REVIEW ARTICLE

Analysis of Magnetic Resonance Imaging with Chemical Exchange Saturation Transfer in Glioma: A Medical Anthropology Perspective

Min Zhang, MM

ABSTRACT

Background • Medical anthropology plays a crucial role in understanding health, disease, and treatment within contemporary anthropology. As the incidence of tumors rises, with cancer posing a significant threat to human health, particularly malignant brain tumors, such as glioma, the need for accurate preoperative diagnosis and effective treatment strategies is paramount.

Objective • This study aims to review the literature on the advancements in medical anthropology and innovative medical technologies to enhance preoperative diagnostics, guide treatment strategies, and ultimately improve the survival rates and quality of life for glioma patients.

Methods • This study reviews and synthesizes existing literature, focusing on chemical exchange saturation transfer (CEST) imaging's potential to provide detailed information about the tumor microenvironment and metabolism. Extensive searches were conducted across reputable databases, including PubMed, Scopus, and relevant medical journals, to identify studies, articles, and reviews relevant to the connection between medical imaging and anthropological perspectives.

Results • Examining CEST imaging in glioma reveals promising insights. Through a medical anthropology lens, we assessed the potential for accurate preoperative diagnosis and the development of targeted treatment strategies. The results highlight the significance of integrating technological innovations in medicine with the theoretical foundations of medical anthropology to achieve more effective outcomes in glioma research and practice. Key findings include the transformative impact of CEST imaging on preoperative glioma assessment, its principles, and its ability to distinguish gliomas from other brain masses. The integration of medical anthropology in clinical oncology was explored, highlighting the sociocultural factors influencing patient care and outcomes.

Conclusions • This study marks a significant milestone in advancing the understanding and treatment of glioma. Integrating medical anthropology with advanced medical imaging technologies improves preoperative diagnostics, fostering innovation in both fields. This integration contributes to the overall advancement of glioma research and elevates the standards of patient care. (*Altern Ther Health Med.* [E-pub ahead of print.])

Min Zhang, MM, Center for Studies of Ethnic Groups in Northwest China of Lanzhou University; Lanzhou, China.

Corresponding author: Min Zhang, MM
E-mail: 13893400601@163.com

INTRODUCTION

Oncology is a field characterized by its unique and intricate challenges and demands an immediate shift from the traditional biomedical model to a modern "bio-psycho-social" framework.[1] Medical anthropology has emerged as a dynamic interdisciplinary research field with the potential for this imperative transformation.[2] This discipline offers practical insights, deploying a scientific, objective, and modern approach to tackle the profound difficulties individuals face when confronted with the realities of disease and mortality. Medical anthropology provides a valuable perspective for analyzing and resolving clinical problems, contributing to a holistic understanding of the complex relationship between biological, psychological, and social factors in oncological care.[2,3]

Brain tumors constitute approximately 5% of malignant lesions and are associated with high mortality and disability rates.[3] Glioma is the most prevalent primary central nervous system tumor and carries a poor prognosis and elevated mortality rate.[4] In recent years, magnetic resonance imaging (MRI) has emerged as the predominant preoperative diagnostic modality for individuals with brain tumors. This progress is attributed mainly to advanced sequence development and the extensive clinical applications of MRI.[5]

MRI scanning is pivotal in providing comprehensive insights into the tumor microenvironment and metabolism.[6]

Its significance extends beyond preliminary diagnosis, encompassing crucial aspects of glioma management such as surgical planning and monitoring therapeutic effects. The abundant information generated from MRI scans contributes to a more holistic approach to understanding and addressing the complexities associated with glioma.[5,6]

Chemical exchange saturation transfer (CEST) imaging, a subtype of MRI, relies on the proton exchange rate between water and endogenous or exogenous macromolecules with exchangeable protons at the molecular level. This modality exhibits heightened sensitivity to alterations in free proteins and other macromolecules within tissues, offering promising prospects for clinical applications. CEST imaging holds the potential for accurate diagnosis and therapeutic evaluation of glioma.[7]

Amide proton transfer (APT) is the most developed branch within CEST imaging. Moreover, a thorough exploration of this method from the medical anthropology perspective and incorporating theoretical insights from related disciplines has the potential to improve glioma management in clinical oncology substantially. This comprehensive approach can contribute to refining clinical practices and serves as a dependable reference for advancing medical technology.[6] This review was conducted to comprehensively explore the role of CEST imaging, mainly focusing on the mature branch of APT in the context of glioma management. Our findings offer valuable insights for clinical practice, fostering interdisciplinary collaboration and enhancing our holistic understanding of glioma management.

METHODS

A comprehensive and systematic approach was undertaken to gather relevant literature on CEST imaging, explicitly focusing on the medical anthropology perspective and its applications in glioma management. Extensive searches were conducted across reputable databases, including PubMed, Scopus, and relevant medical journals, to identify studies, articles, and reviews pertinent to the intersection of medical imaging and anthropological perspectives. The inclusion criteria prioritized works exploring the principles of CEST and APT, their evolution, and their clinical applications in the context of glioma. The synthesis of information was guided by a narrative format, emphasizing the integration of diverse insights from medical imaging technology and anthropological theories to provide a nuanced overview of glioma diagnosis, treatment planning, and therapeutic evaluation.

Medical Anthropology And Advancements In Glioma Diagnosis

Medical Anthropology Integration into Clinical Oncology. Medical anthropology is a discipline that employs anthropological theories and methodologies to investigate medical issues, emphasizing the understanding of health, disease, and treatment within diverse human societies and experiences.[7] The inception of examining medical behavior through a cultural lens began within the broader field of anthropology. Early developments in medical anthropology predominantly involved comparative, cross-cultural studies of non-Western medicine, as anthropologists conducted field research in various nations and cultures.[8]

Medical anthropologists attempt to understand the origins, diagnosis, and treatment modalities of diseases across diverse cultures. Presently, abundant cross-cultural comparative research materials exist within the expansive medical anthropology field.[9] Medical anthropology strives to propose various explanations for the origins of diseases and diverse treatment methods. This approach involves a deep exploration of the cultural difficulties that emphasize various medical issues, aiming for a comprehensive understanding.[10]

Compared to other medical disciplines, oncology stands out for its specificity and complexity, dealing with a disease, such as cancer, characterized by varying cure rates and high mortality.[9,10] The ongoing advancements in diagnostic and treatment technologies contribute to extending the life expectancy of patients, though not without accompanying challenges and suffering. An anthropological perspective emphasizes that the primary goal in oncology should be to extend patients' lives and alleviate the associated suffering.[11]

Therefore, the introduction of medical anthropology into oncology aims to offer humanistic and practical viewpoints, facilitating a comprehensive examination of the challenges within clinical oncology. This inclusion recognizes the relationship between cancer and culture as a distinctive interdisciplinary collaboration method.[12] The acknowledgment of sociocultural factors becomes pivotal in understanding the origins and prognoses of tumors, advocating for their integration into the clinical treatment paradigm. This holistic approach aspires to provide more comprehensive and human-centered care for patients globally struggling with malignancies, ultimately enhancing their treatment outcomes and overall quality of life.[13] The strategies for incorporating medical anthropology into clinical oncology are delineated as follows.

Transforming Traditional Therapies in Clinical Oncology. First and foremost, there is a necessity to shift the paradigm of traditional therapy for patients with tumors. In clinical practice, this approach involves consolidating an individual's therapeutic plan to encompass general, symptomatic, and localized treatments.[4] Upon thoroughly analyzing the patient's overall condition, including factors such as tumor location and pathological type, the recommended course of action involves embracing a multidisciplinary collaborative management approach. This approach encompasses the adoption of the most suitable diagnosis and treatment plan aimed at enhancing the overall prognosis.

Enhancing Psychological Well-being in Oncology Patients. Furthermore, recognizing the inherent need for psychological comfort and support among cancer patients, the sociocultural lens of medical anthropology proves invaluable. This perspective offers a deep understanding of a patient's pain experience and coping mechanisms.[14]

Consequently, medical anthropology is poised to offer tailored psychological intervention and cognitive therapy based on the emotional state of patients. This strategic approach aims to assist individuals in fostering positive and healthy beliefs throughout their cancer journey.

Integrating Cultural Values for Enhanced Oncological Outcomes. Medical anthropology underscores the profound impact of general values within diverse social and cultural contexts on a patient's outlook on cancer. The patient's psychological state, level of family support, and the broader social and cultural environment intricately shape the trajectory of the treatment process and its ultimate outcomes.[15] A notable strength of medical anthropology lies in its active consideration of patients' values and situations, aiming for optimal results. This approach, in turn, holds the potential to broaden the scope and perspectives within the field of oncological research.

Bridging Modern Science with Humanistic Perspectives in Oncology. Medical anthropology has the potential to integrate modern life sciences with humanistic considerations, fostering a comprehensive and pluralistic comprehension of diseases, particularly within the realm of oncology. This discipline facilitates nuanced analysis and research by situating oncological diseases within a cultural context, examining complex mechanisms, and seeking consensus from a methodological standpoint. Leveraging anthropology's emphasis on social culture and recognizing the cultural properties inherent in medicine as a natural science, medical anthropology emerges as a potentially more effective approach to explaining the interconnection between culture, medicine, and technological progress.[16]

Amidst the ongoing advancements in modern medical technology, there is an increasing demand for precise preoperative diagnoses. An accurate diagnosis emerges as the pivotal determinant in enhancing the clinical prognosis, particularly in cases of malignant brain tumors characterized by elevated disability and mortality rates.[17] Therefore, this review concisely outlines the advantages of the continuous evolution of novel MRI technologies for cancer patients, specifically focusing on the medical anthropological perspective in preoperative glioma diagnosis. The intent is to emphasize the significance of technological innovations in extending human life, urging a simultaneous consideration of cultural characteristics from a humanistic perspective.[18]

Glioma Diagnosis Advancements through CEST Imaging in Clinical Oncology

Medical anthropology plays a crucial role in systematically examining and clarifying oncology research, adopting a sociocultural perspective while highlighting technological advancements.[19] Glioma treatment predominantly relies on maximal safe-range surgical resection, complemented by chemoradiotherapy, with the histological diagnosis informed by postoperative pathological biopsy and immunohistochemistry reports.

A pivotal aspect is a preoperative diagnosis encompassing tumor type, grading, and genetic information, which helps shape the clinical treatment plan. In this context, MRI is the primary modality for glioma preoperative diagnosis, offering abundant diagnostic insights in the early stages. This review focuses on CEST imaging, an innovative MRI technology, investigating the progress of glioma diagnosis within clinical oncology.

Principles and Evolution of CEST Technology

In 2000, Ward et al.[20] introduced CEST technology as a groundbreaking MRI modality stemming from magnetic transfer (MT) innovations. Functioning as a non-invasive MRI technique, CEST relies on the chemical exchange of mobile protons among amide (-NH), amine (-NH_2), and hydroxyl (-OH) groups, in addition to free water molecules. This methodology provides insights into the alterations in mobile proton content and pH of proteins or peptides at the molecular level within tissues.

Its applicability extends to detecting and quantifying changes characteristic of glioma. CEST technology facilitates preoperative and differential glioma diagnosis at the molecular level, enabling classification, prediction of molecular categorization, and therapeutic effect evaluation. APT imaging is currently the most extensively researched and implemented subtype of CEST technology. Furthermore, CEST technology exhibits the capability to image hydroxyl (-OH) and amine (-NH_2) groups, creatine, glutamate, inositol, and various other metabolites.

RESULTS

Enhanced Preoperative Assessment Through CEST Technology

CEST technology emerges as a promising tool for the preoperative assessment of glioma. While conventional MRI scanning is commonly employed in such cases, discerning the glioma lesion from surrounding edema poses challenges. Zhou et al.[21] first proposed that APT imaging precisely delineates the boundaries of Gliosarcoma. Moreover, non-invasive APT imaging reveals internal heterogeneous components within high-grade gliomas. Notably, lesions appearing subtly enhanced on conventional T_1-weighted images (T_1WI) manifest as inhomogeneous hyperintensity on APT images.[22] This difference highlights the potential of CEST technology in providing a more detailed and nuanced preoperative assessment of glioma extent.

The average APT signal intensity within the solid tumor area exhibited a significant elevation compared to that in the edema area surrounding the tumor. Conversely, the average APT signal in the central necrotic area was markedly lower than in the solid tumor component. These distinctions may be attributed to tumor cell proliferation activity variations, heightened protein content, and alterations in amide proton concentration. This observation provides valuable guidance for targeted biopsies in gliomas, facilitating precise diagnosis and tailored treatment planning. Moreover, this technology holds promise in identifying microscopic areas of tumor invasion that remain undetectable with conventional MRI.[23,24]

Optimized Preoperative Grading with CEST Technology

The preoperative grading of gliomas plays a pivotal role in tailoring personalized treatment plans. As per the World Health Organization (WHO) classification standard, gliomas are categorized into grades I-IV. However, relying solely on conventional MRI for preoperative classification poses limitations, as 20% of low-grade gliomas exhibit significant enhancement, while 25% of high-grade gliomas show little to no enhancement. The accelerated proliferation of high-grade glioma cells and increased protein expression distinguish them from their low-grade counterparts. Therefore, CEST technology emerges as a valuable tool, providing more accurate diagnostic information for precise glioma classification.

CEST Technology for Differential Diagnosis of Glioma

Distinguishing gliomas from brain metastases, primary central nervous system lymphomas (PCNSLs), and certain infectious masses poses a challenge due to shared signal features and enhancement patterns.[23-24] Conventional MRI and additional sequences, including perfusion-weighted imaging (PWI), diffusion-weighted imaging (DWI), and magnetic resonance spectroscopy (MRS), often lack diagnostic specificity in this context. Notably, Jiang et al.[25] discovered that the APT signal parameters (APT_{max}, $APT_{max\text{-}min}$, $CEST_{total}$) in PCNSL lesions were significantly lower than those in high-grade gliomas. This disparity may be attributed to the higher nuclear-cytoplasmic ratio characteristic of PCNSLs. The exploration of CEST technology holds promise in refining the differential diagnosis of gliomas, offering enhanced specificity in challenging cases.

Considering the invasive nature of gliomas, their APT signal within the peritumoral edema area surpasses that of PCNSLs. These parameters prove helpful in distinguishing between these lesions, with $APT_{max\text{-}min}$ demonstrating the most effective differential diagnostic impact (Area Under the Curve [AUC] 0.963; accuracy 94.1%). Simultaneously, APT imaging significantly elevates the accuracy of distinguishing between glioblastomas and metastases.

Notably, APTmin in the peritumoral edematous area emerges as the most precise parameter for distinguishing metastases from glioblastomas (AUC 0.905 and accuracy 85.2%). Remarkably, this accuracy surpasses that of junior and senior physicians (51.6% and 79.5%, respectively),[26] highlighting the potential of APT imaging in augmenting diagnostic precision. Additionally, histogram analysis of APT imaging is valuable in distinguishing gliomas from infectious lesions.[27]

Molecular Markers for Prediction and Diagnosis of Glioma

In line with the 2021 WHO classification criteria for central nervous system tumors,[28] specific molecular markers significantly impact the prediction and diagnosis of gliomas. Notably, mutations in isocitrate dehydrogenase (*IDH*), inappropriate methylation in the promoter of O^6-methylguanine-DNA-methyltransferase (*MGMT*), K27M mutation in histone H3, and chromosome 1p/19q co-deletion play important roles in glioma classification and grading. These molecular alterations influence the selection of treatment strategies and impact treatment efficacy and prognosis.

Encouragingly, multiple studies have demonstrated that CEST and its variations can non-invasively identify these crucial mutations before surgery.[29–31] This finding underscores the potential of CEST technology as a valuable asset in the molecular characterization of gliomas, aiding in more precise treatment planning and prognostic assessments.

Preoperative APT emerges as an independent prognostic factor for gliomas. An increased APT signal correlates with increased tumor cell proliferation and invasiveness, standing as a robust and independent predictor of low progression-free and overall survival in high-grade glioma patients. The prognostic value of APT surpasses that of other clinically relevant prognostic factors and molecular markers.[32,33] Integrating the APT signal as a parameter into a prediction model significantly enhances its performance. This finding highlights the pivotal role of APT as a supplementary diagnostic method, emphasizing its potential to refine prognostic assessments and contribute to more effective treatment planning for individuals with gliomas.

DISCUSSION

The primary approach for treating gliomas remains maximum safe-distance surgical resection, often complemented by adjuvant radiotherapy and temozolomide chemotherapy. Despite these combined interventions contributing to extended patient survival, the 5-year survival rate for glioblastoma remains dishearteningly low at 5%.[34] Furthermore, the impact of chemotherapy extends beyond targeting malignant cells, potentially causing collateral damage to healthy brain tissue. This unintended consequence may lead to local inflammation, edema, and altered vascular permeability, highlighting the intricate balance required in glioma treatment strategies. To improve therapeutic outcomes, it is crucial to navigate the challenges posed by these interventions adeptly. This strategic approach ensures the optimization of patient care and contributes to an overall improvement in the quality of life for individuals undergoing glioma treatment.

Conventional MRI often depicts these changes as mixed signals and irregular enhancements on T_1-weighted imaging (T_1WI) and T_2-weighted imaging (T_2WI). The challenge lies in differentiating these signals from potential glioma recurrence. Consequently, biomarkers are urgently needed to promptly estimate treatment efficacy and differentiate genuine tumor progression from post-treatment alterations. This quest for biomarkers aims to prevent ineffective treatments, offering a pathway to tailor interventions based on individualized responses, ultimately optimizing the effectiveness of glioma therapies.

Multiple studies have shown the remarkable capability of CEST imaging parameters in promptly assessing the response of glioma patients to chemoradiotherapy, surpassing the sensitivity of morphological changes like tumor volume reduction. Notably, CEST proves very useful in identifying individuals potentially facing early progression even before the initiation of chemoradiotherapy. This early detection empowers timely adjustments to the treatment plan, illustrating the pivotal role of CEST imaging in revolutionizing the monitoring and management of glioma patients.[35,36]

Medical anthropology, a discipline full of theoretical depth and practical application, stands at the forefront of vigorous and progressive development. Systematic exploration of oncological challenges consistently generates innovative strategies to confront the evolving landscape of chronic diseases. The analysis of glioma research progress and its real-world applications not only mirrors the compassionate essence of anthropology but also underscores the scientific rigor intrinsic to medicine. This comprehensive approach considers the cultural and social dimensions, adding a profound layer to our understanding of disease.[37]

Medical anthropology plays a critical role in broadening the collective understanding of the diverse facets of illness and the treatment journey. It serves as a keystone for medical treatment, enhancing both academic and clinical research endeavors.[38] This influential capacity is anticipated to catalyze the advancement of rapid and precise CEST technology for glioma and other diseases. It holds the potential to elevate disease diagnosis by furnishing more extensive diagnostic information, enhancing treatment efficacy monitoring, and ultimately contributing to the improvement of patient prognoses.

Along with societal evolution, medical anthropology is poised to gain increasing visibility and integration across a spectrum of disciplines. Rooted in medical humanistic studies, its application extends beyond professional domains, encompassing clinical practice, imaging, and allied domains.[39] The discipline's expanding influence holds the potential to underscore the role and significance of culture in medical practice. Focusing on the social dimensions of medicine and understanding patients' emotions and health-seeking behaviors, medical anthropology significantly contributes to improving the effectiveness of Western medicine in treating diseases.

Therefore, to thrive in the evolving landscape, this discipline must align with global medical anthropology research trends. It should strengthen its role, expand research institutions and collaborative teams, persist in applied research, and facilitate the translation of studies across diverse nations. Enhancing the anthropological theory and framework, grounded in an understanding of diseases across countries, is paramount. Attention to patient needs, advocacy for humanistic concepts, and the cultivation of humanistic literacy among medical students are crucial. Embedding humanistic care and psychological support within clinical practice lays a robust foundation for the continued advancement of medical anthropology. This ongoing commitment to research holds immense significance for the discipline's future impact and development.

CONCLUSION

In conclusion, this study highlights the pivotal role of medical anthropology in understanding and addressing the complexities of oncological diseases, particularly gliomas. By merging scientific rigor with a humanistic perspective, medical anthropology contributes invaluable insights into the holistic experience of illness and treatment. The exploration of advanced technologies like CEST imaging within this interdisciplinary framework not only enhances diagnostic precision but also propels the field toward more effective treatment strategies. As we navigate the challenges of contemporary healthcare, the continued development of medical anthropology emerges as a potent force in fostering cultural awareness, patient-centric care, and advancements in medical technologies. In the future, the integration of anthropological insights into medical practice is believed to play a pivotal role in shaping more compassionate, culturally attuned, and efficacious healthcare.

CONFLICTS OF INTEREST

All authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

FUNDING STATEMENT

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ACKNOWLEDGMENTS

None.

REFERENCES

1. Fellmann F. From social psychology to cultural psychology: the redemption of personality. *Psychology (Irvine)*. 2017;08(10):1586-1600. doi:10.4236/psych.2017.810105
2. Johnson TM, Sargent CF. *Medical Anthropology: Contemporary Theory and Method*. Praeger Publishers; 1990.
3. Young A. The anthropologies of illness and sickness. *Annu Rev Anthropol*. 1982;11(1):257-285. doi:10.1146/annurev.an.11.100182.001353
4. Vernimmen FJ, Rock K. Technological progress in radiation therapy for brain tumors. *J Cancer Ther*. 2014;05(1):38-43. doi:10.4236/jct.2014.51005
5. Dongas J, Asahina AT, Bacchi S, Patel S. Magnetic resonance perfusion imaging in the diagnosis of high-grade glioma progression and treatment-related changes: A systematic review. *Open J Mod Neurosurg*. 2018;08(3):282-305. doi:10.4236/ojmn.2018.83024
6. Jelenc M. The partnership of public health and anthropology. *Coll Antropol*. 2016;40(2):151.
7. Kleinman A, Eisenberg L, Good B. Culture, illness, and care: clinical lessons from anthropologic and cross-cultural research. *Ann Intern Med*. 1978;88(2):251-258. doi:10.7326/0003-4819-88-2-251
8. Bob. Study on Mongolian medicine with the medical anthropology theory and method. *Zhong Yi Xue*. 2021;10(1):97-100. doi:10.12677/TCM.2021.101012
9. Logan MH. *HEJ. Health and the Human Condition: Perspectives on Medical Anthropology*. Duxbury Press; 1978.
10. Lock MM, Nguyen V-K. *An Anthropology of Biomedicine*. John Wiley & Sons; 2018.
11. Baltić V. Impact assessment of oncology literature published in Serbia. *Arch Oncol*. 2005;13(2):59-61. doi:10.2298/AOO0502059B
12. Atkinson SJ. Anthropology in research on the quality of health services. *Cad Saúde Publ*. 1993;9:283-299. https://doi.org/10.1590/S0102-311X1993000300016.
13. Hahn RA. *Sickness and Healing: an Anthropological Perspective*. Yale University Press; 1995.
14. Varela FJ, Thompson E, Rosch E. *The Embodied Mind*. rev. ed.: Cognitive science and human experience: MIT press; 2017. doi:10.7551/mitpress/9780262529365.001.0001
15. Kleinman A. Concepts and a model for the comparison of medical systems as cultural systems. *Soc Sci Med*. 1978;12(2B):85-95. doi:10.1016/0160-7987(78)90014-5
16. Wan X, Liu JP, Ai YK, Li LJ. [Cultural anthropology of traditional Chinese medicine]. *J Chin Integr Med*. 2008;6(7):674-677. doi:10.3736/jcim20080703
17. Nikitović MR, Golubicić IV, Borojević ND, Pekmezović TD, Grujicić DM, Plesinac-Karapandzić VS. [Pediatric brain tumors--diagnostic and treatment]. *Acta Chir Iugosl*. 2009;56(4):19-24. doi:10.2298/ACI0904019N
18. Csordas TJ. Somatic modes of attention. *Cult Anthropol*. 1993;8(2):135-156. doi:10.1525/can.1993.8.2.02a00010
19. Bukovčan T. How ethnology (Mis) treated medicine: little regional history of transformation of traditional medicine into medical anthropology. *Stud Ethnol Croat*. 2010;22:215-235.
20. Ward KM, Aletras AH, Balaban RS. A new class of contrast agents for MRI based on proton chemical exchange dependent saturation transfer (CEST). *J Magn Reson*. 2000;143(1):79-87. doi:10.1006/jmre.1999.1956
21. Zhou J, Lal B, Wilson DA, Laterra J, van Zijl PC. Amide proton transfer (APT) contrast for imaging of brain tumors. *Magn Reson Med*. 2003;50(6):1120-1126. doi:10.1002/mrm.10651
22. Wen Z, Hu S, Huang F, et al. MR imaging of high-grade brain tumors using endogenous protein and peptide-based contrast. *Neuroimage*. 2010;51(2):616-622. doi:10.1016/j.neuroimage.2010.02.050
23. Warnert EAH, Wood TC, Incekara F, et al. Mapping tumour heterogeneity with pulsed 3D CEST MRI in non-enhancing glioma at 3 T. *Magn Reson Mater Biol Phys Med*. 2022;35(1):53-62. doi:10.1007/s10334-021-00911-6
24. Wu Y, Wood TC, Arzanforoosh F, et al. 3D APT and NOE CEST-MRI of healthy volunteers and patients with non-enhancing glioma at 3 T. *Magn Reson Mater Biol Phys Med*. 2022;35(1):63-73. doi:10.1007/s10334-021-00996-z
25. Jiang S, Yu H, Wang X, et al. Molecular MRI differentiation between primary central nervous system lymphomas and high-grade gliomas using endogenous protein-based amide proton transfer MR imaging at 3 Tesla. *Eur Radiol*. 2016;26(1):64-71. doi:10.1007/s00330-015-3805-1

26. Yu H, Lou H, Zou T, et al. Applying protein-based amide proton transfer MR imaging to distinguish solitary brain metastases from glioblastoma. *Eur Radiol*. 2017;27(11):4516-4524. doi:10.1007/s00330-017-4867-z
27. Debnath A, Gupta RK, Singh A. Evaluating the role of amide proton transfer (APT)-weighted contrast, optimized for normalization and region of interest selection, in differentiation of neoplastic and infective mass lesions on 3T MRI. *Mol Imaging Biol*. 2020;22(2):384-396. doi:10.1007/s11307-019-01382-x
28. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the central nervous system: a summary. *Neuro-oncol*. 2021;23(8):1231-1251. doi:10.1093/neuonc/noab106
29. Yao J, Hagiwara A, Raymond C, et al. Human IDH mutant 1p/19q co-deleted gliomas have low tumor acidity as evidenced by molecular MRI and PET: a retrospective study. *Sci Rep*. 2020;10(1):11922. doi:10.1038/s41598-020-68733-5
30. Jiang S, Rui Q, Wang Y, et al. Discriminating MGMT promoter methylation status in patients with glioblastoma employing amide proton transfer-weighted MRI metrics. *Eur Radiol*. 2018;28(5):2115-2123. doi:10.1007/s00330-017-5182-4
31. Zhuo Z, Qu L, Zhang P, et al. Prediction of H3K27M-mutant brainstem glioma by amide proton transfer-weighted imaging and its derived radiomics. *Eur J Nucl Med Mol Imaging*. 2021;48(13):4426-4436. doi:10.1007/s00259-021-05455-4
32. Joo B, Han K, Ahn SS, et al. Amide proton transfer imaging might predict survival and IDH mutation status in high-grade glioma. *Eur Radiol*. 2019;29(12):6643-6652. doi:10.1007/s00330-019-06203-x
33. Paech D, Dreher C, Regnery S, et al. Relaxation-compensated amide proton transfer (APT) MRI signal intensity is associated with survival and progression in high-grade glioma patients. *Eur Radiol*. 2019;29(9):4957-4967. doi:10.1007/s00330-019-06066-2
34. Chawla S, Bukhari S, Afridi OM, et al. Metabolic and physiologic magnetic resonance imaging in distinguishing true progression from pseudoprogression in patients with glioblastoma. *NMR Biomed*. 2022;35(7):e4719. doi:10.1002/nbm.4719
35. Mehrabian H, Myrehaug S, Soliman H, Sahgal A, Stanisz GJ. Evaluation of glioblastoma response to therapy with chemical exchange saturation transfer. *Int J Radiat Oncol Biol Phys*. 2018;101(3):713-723. doi:10.1016/j.ijrobp.2018.03.057
36. Meissner JE, Korzowski A, Regnery S, et al. Early response assessment of glioma patients to definitive chemoradiotherapy using chemical exchange saturation transfer imaging at 7 T. *J Magn Reson Imaging*. 2019;50(4):1268-1277. doi:10.1002/jmri.26702
37. Farmer P, Kim JY, Kleinman A, Basilico M. *Reimagining Global Health: an Introduction*. University of California Press; 2013.
38. Béhague DP, Gonçalves H, Victora CG. Anthropology and Epidemiology: learning epistemological lessons through a collaborative venture. *Cien Saude Colet*. 2008;13(6):1701-1710. doi:10.1590/S1413-81232008000600002
39. Trostle JA, Sommerfeld J. Medical anthropology and epidemiology. *Annu Rev Anthropol*. 1996;25(1):253-274. doi:10.1146/annurev.anthro.25.1.253