Surfactant based nanobubbles: a combined strategy to enhance brain delivery

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Nanoscale echogenic bubbles (NBs), can be used as a theranostic platform for the localized delivery of encapsulated drugs. Although the generation of NBs is challenging, their short lifetimes and instability limit their application. The aim of our research activity was the optimization of a preparation method for the generation of stable NBs, characterized by measuring: a) acoustic efficiency, b) nano-size, to ensure passive tumour targeting, c) stability during storage and after injection and d) ability to entrap drugs. NBs are monodisperse and ultrastable, their stability achieved by generation of an amphiphilic multilamellar shell able to efficiently retain the PFC gas. The NBs perform as good acoustic enhancers over a wide frequency range and out of resonant conditions, as tested in both in vitro and in vivo experiments, proving to be a potential platform for the BBB opening in presence of Focused Ultrasounds (FUS), encouraging the possibility to deliver NBs in the brain obtaining stable cavitation. Other NBs, made of different surfactants were also proposed for Nose to Brain Delivery (N2B). A new kind of protocol to evaluate an *in vitro* US characterization of NBs was developed and obtained results suggest a stable and controlled probe release, encouraging the possibility to deliver NBs into the brain. In this context, extracellular field recordings in specific area of hippocampus (CA1-CA3) have been carried out in order to assure that synaptic plasticity was not affected in the form of long-term potentiation.