Shape Memory Polymer Foams with Tunable Interconnectivity Using Off-the-Shelf Foaming Components

Natalie Marie Petryk, Grace Haas, Anand Utpal Vakil and Mary Beth Browning Monroe
Biomedical and Chemical Engineering, BioInspired Syracuse, Syracuse University, Syracuse, New York

Statement of Purpose: Polyurethane shape memory polymer (SMP) foams have broad biomedical applications for hemorrhage control, drug delivery, and tissue engineering;[1] different pore sizes and interconnectivities are necessary to facilitate blood permeability, expansion-controlled drug release, and/or cell proliferation, migration, and attachment. The main mechanisms for pore size control in gas-blown foams are to alter premix viscosity and to utilize a chemical or physical blowing agent. Premix viscosity is slow to tune and less precise. Water is a chemical blowing agent that releases carbon dioxide upon reactions with isocyanates, but changing water quantity alters foam chemistry, limiting tunability of pores while maintaining mechanical and thermal properties. Enovate (HFC-254fa) is a physical blowing agent used to open pores, but the Environmental Protection Agency (EPA) considers it unacceptable, because hydrofluorocarbons destroy the ozone and can contribute to global warming.[2] Thus, there exists a need to easily and safely modify pore size and interconnectivity of gas-blown polyurethane foams. This work explores simple alternatives for increasing interconnectivity in porous SMP foams using readily available physical blowing agents outlined as safe for use by the EPA in their Significant New Alternatives Policy (SNAP) Program.[3] The effects of pore interconnectivity on blood and cell interactions is explored.

Methods: *Foam Synthesis:* An isocyanate (NCO) premix was made with 0.35 hydroxyl (OH) molar equivalents (70% hydroxypropyl ethylenediamine (HPED), 30% triethanolamine (TEA)) and 1 isocyanate (NCO) molar equivalent (hexamethylene diisocyanate (HDI) or 2,2,4-trimethylhexamethylene diisocyanate (TMHDI)). The premix was reacted at 50°C for 48 hours after mixing. Then, surfactant was added. The remaining 0.65 molar equivalents of OH (HPED and TEA) were mixed at 3500 rpm with water and catalysts (T-131 and BL-22). The hydroxyl mix, premix, and a physical blowing agent (1, 2, or 3 mL of acetone, dimethyoxymethane (methylal), or methyl formate) were mixed prior to foaming at 50°C. *Foam Characterization:* Before characterization, all foams were washed with 70% ethanol and deionized (DI) water, then dried under vacuum for 24 hours. Differential scanning calorimetry (DSC) was run on 3-5 mg foam pieces to determine the dry glass transition temperature (Tg). Foam samples were heated, radially crimped, and cooled; then, the crimped samples were submerged in a DI water bath at 37°C to determine shape memory behavior and volume expansion. Scanning electron microscopy (SEM) images were taken to analyze average foam pore size; ~1 cm^3 samples were taken from the top, middle, and bottom of the foams along axial and transverse axis. The same images were used to determine percent interconnectivity using GIMP histogram analysis. *Blood and Cell Interactions:* Foams were incubated with whole blood and imaged via SEM to analyze platelet attachment and activation. 3T3 fibroblast attachment and spreading were measured on the surface of synthesized foams using fluorescent images of stained cells.

Results: *Foam Synthesis:* Foams have been synthesized containing no physical blowing agent (control), 1 mL, 2 mL and 3 mL of each physical blowing agent. *Foam Characterization*: The dry Tg was ≥ 50°C for all foam formulations, enabling stable storage in their secondary shape. All foams expanded at 37°C within 5 minutes, demonstrating shape recovery and the ability to quickly shape-fill a defect site after implantation. Although no clear trend in pore size is evident based on the boiling points of the physical blowing agents (acetone: 56°C, methylal: 42°C, methyl formate: 32°C), increased volumes of each blowing agent increased interconnectivity (**Figure 1**). Blood and cell studies are currently underway.

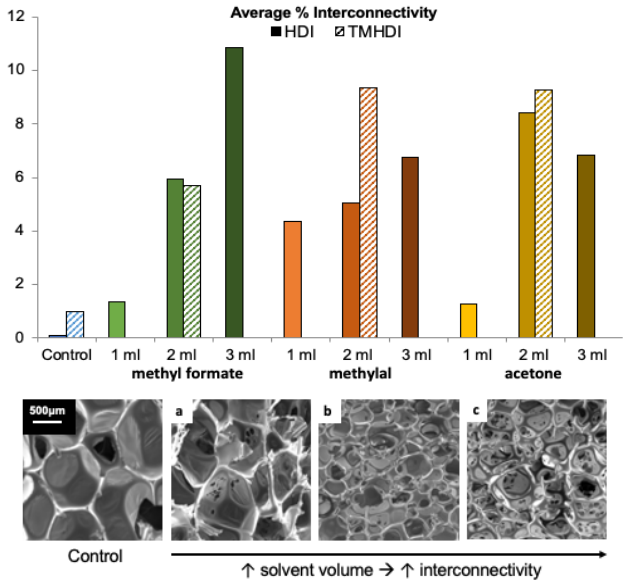

Figure 1: Average % interconnectivity of all synthesized foams (top) and SEM images of control SMP foam and foams containing a) 1 mL, b) 2 mL, and c) 3 mL of methyl formate (bottom).

Conclusions: The physical blowing agents impacted pore size and connectivity of the foams while maintaining thermal and shape memory properties. This work provides a simple, environmentally friendly approach for tuning SMP foam interconnectivity with readily available and EPA-approved agents, which could aid in commercialization efforts. Future work involves testing how varying foam pore size and interconnectivity effects cell attachment and blood-material interactions.

References:

[1] Serrano, M.C. et al. (2012), Macromol. Biosci., 12: 1156-1171. [2] Tsai, W.-T. (2005). *Chemosphere*, *61*(11), 1539–1547. [3] "Substitutes in Flexible Polyurethane | US EPA." https://www.epa.gov/snap/substitutes-flexible-polyurethane.