific diagnostic and therapeutic approaches that should be performed on pediatric cancers of the brain since the pattern and prevalence have great differences between different age groups [7, 8].

In recent decades advances in neurosurgery, chemotherapy and radiotherapy have markedly improved survival rates. However, outcomes for aggressive and diffuse tumors, such as high-risk medulloblastomas and diffuse midline gliomas, continue to be dismal [1]. The biological characteristics of these tumors are reflected in their unique radiologic and molecular signatures, underscoring the necessity of precise imaging methods that can capture both structural and molecular heterogeneity [3, 5]. The establishment of comprehensive pediatric tumor registries and standardized imaging databases, in conjunction with timely and accurate diagnosis, is crucial for the acceleration of therapeutic advancements, the facilitation of multicenter research, and the enhancement of prognosis.

Imaging is the mainstay of pediatric neuro-oncology. Magnetic resonance imaging (MRI) remains the most effective modality for the detection, characterization, and monitoring of malignancies, owing to its superior soft-tissue contrast and absence of ionizing radiation [3, 9]. Advanced MRI sequences, including diffusion- and perfusion-weighted imaging, further improve the evaluation of tumor cellularity, vascularity, and therapeutic response [10]. Computed tomography becomes another diagnostic modality in acute states with osseous, hemorrhagic, or calcified lesions. Its use, however, is intentionally limited to reduce radiation exposure in children [11].

Conventional image interpretation is predominantly qualitative, depending on the observer's subjective evaluations of morphological alterations. This could miss minor imaging biomarkers, which may indicate genetic or microstructural anomalies. This limitation is resolved by radiomics, which extracts a comprehensive array of quantitative imaging features—including intensity, texture, shape, and spatial relationships—that objectively characterize tumor heterogeneity and phenotype [12-14]. Radiomic analysis has been shown to be effective in the differential diagnosis of posterior fossa tumors, the assessment of glioma grades, and the prediction of critical mutations, including H3K27M and BRAF [12, 15-20]. To establish a connection between phenotype and genotype and to facilitate the development of integrated precision oncology, radiogenomics combines genomic and transcriptome profiles with imaging-derived signals.

Artificial intelligence (AI) development has rendered quantitative imaging more advantageous. Classical machine learning techniques, including support vector machines and random forests, are dependent on radiomic characteristics that are human-designed. In contrast, convolutional neural networks (CNNs) are among the deep learning (DL) models that have the ability to autonomously extract intricate, hierarchical representations from imaging data. Artificial intelligence has demonstrated promising applications in predicting survival or treatment response, tumor segmentation, classification, and non-invasive molecular subtyping in pediatric populations [7, 21, 22]. Automated segmentation techniques in the PACS environment allow for immediate assessment, reduce processing time, and minimize manual variation [23]. Integrating clinical and genomic data with AI may yield biologically informed and personalized therapies for pediatric brain tumor patients [18, 21].

However, significant ethical, methodological, and technological challenges continue to exist. The inherently limited size, heterogeneity, and occasional imbalance of pediatric imaging datasets constrain the generalizability and external validity of trained models [9]. The significant alteration of radiomic feature distributions due to differences in scanner types, acquisition methodologies, and image preparation highlights the imperative for harmonization and uniformity among institutions [12, 24]. Moreover, the interpretability of AI-generated biomarkers poses a significant barrier to clinical application, as numerous models operate as opaque "black boxes" with restricted biological transparency [25]. In pediatric research, protecting children and ensuring the long-term security of their data are paramount, alongside ethical considerations including data privacy, equity, and informed consent [26-28].

Radiomics and artificial intelligence are revolutionary tools in pediatric neuro-oncology, notwithstanding the challenges they pose. These technologies provide objective, quantifiable, and physiologically relevant biomarkers that improve diagnosis, facilitate future predictions, and tailor treatment. The combination of genetic, computational, and imaging data announces the beginning of a new era in precision pediatric neuro-oncology. In this new era, AI-generated insights can help physicians make decisions that are more ethical, precise, and timely.

OBJECTIVE

The objective of this review is to provide a comprehensive overview of the current applications of radiomics and artificial intelligence in pediatric brain tumors, identify the primary obstacles to clinical translation, and emphasize emergent opportunities for the integration of these technologies into precision medicine for children.

Research objectives:

1. Synthesis of existing data on the use of radiomics and artificial intelligence in pediatric neuro-oncology.
2. Systematization of AI applications in classification, segmentation, radiogenomics, and prognostication.
3. Description of technical and methodological limitations.
4. Analysis of challenges related to standardization, small cohorts, and reproducibility.
5. Identification of future directions and opportunities for clinical integration of AI.

MATERIALS AND METHODS

This narrative review was conducted in accordance with the Scale for the Assessment of Narrative Review Articles (SANRA) and established methodological standards for medical literature reviews to ensure transparency, comprehensiveness, and methodological rigor.

Search Methodology: A comprehensive search was performed in PubMed, which employed combinations of pediatric, brain tumor, radiomics, artificial intelligence, machine learning, deep learning, and multi-omics in research phrases. We also manually reviewed the reference lists of relevant review papers to identify additional studies that met the requirements.

Selection criteria:

The following were the inclusion criteria:

1. Original or review articles that have undergone peer review and are published in English;
2. Research focused on pediatric brain tumors or specific cohorts within the pediatric population;
3. Research focused on radiogenomics, AI-enhanced imaging methodologies, radiomic analysis, or the integration of multi-omics.
4. The requirement of at least abstract and methodological specifications that enable to judge the study design.

The literature search covered the period from 2010 to 2024. The last search update was performed on 15 November 2024. A total of 67 studies met the inclusion criteria, based on relevance to pediatric neuro-oncology imaging, radiomics, artificial intelligence, or multi omics integration.

The exclusion criteria encompassed conference papers, letters, editorials, case reports devoid of radiomic or AI elements, and studies solely concentrated on adult populations.

Integration and Extraction of Data**:** The texts of qualifying papers were assessed to confirm their pertinence to pediatric neuro-oncology imaging. Data were gathered from each study concerning the imaging modality (MRI, CT, PET/MRI), tumor type, cohort size, computational methodologies (radiomics pipeline, AI algorithm, validation technique), and clinical outcomes (diagnosis, molecular prediction, prognosis, or therapeutic response). The literature was qualitatively synthesized, and the results were narratively organized into thematic areas that corresponded to the sections of this review.

To resolve discrepancies in the study's interpretation, consensus was implemented. Utilizing PubMed or official publisher databases, we verified the authenticity and traceability of all references.

RESULTS

1. RADIOMICS AND ARTIFICIAL INTELLIGENCE IN PEDIATRIC NEURO-ONCOLOGY IMAGING

1.1. Fundamentals of Radiomics

Radiomics is the process of transforming regular scans into high-dimensional datasets that improve precision medicine by comprehensively acquiring superior quantitative traits from medical images [3, 7, 12, 14, 29]. It is an approach that helps to objectively and reproducibly identify malignancies by transforming visual patterns into quantitative data and is effective in practice when combined with traditional radiological evaluation. The spatial and biological heterogeneity of the tumor phenotype is captured by the extracted features, which include first-order intensity, higher-order texture, morphology, and wavelet-transformed patterns, thereby surpassing human perception [7, 8, 12, 14, 30]. These characteristics offer a glimpse into the microstructural complexity, perfusion variability, and necrotic patterns that may be associated with the therapeutic response and aggressiveness of the tumor. Radiomics offers reproducible quantitative biomarkers that are consistent with histology, molecular profiles, and clinical outcomes, thereby enhancing the development of personalized treatment plans and risk stratification in contrast to qualitative interpretation [25, 31, 32].

The integration of genetics and imaging in this data-centric approach facilitates the emergence of radiogenomics, in which the prediction of genetic mutations or changes in pathways is possible through the use of imaging-derived signals. In pediatric neuro-oncology, radiomics-derived texture and perfusion metrics can non-invasively differentiate tumor grades, genetic subtypes, and therapeutic responses [3, 7, 8, 29].

1.2. Radiomics and Advanced MRI Modalities

1.2.1. Diffusion-Weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI)

Diffusion imaging provides important information about the cellularity and microstructure of tumors, thus enabling the observation of the biological behavior of brain tumors beyond that possible with conventional anatomical tests [8]. In fact, DWI and DTI may allow an indirect judgment of the integrity of white matter pathways, cellular architecture, and tissue density by quantifying the stochastic movement of water molecules within tissues. These are significant findings for tumor classification and the development of therapeutic schemes since they reflect histological features, including necrosis, edema, and cellular proliferation [8].

Radiomics, particularly DWI and DTI, have significantly enhanced the capacity to distinguish between primary posterior fossa tumor forms, such as medulloblastomas, pilocytic astrocytomas, ependymomas, and other cerebellar neoplasms, in diffusion MRI. Radiomic analysis enables the acquisition of a broad spectrum of diffusion-based parameters that characterize tumor heterogeneity at the microstructural level. This approach provides an even better depiction than standard diffusion metrics, facilitating the ability to see subtle alterations in the texture of the lesion. The ADC (apparent diffusion coefficient) histogram and texture-derived features are more accurate than traditional mean ADC measures when it comes to determining different types and subtypes of tumors [4, 33-35]. These methods could facilitate noninvasive predictions of tumor behavior and treatment response, as well as enhance diagnostic accuracy.

Further evidence indicates that radiomic parameters from DWI can differentiate between high-grade and low-grade juvenile gliomas [24]. Complex spatial heterogeneity that reflects differences in cellularity and microenvironmental structure within the tumor can be reliably represented by radiomic models that employ diffusion imaging. By assessing the directionality of water diffusion, diffusion tensor imaging (DTI) enhances diagnostic accuracy, enables pre-surgical planning, and provides understanding of tumor infiltration along white matter pathways [8].

The association of texture-based diffusion characteristics with early treatment responses in diffuse midline gliomas suggests their potential as biomarkers for evaluating therapeutic efficacy [1]. The combination of DWI-radiomics and machine learning classifiers makes it possible to combine different diffusion-derived parameters into predictive algorithms. This process improves the specificity of the differentiation between genuine tumor recurrence and post-treatment conditions such as radiation necrosis or pseudoprogression [36].

1.2.2. Perfusion Imaging

Imaging of perfusion gives us significant data about tumor vascularity, hemodynamic condition, and tissue viability, adding to what diffusion-based and structural MRI can provide us with. Perfusion techniques can non-invasively quantify microvascular density, perfusion pressure, and vascular permeability based on the analysis of the passage of contrast substances through brain capillaries. All these features are closely related to the malignancy grade and tumor angiogenesis [1, 3]. Principal techniques for quantifying hemodynamic fluctuations include dynamic contrast-enhanced (DCE) MRI and dynamic susceptibility contrast (DSC) MRI. They provide metrics that include cerebral blood volume, cerebral blood flow, and leakage coefficients, which can be used in the assessment of the effectiveness of blood supply to a tumor and the neovascularization process [1, 3].

Perfusion radiomics enhances conventional imaging biomarkers by extracting high-dimensional quantitative features from perfusion maps. This enables us to look at the physiology and diversity of tumor vascular systems in more detail [30]. To identify subtle variations in blood volume and flow patterns that are undetectable to the human eye,

perfusion radiomics employ texture, shape, and histogram-based descriptors. These attributes have shown significant efficacy in the classification and prognostic assessment of gliomas in pediatric neuro-oncology, despite occasional restrictions on the histopathological sample. In pediatric patients with high-grade gliomas, texture-based perfusion characteristics have been associated with clinical outcomes, including progression-free survival and overall survival, and have revealed microvascular heterogeneity in tumors [30].

The incorporation of DSC and DCE-derived radiomic characteristics enhances the noninvasive prediction of molecular subtypes, which is crucial for the detection of H3K27M mutations. The identification of the most efficacious treatments for diffuse midline gliomas is contingent upon these mutations [19, 30]. Integration of clinical and genetic data with radiomic parameters from perfusion improves prognostic modeling by facilitating more accurate risk stratification and survival prediction in pediatric glioblastoma [1, 3]. This comprehensive approach extends the conventional imaging review for clinicians by providing information on the biological aggressiveness of the tumor and the expected response to treatment.

Perfusion radiomics is able to differentiate between and determine the risk of posterior fossa malignancies through the analysis of vascular patterns, yielding significant diagnostic insights. Perfusion-derived characteristics may function as preliminary indicators of treatment response by detecting changes in tumor perfusion prior to the emergence of structural abnormalities on MRI, and also facilitating diagnostic classification [37].

1.2.3. MR Spectroscopy

Magnetic resonance spectroscopy (MRS) quantifies essential metabolites, including choline, lactate, N-acetylaspartate (NAA), and myo-inositol, providing significant insights into the metabolic processes of brain tumors. These metabolites are indicative of energy utilization, neuronal functionality, and cellular turnover. By providing clinicians with a way to examine the chemical composition of tissue, MRS enables them to evaluate the aggressiveness of tumors as well as to differentiate between ongoing disease and treatment-induced alterations. This feature is distinct from conventional magnetic resonance imaging (MRI), which examines structural and morphological features. This method is especially important in juvenile neuro-oncology, as metabolic changes often occur before anatomical changes and can serve as an indicator of the efficacy of a treatment [8].

Radiomics, in conjunction with multi-voxel spectroscopy, has the potential to extract quantitative features from metabolite maps, thereby converting spectroscopic data into high-dimensional descriptors that illustrate spatial variations in tumor metabolism. This technique distinguishes between post-treatment effects and tumor recurrence, which may appear identical on conventional imaging. The synergistic importance of metabolic and morphological data in pediatric tumor evaluation is highlighted by the substantial enhancement in categorization accuracy when features from spectroscopy are integrated with those from structural MRI radiomics.

The most effective way to distinguish between active tumor tissue and necrosis or inflammation is to combine spectroscopy-based radiomics with diffusion and perfusion models, thereby significantly enhancing diagnostic accuracy [36]. Spectroscopic radiomics facilitates molecular and histological subtyping, as alterations in metabolite ratios, such as choline-to-NAA, are associated with aggressive biological behavior and unfavorable outcomes in pediatric gliomas [8]. Furthermore, early changes in lactate and choline-derived radiomic parameters may improve adaptive treatment strategies for pediatric brain tumor patients and can be considered as non-invasive biomarkers of response to therapy.

These applications are further extended by the inclusion of three-dimensional spectroscopic radiomics, which identifies metabolic heterogeneity across the whole tumor volume. This volumetric analysis extends our knowledge in terms of the unique characteristics of the different tumor components; it further allows personalized adjustment of treatment, targeted biopsies, and radiation planning. In the end, MRS poses a robust multiparametric imaging technique with a combination of metabolic and structural information that allows for increased diagnostic specificity, proper monitoring of treatment response, and finally personalized care in pediatric neuro-oncology.

1.3. Fundamentals of AI and Machine Learning

AI in medical imaging is an entirely new approach in data analysis, whereby computers detect complex patterns and make diagnostic predictions that augment the knowledge of radiologists. The AI in pediatric neuro-oncology empowers clinicians to obtain the most crucial knowledge from high-dimensional imaging data in order to reach a molecular categorization, early diagnosis, and even treatment monitoring. Deep learning and machine learning are two of the main types of artificial intelligence in imaging, which acquire knowledge and understanding of imaging characteristics through a variety of methods [7, 24, 29, 39].

Random forests, logistic regression, and support vector machines are machine learning algorithms that employ meticulously selected radiomic characteristics that are derived from imaging data. The intensity, morphology, and texture of the tumor are the characteristics that are quantified by these features, which allows the model to understand the correlations between these factors and histopathologic or molecular outcomes [7, 24, 29, 39, 40]. With proper feature selection, normalization, and cross-validation practices - even with small pediatric datasets that

exhibit a high amount of variability in the data - machine learning models can accurately predict different outcomes [12]. On the other hand, they depend on intensive data preprocessing, precise segmentation, and consistent feature extraction for best results in establishing repeatable findings in various settings and conditions [25, 29].

One of the deep learning methods that acquires hierarchical picture representations from raw data and thereby eliminates the need for human feature construction is convolutional neural networks (CNNs) [12, 24, 31, 41]. These networks independently recognize complex spatial and textural patterns, which allows for the training of a model from its inception to its completion, with feature extraction, selection, and classification all taking place within the same computational framework. With deep learning algorithms, several MRI inputs can be analyzed at the same time to pick out even slight imaging biomarkers of tumor biology that might not be detected by other methods. They can generalize well on a wide variety of datasets as well as are applied to enhance the interpretation of MRI imaging by radiologists through the conversion of standard MRI data into important biomarkers.

The integration of automated algorithms into pediatric neuro-oncology represents the next leap in personalized imaging diagnostics, enabling clinicians to rapidly, precisely, and reproducibly quantify tumor characteristics and response to therapy.

2. CLINICAL APPLICATIONS OF INTEGRATED RADIOMICS AND ARTIFICIAL INTELLIGENCE IN PEDIATRIC BRAIN TUMORS

2.1. Automated Segmentation

Precise tumor segmentation is a vital component of neuro-oncologic imaging and serves as a necessity for diagnosis, treatment planning, and response assessment. Segmentation is particularly important for pediatric brain tumors due to the considerable morphological differences between molecular subtypes and the often indistinct margins of the lesions. The manual delineation of tumor areas, which is considered the reference standard, is time-intensive, arduous, and subject to significant inter- and intra-observer variability, thereby compromising diagnostic consistency and repeatability [23, 24, 42]. The necessity of automated and standardized methods is underscored by the complexity of pediatric brain architecture and the small size of lesions, which complicate manual segmentation.

Deep learning models that have been trained on pediatric brain tumor datasets have exhibited segmentation accuracy that is comparable to that of experienced neuroradiologists [23, 36, 43, 44]. These models primarily employ convolutional neural networks (CNNs), which can directly learn to characterize tumor regions in terms of spatial and textural characteristics from imaging data. By automatically delineating tumor core, edema, and necrotic elements, deep learning-based segmentation enables volume measurement with unprecedented precision and allows for temporal and inter-center comparisons. Such automation will lighten the workload of physicians and allow the objective assessment of the treatment effect and tumor size.

The model may employ both structural and functional information as it incorporates different types of MRI data, such as diffusion, perfusion, and spectroscopy, thus enhancing segmentation. This multiparametric integration improves accuracy in various malignancies, including diffuse midline gliomas, where traditional single-sequence segmentation often may be inaccurate [1, 18]. Automated segmentation diminishes observer variability and produces consistent volumetric data across various institutions, facilitating comprehensive longitudinal and multicenter studies [18, 23, 42]. This uniform measurement is very important in the standardization of trials, performance of radiomics analysis, and evaluation of therapy.

Segmentation represents a critical step as it provides the foundation for the subsequent radiomic and radiogenomic analyses. The precise delineation of tumor regions markedly influences the clinical value of imaging biomarkers. Due care in segmentation is highly important for establishing a relationship between image-derived features such as texture, shape, and perfusion heterogeneity with molecular composition and gene expression changes. AI-driven segmentation pipelines represent methodologies to approach radiogenomic modeling, which provide high-quality, spatially resolved input that can be integrated with genomic and transcriptomic data for the detection of biologically significant imaging anomalies [18, 45].

Automated segmentation facilitates the consistent extraction of radiomic properties from different datasets and institutions through the establishment of reproducible regions of interest. This facilitates the identification of noninvasive imaging surrogates for tumor genotype in multicenter radiogenomic studies.

Automation is vital in differentiating tumor tissue from treatment effects, such as radiation necrosis or pseudoprogression, which can appear similarly on imaging studies [24, 32]. Deep learning algorithms can objectively discern complex imaging appearances more accurately than humans and are able to appreciate subtle patterns of intensity and texture. This can be achieved by embedding deep learning representations and handcrafted radiomic features within the hybrid machine learning and deep learning approaches, with much better accuracy and robustness than is possible by either approach independently [17].

2.2. Pediatric Brain Tumor Classification

Radiomics and artificial intelligence (AI) are revolutionizing pediatric neuro-oncology by rendering the objectivity and accuracy of brain tumor classification. To distinguish the most prevalent types of pediatric brain tumors, it is essential to analyze the spatial patterns and variability of MRI data. Multimodal models incorporating diffusion, perfusion, and MR spectroscopic characteristics are superior in tumor classification compared to single-sequence analyses, as they yield complementary information regarding the tumor's microstructure, vascularity, and metabolism [3, 17, 33, 46]. These combined computational methods show imaging biomarkers that are highly comparable to histopathologic and molecular traits, which boosts diagnostic confidence and enables biologically informed therapy planning. The apparent diffusion coefficient (ADC) histogram and texture-based features significantly improve diagnostic accuracy in differentiating medulloblastomas, pilocytic astrocytomas, ependymomas, and other cerebellar tumors compared to conventional mean ADC measurements [33-35, 38].

Artificial intelligence algorithms have improved these capabilities by automatically extracting discriminative image representations from large datasets. Indeed, several works have emphasized the performances of deep learning architectures, in particular CNNs, in classifying pediatric brain tumors, many of them reporting professional radiologist performance or even outperforming them [22, 47, 48]. Such algorithms identify diagnostic trends quite expertly across various types of imaging and across hospitals by capturing complex spatial correlations in imaging data [23]. AI models utilizing radiomic features from diffusion and perfusion have proven to be particularly effective in several applications, such as the detection of diffuse midline gliomas and posterior fossa tumors. Under these conditions even slight changes may make an important difference in the outcomes of treatment [1, 3, 8].

New radiogenomic methodologies expand these frameworks by incorporating noninvasive imaging with tumor genomics, thereby allowing correlations between imaging features and critical molecular and genetic alterations. Radiogenomic models can non-invasively identify WNT- and SHH-activated subgroups in medulloblastoma and differentiate between Group 3 and Group 4 tumors, thereby facilitating early molecular stratification [18, 28]. Diffusion and perfusion radiomics in genetically defined gliomas emphasize their biological interpretability through their association with MAPK/ERK signaling and metabolic reprogramming [36].

Integrating clinical variables, including patient age, tumor location, and presenting symptoms, into AI models improves their diagnostic accuracy and expands their applicability, allowing systems to emulate comprehensive clinical reasoning. These integrated pipelines exhibit tumor categorization accuracy that is either at or above the level of specialists [17, 22, 23, 33, 48, 49]. This standardizes, replicates, and improves the efficacy of diagnostic workflows. Thanks to all these improvements, contemporary pediatric neuro-oncology is progressing toward a precision imaging paradigm that combines quantitative biomarkers and computational intelligence to enable personalized diagnoses and therapies.

2.3. Molecular Subtyping of Pediatric Brain Tumors and Radiogenomics

Radiomics and artificial intelligence (AI) are crucial tools for the non-invasive molecular characterization of pediatric brain tumors, as they correlate imaging characteristics with their corresponding genomic profiles. Genetic differences substantially influence treatment strategies and prognoses, making precise molecular classification essential for guiding therapy. For deep-seated or widespread tumors, traditional molecular testing necessitates invasive biopsy, which may pose challenges or hazards in juvenile patients. By analyzing comprehensive tumor imaging data, which includes significant spatial and microstructural heterogeneity reflective of biological behavior and molecular state, radiomic–AI pipelines mitigate these limitations [1, 7, 38].

Radiomics offers quantitative, dependable alternatives for molecular classification and histopathologic grading. Quantitative metrics extracted from structural, diffusion, and perfusion magnetic resonance imaging (MRI) exhibit correlations with tumor cellularity, angiogenesis, and necrosis—critical indicators of malignant transformation [1, 7, 38]. Numerous investigations have demonstrated that radiomics can accurately predict BRAF mutations and fusions in low-grade gliomas [7, 16, 20, 21] - these mutations and fusions are crucial biomarkers for the selection of targeted therapy. Similarly, advanced MRI-derived radiomic signatures have been able to ascertain the H3K27M mutation status, which is a genetic mutation influencing the prognosis and treatment strategy in diffuse midline gliomas [7, 19]. The substantial repeatability of machine learning models in employing cerebral blood volume-derived radiomic parameters from a large number of locations has underlined the feasibility of a multicenter standardization for practical application [8]. Radiomic analysis showed that standard sequences such as T2 and FLAIR provide important indicators that allow for accurate molecular prediction and grading without requiring sophisticated specialized imaging techniques [7, 50].

Artificial intelligence enhances such capabilities by generating deep representations of tumor genetics as images on their own. AI-driven radiogenomic models merge deep learning frameworks with manually curated radiomic features to produce molecular predictions that are both generalizable and resilient across diverse institutions. These integrated models have appropriately identified BRAF-mutant low-grade gliomas [16, 20, 21, 24] and H3K27M-positive diffuse midline gliomas [19, 24] by including features from FLAIR, T1, and diffusion-weighted imaging. A random forest model employing FLAIR-based radiomics successfully distinguished BRAF V600E from BRAF fusion-positive

malignancies [16], while transfer learning improved repeatability across cohorts [21]. The integration of perfusion-based radiomic features and convolutional neural networks (CNNs) markedly enhanced the prediction of H3K27M mutations while also demonstrating correlations with molecular status and prognosis [8, 19, 30].

In medulloblastoma, radiogenomics and artificial intelligence have facilitated the precise molecular subtyping that is essential due to the significant differences in prognosis, treatment intensity, and survival rates among the WNT-activated, SHH-activated, and Group 3 and 4 subgroups [8, 24, 51]. The variability resulting from numerous chromosomal and epigenetic factors is clarified by radiomic analyses that utilize both conventional and sophisticated MRI sequences [1, 7, 8, 15, 38]. Multimodal approaches have been used to characterize the unique complexity of blood vessels and cells in each category, while texture- and wavelet-derived features are used to quantify tumor architecture. AI-augmented models, particularly CNN-based pipelines, have shown exceptional skill in differentiating Group 3 from Group 4 cancers, a differential diagnosis that is challenging given the similar imaging and histologic appearance of both tumors [18]. The interpretability of conventional radiomics is combined with the ability of artificial intelligence to acquire new features in novel deep learning–radiomics frameworks that have been developed for medulloblastoma. This integration facilitates risk-adapted therapy by enabling robust and consistent predictions regarding molecular subtypes [24, 51].

AI-driven multi-omics pipelines have now established a connection between imaging phenotypes and transcriptome, proteomic, and metabolomic profiles, superseding the integration of single-omics [18, 26, 45]. These radiomic-multi-omics models improve the biological interpretability and predictive accuracy, thereby enabling a more profound understanding of tumor heterogeneity, treatment response, and survival [15, 45]. Radiogenomics is transitioning from a descriptive approach to a multifaceted biomarker discovery platform that incorporates computational biology, pathology, and radiography. It is anticipated that multi-omics radiogenomic models will become indispensable in personalized care as a result of the continuous improvement of computational power and collaborative data infrastructures. The results will enable clinicians to deliver therapies that are both more effective and more precisely tailored to the personalized needs of each child.

2.4. Prognostication and Treatment Response

In pediatric neuro-oncology, prognostic modeling and treatment response evaluation are being transformed by radiomics and artificial intelligence (AI). The above techniques enable the development of non-invasive biomarkers that improve traditional histopathological and genomic data [8, 29]. These quantitative imaging characteristics yield significant insights into tumor biology and exhibit robust correlations with progression-free and overall survival in multicenter studies.

Radiomics analyses of diffusion and perfusion MRI sequences uncover texture and intensity patterns correlated with biological aggression, treatment responsiveness, and long-term outcomes. When combined with clinical data, radiomic models substantially improve the accuracy of risk assessment and survival predictions [6]. The selection of suitable treatment intensity can be guided by the classification of patients into high- and low-risk prognostic groups prior to treatment, utilizing baseline MRI-derived radiomic characteristics. Furthermore, metabolic radiomics derived from MR spectroscopy enhance the early identification of therapeutic response, as modifications in metabolite characteristics typically precede observable morphological changes [15].

Radiomics is crucial for both static predictions and therapy monitoring, especially in distinguishing between pseudoprogression and true progression, a persistent challenge following chemoradiotherapy [3, 24, 25, 50, 52]. Texture-noninvasive and perfusion-based radiomic signatures reveal subtle geographical and temporal variations, thereby diminishing diagnostic uncertainty during follow-up by differentiating transient treatment-related effects from true tumor recurrence. The use of machine learning classifiers on these variables has rendered clinical decision-making more specific and less difficult for patients to comprehend [9, 25, 32]. Moreover, sophisticated models integrating texture and perfusion data have attained enhanced predictive accuracy for long-term survival [3, 9]. All of these technologies point to a shift towards dynamic, image-guided precision therapy in pediatric neuro-oncology.

AI-driven frameworks enhance these capabilities by autonomously identifying intricate, nonlinear relationships among imaging, molecular, and clinical data. Deep learning (DL) and convolutional neural network (CNN) architectures have shown expert-level competency in predicting treatment response, recurrence, and outcomes when trained on multiparametric MRI [15, 22]. Convolutional Neural Networks (CNNs) are able to differentiate between pseudoprogression and real progression with a greater degree of accuracy than humans by analyzing the subtle variations in the intensity and spatial distribution of imaging signals [24, 25, 31, 32]. Application of these instruments reduces variability in the results among radiologists, thus improving data interpretation.

Long-term surveillance systems, enabled by AI, follow disease progression over time and change the way we assess treatment. Volumetric and texture analysis, through automation, can identify changes in tumor burden far earlier, thus enabling timely adjustment in therapeutic strategies, including adaptive treatments [53].

The table below summarizes the main themes addressed and their clinical relevance.

Table 1. Comparative overview of thematic pillars and clinical implications of radiomics and AI in pediatric neuro oncology

Dimension	Key points addressed	Clinical meaning
Radiomics foundations	Transformation of imaging into quantitative biomarkers linked to tumour biology and heterogeneity [1,15]	Enables noninvasive diagnosis and risk stratification [1,15]
AI and machine learning	Automated segmentation classification prognostication and radiogenomics including detecting progression versus pseudoprogression [17,22]	Improves diagnostic accuracy and clinical decisions [17,22]
Challenges	Small datasets lack of standardization, limited reproducibility, restricted interpretability, ethical and regulatory barriers [9,3]	Limits clinical implementation [9,3]
Opportunities	Collective data sharing privacy preserving model training reuse of existing models, understandable AI and development that reduces global disparities [58,59]	Creates pathways for scalability fairness and integration [58,59]
Clinical implications	Potential for personalised treatment, early prognostication, noninvasive monitoring treatment optimisation and reduced invasive procedures [5,29]	Supports a new precision imaging paradigm [5,29]

DISCUSSION

3. CHALLENGES ACROSS RADIOMICS AND AI

3.1. Limited Data Availability and Small Pediatric Cohorts

One of the most important translational challenges in radiomics and AI with regard to clinical application in pediatric neuro-oncology is the rarity of comprehensive, balanced datasets. With rare diseases such as pediatric brain cancers, let alone specific subtypes, statistically representative databases for the population are extremely hard to develop [1, 3, 8, 14, 18, 22]. This limitation complicates the application of AI models in a variety of healthcare settings and increases the probability of overfitting the data. The translational potential of artificial intelligence in pediatrics has been notably limited by the scarcity and heterogeneity of pediatric data, unlike adult oncology, which benefits from extensive imaging databases [21, 54].

Diffuse midline gliomas with H3K27M mutations exemplify this issue, as studies often encompass a restricted number of patients per cohort, thereby severely limiting external validation and statistical power [8]. Most AI evaluations, due to the infrequent inclusion of rare tumor subtypes, yield only models that fail to capture the full biological and clinical spectrum of pediatric brain cancers [1, 21]. Sampling bias may result from scanty and imbalanced datasets when the algorithm learns patterns specific to the training cohort rather than the underlying tumor biology. This issue elevates the likelihood that the model will deliver inaccurate outcomes, reduces the model's robustness, and limits clinical reliability [1, 14, 30, 36, 39, 40].

3.2. Reproducibility and Lack of Standardization

The clinical implementation of radiomics and artificial intelligence is significantly impeded by the issue of reproducibility. Radiomic features are highly susceptible to changes in imaging protocols, scanner hardware, acquisition parameters, and segmentation methods, which can significantly impact feature distributions and subsequent biomarkers [1, 12, 15, 43, 55]. Models developed at a single site frequently fail to replicate in external cohorts due to technical variability and inadequate harmonization [1]. The instability of numerous sophisticated radiomic parameters is illustrated by the significant impact that minor alterations in the acquisition or reconstruction of MRI can have on the values of texture- and wavelet-based features [55].

Variability among scanners stems from disparities in voxel resolution, contrast timing, magnetic field intensity, or

vendor-specific reconstruction techniques [1]. The variations in pediatric imaging are especially concerning as they add more uncertainty due to patient movement, sedation requirements, and the diversity of equipment across children's hospitals. Therefore, the predictive validity of even high-performing characteristics found in one dataset may decrease when evaluated in another dataset.

External validity is limited, and model outputs are inconsistent, which is further exacerbated by the lack of standardized preprocessing pipelines and quality control measures [1, 12, 55]. The lack of standardized methods for feature extraction, segmentation, and image acquisition can lead to inconsistent results among different institutions, which further complicates reproducibility and undermines trust in therapeutic applications. The Image Biomarker Standardization Initiative (IBSI), among other similar projects, aims to make the methods more harmonized, but those have not yet seen wide adoption. Standardization must be the primary objective for radiomics research at all stages, from acquisition to analysis. To ensure dependable translation into clinical practice, it is essential to establish open-access datasets, transparent reporting, and rigorous validation strategies that facilitate reproducibility testing across multiple centers.

3.3. Biological Interpretability and Validation

The derived features' limited biological interpretability is a significant challenge that radiomics has encountered, despite its strong prediction capabilities in numerous investigations. The majority of radiomic measures evaluate the geometric configuration, texture, or intensity of an image; however, their relationship with molecular or histopathological processes is frequently uncertain [9, 13, 25, 55]. The absence of transparency impedes the implementation of radiomics-based technologies in clinical practice, complicates regulatory assessment, and diminishes clinician confidence. Radiomic models devoid of a biological basis may function as "black boxes", generating statistically valid predictions without clarifying their underlying mechanisms [12, 25, 39, 56].

To attain clinical significance and credibility, radiomics must clarify the mechanistic relationships between tumor biology and image-derived attributes. Radiomic signals are generally more resilient and relevant across diverse datasets when biologically interpretable features correlate with molecular and genetic modifications, such as MGMT promoter methylation, IDH mutation, or 1p/19q co-deletion, as evidenced by studies [15]. These correlations indicate that specific imaging textures and intensity patterns may represent cellular density, necrosis, angiogenesis, or metabolic reprogramming, thereby connecting radiomic descriptions to tangible biological processes.

Biologically based radiomics enhances scientific credibility and clinical trust. Imaging biomarkers that have been validated against genetic or histological references are more robust in the face of variability across patient populations, institutions, and scanners. To ensure that radiomic characteristics accurately represent authentic biological processes rather than mere technological artifacts, it is essential to develop biological validation pipelines that include cross-modal correlation with genomic, proteomic, and metabolomic data [3, 7, 13, 45]. These pathways ultimately connect image-based analytics to clinical decision-making, facilitate regulatory acceptability, and enhance reproducibility. As radiomics continues to move toward integration with radiogenomics and multi-omics, biological interpretability will be an essential focus during clinical translation of radiomics in pediatric neuro-oncology.

3.4. Generalizability and External Validation

Restricted generalizability continues to pose a substantial obstacle in the field of clinical translation [1, 13, 24, 30, 39, 40, 55]. Models that have been trained on homogeneous datasets often overfit to the imaging properties, scanner parameters, or patient demographics that are unique to a particular institution. Such bias can lead to a decrease in performance when faced with unfamiliar data. These discrepancies illustrate the need for multicenter collaboration and external validation in radiomics research.

Numerous scientific publications indicate that perfusion-radiomics classifiers exhibiting outstanding performance in internal validation significantly underperformed on independent datasets, which demonstrates the vulnerability of models in the absence of external validation [30]. In the same vein, radiomic models that are derived from single-institution pediatric glioma cohorts have demonstrated a significant decline in multi-center evaluations. This decline is often attributed to demographic variability, variable imaging methodologies, and the lack of systematic preprocessing. Such limitations show that even the best-performing models could lack transferability in the absence of standardization across scanners and organizations.

The inadequate representation of rare tumor subtypes in training datasets significantly undermines generalizability [15, 17, 36]. As an example, the diagnostic accuracy decreases, even within the same institution, due to AI algorithms being unable to learn the imaging features of embryonal tumors or atypical teratoid/rhabdoid tumors (AT/RT) when not included in training [17]. Such systemic bias, resulting from the exclusion of some entities, undermines the clinical reliability of the models, which then tend to prefer more common tumor types.

Demographic and ethnic diversity also affect external validity. Models trained on pediatric cohorts from one region may have suboptimal performance with alternative populations. Imaging biomarkers influenced by genetic, anatomical, or environmental changes might show divergent behaviors across demographic groups, leading to

inconsistent predictive efficacy.

To address these limitations, forthcoming research must incorporate multi-institutional, demographically varied datasets and employ federated learning frameworks that enable collaborative model training while ensuring data confidentiality. Through such varieties of integrated endeavors, AI and radiomics can achieve the necessary reliability for clinical application. This will ensure that prediction technologies function effectively and equitably in real pediatric neuro-oncology practice.

3.5. Ethical, Legal, and Regulatory Issues

The integration of AI into pediatric neuro-oncology introduces complex ethical, legal, and regulatory challenges far beyond that posed in adult populations. Information related to children is considered particularly sensitive, as it may contain genetic and long-term health information with potential lasting consequences for privacy, identity, and insurability [7, 26, 28, 57]. Thus, it is essential to protect data and maintain ethical governance to facilitate AI research and its implementation. Given the rarity of pediatric brain malignancies, the development of a substantial AI model typically necessitates the collaboration of multiple institutions and the integration of genomic and imaging data. This requirement also raises new privacy issues that need to be addressed through advanced security measures, including federated learning, homomorphic encryption, and differential privacy. These protections facilitate collaborative model training while maintaining data confidentiality [26, 48].

Algorithmic bias is a significant ethical issue, particularly regarding data privacy [40, 58]. Most AI models are trained using data acquired from affluent institutions or from specific geographic regions and perform poorly in low-resourced settings, which might exacerbate health problems worldwide [58]. The underrepresentation of ethnic, socioeconomic, or demographic groups will lead to lower diagnostic performance and biased results within those populations [28]. This constitutes a grave ethical concern related to the benefits of technology being equitably shared pertaining to pediatric healthcare, as well as justice and inclusion.

AI applications in pediatric oncology are currently lagging behind those in adults because of the challenges related to meeting strict legal and regulatory requirements of safety, interpretability, and generalizability in rare diseases. The regulatory authorities require definitive evidence of algorithmic reliability and explainability before granting clinical approval; however, the small sample sizes and significant heterogeneity typical for pediatric neuro-oncology impede such validation.

This complicates matters for children, as AI tools must comply with data governance, ethical review, and regulations regarding parental consent. In the interest of patient safety and to comply with ethical considerations, it is important that standard international mechanisms for the validation and regulation of pediatric AI are established.

3.6. Integration into Clinical Workflows

Even the most innovative and most thoroughly tested AI algorithms will have a minimal impact on patient care if they are unable to be seamlessly incorporated into practical radiology workflows [25]. In pediatric neuro-oncology, the seamless integration with the existing hospital infrastructure is essential, as diagnostic decisions are time-sensitive and necessitate the collaboration of multiple specialists. To integrate AI tools effectively in their regular imaging responsibilities for the analysis of AI-generated results, radiologists need to connect directly to Picture Archiving and Communication Systems (PACS), Electronic Health Records (EHRs), and vendor-neutral archives. The utilization of systems that function as independent "add-ons" external to conventional radiography software may be restricted as a result of their alteration of operational procedures, which leads to reduced clinician engagement [40].

The interpretability and therapeutic utility of the AI output are equally important. Forecasts and visualizations should be transparent, accessible, and comprehensible to enable physicians, whether individually or at multidisciplinary tumor board meetings, to make decisions in a timely manner [1, 22, 40, 56]. Explainable AI frameworks, such as those providing confidence scores, feature importance analyses, or heatmaps, help engender trust and accountability for physicians in daily practice. This approach is especially important in pediatric diagnoses because these conditions have long-ranging effects on cognitive and developmental outcomes across the life course.

In most successful workflow integrations, immediate reactivity is usually important. AI outcomes must be accessible within seconds in urgent clinical scenarios, such as surgical planning or therapy modification, to influence immediate decision-making [39, 56]. AI tools should not replace experts; they should assist them in their decision-making processes. By seamlessly integrating them into the standard procedures of radiologists, they can standardize image interpretation, minimize variability, and enhance diagnostic efficiency, thus enabling the delivery of more consistent and expedited care for children.

3.7. Resource and Infrastructure Limitations

Beyond that, however, there are a number of problems that go far beyond the simply technical issues in terms of limiting the implementation of AI in pediatric neuro-oncology. What is more, variability in infrastructure, finances, and

human expertise further complicates its use. It is strikingly different between different universities in terms of secure data storage, fast processors, and robust digital infrastructure. This leads to a gradient of AI readiness throughout the world, with some areas being more ready than others [25, 48]. In many low-income or middle-income countries, limited access to sophisticated imaging technology, reliable internet, or adequate computer facilities hinders the carrying out of research on AI or the application of AI in clinical settings [25, 58]. As a result, the benefits of AI, such as early detection, prognostic modeling, and predicting therapeutic response, are often only available to well-funded academic institutions [43, 58].

The use of AI is further complicated by the necessity of human expertise. Professionals need to know more than the basics of radiology; they also need to possess knowledge about medical data science, software integration, and AI ethics [58]. This information is not evenly disseminated, and a significant number of hospitals are unable to manage AI workflows or understand algorithmic outputs due to a dearth of personnel. In low-resource environments, clinicians and data scientists are not provided with structured training programs. It indicates that AI programs depend on external sources, thereby rendering them of less value.

Yet, scalability is mostly limited by the high costs of maintaining infrastructure and software licensing, especially for public healthcare systems. These discrepancies therefore point to the need for capacity-building programs such as training programs, accessible AI tools, and international partnerships that foster equitable development and use. The healthcare landscape will otherwise continue to be unequal in the global distribution of AI's capacity for improvement in diagnostic accuracy and patient outcomes in the field of pediatric neuro-oncology [58].

4. OPPORTUNITIES AND FUTURE DIRECTIONS

4.1. Multicenter Collaboration and Data Sharing

The development of credible AI and radiomics models is contingent upon the extensive collaboration among multiple institutions and the sharing of substantial data, as juvenile brain tumors are rare and heterogeneous [7, 15, 25, 29, 36]. As previously mentioned, single-center studies, which are still prevalent in pediatric neuro-oncology research, frequently involve restricted disease ranges and limited patient populations, resulting in overfitting, insufficient reproducibility, and limited generalizability [1, 14, 15, 36, 40]. These narrow, homogeneous data sets undermine the validity of predictive and prognostic models as they cannot capture the wide biological and imaging heterogeneity between institutions and among individuals.

Large amounts of clinical data and imaging from different locations can be integrated to develop more complete and representative data sets that reflect the biological features of various kinds of pediatric cancers. Such collaborations bring in a wider array of imaging modalities, scanner types, and acquisition techniques that enhance the effectiveness of the model and increase its statistical power. They facilitate the inclusion of underrepresented groups and the development of rare tumor subtypes; hence, AI-driven analyses become clinically more relevant and equitable.

Successful collaboration between multiple centers requires an institutional commitment and establishment of clear regulations for standards related to data, its governance, and interoperability. The consistency in imaging techniques, protocols that define conditions for the acquisition of radiomic features, and cross-center calibration methodologies are decisive to reduce variability, thereby reinforcing outcomes' reliability [3, 7, 25, 29, 59]. Collaboration amongst institutions, made easier by shared ontologies and standardized data elements, allows for comparisons that are necessary and results in meta-analyses.

At the same time, it is essential to guarantee that all individuals have equal access to data. To participate in multicenter research networks, resource-constrained centers require support for their infrastructure and technology [28, 58]. Improving open-access databases, standardized imaging repositories, and collaborative algorithmic resources could help close the disparities in technology access between poor areas. Such collaborations ensure that AI technologies for pediatric neuro-oncology will help children worldwide, irrespective of their financial background and location, while enhancing the reliability of scientific endeavors.

4.2. Federated Learning (FL) and Transfer Learning (TL)

Institutions often restrict data sharing due to privacy regulations and ethical concerns about children's data, despite its essential nature. Indeed, FL has emerged as a transformative solution to these challenges. It allows institutions to collaborate in the training of AI models without the exchange of raw data [48, 54, 58, 60]. In this method, each participating site autonomously trains its models, sharing only the acquired parameters, with a single location that integrates these parameters together subsequently. The approach ensures data protection laws are adhered to and at the same time keeps children's sensitive genetic and imaging data safe.

Federated learning ensures the privacy of patient data and increases participation from all over the world, even from institutions with low computation resources or with legal restrictions on sharing the data. By combining data from various tumor subtypes and populations, federated learning models enhance representativeness and reduce single-center training biases [9, 56, 58, 60]. Federated frameworks can therefore accelerate global collaboration among

academic and clinical institutions to expedite the clinical and ethical development of AI systems for pediatric neuro-oncology.

TL helps FL address the significant problem of limited pediatric datasets. Transfer learning enhances models trained on large adult neuro-oncology datasets through the addition of smaller pediatric cohorts. This allows them to improve predictive accuracy by using the acquired image patterns [9, 54, 61], which is especially beneficial for molecular subtyping, predicting outcomes, and forecasting responses in medulloblastomas and gliomas [21]. Transfer learning enables pediatric models to initiate with a robust foundational representation derived from imaging of adult glioblastoma, thereby minimizing the volume of pediatric data required for effective model training.

Combined, the potential of federated learning and transfer learning opens great avenues to future improvements. Federated networks may establish their own respective privacy-protecting data ecosystems, while transfer learning can expedite progress by quickly adapting existing adult models for application to children. These techniques together mark an important juncture in the advance of AI in pediatric neuro-oncology toward a more scalable, ethical, and collaborative paradigm. This approach will lead to the development of precision medicine that is truly global in scope.

4.3. Understandable and User-Centered AI

For artificial intelligence (AI) to be useful in pediatric neuro-oncology, it needs to be accurate, technically sound, easy to understand, and open and reliable for doctors. The comprehension and evaluation of data within a therapeutic context are further complicated by the enduring existence of numerous models as "black boxes," notwithstanding the swift progress of AI-driven image analysis [62, 63]. Because of a lack of transparency, regulatory approval and broad clinical application remain considerably hindered, especially in pediatric care, where the ethical and patient safety standards are very high [27, 62, 63].

To overcome these weaknesses, the new field of XAI has developed techniques that explain algorithmic decisions, making them more understandable to humans [63, 64]. Techniques such as saliency maps, attention mechanisms, and feature attribution analyses can help explain a model's prediction by showing which parts of an image or which radiomic feature are highly influential. XAI supports radiologists and oncologists in deciding whether an algorithm's output is clinically valid by providing them with visual or numerical explanations for every decision. This boosts their assurance that AI may assist with diagnosis and treatment planning [22, 27, 59, 65]. This level of interpretability facilitates communication among various disciplines, thereby enhancing the ability of radiologists, oncologists, and surgeons to utilize AI insights more effectively in collaborative decision-making.

It is essential to seamlessly integrate explainability and usability [56]. AI systems that present data in straightforward and understandable formats, such as interactive interfaces or color-coded probability maps, enhance workflow efficiency and bolster diagnostic confidence. Research findings indicate that the incorporation of AI-generated results into the regular viewing environments of radiologists, supplemented by explicit visual explanations, enhances clinician trust and increases the likelihood of integrating these technologies into routine procedures [22]. User-centered design not only reduces the time required for data interpretation but also reduces diagnostic uncertainty. It also reinforces AI's role as a supportive clinical assistant rather than a substitute for human expertise by emphasizing the seamless integration of AI within clinical workflows and its comprehensibility [28, 56, 66].

In pediatrics, explainability encompasses an additional ethical dimension. Transparent AI technologies enable healthcare providers to elucidate complex diagnostic results for families and caregivers, thereby fostering collaborative decision-making and building trust in emotionally charged situations [27, 66]. Clinical integrity and ethical accountability should be preserved in pediatric neuro-oncology, in which many critical decisions are frequently necessary. Thus, more explainable and user-friendly AI is much needed. Integration of XAI into the clinical workflow will set a standard for the use of AI in pediatric medicine that is appropriate, understandable, and safe for patients.

4.4. Equity and Global Health Perspectives

Artificial intelligence could serve as a game-changer in improving global health disparities in pediatric neuro-oncology through enhanced diagnostic capabilities in resource-constrained settings [48]. In many low- and middle-income countries, timely and accurate diagnoses are limited due to a lack of high-resolution imaging, computational infrastructure, and fully trained radiologists. Application of AI diagnostic software on cloud-based or transportable systems enables smaller community hospitals to achieve diagnostic results comparable to specialized tertiary care institutions [58].

A tactical approach to ensuring fair usage of AI is by putting justice and inclusion first. Algorithm performance may differ in marginalized populations from those developed using data predominantly from wealthy groups, leading to systemic bias and inequities in health outcomes [28, 58]. To date, validation in subgroups, performance auditing of AI models across demographic variables, and transparency regarding the composition of datasets used are mandatory. International standards and fairness criteria have to be established for pediatric AI with further judgment in order to prevent new technologies from increasing existing unfairness - these tools must link areas where diagnosis and treatment exhibit significant differences.

While cloud-based AI systems with mobile health networks ensure more accessible diagnostics to low-resource settings, cloud-based AI with mobile health networks facilitates the feasibility of obtaining diagnostics in resource-constrained settings [58]. Such infrastructures would allow local clinicians to access international imaging datasets, expert consultations, and AI-driven analyses in real time. These solutions enable secure data sharing and remote model deployment over networked hospitals worldwide, thereby creating a continuous learning environment with shared knowledge.

These technologies will only be equitably available to all children if there is global collaboration on a delicate balance between ethical responsibility and technological advancement. This investment in open-access datasets, physician training, and digital infrastructure can ensure that artificial intelligence—in particular, personalized care, timely treatment monitoring, and improved diagnostic accuracy for all children, irrespective of their socioeconomic background and location—becomes a reality. If built on the principles of impartiality, inclusiveness, and collaboration, artificial intelligence has immense potential to enhance medical knowledge and promote global health equity in pediatric oncology.

CONCLUSION

Pediatric neuro-oncology is currently experiencing a transformative era powered by radiomics, artificial intelligence, and the integration of multi-omics. Conventional imaging, although essential for diagnosis and surveillance, no longer fully captures the biological intricacy of pediatric brain tumors. With radiomics and AI, high-dimensional imaging features can be acquired that reflect molecular alterations, treatment response, and outcomes to support precision medicine tailored to children. The current evidence indicates that AI improves tumor segmentation, molecular subtyping, and early treatment evaluation, while radiogenomic and federated learning frameworks foster reproducibility and data confidentiality. These advancements hold the potential for noninvasive, biologically significant biomarkers that minimize invasive procedures and enhance personalized therapy. However, progress remains limited due to small and different pediatric cohorts, protocol variability, limited interpretability, and ethical questions regarding privacy and bias. This calls for harmonized imaging standards, transparent algorithms, and fairness-driven regulation that ensures safety and equity in clinical translation. Establishing multicenter collaboration, robust validation, clinician education, and pediatric-specific regulatory frameworks is necessary for a successful future. When pursued collaboratively, radiomics and AI will emerge as essential elements of precision pediatric neuro-oncology, ensuring technical soundness, ethical responsibility, and accessibility for all children.

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AUTHORS' CONTRIBUTIONS

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USE OF ARTIFICIAL INTELLIGENCE

The authors state that artificial intelligence (ChatGPT) was employed only to assist with language refinement and manuscript organization. All aspects concerning paper design, data interpretation, content development, writing, and final approval were entirely the responsibility of the authors. This approach guarantees that the article's accuracy, integrity, and scientific value reflect the authors' independent scholarly work.

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