Research paper

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Ultrasound-mediated nanoparticle delivery across *ex vivo* bovine retina after intravitreal injection

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Abstract

Intravitreal injection is the most common administration route for the treatment of retinal diseases. However, the vitreous and some of the retinal layers themselves act as significant barriers to efficient delivery of drugs administered intravitreally. This study aimed to improve the diffusive mobility of nanoparticles (NPs) in the vitreous and enhance their permeation across the retina after intravitreal injection by application of ultrasound (US). *Ex vivo* posterior bovine eye cups were used and the vitreous was either left intact or removed gently from the neural retina. Hyaluronic acid coated human serum albumin NPs were administered into the eye cups and continuous US with a frequency of 1 MHz, an intensity of 0.5 W/cm^2, and a duration of 30 s was applied once or repeatedly via the transscleral route. After pre-determined time points, fluorescence intensities in the vitreous and the retina were analyzed. Short pulses of US significantly improved the diffusive mobility of NPs through the vitreous as well as their penetration across the neural retina into the retinal pigment epithelium and choroid without causing any detectable damage to the ocular tissues. Therefore, transscleral US could be a powerful and safe tool to enhance retinal delivery of intravitreally injected NPs.

Keywords

Ultrasound; Nanoparticles; Ocular drug delivery; Retinal penetration; Intravitreal mobility; Safety

Highlights

- Ultrasound enhanced nanoparticle penetration across the retina
- Ultrasound improved the diffusive mobility of nanoparticles in the vitreous
- Ultrasound did not cause any detectable damage to the ocular tissues