

Radiomics Utilization in Neuro-Oncology Brief Review of the State-of-art

Nöro-Onkolojide Radyomik Kullanımı: Son Teknolojinin Kısa İncelemesi

Moamin JAMEEL^a, Muslim JAMEEL^a, Soner SAHİN^{a,b}

^aBahçeşehir University, School of Medicine, Department of Neurosurgery, Istanbul, Turkey

^bBahçeşehir Institution of Graduate School of Health Sciences, Tissue Engineering and Regenerative Medicine, Istanbul, Turkey

Abstract: Radiomics is nascent field that involves extracting quantitative features - radiomic features from medical images that correlate with the properties of the concerned lesion, such as the heterogeneity, shape, volume, proteomic, demographic and histology that have personalized clinical value in diagnosis, prognosis and treatment. Our article aims to explore and review the state-of-art Radiomics and texture analysing in neuro-oncology, address the challenges a provide a prospect for future studies.

Keywords: radiomics, neurosurgery, oncology

Özet: Radyomik, tanı, prognoz ve tedavide kişiselleştirilmiş klinik değere sahip heterojenlik, şekil, hacim, proteomik, demografik ve histoloji gibi ilgili lezyonun özellikleriyle uyumlu tıbbi görüntülerden radyomik özellikler olan nicel özelliklerin çıkarılmasını içeren yeni bir alandır. Makalemiz nöro-onkolojide son teknoloji Radyomikleri ve doku analizini keşfetmeyi ve gözden geçirmeyi, zorlukları ele almayı ve gelecekteki çalışmalar için bir umut sunmayı amaçlamaktadır.

Anahtar Kelimeler: radyomik, beyin cerrahisi, onkoloji

Correspondence Address : Soner Sahin

Bahçeşehir University, School of Medicine, Department of Neurosurgery, Istanbul, Turkey

soner.sahin@med.bau.edu.tr

ORCID ID of the authors: M.J. 0000-0001-8934-5803

M.J. 0000-0001-8397-1280, S.S. 0000-0001-9391-8088

Please cite this article in press at: JAMEEL M., JAMEEL M., SAHİN S., Radiomics Utilization in Neuro-Oncology Brief Review of the State-of-art, Journal of Medical Innovation and Technology, 2020; 2 (2):143-147

1.Introduction

Radiomics is nascent field that involves extracting quantitative features - radiomic features from medical images that correlate with the properties of the concerned lesion, such as the heterogeneity, shape, volume, proteomic, demographic and histology that have personalized clinical value in diagnosis, prognosis and treatment (1,2).

Large number of image features (e.g. >400), including texture features, are extracted from medical images derived from large medical radiologic images from database after manual, semi- or automated segmentation. Then radiomic features are selected based on their stability as well as their contributions to the prognoses (3).

A popular approach in computer-aided diagnosis using machine learning is the classification of lesions into classes such as lesion and non-lesion or malignant and benign lesion. All based on input features that allow machine learning to determine the boundaries for the separating classes. When images are fed into the system, lesions are segmented by different methods including thresholding, edge-based segmentation. After the extraction of features from the segmented lesions, they are processed by a model such as linear or quadratic discriminant analysis and support vector machine (SVM), the training is performed for determination of "optimal" boundaries for separating classes (4).

Although the field is still in its embryogenesis, yet it shows assuring results that would revolutionize the clinical practice and applications in grading and precisely diagnosing tumors. Radiomics are capable to provide data regarding the temporal and spatial heterogeneity non-invasively and even characterize the microenvironment of tumors that otherwise require biopsy. Furthermore, Delta radiomics introduce innovative approach to prognosis and disease response to therapeutics over the course of treatment by extracting quantitative features from images and show their value changes (5,6,7).

The field of Radiomics is attracting much attention in neuro-oncology due to its feasibility and accuracy in classification, grading and providing genomic and molecular profile of CNS tumors (8,9).

Our article aims to explore and review the state-of-art Radiomics and texture analysing in neuro-oncology, address the challenges and provide a prospect for future studies.

Radiomics In Neuro-Oncology

Although clinical symptoms of metastasis and Glioma overlap, it is essential to distinguish between the two as their clinical management is different. A study done by Moushi et al. Assessed retrospectively 50 patients' T2/FLAIR/T1 post-contrast and PWI images. Estimating Perfusion and Texture (Haralick's second order statistics) parameters. Found that by combining visual texture features from the peritumoral area with rCBVlesion and rCBVperilesion measurements, classifier sensitivity was increased by 12% and specificity was increased by 7% compared with perfusion parameters alone. Differentiated MET from GBM with a sensitivity of 92% and a specificity of 71% (10).

Utilization of Radiomics show promising results in non-invasive Glioma grading. However, it still lacks standardized methodologies.

A study done by Tian et al. Divided patient population of 153 with Glioma grade II, III and IV into two groups, the feature Groups I and II were comprised of 420 texture features and 90 histogram features, respectively, from 10 VOIs of each patient. The study showed the superiority of texture parameters with accuracy, Sensitivity and specificity of Overall 96.8%, 96.4%, 97.3% respectively (P <0.001) for classifying LGGs from HGGs, and 98.1% for classifying grades III from IV, which were more promising than using histogram parameters (accuracy, sensitivity and specificity of 91.4%, 83.8%, 99.1%, P<0.001, Respectively) or using the single sequence MRI. Concluding the texture features and combined application of multiparametric MRI provided higher non-invasive glioma grading efficiency (11).

Skogen et al. Were able to achieve a sensitivity and specificity of 93% and 81% (AUC 0.910, p < 0.0001). Using MR Tissue analysis MRTA to differentiate Low and High grade glioma by filtering and extracting texture features from 2 mm (fine features) to 6 mm (coarse features) and obtaining statistical parameter standard deviation (SD). However, such method showed lower but still significant ability to differentiate sub-groups gliomas. Concluding that texture from necrosis is probably more applicable to extract from CT and ADC textural analysis than MRTA. Advicing a multimodal or multiparametric approach of combining ADC and contrast-enhanced SPGR to gain more complete tumor heterogeneity profile (12).

Furthermore, Ditmer et al. expanded on the work of Skogen et al. using The histogram parameters including mean, standard deviation, entropy, mean of the positive pixels, skewness, and kurtosis were analyzed at spatial scaling factors ranging from 0 to 6 mm to assess High and Low grade gliomas heterogeneity. Low and high-grade gliomas

were best-discriminated using mean of 2 mm fine texture scale, with a sensitivity and specificity of 93% and 86% (AUC of 0.90) (13).

Studies in radiomics utilization in gliomas detection and grading show significant and promising result. However more studies with larger patients population and focused on the ability to differentiate the sub-groups of gliomas are needed. In addition the lack of consensus regarding the approaches renders a standardized methods essential for future studies.

Radiogenetics

Eversince the introduction of WHO classification of CNS tumors in 2016, Molecular and genetic profile of tumors gained essential role in diagnosis process. Restructuring and incorporating new types, subtypes and identities by both histology and molecular features. directing toward more precise and objective classification in order to customize personalized treatment (14).

Radiomics on the other hand is a rapidly evolving and promising field that relies on feature extraction and analysis of medical images. The integration of radiomics and machine learning and availability of large and annotated data bank, allow the algorithm to predict crucial information for accurate non-invasive diagnosis like the microenvironment, biologic markers and even the genetic profile of tumors (15).

the nascent field of radiogenomics has auspicious potential contribution to the advancement of neuro-oncology by extracting information regarding genetic mutation and expression patterns from radiologic imaging.

Radiogenomics also has the power to dynamically monitor the microenvironment over the course of treatment, potentially allowing for a reduced number of repeat biopsies or resections (16).

In a study done by S.Hu et.al that assessed the feasibility of multiparametric MRI and tissue texture analysis feasibility of using multiparametric MRI and texture analysis to characterize regional genetic heterogeneity throughout MRI-enhancing and nonenhancing tumor segments. The study looked 6 driving genes: EGFR, PDGFRA, PTEN, CDKN2A, RB1, and TP53 from 48 biopsies from region of enhancement and nonenhancement paranchyma using univariate analysis. The result showed Highest accuracies were observed for PDGFRA (77.1%), EGFR (75%), CDKN2A (87.5%), and RB1 (87.5%), while lowest accuracy was observed in TP53 (37.5%) (17).

Hong et.al showed Significant correlation between radiological parameters such as volumetric and ADC values and major genomic profiles of tumors.

The IDH-mut group showed a larger volume on T2WI and a higher volume ratio between T2WI and CETWI than the IDH-wt group ($P < 0.05$). while IDH-wt tumours, IDH-wt, ATRX-loss tumours revealed higher 5th percentile nADC values than the IDH-wt, ATRX-noloss tumours ($p = 0.03$). PFS was the longest in the IDH-mut group, followed by the IDH-wt, ATRX-loss groups and the IDH-wt, ATRX-noloss groups, consecutively ($p < 0.05$) (18).

Predictive genomic profile of gliomas can be derived from radiologic images. A positive association between previously identified tumor genomic subtypes in lower-grade glioma the tumor shape as seen in MRI. By analysing FLAIR images using five quantitative measurement of tumor shape in two and three dimensions with genomic data based on IDH mutation and 1p/19q co-deletion, DNA methylation, gene expression DNA copy number, and microRNA expression. Mazurowski et.al. Reported a strong association between angular standard deviation (ASD), which measures irregularity of the tumor boundary, and the IDH-1p/19q subtype ($p < 0.0017$), RNASeq cluster ($p < 0.0002$), DNA copy number cluster ($p < 0.001$), and the cluster of clusters ($p < 0.0002$). The RNASeq cluster was also associated with bounding ellipsoid volume ratio ($p < 0.0005$). Tumors in the IDH wild type cluster and R2 RNASeq cluster which are associated with much poorer outcomes generally had higher ASD reflecting more irregular shape (19).

The accumulation of supportive evidences that reflect the genomic heterogeneity correlation with radiological imaging pave a way for non-invasive, precise and cost effective approaches to diagnose cerebral tumors allowing better treatment, monitoring and better assessment in prognosis. However, more studies with larger population and focus on texture features can direct future studies in this field.

2.Conclusion

Various studies conducted prove the practicability of Radiomics in medicine due to its accuracy, cost-effectiveness, non-invasive methods in detecting, classifying, grading and prognosis of tumors. However issues regarding the standardization of methodologies need to be addressed. Furthermore, optimization of criteria regarding feature selection, segmentation methods to achieve best possible results need to be set.

References

1. Mayerhoefer ME, Materka A, Langs G, Häggström I, Szczypiński P, Gibbs P, Cook G. Introduction to Radiomics. *J Nucl Med*. 2020;61:488-95.
2. Liao X, Cai B, Tian B, Luo Y, Song W, Li Y. Machinelearning based radiogenomics analysis of MRI features and metagenes in glioblastoma multiforme patients with different survival time. *J Cell Mol Med*. 2019;23:4375-85.
3. Arimura H, Soufi M, Kamezawa H, Ninomiya K, Yamada M. Radiomics with artificial intelligence for precision medicine in radiation therapy. *J Radiat Res*. 2019;60:150-57.
4. Suzuki K. Overview of deep learning in medical imaging. *Radiol Phys Technol*. 2017;10:257-73.
5. Tselikas L, Sun R, Ammari S, Dercle L, Yevich S, Hollebecque A, Ngo-Camus M, Nicotra C, Deutsch E, Deschamps F, de Baere T. Role of image-guided biopsy and radiomics in the age of precision medicine. *Chin Clin Oncol*. 2019;8:57.
6. Lambin P, Leijenaar RTH, Deist TM, Peerlings J, de Jong EEC, van Timmeren J, Sanduleanu S, Larue RTHM, Even AJG, Jochems A, van Wijk Y, Woodruff H, van Soest J, Lustberg T, Roelofs E, van Elmpst W, Dekker A, Mottaghy FM, Wildberger JE, Walsh S. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol*. 2017;14:749-62.
7. Mirestean CC, Pagute O, Buzea C, Iancu RI, Iancu DT. Radiomic Machine Learning and Texture Analysis - New Horizons for Head and Neck Oncology. *Maedica (Bucur)*. 2019;14:126-30.
8. Park JE, Kickingereder P, Kim HS. Radiomics and Deep Learning from Research to Clinical Workflow: NeuroOncologic Imaging. *Korean J Radiol*. 2020;21:1126-37.
9. Leng Y, Wang X, Liao W, Cao Y. Radiomics in gliomas: A promising assistance for glioma clinical research. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2018;43:354-59.
10. Mouthuy N, Cosnard G, Abarca-Quinones J, Michoux N. Multiparametric magnetic resonance imaging to differentiate high-grade gliomas and brain metastases. *J Neuroradiol*. 2012;39:301-7.
11. Tian Q, Yan LF, Zhang X, Zhang X, Hu YC, Han Y, Liu ZC, Nan HY, Sun Q, Sun YZ, Yang Y, Yu Y, Zhang J, Hu B, Xiao G, Chen P, Tian S, Xu J, Wang W, Cui GB. Radiomics strategy for glioma grading using texture features from multiparametric MRI. *J Magn Reson Imaging*. 2018;48:1518-28.
12. Skogen K., Schulz A., Dormagen J.B., Ganeshan B., Helseth E., Server A. Diagnostic performance of texture analysis on MRI in grading cerebral gliomas. *Eur. J. Radiol*. 2016;85:824-29.
13. Ditmer A, Zhang B, Shujaat T, et al. Diagnostic accuracy of MRI texture analysis for grading gliomas. *Journal of Neuro-oncology*. 2018;140:583-89.
14. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*. 2016;131:803-20.
15. VIAL, A., STIRLING, D., FIELD, M., ROS, M., RITZ, C., CAROLAN, M., HOLLOWAY, L., MILLER, A.. The role of deep learning and radiomic feature extraction in cancer-specific predictive modelling: a review. *Translational Cancer Research, North America*, 7, jun. 2018. Available at: <<http://tcr.amegroups.com/article/view/21823>>. Date accessed: 26 Dec. 2020
16. Rudie JD, Rauschecker AM, Bryan RN, Davatzikos C, Mohan S. Emerging Applications of Artificial Intelligence in Neuro-Oncology. *Radiology*. 2019;290:607-18.
17. Hu LS, Ning S, Eschbacher JM, Baxter LC, Gaw N, Ranjbar S, Plasencia J, Dueck AC, Peng S, Smith KA, Nakaji P, Karis JP, Quarles CC, Wu T, Loftus JC, Jenkins RB, Sicotte H, Kollmeyer TM, O'Neill BP, Elmquist W, Hoxworth JM, Frakes D, Sarkaria J, Swanson KR, Tran NL, Li J, Mitchell JR. Radiogenomics to characterize regional genetic heterogeneity in glioblastoma. *Neuro Oncol*. 2017;19:128-37.
18. Hong EK, Choi SH, Shin DJ, Jo SW, Yoo RE, Kang KM, Yun TJ, Kim JH, Sohn CH, Park SH, Won JK, Kim TM, Park CK, Kim IH, Lee ST. Radiogenomics correlation between MR imaging features and major genetic profiles in glioblastoma. *Eur Radiol*. 2018;28:4350-61.
19. Mazurowski, M.A., Clark, K., Czarnek, N.M. et al. Radiogenomics of lower-grade glioma: algorithmically assessed tumor shape is associated with tumor genomic subtypes and patient outcomes in a multi-institutional study with The Cancer Genome Atlas data. *J Neurooncol* 2017;133, 27-35