

**ADVANCED
HEALTHCARE
MATERIALS**

Supporting Information

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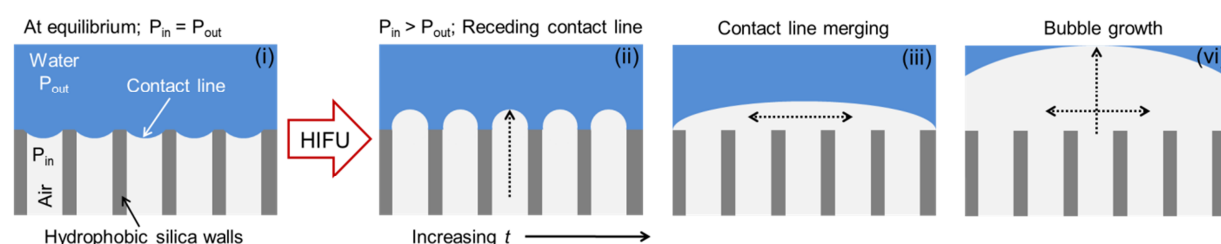
Stable Encapsulation of Air in Mesoporous Silica
Nanoparticles: Fluorocarbon-Free Nanoscale Ultrasound
Contrast Agents

*Adem Yildirim, Rajarshi Chattaraj, Nicholas T. Blum, Galen
M. Goldscheitter, and Andrew P. Goodwin**

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Stable Encapsulation of Air in Mesoporous Silica Nanoparticles: Fluorocarbon-Free Nanoscale Ultrasound Contrast Agents

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Scheme S1. Schematic representation of proposed mechanism for bubble growth from air pockets of P-hMSN. (i) In the absence of pressure difference water contact line is in equilibrium on the surface of the particles. (ii) Application of HIFU decreases the P_{out} and air starts push out the contact line to reach the equilibrium again. (iii) Neighboring air pockets merge to form larger bubbles. (iv) Bubble continues on its growth by merging with the other bubbles on the surface. Note that, in this schematic, we do not show the F127 molecules, which should be normally at the air-water interface, to simplify the schematic.

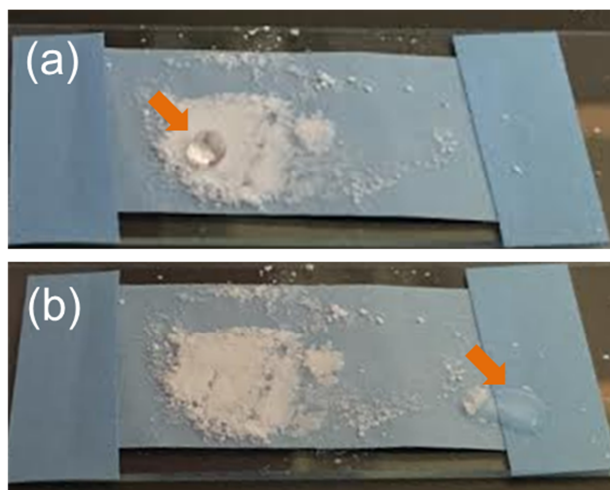


Figure S1. Water droplet sitting on surface produced from powder of hMSN before (a) and after (b) slight tilting.

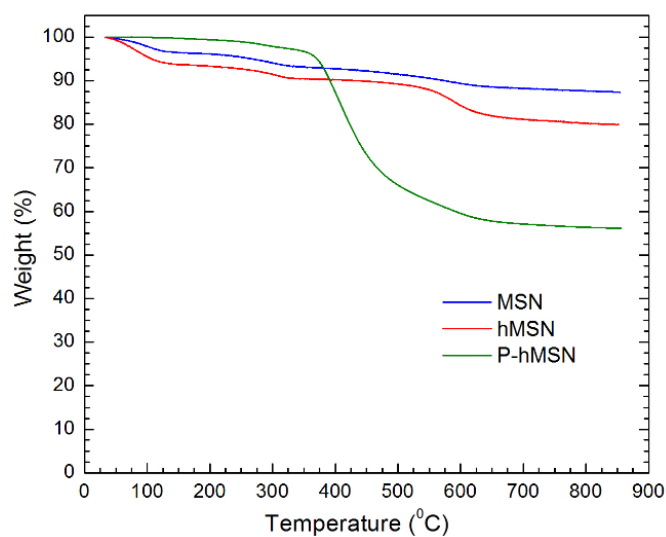


Figure S2. TGA analysis of the MSN, hMSN, and P-hMSN.

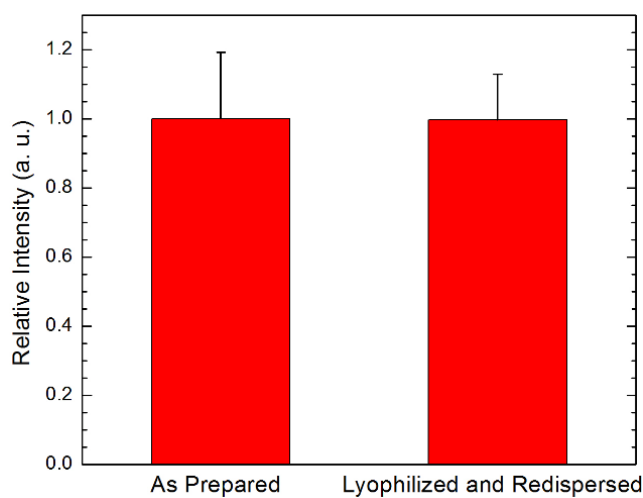


Figure S3. Ultrasound response of as prepared and lyophilized/redispersed P-hMSN samples in PBS (particle concentration was $200 \mu\text{g mL}^{-1}$ and 12 HIFU cycles was applied). Error bars = 1 SD, studies were run in triplicate.

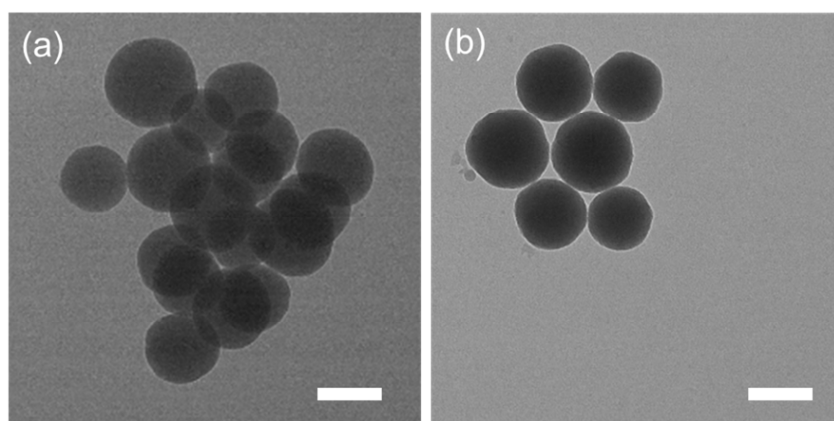


Figure S4. TEM images of (a) SSN and (b) P-hSSN. Scale bars are 100 nm.



Figure S5. Photograph of hMSN dispersion in ethanol.

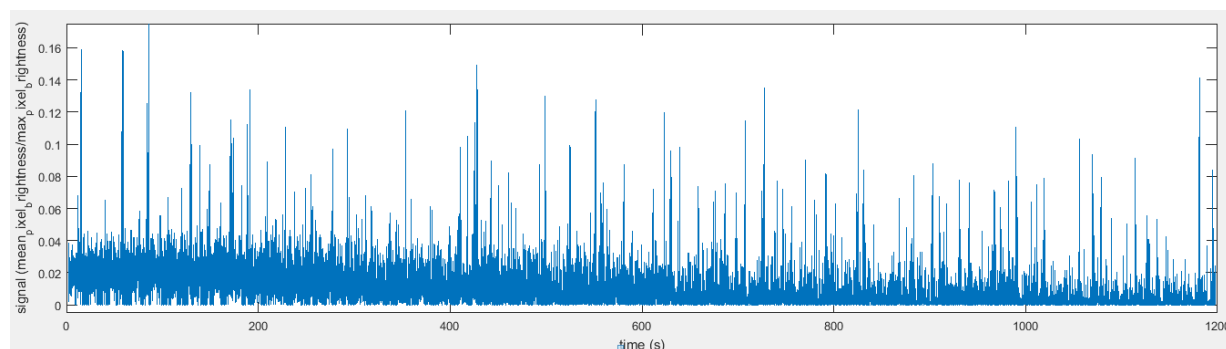


Figure S6. Graph showing the calculated intensities for each frame of the complete video of HIFU exposed (12 cycles) P-hMSN ($200 \mu\text{g mL}^{-1}$) for 20 min.

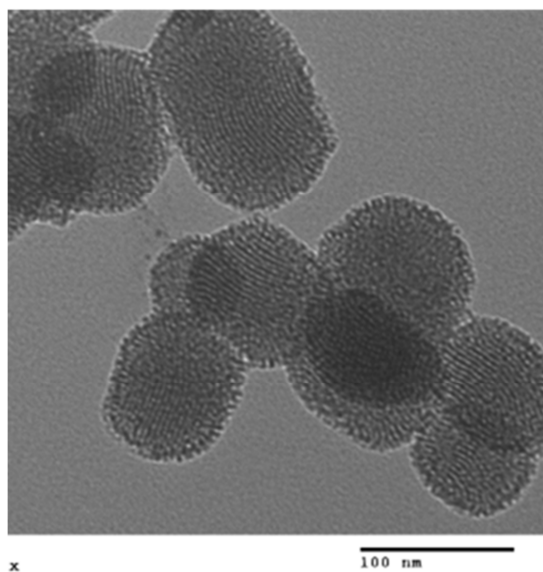


Figure S7. TEM image of the P-hMSN after exposing the particles with HIFU (12 cycles) for 20 min.

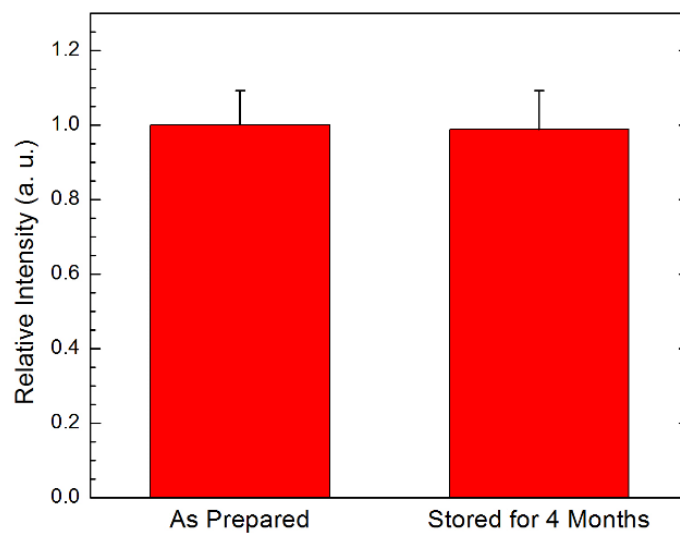


Figure S8. Ultrasound response of as prepared and stored (in PBS, for four months) P-hMSN samples in PBS (particle concentration was $200 \mu\text{g mL}^{-1}$ and 12 HIFU cycles was applied). Error bars = 1 SD, studies were run in triplicate.

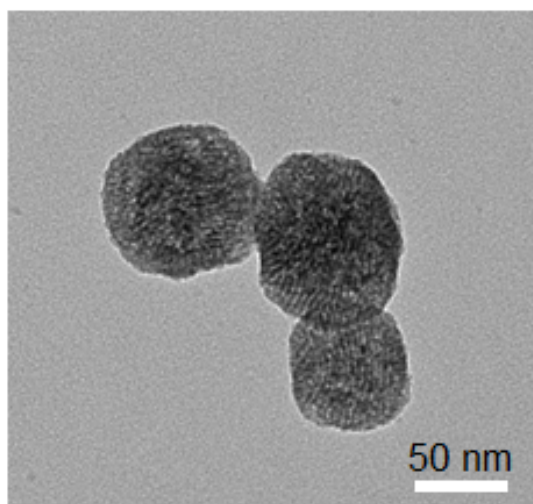


Figure S9. TEM image of the stored (four months in PBS) P-hMSN in PBS.

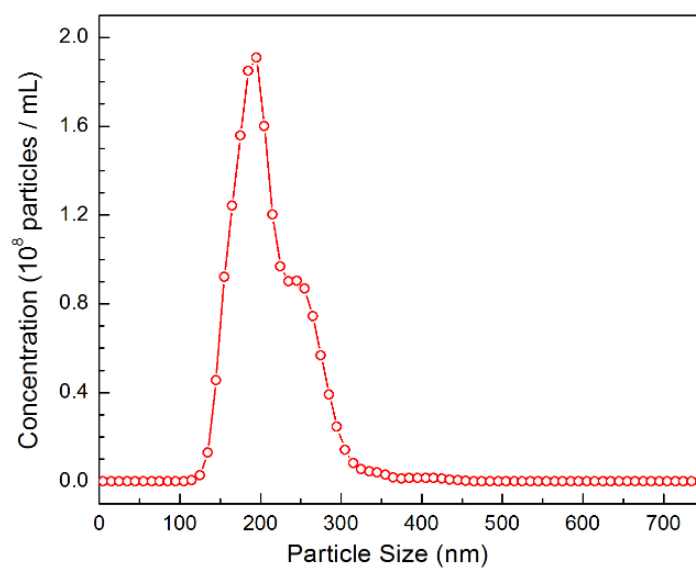


Figure S10. Size distribution of the stored (four months in PBS) P-hMSN in PBS as determined by Nanoparticle Tracking Analysis.

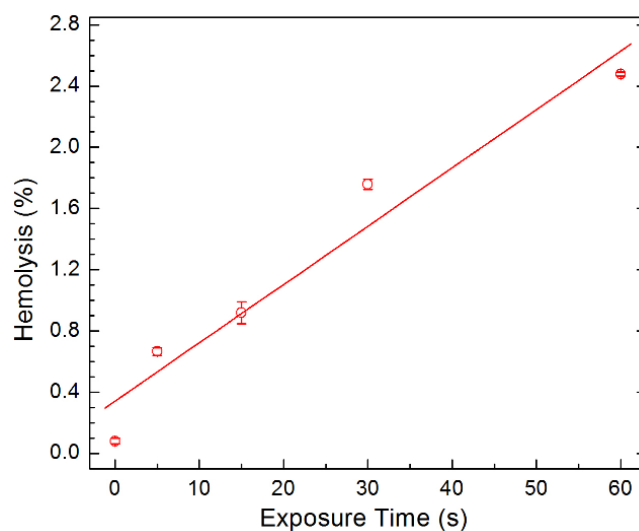


Figure S11. Hemolytic activity of P-hMSN ($200 \mu\text{g mL}^{-1}$) with respect to the HIFU exposure time at 12 cycles. Error bars = 1 SD, studies were run in triplicate.

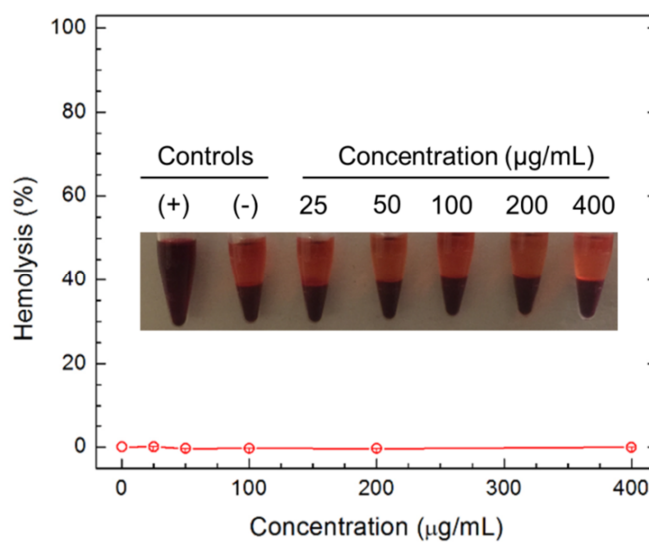


Figure S12. Hemolytic activity of P-hMSN in the absence of HIFU. Error bars = 1 SD, studies were run in triplicate.

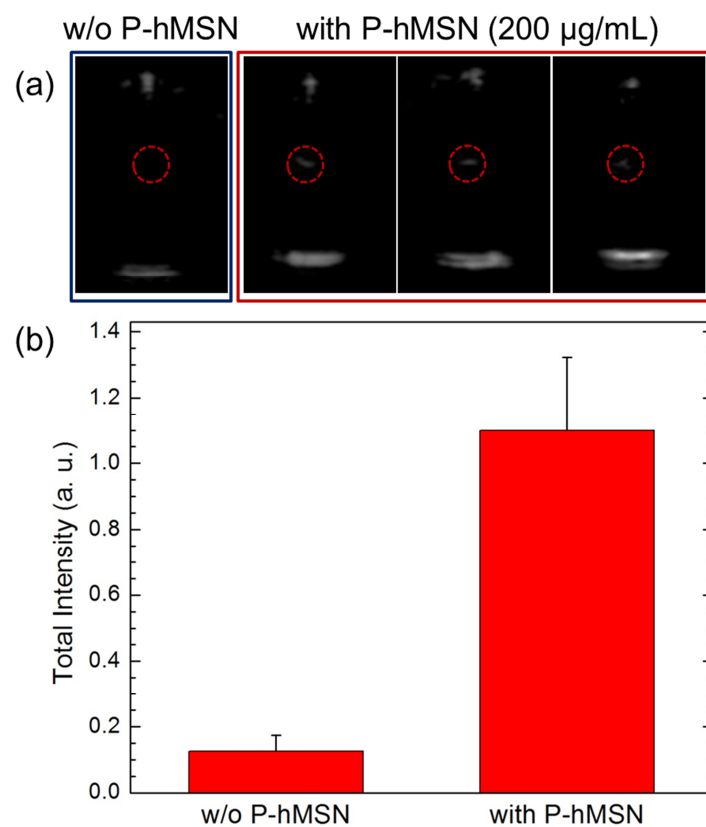


Figure S13. (a) Representative images were taken from movies acquired during HIFU irradiation at 12 cycles of the agarose gels without and with P-hMSN ($200 \mu\text{g mL}^{-1}$). The three images for the agarose gel containing P-hMSN were taken from three separate gels. (b) Calculated total intensities from the acquired movies of agarose gels with and without P-hMSN exposed with 12 HIFU cycles. Error bars = 1 SD, studies were run in triplicate.