Novel Acrylic-Based Composite Bone Cement for Craniotomy Defect Filler

Lucas C Rodriguez[1], Dustin Simon[2], Dane W Grasse[1,3], Robert Rennaker[1,3], Danieli C Rodrigues[1]
[1]*Department of Biomedical Engineering;* [2]*Department of Materials Science and Engineering;* [3]*Texas Biomedical Devices Center, The University of Texas at Dallas, Richardson, TX 75080*

Statement of Purpose: Acrylic allografts are widely used as synthetic head caps following craniectomies. Acrylics provide many advantages over other materials (e.g. titanium) for such applications including being lightweight, radiolucent, and easily moldable [1]. However, methyl methacrylate toxicity, high curing temperature (up to 107°C), and lack of interdigitation with bone restricts further development for such polymer materials. Because currently available acrylics do not strongly bind to bone, gaps between the acrylic and skull can be created, which encourage granular tissue growth and bacterial colonization [2]. The goal of this study was to develop, characterize, and test a novel PMMA-Brushite composite bone cement for cranioplasty head caps. This partially acrylic, bioactive material was designed to increase avenues for bone interdigitation and adhesion to the skull, retain mechanical stability to provide a protective environment, as well as demonstrate ideal viscosity (low enough to allow the material to be easily injected from a small cannula while forming a smooth coat). An antimicrobial formulation of the material was also investigated to determine the feasibility of adding such a phase to prevent granular tissue proliferation.

Methods: *Cement Preparation*: Material preparation was adapted from protocols described in previous studies [3,4]. Brushite was utilized as a bioactive phase in varying concentrations to replace the PMMA concentration. *Rheology Testing:* For rheology characterization, a Discovery HR 3 Rheometer (TA Instruments) was used. The testing parameters (Oscillatory Shear) remained constant for each composition tested. Parameters investigated included storage and loss modulus, complex viscosity, tangent delta, temperature, and time. *Mechanical/Exothermal Investigation:* Mechanical/Exothermal property evaluation was conducted on the material post-polymerization according to ASTM standard F451 [5]. *Antimicrobial Testing:* Zone of inhibition and microbial proliferation assays were carried out to determine the extent to which the material was capable of releasing antimicrobials from its matrix post-polymerization. *Animal Model: Inflammation/Systemic Reaction:* Material was implanted as a head cap into a rat model and was monitored for inflammatory and systemic reactions to determine the safety and efficacy of continued testing of the investigative material. *Interdigitation Analysis:* Material was implanted into rat models for set time points before sacrifice to allow for skull-material gap quantification and skull-material interdigitation analysis using a Digital Microscope (Keyence VHX-2000).

Results: Rheological characterization displayed the materials highly pseudoplastic behavior. The zero-shear viscosity (~532 KPa) is comparable to commercially available materials ($p>0.05$). Exothermal temperatures recorded from the investigative material (~62°C) are approximately 30°C lower than many currently available materials. Further, the mechanical strength (~55MPa compressive strength) of this material is still suitable for cranioplasty procedures. After implantation into an animal model, there was no notable inflammatory or systemic reaction, and histology characterization is being finalized to determine the viability of brain tissue post-material interaction. The adhesion and interdigitation of the investigative material was observed to be superior to available acrylics (skull-material gap compared to Figure 1). The antimicrobial formulation was demonstrated to effectively prevent fibroblast proliferation below the material surface (Figure 2).

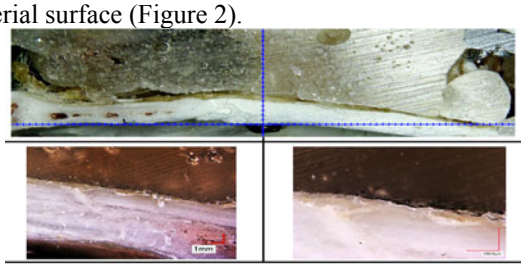

Figure 1: (Top) Assessment of acrylic materials used as head cap for a rat model. 2mm gap throughout the sagittal midline of the head cap illustrating the poor skull-acrylic binding allowing for granular tissue proliferation or bacterial colonization. (Bottom) Although acrylics can have contact, there is no discernible osteointegration between the bone and acrylic.

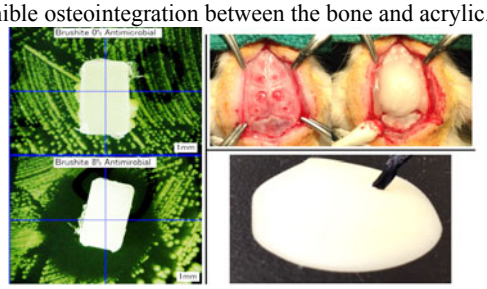

Figure 2: (Left) Antimicrobial effectiveness of the material was demonstrated to last 65 days in a hypothetical environment. The placement of the craniotomies and the investigative material (upper right), and a polymerized sample of material demonstrating the smooth finished surface (lower right).

Conclusions: The investigative material developed demonstrated superior characteristics compared to available acrylics used in cranioplasty procedures. This material will be further tested and characterized for neurodegeneration, cell viability, and myelin characteristics by staining (fluoro-jade, cresyl violet, and luxol fast blue) and imaging brain tissue after prolonged contact with the investigative material. Long term testing will commence to determine the feasibility of using this material as permanent craniotomy defect filler in patients.

References: *1.Aydin, S, et al. (2011) J Neurosci Rural Pract. 2(2): 162-167. 2. McAndrew, RM, et al. (2012) J Neurosci Methods. 207(1): 86-90. 3. Hasenwinkel, JM, et al. (1999) JBMR-B. 47:36-45. 3. Rodrigues DC, et al. (2009) JBMR-B: Appl Biomater 91:248-256. 5. ASTM Standard F451 (2008), ASTM International,www.astm.org.*