Open Peer Review on Qeios

[Perspective] Delta Radiomics — Potential Role in Head Neck Cancer

Shrikant Mali¹

1 Karmaveer Bhausaheb Hiray Dental College and Hospital

Funding: No specific funding was received for this work.Potential competing interests: No potential competing interests to declare.

Abstract

Introduction: Delta radiomics is a tool used to assess the response of oncologic patients undergoing immunotherapy. It extracts high-dimensional quantitative features from medical images, providing information about cancer's phenotype, genotype, and tumoral microenvironment. This analysis could help avoid invasive procedures and help choose the most suitable therapeutic in multiple therapeutic options. Radiomics has gained interest as an imaging biomarker for predicting response to various immunotherapies. Delta radiomics assesses feature variations from one time point to another based on subsequent images, offering higher value for treatment-outcome prediction or patient stratification into risk categories. It has potential benefits for clinical endpoints in oncology, such as differential diagnosis, prognosis, treatment response prediction, and evaluation of side effects. Further research with prospective and multicentre studies is needed for clinical validation of delta radiomics approaches.

Statement of CLINICAL SIGNIFICANCE: In head and neck oncology, delta radiomics can be used to enhance the precision of diagnosis, assess tumor response, forecast normal tissue toxicity, predict clinical outcome, and pinpoint characteristics for treatment modification. Patients' quality of life may be enhanced by it. It can support post-treatment surveillance. Additionally, it can support the delivery of individualized care based on a patient's reaction to medication and radiation.

Dr. Shrikant B Mali^{*}

MDS oral and maxillofacial surgery Associate professor Mahatma Gandhi Vidya Mandir's Dental College and Hospital Nashik

*<u>Shrikantmali@gmail.com</u>

Keywords: Radiomics, delta radiomics, cancer, head neck cancer.

Introduction

For patient monitoring, treatment response assessment, and diagnosis, medical imaging is essential. Radimic image analysis has enhanced clinical decision-making through sophisticated mathematical and statistical analysis, based on phenotype, genotype, and molecular features. Additionally, ^[1] AI techniques have increased the precision of image segmentation, detection, classification, and treatment outcome prediction. One can classify radiomic features into statistical, model-based, texture-based, transform-based, statistical, and shape-based categories. In order to enhance readability, they can be taken out of 3-dimensional (3D) volumes or 2-dimensional (2D) regions of interest (ROIs). Unmodified or discretized gray-level intensities can be used to compute statistical features. For head and neck cancer, radiomics has been suggested as a prognostic biomarker. The International Working Group created Response Assessment Criteria in Solid Tumours, and it is essential to use oncological imaging to assess treatment response. Rapid technological advancements have necessitated modifications, though, including the assessment of target lesions, pathological lymph nodes, disease progression, and the application of 18F-FDG PET to identify novel lesions. Immunotherapy's unique mechanisms of action and unusual response patterns that approximate tumor growth have changed imaging data since its introduction. ^{[2][3][4][5]}

In order to detect cancer, predict patient outcomes, and make clinical decisions, texture analysis is a technique used to extract quantitative imaging characteristics from medical images. It is a difficult field of study before practical implementation, though, because of issues with the robustness and consistency of derived parameters between scans or with varying acquisition settings. ^{[6][7][8][9]}

Medical imaging methods such as radiomics and delta-radiomics are essential to personalized precision medicine. Radiomics offers data on tumor microenvironment, genotype, and cancer phenotype that can be used for prognostication and diagnosis. In order to predict treatment response early, delta radiomics evaluates treatment-induced net change in radiomic characteristics over time. It looks at feature variance frequently before and after treatment at different acquisition time points. More precise clinical outcome prediction is possible with deep learning techniques, particularly for aggressive, radioresistant tumors. To help with early therapy evaluation, delta analysis takes texture characteristics into account as proxy biomarkers of clinical endpoints. ^{[10][11][12]}

Due to its reliance on image capture and reconstruction parameters, which cause notable differences between datasets, radiomics has certain limitations. To take acquisition date variations in features into consideration, "delta radiomics" was developed. This methodology allows for the examination of the effects of feature modifications following designated stages in the patient's workflow, such as biological events, therapy, or time. Delta radiomics is a fascinating field of research, but its results are controversial and varied, making it difficult to generalize and apply. Individualized therapy is made possible by the removal of inter-patient variability through the use of delta radiomics, which analyzes data for one patient over time. [13][14][15][16][17][18][19]

In metastatic melanoma patients, combining conventional and delta radiomics improves treatment response prediction by differentiating between pseudo-progression and advancement of the disease. While differences in image processing and

segmentation techniques may lead to biased data interpretation, delta radiomics can forecast radiologic responses. Suggestions for harmonization are essential for future expansion. ^{[20][21]}

Head neck cancer

The distinct anatomy and radiobiology of head and neck carcinomas make them formidable therapeutic challenges, frequently leading to treatment failure or recurrence. Effective treatment requires an evaluation of critical characteristics such as hypoxia, proliferative capacity, proportion of cancer stem cells, radioresistance, and HPV status. Monitoring tumor response and treatment-related side effects enhances the therapeutic index and patient quality of life, while biomarkers and pharmacogenetics can help stratify patients and improve management. Progress in molecular and functional imaging facilitates precise diagnosis and treatment planning. ^{[13][22][23]}

The term "delta-radiomics features" refers to radiographic techniques that employ machine learning to quantify features from radiological images. These features measure changes in tumor areas brought about by therapy and are associated with treatment response or outcome in a variety of cancer types. Because there are few patient cohorts available, machine learning techniques for predicting treatment outcomes in medical physics applications frequently encounter limitations. Deep learning techniques may only observe a small area around training samples and overfit training data, which may result in an inaccurate representation of all patients. The current research focuses on enhancing model performance by utilizing new imaging or detection modalities, selecting new features, investigating features, and introducing novel classifiers. ^{[24][25][26][27]} For early HNC locoregional recurrence prediction, the study proposes a robust post-treatment model that can be enhanced by adding new algorithms to the model or by gathering additional patient data. The method increases clinicians' confidence in predictions for particular patient groups by defining an acceptable reliability threshold for HNC locoregional recurrence prediction. ^[28]

Early detection of adverse events in head and neck cancer can be achieved by using delta radiomics, a technique that detects changes in radiomic features on CT images and salivary functionality. Reductions in the surface area of the parotid gland were found to be strongly correlated with the development of xerostomia 6 and 12 months after radiation therapy, indicating a correlation between delta radiomics changes in the parotid gland and later xerostomia. ^[29] Barua and associates ^[30] According to the study, 21 patients with oropharyngeal carcinoma had an early prediction of mandibular osteoradionecrosis using quantitative ultrasound (QUS) delta radiomics, which may improve the prognosis in HNSCC. When the endpoint is closer to hand, delta radiomics analysis is the best surrogate biomarker, which facilitates the testing of various approaches. Although more clinical research is required to confirm these findings, a study found that Delta Texture analysis features were more robust than Texture analysis features, suggesting their potential for early treatment response assessment and tailored therapies. ^[6]

Limitations challenges

Radiomics has shortcomings such as lack of robustness and reproducibility, despite its potential. A subfield of radiomics called delta-radiomics compares CT scans and evaluates changes that occur during treatment or due to outside influences by concentrating on variations of radiomic features at various times. This technique's consistent acquisition parameters make it more repeatable across centers. Notwithstanding these drawbacks, radiomics continues to be of great scientific interest. ^{[6][31]}

As shown by Liu et al., who used a delta radiomics signature to predict anti-PD-1 immunotherapy response in advanced NSCLC, delta-radiomics signatures can differentiate responders in advanced NSCLC, bladder cancer, and melanoma, predict free-progression-survival in gastric cancer treated with ICIs, and offer a solution when conventional radiomics fails. ^[32] Although Welch et al. ^[33] have put safety measures in place for radiomic models, patients' compliance with imaging schedules and the creation of datasets are hampered by standardized image parameters and hybrid imaging fusion algorithms.

Conclusion

Although delta radiomics has intriguing implications for evaluating treatment response, more large-scale multicentric cohort studies and prospective designs are required to validate these results. It is necessary to demonstrate in clinical settings the role of delta radiomics in various cancer types. In head and neck oncology, delta radiomics can be used to enhance the precision of diagnosis, assess tumor response, forecast normal tissue toxicity, predict clinical outcome, and pinpoint characteristics for treatment modification. Patients' quality of life may be enhanced by it. It can support post-treatment surveillance. Additionally, it can support the delivery of individualized care based on a patient's reaction to medication and radiation.

Statements and Declarations

Conflict of interests

No conflict of interest.

Funding

No funding received.

Other References

• Ciolina M, Vinci V, Villani L, Gigli S, Saldari M, Panici PB, Perniola G, Laghi A, Catalano C, Manganaro L. Texture analysis versus conventional MRI prognostic factors in predicting tumor response to neoadjuvant chemotherapy in

patients with locally advanced cancer of the uterine cervix. Radiol Med. 2019 Oct;124(10):955-964. doi: 10.1007/s11547-019-01055-3. Epub 2019 Jun 28. PMID: 31254220.

Nardone V, Tini P, Croci S, Carbone SF, Sebaste L, Carfagno T, Battaglia G, Pastina P, Rubino G, Mazzei MA, Pirtoli L. 3D bone texture analysis as a potential predictor of radiation-induced insufficiency fractures. Quant Imaging Med Surg. 2018 Feb;8(1):14-24. doi: 10.21037/qims.2018.02.01. PMID: 29541619; PMCID: PMC5835655.

References

- [^]Wong OL, Yuan J, Zhou Y, Yu SK, Cheung KY. Longitudinal acquisition repeatability of MRI radiomics features: An ACR MRI phantom study on two MRI scanners using a 3D T1W TSE sequence. Med Phys. 2021 Mar;48(3):1239-1249. doi: 10.1002/mp.14686. Epub 2021 Feb 2. PMID: 33370474.
- [^]Nardone V, Reginelli A, Grassi R, Boldrini L, Vacca G, D'Ippolito E, Annunziata S, Farchione A, Belfiore MP, Desideri I, Cappabianca S. Delta radiomics: a systematic review. Radiol Med. 2021 Dec;126(12):1571-1583. doi: 10.1007/s11547-021-01436-7. Epub 2021 Dec 4. PMID: 34865190.
- Abbas E, Fanni SC, Bandini C, Francischello R, Febi M, Aghakhanyan G, Ambrosini I, Faggioni L, Cioni D, Lencioni RA, Neri E. Delta-radiomics in cancer immunotherapy response prediction: A systematic review. Eur J Radiol Open. 2023 Jul 18;11:100511. doi: 10.1016/j.ejro.2023.100511. PMID: 37520768; PMCID: PMC10371799.
- ^ATazdait M, Mezquita L, Lahmar J, Ferrara R, Bidault F, Ammari S, Balleyguier C, Planchard D, Gazzah A, Soria JC, Marabelle A, Besse B, Caramella C. Patterns of responses in metastatic NSCLC during PD-1 or PDL-1 inhibitor therapy: Comparison of RECIST 1.1, irRECIST and iRECIST criteria. Eur J Cancer. 2018 Jan;88:38-47. doi: 10.1016/j.ejca.2017.10.017. Epub 2017 Nov 26. PMID: 29182990.
- [^]Beer L, Hochmair M, Prosch H. Pitfalls in the radiological response assessment of immunotherapy. Memo. 2018;11(2):138-143. doi: 10.1007/s12254-018-0389-x. Epub 2018 Mar 21. PMID: 29983829; PMCID: PMC6006274.
- ^{a, b, c}Nardone V, Reginelli A, Guida C, Belfiore MP, Biondi M, Mormile M, Banci Buonamici F, Di Giorgio E, Spadafora M, Tini P, Grassi R, Pirtoli L, Correale P, Cappabianca S, Grassi R. Delta-radiomics increases multicentre reproducibility: a phantom study. Med Oncol. 2020 Mar 31;37(5):38. doi: 10.1007/s12032-020-01359-9. PMID: 32236847.
- [^]Nardone V, Reginelli A, Scala F, Carbone SF, Mazzei MA, Sebaste L, Carfagno T, Battaglia G, Pastina P, Correale P, Tini P, Pellino G, Cappabianca S, Pirtoli L. Magnetic-Resonance-Imaging Texture Analysis Predicts Early Progression in Rectal Cancer Patients Undergoing Neoadjuvant Chemoradiation. Gastroenterol Res Pract. 2019 Jan 17;2019:8505798. doi: 10.1155/2019/8505798. PMID: 30847005; PMCID: PMC6360039.
- [^]Nardone V, Tini P, Nioche C, Mazzei MA, Carfagno T, Battaglia G, Pastina P, Grassi R, Sebaste L, Pirtoli L. Texture analysis as a predictor of radiation-induced xerostomia in head and neck patients undergoing IMRT. Radiol Med. 2018 Jun;123(6):415-423. doi: 10.1007/s11547-017-0850-7. Epub 2018 Jan 24. PMID: 29368244.
- [^]Biondi M, Vanzi E, De Otto G, Carbone SF, Nardone V, Banci Buonamici F. Effects of CT FOV displacement and acquisition parameters variation on texture analysis features. Phys Med Biol. 2018 Dec 4;63(23):235021. doi: 10.1088/1361-6560/aaefac. PMID: 30511662.

- [^]Rizzo S, Botta F, Raimondi S, Origgi D, Fanciullo C, Morganti AG, Bellomi M. Radiomics: the facts and the challenges of image analysis. Eur Radiol Exp. 2018 Nov 14;2(1):36. doi: 10.1186/s41747-018-0068-z. PMID: 30426318; PMCID: PMC6234198.
- [^]G. Aghakhanyan, G. Di Salle, S.C. Fanni, et al., Radiomics insight into the neurodegenerative "hot" brain: a narrative review from the nuclear medicine perspective, Front. Nucl. Med. 3 (2023), https://doi.org/10.3389/ fnume.2023.1143256.
- Aringhieri G, Fanni SC, Febi M, Colligiani L, Cioni D, Neri E. The Role of Radiomics in Salivary Gland Imaging: A Systematic Review and Radiomics Quality Assessment. Diagnostics (Basel). 2022 Dec 1;12(12):3002. doi: 10.3390/diagnostics12123002. PMID: 36553009; PMCID: PMC9777175.
- ^{a, b}Marcu DC, Grava C, Marcu LG. Current Role of Delta Radiomics in Head and Neck Oncology. Int J Mol Sci. 2023 Jan 22;24(3):2214. doi: 10.3390/ijms24032214. PMID: 36768535; PMCID: PMC9916410.
- [^]Pfaehler E, Beukinga RJ, de Jong JR, Slart RHJA, Slump CH, Dierckx RAJO, Boellaard R. Repeatability of 18 F-FDG PET radiomic features: A phantom study to explore sensitivity to image reconstruction settings, noise, and delineation method. Med Phys. 2019 Feb;46(2):665-678. doi: 10.1002/mp.13322. Epub 2018 Dec 28. PMID: 30506687; PMCID: PMC7380016.
- 15. [^]Gao Y, Kalbasi A, Hsu W, Ruan D, Fu J, Shao J, Cao M, Wang C, Eilber FC, Bernthal N, Bukata S, Dry SM, Nelson SD, Kamrava M, Lewis J, Low DA, Steinberg M, Hu P, Yang Y. Treatment effect prediction for sarcoma patients treated with preoperative radiotherapy using radiomics features from longitudinal diffusion-weighted MRIs. Phys Med Biol. 2020 Aug 27;65(17):175006. doi: 10.1088/1361-6560/ab9e58. PMID: 32554891.
- [^]Mazzei MA, Nardone V, Di Giacomo L, Bagnacci G, Gentili F, Tini P, Marrelli D, Volterrani L. The role of delta radiomics in gastric cancer. Quant Imaging Med Surg. 2018 Aug;8(7):719-721. doi: 10.21037/qims.2018.07.08. PMID: 30211038; PMCID: PMC6127523.
- [^]Boldrini L, Bibault JE, Masciocchi C, Shen Y, Bittner MI. Deep Learning: A Review for the Radiation Oncologist. Front Oncol. 2019 Oct 1;9:977. doi: 10.3389/fonc.2019.00977. PMID: 31632910; PMCID: PMC6779810.
- [^]Reginelli A, Nardone V, Giacobbe G, Belfiore MP, Grassi R, Schettino F, Del Canto M, Grassi R, Cappabianca S. Radiomics as a New Frontier of Imaging for Cancer Prognosis: A Narrative Review. Diagnostics (Basel). 2021 Sep 29;11(10):1796. doi: 10.3390/diagnostics11101796. PMID: 34679494; PMCID: PMC8534713.
- [^]Nardone V, Boldrini L, Grassi R, Franceschini D, Morelli I, Becherini C, Loi M, Greto D, Desideri I. Radiomics in the Setting of Neoadjuvant Radiotherapy: A New Approach for Tailored Treatment. Cancers (Basel). 2021 Jul 17;13(14):3590. doi: 10.3390/cancers13143590. PMID: 34298803; PMCID: PMC8303203.
- [^]Marcu, L.G., Boyd, C. & Bezak, E. Current issues regarding artificial intelligence in cancer and health care. Implications for medical physicists and biomedical engineers. Health Technol. 9, 375–381 (2019). https://doi.org/10.1007/s12553-019-00348-x
- [^]Marcu, L.G.; Marcu, D. Points of view on artificial intelligence in medical imaging—One good, one bad, one fuzzy. Health Technol. 2021, 11, 17–22.
- 22. [^]Marcu LG, Reid P, Bezak E. The Promise of Novel Biomarkers for Head and Neck Cancer from an Imaging Perspective. Int J Mol Sci. 2018 Aug 24;19(9):2511. doi: 10.3390/ijms19092511. PMID: 30149561; PMCID:

PMC6165113.

- [^]Marcu LG, Marcu DC. Current Omics Trends in Personalised Head and Neck Cancer Chemoradiotherapy. J Pers Med. 2021 Oct 26;11(11):1094. doi: 10.3390/jpm11111094. PMID: 34834445; PMCID: PMC8625829.
- 24. [^]Zhou Z, Wang K, Folkert M, Liu H, Jiang S, Sher D, Wang J. Multifaceted radiomics for distant metastasis prediction in head & neck cancer. Phys Med Biol. 2020 Aug 7;65(15):155009. doi: 10.1088/1361-6560/ab8956. PMID: 32294632.
- [^]Wang K, Zhou Z, Wang R, Chen L, Zhang Q, Sher D, Wang J. A multi-objective radiomics model for the prediction of locoregional recurrence in head and neck squamous cell cancer. Med Phys. 2020 Oct;47(10):5392-5400. doi: 10.1002/mp.14388. Epub 2020 Aug 5. PMID: 32657426.
- 26. [^]Jeon SH, Song C, Chie EK, Kim B, Kim YH, Chang W, Lee YJ, Chung JH, Chung JB, Lee KW, Kang SB, Kim JS. Delta-radiomics signature predicts treatment outcomes after preoperative chemoradiotherapy and surgery in rectal cancer. Radiat Oncol. 2019 Mar 12;14(1):43. doi: 10.1186/s13014-019-1246-8. PMID: 30866965; PMCID: PMC6417065.
- 27. [^]Chiesa S, Bartoli FB, Longo S, et al. Delta radiomics features analysis for the prediction of patients outcomes in glioblastoma multiforme:the generating hypothesis phase of GLIFA project. Int J Radiat Oncol. 2018;102(3):S213-S213
- [^]Wang K, Dohopolski M, Zhang Q, Sher D, Wang J. Towards reliable head and neck cancers locoregional recurrence prediction using delta-radiomics and learning with rejection option. Med Phys. 2023 Apr;50(4):2212-2223. doi: 10.1002/mp.16132. Epub 2022 Dec 17. PMID: 36484346; PMCID: PMC10121744.
- 29. ^Liu Y, Shi H, Huang S, Chen X, Zhou H, Chang H, Xia Y, Wang G, Yang X. Early prediction of acute xerostomia during radiation therapy for nasopharyngeal cancer based on delta radiomics from CT images. Quant Imaging Med Surg. 2019 Jul;9(7):1288-1302. doi: 10.21037/qims.2019.07.08. PMID: 31448214; PMCID: PMC6685806.
- 30. [^]Barua S, Elhalawani H, Volpe S, Al Feghali KA, Yang P, Ng SP, Elgohari B, Granberry RC, Mackin DS, Gunn GB, Hutcheson KA, Chambers MS, Court LE, Mohamed ASR, Fuller CD, Lai SY, Rao A. Computed Tomography Radiomics Kinetics as Early Imaging Correlates of Osteoradionecrosis in Oropharyngeal Cancer Patients. Front Artif Intell. 2021 Apr 9;4:618469. doi: 10.3389/frai.2021.618469. PMID: 33898983; PMCID: PMC8063205.
- [^]Koçak B, Cuocolo R, dos Santos DP, Stanzione A, Ugga L. Must-have Qualities of Clinical Research on Artificial Intelligence and Machine Learning. Balkan Med J. 2023 Jan 23;40(1):3-12. doi: 10.4274/balkanmedj.galenos.2022.2022-11-51. Epub 2022 Dec 29. PMID: 36578657; PMCID: PMC9874249.
- 32. [^]Khorrami M, Prasanna P, Gupta A, Patil P, Velu PD, Thawani R, Corredor G, Alilou M, Bera K, Fu P, Feldman M, Velcheti V, Madabhushi A. Changes in CT Radiomic Features Associated with Lymphocyte Distribution Predict Overall Survival and Response to Immunotherapy in Non-Small Cell Lung Cancer. Cancer Immunol Res. 2020 Jan;8(1):108-119. doi: 10.1158/2326-6066.CIR-19-0476. Epub 2019 Nov 12. PMID: 31719058; PMCID: PMC7718609.
- 33. [^]Welch ML, McIntosh C, Haibe-Kains B, Milosevic MF, Wee L, Dekker A, Huang SH, Purdie TG, O'Sullivan B, Aerts HJWL, Jaffray DA. Vulnerabilities of radiomic signature development: The need for safeguards. Radiother Oncol. 2019 Jan;130:2-9. doi: 10.1016/j.radonc.2018.10.027. Epub 2018 Nov 8. PMID: 30416044.