Access this article online

Quick Response Code:

Website: www.neurologyindia.com

DOI: 10.4103/neurol-india.neurol-india_88_24

Radiogenomics In Neuro-Oncology: A Noninvasive Way of Understanding Tumor Biology

Ramesh Doddamani, Poodipedi Sarat Chandra

Brain tumours have spatial and temporal heterogeneity at different levels: genes, proteins, cells, microenvironment, tissues and organs. Molecular assays obtained from the biopsy of these lesions may not always represent the true nature of the entire lesion. This could very well explain the discrepancy noted in certain histologically diagnosed low grade lesions demonstrating aggressive behaviours in terms of progression free survival/recurrences and outcomes. This limits the use of biopsy based molecular assays but in contrast gives a huge potential for non-invasive imaging, which has the ability to capture intra-tumoral heterogeneity in a non-invasive way. Medical imaging has traditionally been focussed on the qualitative assessment of visually appreciable features like the size, shape and enhancement pattern of a lesion. The field of Radiomics allows for a quantitative assessment of such features along with mathematical extraction of the visually imperceptible features, which can serve as biomarkers.[1,2]

Radiomics represents a method of extracting undiscovered imaging features by converting routinely acquired medical images into higher dimensional data with the help of artificial intelligence (AI), which are otherwise not accessible by conventional visual image analysis. After the introduction of the concept by Lambin and colleagues, radiomics has gained relevance in medical subdisciplines especially neuro-oncology by generating prognostic or predictive mathematical models.[2]

The potential utility of Radiomics in neuro oncology has been shown by several studies, with respect to prediction of survival; assessment of treatment response; the identification of important biomarkers, such as isocitrate dehydrogenase (IDH) mutation status or O-6-methylguanine-DNA-methyltransferase (MGMT) promoter methylation status; and differentiation between treatment-induced changes from local brain tumour relapse. The other advantages are; it is non-invasive (without the need for biopsy) and less time consuming compared to the conventional visual analysis of imaging. The time taken to interpret the histopathology findings can also be reduced if good predictive models are developed, thereby expediting the institution of appropriate treatment strategy in a timely fashion.[3-6]

One of the important contribution of radiomics to neuro oncology is the ability to predict the genetic makeup of the tumour. Qureshi and colleagues, retrospectively analysed the status of MGMT promotor methylation status using Radio-genomics. The MGMT is a DNA repair enzyme and under normal circumstances is beneficial for cellular growth and proliferation. However, in high grade gliomas this enzyme is counterproductive and may render the tumour resistant to alkylating chemotherapeutic agents. However, MGMT promoter gene methylation results in favourable chemotherapeutic response/outcomes to these alkylating agents by silencing the MGMT enzymes. The MGMT promotor gene methylation status is currently identified by the biopsy specimen processing, obtained from the operating room. The tissue processing and special staining necessary to identify the molecular markers is tedious and time consuming (up to few weeks). The availability of these special

Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence:
Dr. Poodipedi Sarat Chandra, Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi – 110 029, India.
E-mail: drpsaratchandra.editor.ni@gmail.com

How to cite this article: Doddamani R, Chandra PS. Radiogenomics In Neuro-Oncology: A Noninvasive Way of Understanding Tumor Biology. Neurol India 2024;72:698-9.

Submitted: 26-Aug-2024 **Revised:** 26-Aug-2024
Accepted: 26-Aug-2024 **Published:** 31-Aug-2024

stains may not be universal especially in the resource limited settings. Hence, MRI based radio-genomics offers an excellent non-invasive alternative to identify the molecular markers pre-surgery, thereby providing valuable insights into the disease prognosis. Several authors have studied the MGMT radiomics and demonstrated its superior ability to correctly identify the MGMT promotor methylation status.[7]

BRAF (v-Raf murine sarcoma viral oncogene homolog B1) mutations is noted in nearly 50% of melanomas, Low grade gliomas (Gangliogliomas and DNETs), Optico chiasmatic gliomas. The most frequent mutation V600E, is noted in about 70% of cases, (i, e, substitution of valine for glutamic acid). This mutation is a prerequisite for an effective response to targeted therapies using BRAF inhibitors like; vemurafenib and dabrafenib. These agents have shown considerable intracranial response rates in clinical trials with a significant improvement of overall and progression-free survival. Meißner *et al*., using predictive Machine learning (ML) algorithms could noninvasively predict the BRAF V600E. The authors noted 50-60% prediction rate of this mutation based on the imaging features and when clinical parameter like age was incorporated in the model, the prediction rate enhanced up to 85%.[8]

In this issue of Neurology India, Vaidya and colleagues have tried to analyse the imaging features and tried to correlate retrospectively with the BRAF mutations noted on histopathology in twenty-six patients of Optic pathway hypothalamic gliomas (OPHGs). It is well known the OPHGs are classified as WHO grade 1 tumours. Despite being classified as benign, some of these tumours have aggressive lesions on radiology in terms of extensions beyond the primary location. The authors used visual analysis of the MRI and noted characteristically, presence of solid cystic lesion along with central necrosis pointed towards OPHGs. The authors also noted presence of multiple cysts and minimal necrosis to be strongly associated with BRAF V600E mutations, while Marked necrosis in the solid component significantly correlated with *BRAF* wild genotype. A single peripherally located cyst was noted in the presence of BRAF Fusion.[9]

Similarly, Lijima and colleagues utilized visual analysis by three expert neuroradiologists to understand the role of BRAF V600E and seizure outcomes in low-grade epilepsy-associated neuroepithelial tumours (LEATs). The authors divided 3 groups based on imaging characteristics. Group 1 had indistinct borders and iso T1-weighted and slightly high or high T2-weighted signal intensities without a diffuse mass effect, associated with 93.8% sensitivity and 100% specificity to *BRAF* V600E mutations; Group 2 exhibited sharp borders and very or slightly low T1-weighted and very high T2-weighted signal intensities with a diffuse mass effect and 100% sensitivity and specificity for *FGFR1* mutations; and Group 3 displayed various characteristics. The authors noted excellent seizure outcomes in Group-1 patients compared to the group-2. The use of radiomics by the authors, with larger sample size would have been more informative.[10]

Despite the large number of studies suggesting an added value of radiomics for diagnosis and disease monitoring in patients with brain tumours, this technique still underutilized in neuro-oncological clinical trials. The main reasons are probably lack of standardisation of imaging protocols as well as the reporting of the results. Absence of validation of the developed machine-learning model in large multicentre trials and lack of emphasis on the interobserver interpretation and biological meaning of identified radiomics features. Future multicentre studies conducted prospectively focussing on the uniformity of the data interpretation, standard image acquisition protocols will definitely provide insights in this field leading to better management strategies. Radiogenomics has a promising future, as Gillies and colleagues rightly stated "Images are more than pictures, they are data".[11]

References

1. Van Timmeren JE, Cester D, Tanadini-Lang S, Alkadhi H, Baessler B. Radiomics in medical imaging-"how-to" guide and critical reflection. Insights Imaging 2020;11:91.
2. Lambin P, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RG, Granton P, *et al*. Radiomics: extracting more information from medical images using advanced feature analysis. Eur J Cancer 2012;48:441-6.
3. Jiang C, Kong Z, Liu S, Feng S, Zhang Y, Zhu R, *et al*. Fusion Radiomics Features from Conventional MRI Predict MGMT Promoter Methylation Status in Lower Grade Gliomas. Eur J Radiol 2019;121:108714.
4. Li ZC, Bai H, Sun Q, Li Q, Liu L, Zou Y, *et al*. Multiregional radiomics features from multiparametric MRI for prediction of MGMT methylation status in glioblastoma multiforme: A multicentre study. Eur Radiol 2018;28:3640-50.
5. Malhotra KP, Kaif M, Malhotra HS, Husain N. A Novel Case of Primary Conus Medullaris Epithelioid Glioblastoma with Gliosarcomatous Differentiation. Neurol India. 2023 Jan-Feb; 71:132-4.
6. Jiang B, Zheng Y, She D, Xing Z, Cao D. MRI characteristics predict BRAF V600E status in gangliogliomas and pleomorphic xanthoastrocytomas and provide survival prognostication. Acta Radiologica 2024;65:33-40.
7. Qureshi SA, Hussain L, Ibrar U, Alabdulkreem E, Nour MK, Alqahtani MS, *et al*. Radiogenomic classification for MGMT promoter methylation status using multi-omics fused feature space for least invasive diagnosis through mpMRI scans. Sci Rep 2023;13:3291.
8. Meißner AK, Gutsche R, Galldiks N, Kocher M, Jünger ST, Eich ML, *et al*. Radiomics for the noninvasive prediction of the BRAF mutation status in patients with melanoma brain metastases. Neuro Oncol 2022;24:1331-40.
9. Vaidya T, Sahu A, Epari S, Shetty O, Gurav M, Sahay A, *et al*. Magnetic Resonance Imaging Features of Sporadic Optic Chiasmatic–Hypothalamic Gliomas and Correlation with Histopathology and Braf Gene Alterations. Neurol India 2024;72:747-55.
10. Iijima K, Komatsu K, Miyashita S, Suyama K, Murayama K, Hashizume K, *et al*. Transcriptional features of low-grade neuroepithelial tumors with the BRAF V600E mutation associated with epileptogenicity. Genes Cells 2024;29:192-206.
11. Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images Are More than Pictures, They Are Data. Radiology 2016;278:563-77.