Hybrid devices based on the association of iron oxides with lipid nanoscale particles play an increasing role for targeted delivery of chemotherapeutics, mainly due to their recognized biocompatibility and intrinsic efficacy as contrast agents for in-vivo Magnetic Resonance Imaging (MRI). In this study, we aim to target human U87 glioblastoma, implanted into the striatum of mice, using magnetic-fluid-loaded liposomes (MFLs), sterically stabilized by hydrophilic poly(ethylene glycol) chains and loaded with a suspension of superparamagnetic nanocrystals of maghemite. MFLs targeting was achieved by applying a 190-T/m magnetic field gradient, produced by an external 0.4-T magnet placed onto the head of the mice.

In-vivo monitoring of MFLs trafficking was performed by a 7-T MRI as a function of time. MRI demonstrated a significant increase in intra-tumoral concentration of the magnetoliposomes for magnet-exposed mice, compared to not exposed ones. Animals were then sacrificed and their brains were sliced and alternatively processed for confocal microscopy or transmission electron microscopy (TEM), to perform histological and cytological analysis. Primary, detection of the rhodamine-labelling of MFLs lipid membranes in confocal microscopy revealed accumulation of magnetoliposomes in brain tumour. TEM observation of the same regions, in adjacent slices, revealed the presence of clustered electron-dense nanoparticles in the extracellular matrix space and within endosomal-structures in the cytoplasm of tumour cells and in cells lining the vascular lumen. Finally, electron energy-loss spectroscopy (EELS), coupled to energy-filtered imaging in TEM showed the iron composition of these electron-dense nanoparticles, confirming their MFLs identity.

The overall observations showed that MFLs were successfully delivered and concentrated into glioblastoma via the vasculature where they pass through the vascular endothelium as intact structures due to enhanced permeation and retention effect before to be internalized by the tumor cells. Interestingly, the magnetic field gradient does not affect the amounts of the MFLs recovered in the healthy part of brains, which comparatively remain very low according to the different imaging methods we used.

The results in their whole revealed MFLs as potent tools for selective targeting of malignant brain tumors, especially promising for therapeutic issue as it can be expected that healthy brain tissue will be spared upon treatments by deleterious anticancer drugs carried by MFLs.