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EDITORIAL

Editorial for "Functional MRI and Tumor Vasculature Correlation in Ewing Sarcoma Xenografts: A Prospective Study Based on MRI-Pathology Co-Alignment"

Zubkov Mikhail

GIGA-Institute, CRC-Human Imaging, University of Liège, Liège, Belgium

Correspondence: Zubkov Mikhail (m.zubkov@uliege.be)

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The work "Functional MRI and Tumor Vasculature Correlation in Ewing Sarcoma Xenografts: a Prospective Study Based on MRI-Pathology Co-alignment" [1] approaches several research questions with appealing rigor and sufficient detail. Briefly, the authors have employed a meticulous scan and tissue preparation protocol [2] ensuring through placement of well-thought out markings the co-alignment between the imaging and the histopathological data, and have applied it to the Ewing sarcoma human cells grafted into the animal model for growth, imaging, and further excision. At the imaging step, the mice were subjected to a 3T MRI scan, including classical anatomical imaging, and a number of quantitative approaches: intravoxel incoherent motion, and dynamic contrast enhancement analyzed with Tofts model, in this case. After the following excision, the tissues have been accordingly prepared to allow quantification of vascular endothelial growth factor, microvessel density, and vascular mimicry—the three being critical in Ewing sarcoma malignancy regulation. The subsequent statistical analysis of the histopathologically derived and imaging-derived vascularity measures revealed the connection between a number of quantitative perfusion metrics and the underlying tumor vascularity.

This seemingly straightforward approach features at least three vital traits that make it stand out in a biomedical research field. To start with, a substantial section of [1] is dedicated to the analysis of the predictive power of quantitative MRI in Ewing sarcoma. The analysis of the predictive power of the biophysical tumor model is a rare finding in biomedicine, where the field is dominated by inference studies, which serve their own vital but substantially different purpose when compared to establishing clinical significance or diagnostic power. Second, the pathology itself: Ewing sarcoma MRI is a scarcely examined topic, primarily due to the relatively rare prevalence of the tumor [3], but also due to its strong heterogeneity, resulting in a complex imaging appearance. The conventional anatomical MRI is nevertheless critical for Ewing sarcoma operation planning, as it has the potential to improve the post-operative quality of life, although it is not possible to use it to discriminate between active tumor recurrence and reactive changes [4]. This downside of conventional MRI is commonly tackled via multiparametric and quantitative imaging [5]. In Ewing sarcoma, this is complicated due to high tumor heterogeneity, hindering quantitative analysis of the imaging data, particularly acquiring reference values for this particular tumor type. This highlights the third and the main hallmark of [1], which supports the quantitative MRI findings with the histopathological immunohistochemistry data, the latter being the reference method for Ewing sarcoma diagnostics and validation. Works like this are rare and foundational in quantitative MRI, as they set the standards and build normative databases for future methods developments. Such research has been recently conducted for the central nervous system [6], laying forth the basis for major research directions in the fields of healthy aging and pathologic neurodegeneration such as Alzheimer's and Parkinson's disease. Outside of the brain, research combining immunohistochemistry measures with quantitative MRI was conducted for colon cancer [7]. In sarcoma studies, investigation has been performed in a substantial cohort of human subjects, revealing a connection of the same perfusion parameters as in [1], but to the hypoxia-inducible factor 1-alpha instead [8], which has been related to tumor recurrence and

treatment resistance. Smaller studies have also employed the same approach to identify sarcoma proliferation and radiotherapy response [9, 10].

"Functional MRI and Tumor Vasculature Correlation in Ewing Sarcoma Xenografts: a Prospective Study Based on MRI-Pathology Co-alignment" [1] thus follows the line of employing distilled methodology when tackling original challenges, which suggests it might be paving the path for an extended leap into quantitative imaging-based research of Ewing sarcoma in the near future, as there is still a number of possible extensions of the presented findings: the relaxivity measurements in the tumor, the ultra-high field MRI quantification, and the possible extension into the well-suited for musculoskeletal imaging low-field imaging to name a few. Finally, supporting the presented quantification in xenografts with in vivo human imaging and the analysis of post-operative tissue, as it was done for soft tissue sarcomas and hypoxia-inducible factor 1-alpha, seems to be the logical continuation of this work, which is likely to follow.

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References

1. X. Liu, K. Zhang, Y. Song, et al., "Functional MRI and Tumor Vasculature Correlation in Ewing Sarcoma Xenografts: A Prospective Study Based on MRI-Pathology Co-Alignment," *Journal of Magnetic Resonance Imaging* (2025), https://doi.org/10.1002/jmri.29770.

2. Y. Yuan, D. Zeng, Y. Liu, et al., "DWI and IVIM Are Predictors of Ki67 Proliferation Index: Direct Comparison of MRI Images and Pathological Slices in a Murine Model of Rhabdomyosarcoma," *European Radiology* 30 (2020): 1334–1341.

3. S. C. Kaste, "Imaging Pediatric Bone Sarcomas," *Radiologic Clinics* 49 (2011): 749–765.

4. C. Frouge, D. Vanel, C. Coffre, D. Couanet, G. Contesso, and D. Sarrazin, "The Role of Magnetic Resonance Imaging in the Evaluation of Ewing Sarcoma," *Skeletal Radiology* 17 (1988): 387–392.

5. E. J. Inarejos Clemente, O. M. Navarro, M. Navallas, et al., "Multiparametric MRI Evaluation of Bone Sarcomas in Children," *Insights Into Imaging* 13, no. 33 (2022): 1–18.

6. A. Alkemade, P.-L. Bazin, R. Balesar, et al., "A Unified 3D Map of Microscopic Architecture and MRI of the Human Brain," *Science Advances* 8, no. 17 (2022): eabj7892, https://doi.org/10.1126/sciadv.abj7892.

7. J. Liang, Q. Cheng, J. Huang, et al., "Monitoring Tumour Microenvironment Changes During Anti-Angiogenesis Therapy Using Functional MRI," *Angiogenesis* 22 (2019): 457–470.

8. X. Li, Y. Xie, Y. Hu, et al., "Soft Tissue Sarcoma: Correlation of Dynamic Contrast-Enhanced Magnetic Resonance Imaging Features With HIF-1α Expression and Patient Outcomes," *Quantitative Imaging in Medicine and Surgery* 12 (2022): 4823836–4824836.

9. J. H. Lee, Y. C. Yoon, S. W. Seo, Y.-L. Choi, and H. S. Kim, "Soft Tissue Sarcoma: DWI and DCE-MRI Parameters Correlate With Ki-67 Labeling Index," *European Radiology* 30 (2020): 914–924.

10. M. Jung, B. Bogner, T. D. Diallo, et al., "Multiparametric Magnetic Resonance Imaging for Radiation Therapy Response Monitoring in Soft Tissue Sarcomas: A Histology and MRI Co-Registration Algorithm," *Theranostics* 13 (2023): 1594–1606.