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Design of multi-functional core-shell nanoparticles and investigation of their transport kinetics after intracranial injection in a brain cancer model

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Abstract:

Glioblastoma multiforme (GBM) is the most common primary brain tumor in adults. Because of its aggressive and infiltrative nature, efficient treatment with systemic chemotherapy remains a major challenge.
In this work, multifunctional polymer nanoparticles (PNPs) for concomitant loading of multiple payloads and imaging agents were designed and characterized for the intracranial (i.c.) drug delivery in GBM. Their transport/clearance kinetics were investigated after i.c. administration in a highly infiltrative GBM model.
Core-shell PNPs were prepared by a nano-precipitation/self-assembly method to obtain a biocompatible lipid shell for long circulation and ready conjugation with imaging agents and a polymer core of multi-block polyurethanes (PURs).
These particles showed a high efficiency in loading multiple payloads and remarkable imaging capabilities, showing high selectivity as MRI contrast agents as well as a high Contrast to Noise Ratio (CNR) in fluorescent/photoacustic imaging.
Cyanine-7 tagged PNPs loaded with BODIPY, a model fluorescent molecule simulating a therapeutic payload, were i.c. administered in glioblastoma-bearing mice (15 days after tumor inoculation) and transport kinetics were investigated using IVIS imaging and ex vivo fluorescence imaging.
PUR PNPs demonstrated high tissue penetration ability, potential to combine imaging and therapy, long-term retention inside the brain up to 20 days post i.c. injection, warranting further investigation as drug carriers in GBM treatment.