Ultrasmall MoS_2 Nanoparticle Contrast Agents for Dual Energy Mammography

Emily K. Berkow[1], Katherine J. Mossburg[2], Lenitza M. Nieves[3], Derick N. Rosario[3], Andrew D.A. Maidment[4], David P. Cormode[2,4]
[1]Department of Chemistry (2024), [2]Department of Bioengineering, [3]Department of Biochemistry and Molecular Biophysics,
[4]Department of Radiology, University of Pennsylvania

Background

- Routine mammography screenings have been shown to lower mortality rates due to breast cancer. However, conventional mammography has a low sensitivity for the population of women with dense breasts.
- Contrast enhanced dual energy mammography (DEM) can improve tumor detection for this population (Fig. 1).
- Currently used iodine-based contrast agents for DEM have several drawbacks such as their contraindication for use with renal insufficiency, high-dose requirement, and sub-optimal contrast.

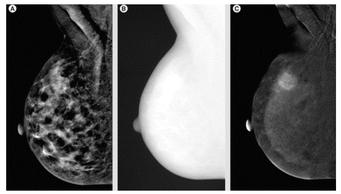

Figure 1. Example of contrast-enhanced DEM. Three images are created in DEM: A) low energy image, B) high energy image, and C) subtraction image which clearly shows a mass in the upper breast. Image from Lalji and Hobbes.

Introduction

- Molybdenum disulfide nanoparticles (MoS_2 NPs) are known to produce x-ray contrast at clinically reasonable energies.
- Clinical translation of MoS_2 NPs as contrast agents is dependent on their ability to be rapidly eliminated from the body to minimize long-term toxicity concerns (Fig. 2).

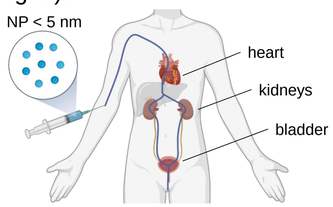

Figure 2. Renal clearance of nanoparticles. Ultrasmall particles (< 5 nm) can be rapidly cleared through renal filtration and urinary excretion pathways.

- Objective: Develop ultrasmall MoS_2 NP contrast agents for DEM with the aim of improved contrast, stability, clearance, and biocompatibility.

Synthesis and Purification

- Aqueous solutions 2-mercaptopropionic acid (2MPA), sodium sulfide (Na_2S), and sodium molybdate (Na_2MoO_4) were combined (Fig. 3).
- The particles were purified by dialysis overnight, filtered using 20 nm filters, and concentrated by lyophilization.
- The molybdenum concentration in each sample was determined using inductively coupled plasma optical emission spectroscopy (ICP-OES).

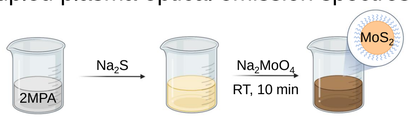

Figure 3. Synthesis of MoS_2 nanoparticles with 2MPA coating.

MoS_2 NP Characterization

- 2MPA-MoS_2 NPs had an average core size of 2.6 ± 0.4 nm (Fig. 4A).
- A characteristic peak of MoS_2 NPs, 215 nm, was observed (Fig. 4B).
- Fourier transform infrared spectroscopy (FT-IR) analysis suggests the successful incorporation of the 2MPA coating onto MoS_2 NPs (Fig. 4C).

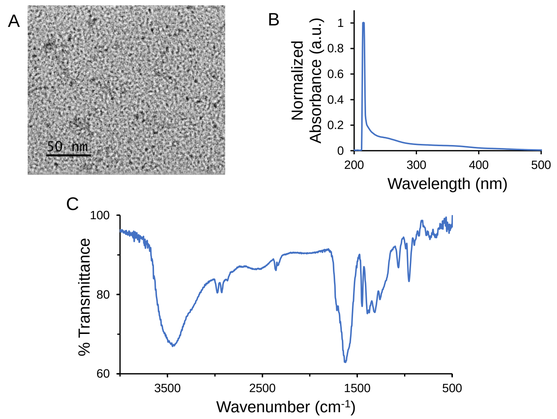

Figure 4. Characterization of MoS_2 NP. A) Transmission electron micrograph, B) UV-vis spectra, and C) FT-IR spectra of 2MPA-MoS_2 NPs.

Phantom Imaging

- MoS_2 NP produce strong contrast in both DEM (Fig. 5A) and computed tomography (CT) (Fig. 5B) imaging modalities.

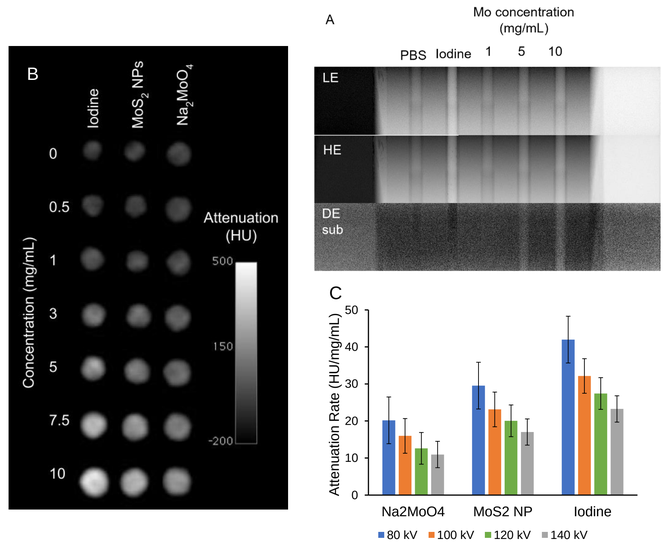

Figure 5. Phantom imaging. A) Representative DEM image of GSH-MoS_2 NPs collected on a Hologic Dimensions clinical mammography system using a tissue-mimicking phantom. B) Representative CT image collected on a Siemens SOMATOM clinical CT scanner at 80 kV. C) Quantification of CT attenuation rates at varying x-ray energies.

MoS_2 NP Stability

- MoS_2 NPs were incubated in water, PBS, and a solution of PBS/10% FBS for 48 hours. Their UV-Vis spectra was recorded at several timepoints.

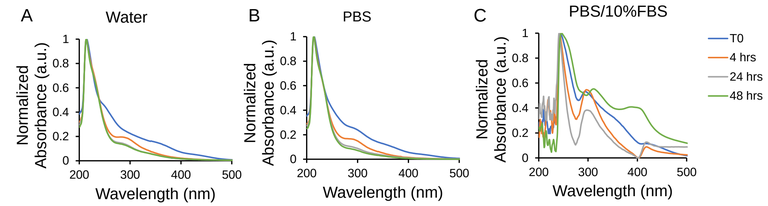

Figure 6. Stability of MoS_2 NPs in different media. UV-Visible spectra of particles in A) water, B) PBS, and C) PBS + 10% FBS at 0, 4, 24, and 48 hours post incubation.

In Vitro Biocompatibility

- MoS_2 NP were incubated with HepG2 (hepatocytes) cells at a range of Mo concentrations. Cell viability was determined after 4 hours.

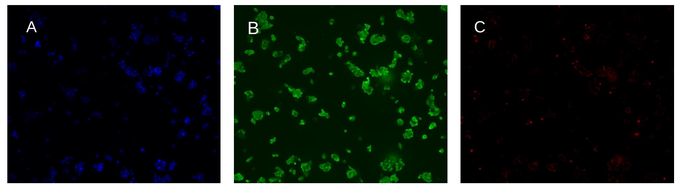

Figure 7. Cell viability of HepG2 after incubation with 2MPA-MoS_2 NPs at 1 mg/mL Mo. Color stain highlights A) nuclei, B) live cells, C) dead cells after 4 hours of incubation post-treatment.

Conclusions and Future Directions

Conclusions

- Ultrasmall MoS_2 NP (2.6 ± 0.4 nm) coated with 2MPA were successfully synthesized. These particles are stable for at least 48 hours in water and PBS, have good contrast, and show promise for being biocompatible.

Future Directions

- Further *in vitro* studies. Examine cell viability with varied cell lines, DNA damage quantification, and reactive oxygen species generation.
- Determine the biocompatibility of 2MPA-MoS_2 NP *in vivo*. Inject female mice with a dose of MoS_2 NPs to provide information about the particles' clearance, biocompatibility, contrast in real tissue, and potential unwanted retention in organs.

Acknowledgments

Support for this work was provided by the Cormode Group and the Penn Center for Undergraduate Research and Fellowships through the Benjamin Franklin Scholars summer research grant.

References

Figure 1: Lalji U, Lobbes M. Contrast-enhanced dual-energy mammography: a promising new imaging tool in breast cancer detection. *Women's Health* (2014) 10(3): 290.