Delayed Disintegration of Glioblastoma Spheroids After Magnetic Hyperthermia Without Proportional Increase in Detected Cell Death

Mazzitelli Fuentes, Laura[1]; Morales Ovalle, Marco[2]; Vasquez Mansilla, Marcelo[2]; Lima Jr, Enio[2]; Winkler, Elin[2,3]; Negrin, Lara[1]; Zysler, Roberto[2,3]; Raineri, Mariana[2,4]

[1] Instituto de Tecnologías Nucleares para la Salud (INTECNUS), CNEA, San Carlos de Bariloche, Argentina.
[2] Instituto de Nanociencia y Nanotecnología, Nodo Bariloche, CNEA-CONICET, San Carlos de Bariloche, Argentina
[3] Departamento de Magnetismo y Materiales Magnéticos, Gerencia de Física (CNEA), San Carlos de Bariloche, Argentina.
[4] Instituto Balseiro, San Carlos de Bariloche, Argentina
[5] Facultad de Medicina, Universidad Nacional de Río Negro sede Andina, San Carlos de Bariloche, Argentina.

rainericab@gmail.com

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Magnetic hyperthermia is a promising therapeutic approach; however, its impact on three-dimensional tumor organization and delayed responses remains incompletely characterized. Here, we evaluated the effects of magnetic hyperthermia on glioblastoma multicellular spheroids, focusing on the relationship between structural integrity, metabolic activity, and cell viability.

Spheroids were exposed to nanoparticle-mediated hyperthermia under conditions reaching therapeutic temperature ranges. Responses were assessed over several days using metabolic assays, confocal microscopy, flow cytometry, and morphological analysis.

At early time points, spheroids retained a substantial fraction of metabolic activity, as determined by an acid phosphatase assay. By day 4 post-treatment, a pronounced loss of structural integrity was observed exclusively in the nanoparticle-mediated hyperthermia group, with most spheroids exhibiting fragmentation and collapse. Notably, flow cytometry of cells recovered at day 4 revealed predominantly viable populations in both control and treated samples, despite the marked disintegration observed only in the treated group.

These findings indicate a dissociation between structural integrity and detectable cell death following magnetic hyperthermia. This behavior may reflect alterations in cell–cell interactions, mechanical stability, or selective recovery of viable subpopulations. Overall, our results highlight the importance of incorporating structural and recovery-dependent endpoints when evaluating hyperthermia responses in 3D tumor models.