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Letter to the Editor of Radiotherapy and Oncology regarding the paper titled "MRI and FUNDUS image fusion for improved ocular biometry in Ocular Proton Therapy" by Via et al.

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Letter to the Editor of Radiotherapy and Oncology regarding the paper titled "MRI and FUNDUS image fusion for improved ocular biometry in Ocular Proton Therapy" by Via et al.

Jan-Willem M. Beenakker PhD ^{1,2,3}, Coen R.N. Rasch MD PhD¹

Affiliations:

¹Department of Radiation Oncology, Leiden University Medical Center, 2333ZA Leiden, The Netherlands ²Department of Radiology, Leiden University Medical Center, 2333ZA Leiden, The Netherlands

³Department of Ophthalmology, Leiden University Medical Center, 2333ZA Leiden, The Netherlands

Corresponding author:

Jan-Willem Beenakker, PhD

With great interest have we read the recent publication of Via et al.,[1] who propose a method to combine optical fundus photographs and magnetic resonance images (MRI) of the eye. Combining the strengths of different imaging modalities is an important path to improve the outcomes for patients with an intraocular tumor. Based on a flat tumor component that was missed on the MRI of two patients, the authors conclude that MRI is limited in determining the tumor extent. However, in the last decade, ocular MRI has seen a number of considerable technical advances,[2] resulting in significant improvements in image quality. Unfortunately, the MR-protocol used by Via et al. lacks most of these advances.[3]

Contrast enhancement: Similar to tumors in other body parts, MR-imaging of eye tumors should include contrast-enhanced scans to reliably determine the (enhancing) tumor extent.[4–7] Unfortunately, the vast majority (83%) of the patients were scanned without contrast, making it indeed difficult to differentiate flat tumor components from the choroid. Motion artifacts: Although the authors obtained a good image resolution of 0.5mm isotropic, the used sequences took up to five minutes to acquire, in contrast to modern 3 Tesla sequences which only take 2 minutes[8]. As a result, the actual image quality will not be limited by resolution but by eye-motion artefacts, as patients cannot maintain a stable gaze for such a prolonged period of time.[9,10] Combined with the applied smoothing filter in the post-processing, the used scans likely contain too much blurring to reliably detect small details. Unfortunately, we could not assess the impact of these limitations, as the MR-images of these cases have not been included in the publication.

With a modern MRI protocol, however, detailed anatomical images of the eye and tumor can be acquired, which proved to reveal clinically relevant details that were not visible on conventional fundus and/or ultrasound imaging.[6,8,11] MRI, for example, can reveal tumor invasion into the optic nerve not visible on ophthalmic imaging.[11]

As a result, we wonder if the authors would agree that the observed MRI limitations are more a reflection of the used MRI protocol than of a limitation of ocular MRI in general.

References

[1] Via R, Pica A, Antonioli L, Paganelli C, Fattori G, Spaccapaniccia C, et al. MRI and FUNDUS image fusion for improved ocular biometry in Ocular Proton Therapy. Radiotherapy Oncol J European Soc Ther Radiology Oncol 2022. https://doi.org/10.1016/j.radonc.2022.06.021.

[2] Niendorf T, Beenakker J-WM, Langner S, Erb-Eigner K, Cuadra MB, Beller E, et al. Ophthalmic Magnetic Resonance Imaging: Where Are We (Heading To)? Curr Eye Res 2021:1–20. https://doi.org/10.1080/02713683.2021.1874021.

[3] Via R, Hennings F, Pica A, Fattori G, Beer J, Peroni M, et al. Potential and pitfalls of 1.5T MRI imaging for target volume definition in ocular proton therapy. Radiother Oncol 2021;154:53–9. https://doi.org/10.1016/j.radonc.2020.08.023.

[4] Graaf P de, Göricke S, Rodjan F, Galluzzi P, Maeder P, Castelijns JA, et al. Guidelines for imaging retinoblastoma: imaging principles and MRI standardization. Pediatric Radiology 2012;42:2–14. https://doi.org/10.1007/s00247-011-2201-5.

[5] Ferreira TA, Fonk LG, Jaarsma-Coes MG, Haren GGR van, Marinkovic M, Beenakker J-WM. MRI of Uveal Melanoma. Cancers 2019;11:377. https://doi.org/10.3390/cancers11030377.

[6] Foti PV, Travali M, Farina R, Palmucci S, Spatola C, Raffaele L, et al. Diagnostic methods and therapeutic options of uveal melanoma with emphasis on MR imaging—Part I: MR imaging with pathologic correlation and technical considerations. Insights Imaging 2021;12:66. https://doi.org/10.1186/s13244-021-01000-x.

[7] D'Arco F, Mertiri L, Graaf P de, Foer BD, Popovič KS, Argyropoulou MI, et al. Guidelines for magnetic resonance imaging in pediatric head and neck pathologies: a multicentre international consensus paper. Neuroradiology 2022;64:1081–100. https://doi.org/10.1007/s00234-022-02950-9.

[8] Jaarsma-Coes MG, Ferreira TA, Marinkovic M, Vu THK, Vught L van, Haren GR van, et al. Comparison of MRI-based and conventional measurements for proton beam therapy of uveal melanoma. Ophthalmology Retina 2022. https://doi.org/10.1016/j.oret.2022.06.019.

[9] Tang MCY, Jaarsma-Coes MG, Ferreira TA, Fonk LZ- G, Marinkovic M, Luyten GPM, et al. A Comparison of 3 T and 7 T MRI for the Clinical Evaluation of Uveal Melanoma. J Magn Reson Imaging 2022;55:1504–15. https://doi.org/10.1002/jmri.27939.

[10] Berkowitz B, Detroit M, Canfield D, McDonald C, Ito Y, Tofts P, et al. Measuring the human retinal oxygenation response to a hyperoxic challenge using MRI: Eliminating blinking artifacts and demonstrating proof of concept. Magnetic Resonance in Medicine 2001;46:412–6. https://doi.org/10.1002/mrm.1206.

[11] Ferreira TA, Jaarsma-Coes MG, Marinkovic M, Verbist B, Verdijk RM, Jager MJ, et al. MR imaging characteristics of uveal melanoma with histopathological validation. Neuroradiology 2021:1–14. https://doi.org/10.1007/s00234-021-02825-5.