Development and Characterization of Bovine Milk Ultrasound Responsive Exosomes

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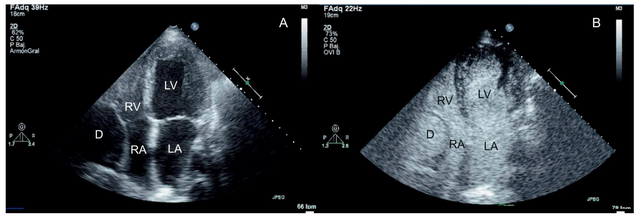
Objective

Develop a new, nanosized ultrasound contrast agent with natural morphology

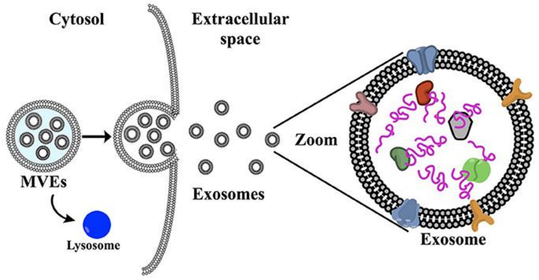


. Sánchez-Brotons et al[2](2013)

Other contrast agents (microbubbles, liposomes, polymersomes) developed limited by large size, induced immune response, and rapid clearance rates

Background

Exosome: Natural Nanoparticle (40-130 nm)



Potential Benefits: de la Torre Gomez et al[1] (2018)

- Natural morphology = reduced clearance rate of particles
- No immune response triggered
- Can extend to beyond vasculature and into tissue due to small size

Experimental Setup

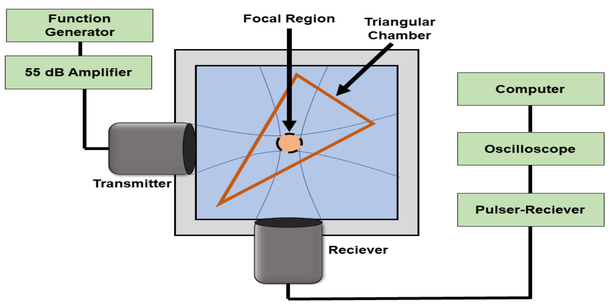


Fig 1. Experimental set for measuring linear and non-linear scattering of echogenic exosomes

Creating Echogenic Exosomes

Isolation from Bovine Milk through intense centrifugation → Sonicated and mixed with Mannitol solution → 3 Freeze Dry Cycles → Lyophilization

Resulting Particle Size and Concentration

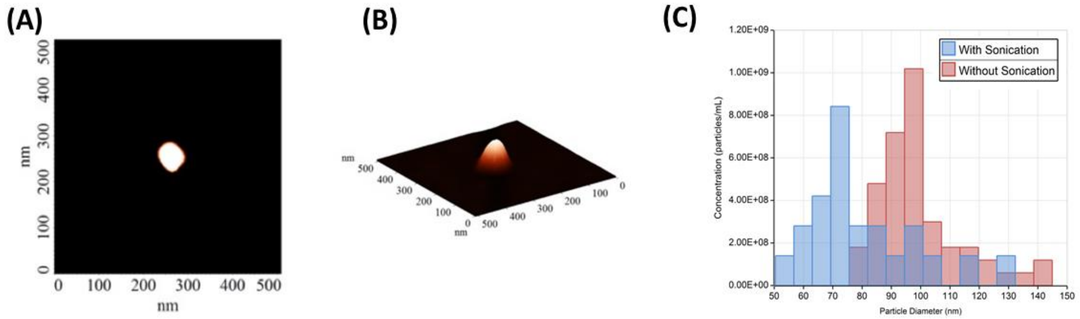


Fig 2. (A) & (B) Atomic Force Microscopy Images of Echogenic Exosomes (C) Size Distributions of Echogenic Exosomes measured by qNano

Average Size: ~100 nm

Concentration: 4.1 ± 1.8 x 10^9 particles/mg lyophilized powder

Linear and Nonlinear Scattering Behavior

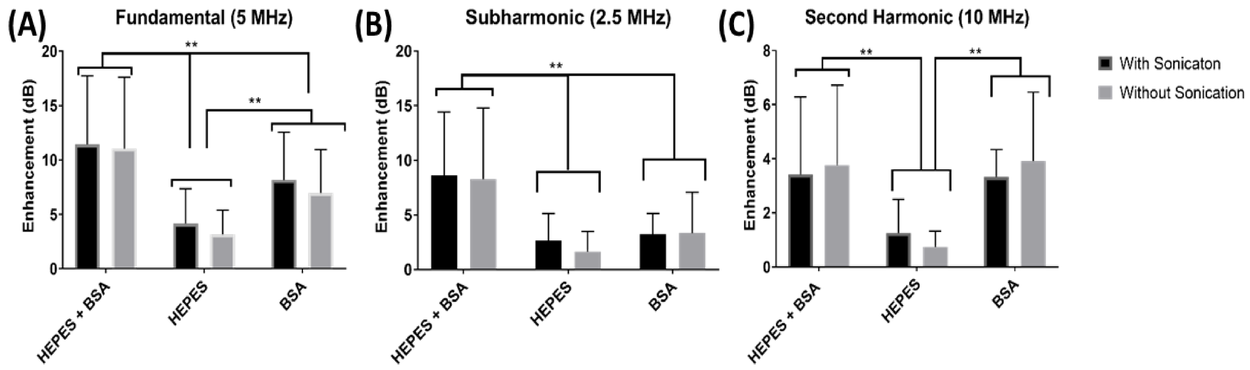


Fig 4. hMSCs after 1 day (1D) and 3 days (3D) with different MB concentrations (% v/v)

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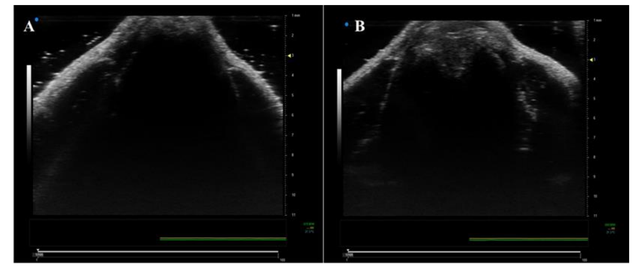
In Vivo Imaging

Synovial Space in Sprague Dawley Rat

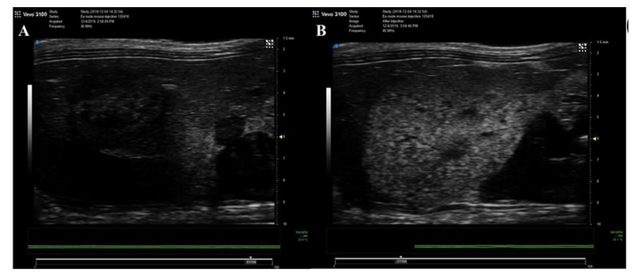
WITHOUT EXOSOMES **WITH EXOSOMES**



36.2% increase **in Brightness**

Tail Vein of an NSG mouse

WITHOUT EXOSOMES **WITH EXOSOMES**



3-fold increase **in Brightness**

Conclusions

- Successful in making exosomes ultrasound responsive
- Prove to be a promising new ultrasound contrast
- Could be extended to possible targeted, drug delivery applications

References

[1]de la Torre Gomez C, Goreham RV, Bech Serra JJ, Nann T and Kussmann M (2018) "Exosomics"—A Review of Biophysics, Biology and Biochemistry of Exosomes With a Focus on Human Breast Milk. Front. Genet. 9:92

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