Three-dimensional models for a deep investigation of ultrasound-based anticancer treatments

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Three-dimensional (3D) cell cultures represent an innovative platform where cells grow and interact with each other in all three dimensions thanks to an artificial environment. 3D models are more reliably predicting in vivo efficacy from in vitro data compared to classic two-dimensional (2D) models, as cells in 3D models show several improvements in i) morphology, proliferation and differentiations; ii) response to external and internal stimuli and iii) drug metabolism and efficacy. For this reason, 3D models have been taken into consideration to facilitate the development of ultrasound (US)-based treatments. Specifically, US has been used for various therapeutic approaches such as promoting tissue healing, decreasing chronic pain, tumor ablation and drug release from drug delivery systems but, one of the most attractive approaches, remains the sonodynamic therapy (SDT). SDT is an anticancer approach based on the use of US to activate a chemical compound, called sonosensitizer. The way in which SDT achieves cytotoxic effects is still under debate, but acoustic cavitation has been considered responsible to trigger sonosensitizer cytotoxicity, through reactive oxygen species (ROS) production, considered the main biological mechanism involved. Therefore, in this work various US-based treatments will be discussed, with a special focus on the use of 3D models for their investigation.