The diffusion dynamics of PEGylated liposomes in the intact vitreous of the ex vivo porcine eye: A fluorescence correlation spectroscopy and biodistribution study

The diffusion dynamics of nanocarriers in the vitreous and the influence of nanocarrier physicochemical properties on these dynamics is an important aspect of the efficacy of intravitreal administered nanomedicines for the treatment of posterior segment eye diseases. Here we use fluorescence correlation spectroscopy (FCS) to determine liposome diffusion coefficients in the intact vitreous (DVit) of ex vivo porcine eyes using a modified Miyake-Apple technique to minimize the disruption of the vitreous fine structure. We chose to investigate whether the zeta potential of polyethylene glycol functionalized (i.e. PEGylated) liposomes altered liposome in situ diffusion dynamics in the vitreous. Non-PEGylated cationic nanocarriers have previously shown little to no diffusion in the vitreous, whilst neutral and anionic have shown diffusion. The liposomes investigated had diameters below 150nm and zeta potentials ranging from -20 to +12mV. We observed that PEGylated cationic liposomes had significantly lower DVit values (1.14μm²s⁻¹) than PEGylated neutral and anionic liposomes (2.78 and 2.87μm²s⁻¹). However, PEGylated cationic liposomes had a similar biodistribution profile across the vitreous to the other systems. These results show that PEGylated cationic liposomes with limited cationic charge can diffuse across the vitreous and indicate that the vitreous as a barrier to nanocarriers (Ø< 500 nm) is more complicated than simply an electrostatic barrier as previously suggested.