(Research Article)

Artificial intelligence for radiomics; diagnostic biomarkers for neuro-oncology

Farzan Vahedifard [1, *], Sara Hassani [2], Ali Afrasiabi [3] and Armin Modarresi Esfe [4]

[1] Department of Diagnostic Radiology and Nuclear Medicine, Rush Medical College, Chicago, USA.
[2] Goddard lab, Radiology department. Penn Medical University, Philadelphia, Pennsylvania, USA.
[3] Department of Internal Medicine, Iran University of Medical Science, Tehran, Iran.
[4] Department of Radiology, Ahwaz Jondishapour Medical University, Ahwaz, Iran.

Abstract

Recent advances in medical image analysis have been made to improve our understanding of how disease develops, behaves, and responds to treatment. Magnetic resonance imaging (MRI) and positron emission tomography (PET) advanced imaging strategies provide structural and functional phenotypic biomarkers that correlate with key disease processes.

Through radiomics and radiogenomics, ML-medical imaging has opened up new perspectives in high-grade glioma diagnosis. As a result, non-invasive and in vivo biomarkers for patient survival, tumor recurrence, and genomics are identified. Tumor genomic imaging signatures can help identify patients who benefit from targeted therapies. Molecular characterization of gliomas and prediction of their evolution would allow treatment optimization.

Radiomics-based biomarkers allow for a more in-depth analysis of pathophysiologic processes and insights into diagnosing better, classifying, stratifying, and prognosticating brain tumors and assessing their response to therapy. Radiomics is a new data-driven approach that can help answer clinical questions like diagnosis, prognosis, and treatment response. With encouraging outcomes in brain tumor patients, radiomics and deep learning are still not widely used in clinical practice, requiring more extensive and practical clinical studies.

Keywords: Brain Tumor; Artificial Intelligence; Biomarkers; Radiology; Deep Learning; Cancer

1. Introduction

Neuro-oncology addresses brain and CNS tumors, both primary and metastatic. Neuroimaging, together with histomolecular analysis of tissue samples from resection or biopsy, is used to diagnose in neuro -onclogoy. Contrast-enhanced MRI is preferred for brain tumor diagnosis, therapy planning, and monitoring. Advanced MRI and amino acid PET are now being used to generate a wide range of imaging characteristics for brain tumor diagnosis. The increased availability of combination PET/CT and PET/MRI scanners also helps [1]. Artificial intelligence (AI) algorithms can evaluate complicated multi-parametric imaging data, possibly assisting clinicians in clinical procedures [2]. Manual tasks like lesion identification and segmentation may be totally automated. In addition, the outcomes are more consistent, and inter-institutional comparability is improved [3].

One of the current clinical challenges in neuro-oncology is tailoring therapy to individual patients based on their survival results or reaction to conventional or experimental medicines. A powerful data-driven method, Radiomics extracts subvisual data from conventional radiographic imaging to provide clinically useful insights into diagnosis,

[*] Corresponding author: Farzan Vahedifard; Email: farzanvahedi@yahoo.com
Department of Diagnostic Radiology and Nuclear Medicine, Rush Medical College, Chicago, USA.

prediction, prognosis, and therapy response. Imaging biomarkers can help advance precision diagnoses by studying biological changes before, during, and after brain tumor treatment. A new field of imaging study, Radiomics, offers an almost infinite supply of potential imaging biomarkers for better patient and disease identification.

2. Precision disease diagnosis and classification

Because primary and metastatic brain cancers are histologically and genetically diverse, it is critical to understand how tumor heterogeneity affects cancer progression, therapeutic response, and prognosis/outcomes [4].

3. Neuro-Oncology Radiomics

Radiomics is a method of image analysis that entails extracting measurable characteristics that serve as biomarkers for structural and pathophysiological alterations in disease entities. Using radiomics, a numerical dataset is generated that can be parsed, processed, and evaluated using machine learning algorithms [5, 6]. Radiomics-based biomarkers may give critical information for diagnosing, classifying, and treating a variety of solid cancers. It also affects the treatment of neuro-oncological illnesses, such as low-grade gliomas, glioblastoma multiforme (GBM), and brain metastases [7]. The next-generation imaging biomarkers provided by radiomic signatures have implications for treating brain malignancies. There are several radiomics applications in this sector, including correct categorization of brain lesions (gliomas versus metastases, IDH-wild type vs. IDH-mutant tumors), therapy planning (prediction of radiation therapy response), and immunotherapy response evaluation.

4. Radiomics for GBM

One relevant example is GBM. GBM is a notoriously aggressive malignancy with high therapy resistance and recurrence rates due to molecular heterogeneity [8]. Radiomics has revealed tissue and molecular heterogeneity and linked it to genetic changes [9]. Furthermore, radiomics can measure GBM molecular heterogeneity at the transcriptome level, which may help classify/stratify GBMs [10]. Shofty et al. [11] used radiomics analysis of multi-parametric MRI to stage 1p/19q co-deleted low-grade gliomas with 92, 83, and 87 percent sensitivity, specificity, and accuracy. Many cancer types are being reclassified from histology to radiogenomic characteristics, which better align with therapy responsiveness [12].

5. Quantitive Imaging Biomarkers

A non-invasive imaging biomarker is a characteristic feature of an imaging study that tells us about a disease process [13]. These new biomarkers need to be linked to ground truths, such as imaging-based "gold standards," clinical outcomes, or pathologic evidence. This is the first step. Quantitative imaging biomarkers (QIB) are being used more and more in precision medicine because they help doctors figure out what is wrong with people [14]. The QIBs can be used as surrogate endpoints, which can significantly cut down on the time and costs [15] and speed up determining who responds and who does not.

6. Neuroradiology Biomarker in Challenging Situations

Neuroradiology can be employed in various situations, including when a diagnosis is in doubt or when a patient is not ready for intervention. The gold standard for carpal tunnel syndrome, for example, is a nerve conduction test, which is uncomfortable in pregnant patients (who have more carpal tunnel syndrome). However, we can use high-frequency ultrasonography instead. As a result, the median nerve can be utilized as a reliable diagnostic biomarker, according to Mirzasgari et al. study [16].

7. Brain tumor biomarker

Brain metastases from various primary tumors have multiple imaging biomarkers. Multiparametric MRI with ADC and perfusion-weighted sequences are commonly used. Also, Perfusion-weighted and permeability MRI have been used to detect and characterize malignant brain lesions [17]. Dynamic susceptibility contrast-enhanced MRI (DSC-MRI) data produced from relative cerebral blood volume (rCBV) and cerebral blood flow (rCBF) helped establish quantitative picture biomarkers. Conventional radiology plus specific maneuvers showed increased diagnostic accuracy [18, 19]. Higher rCBV in the peritumoral edema indicates a primary intrinsic tumor rather than pure vasogenic edema reported

in metastatic disease [20]. But ADC is unlikely to follow likewise. rCBV measurement from the solid tumoral area is a well-established biomarker for GBM [21].

8. New biomarkers for old diseases

Numerous diagnostic biomarkers can be used to detect cancer; some have received more attention than others. We can apply ancient pathological biomarkers in novel diagnostic criteria, which is intriguing. Tabriz et al., for example, demonstrated that Mast Cell Density had a positive connection with tumor grade in Transitional Cell Carcinoma [22]. Expression patterns of DNA repair proteins, such as those linked to microsatellite instability (MSI), have recently been discovered to be effective in predicting the prognosis of solid tumors [23].

9. Modeling disease prognosis

The histologic subtype and genetic alterations are not the only prognostic factors for brain tumors. Radiomics analysis can quantify most of these processes using wavelet transforms or Minkowski functionals [12]. In GBM, MR-based radiomics analysis predicts overall survival and progression-free survival [24]. Key molecular biomarkers like Ki-67 expression in low-grade gliomas or IDH mutation in GBM are predicted by Radiomics signatures [25]. By reclassifying malignancies depending on progression and prognosis, indolent cancers might be managed more conservatively, whereas aggressive tumors could be treated with a more aggressive therapeutic strategy. According to Davatzikos et al., radiomics-based molecular characteristics gave superior risk stratification of GBM than WHO classification [26]. Radiomics can also help identify medical consequences of brain tumors, such as epilepsy in low-grade glioma patients, allowing for better disease treatment [27].

10. Role of MRI

MRI is undeniably important in neuro-oncology. The approach is used in clinical practice and clinical studies to diagnose and monitor disease activity, guide therapy decisions, and assess treatment response. However, clinical MRI is still employed for qualitative, subjective interpretation of macrostructural characteristics rather than quantitative analyses that consider numerous pathophysiological aspects [28]. But quantitative imaging and imaging biomarker development is maturing. Advanced imaging techniques also reach the clinical arena, giving quantitative physiological imaging characteristics that drive imaging biomarkers' development, validation, and clinical use. Also, researchers are increasingly using computer analysis to turn medical images into objective high-dimensional data and create radiomic fingerprints of disease states [29].

Preoperative multi-parametric magnetic resonance imaging (MP-MRI) scans can characterize tumor infiltration and predict future tumor recurrence, maximizing resection extent, radiation dose, and target area [30]. After intravenous administration of gadolinium-based contrast agents, MRI perfusion can also investigate underlying tumor angiogenesis using metrics related to tumor perfusion and permeability [31]. MRI perfusion can offer information regarding tissue cerebral blood volume and perfusion (using dynamic susceptibility contrast-enhanced [DSC] MRI) or microvessel permeability and the extracellular space, depending on the technology used (using T1-weighted dynamic contrast-enhanced [DCE] MRI). The most typically estimated metrics in DSC-MRI for brain tumor evaluation are relative cerebral blood volume (rCBV), relative cerebral blood flow (rCBF), and mean transit time (MTT) [32].

Radiomics have been shown to be effective in patients with brain malignancies using MRI. Studies have shown that combining PET and MRI radiomics encodes more diagnostic information than each modality alone [33]. For example, coupled PET/MRI radiomics can predict molecular indicators like O6-methylguanine-DNA-methyltransferase promoter methylation or ATRX genotype.

11. Magnetic resonance spectroscopy (MRS)

The choline (Cho)/creatinine (Cr) ratio, for example, is lower in brain metastases than in GBMs when using magnetic resonance spectroscopy (MRS) to examine tissue metabolites noninvasively [34]. The peritumoral Cho/NAA ratio has also been useful in this regard [35]. A better prognosis in terms of more extended progression-free periods and later malignant transformation has been demonstrated to be associated with lower levels of creatine/phosphocreatine (Cr) in patients with low-grade gliomas (WHO grade II) [36]. Glycine levels are elevated in the biopsies of GBM patients [37]. Metabolites like these are useful MRS indicators for the detection of brain cancers.

Using multicenter neuroimaging data, some authors found glioma biomarkers for isocitrate dehydrogenase mutations or EGF receptor variant III . A radiomics approach can identify undefined diagnostic biomarkers from imaging data alone. While established and emerging tumor tissue biomarkers are usually molecularly described [38].

12. Using Machine Learning for Radiomic

Artificial intelligence for image-based analysis and prediction algorithms represents a new era for non-invasive biomarker discovery[39]. Recent research shows that radiologic pictures can be mined for quantitative aspects of clinical relevance. Texture or radiomic analysis is the extraction and study of these quantitative properties. Many research has shown that texture and radiomic characterization methods can improve non-invasive forecasts of tumor histologic characteristics, molecular profile, treatment-related alterations, and patient survival. Brain tumor image analysis and prediction algorithms have employed texture or radiomic-based techniques with machine learning. This technique can enable more precise, individualized therapy [40].

Deep learning-based radiomics is another novel approach. Unlike feature-based radiomics, deep learning radiomics uses artificial neural networks to generate and extract non-predefined high-dimensional features. Thus, deep learning-based radiomics workflow differs from feature-based radiomics methodology. The authors examined the problems and limitations of deep learning for automatic lesion detection and segmentation of brain tumors, among other therapeutic applications [41]. For example, Yogananda et al. used deep learning to predict molecular markers [42].

13. Combined use of Radiomic-Pathology Biomarkers

Developing statistical correlations of radiomic characteristics with point mutations and next-generation sequencing data allows routine MRI scans to function as "virtual biopsy" maps. A brief description of the workflow involving preprocessing, tumor segmentation, extraction of "hand-crafted" features from the segmented region of interest, as well as identifying radiogenomic associations that could ultimately lead to the development of reliable prognostic and predictive models in neuro-oncology applications, is provided in this review [43]. Radiomic tumor signatures can be used to develop a multidimensional multi-omics model incorporating genetic/molecular factors to create a holistic genotype-phenotype landscape of cancer, helping predict/evaluate therapeutic response [30]. For example, the Multi Assay Experiment (MAE) as a container for multi-omics research simplifies data collection and integration [44]. The rating scales can also be used in clinical management and "go/no-go" decisions in clinical studies [45].

14. Images biomarkers for assessing tumor response

Response Evaluation Criteria in Solid Tumors (RECIST) is the gold standard for assessing therapy response in solid malignancies. The RECIST morphologic tumor size change is commonly connected with survival and considered a surrogate endpoint of treatment success. Morphologic change may not be sufficient to determine responsiveness to new anticancer medications in all solid tumors. In the last fifteen years, several molecular-targeted treatments and immunotherapies have evolved to treat cancer. Even without tumor shrinkage, a good therapeutic response is associated with tumor necrosis or non-progression. Thus, using unmodified RECIST criteria to assess tumor morphology alone may not be sufficient to assess tumor response to these novel anticancer medications [32]. RECIST is unreliable in assessing therapy response in malignancies such as brain glioma. New medical imaging biomarkers are needed because changes in tumor viability, metabolic activity, and attenuation are linked to early tumor response. Experiments with 18 F-fluorodeoxyglucose (FDG) positron emission tomography (PET) are promising alternatives to RECIST (PET). Review of current RECIST and upcoming concepts of imaging biomarkers in oncology.

As an interesting future application, Neuroimaging biomarkers and innovative neuro interventions -such as neurostimulators and radiofrequency- can be used to ablate the tumor and reduce its size. Several innovative image-guided tumor ablation indications are given, which will be calibrated with imaging biomarkers [46].

15. Set Guidelines

The European Society of Radiology and the Radiological Society of North America have developed guidelines and criteria for developing and eventually adopting imaging biomarkers.

Limitation

There are general obstacles to the widespread application and acceptance of radiomics in neuro-oncology. Although groundbreaking, some evidence of machine learning and glioma imaging biomarkers is retrospective and single-center. Studies utilizing ML to develop neuro-oncology monitoring biomarker models have yet to show a statistical advantage. To develop and validate ML models for neuro-oncology, interdisciplinary and multicenter cooperation are required [47]. There are no user-friendly, FDA-approved radiomic analysis software applications, no generalizable model for predictions, and no prospective study to illustrate the enhanced utility of radiomics above conventional ROI and histogram analysis. The processes of image acquisition, data analysis, and radiological assessment are among the problems of standardizing imaging in multicenter clinical trials [48]. With encouraging outcomes in brain tumor patients, radiomics and deep learning are still not widely used in clinical practice. One reason is the current over-standardization of methods. This limits the use of developed radiomics models across universities and clinical contexts [49].

16. Conclusion

Oncology advanced learners will understand Artificial Intelligence, Radiomics, and Deep Learning in this rapidly growing discipline. Radiologists and oncologists should recognize new imaging techniques such as CT/MRI-based perfusion, DWI, MRS, PET, and radiomics for tumor response evaluation due to the rapid progress in anticancer therapies nowadays. Radiomics is a new data-driven approach that can help answer clinical questions like diagnosis, prognosis, and treatment response. Using radiomics and radiogenomics to personalize treatment decisions in neuro-oncology will rely heavily on the ability to replicate across large multi-institutional cohorts.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest for the authors in this paper.

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