Bone Marrow Analogs for Flight-ready System to Test Countermeasures of Bone Loss

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Objective: Bone homeostasis is influenced by mechanical forces that alter anabolic responses and bone quantity/quality. Astronauts lose bone during spaceflight similar to age-related bone adaptation. To investigate low-intensity vibration (LIV) as a countermeasure to bone loss, we developed 3D bone marrow analogs (BMAs) to be studied aboard the International Space Station (ISS). The ISS-compatible CubeLab is equipped with thermal controls, automated fluidic systems, sensors, and actuators to maintain vibration protocols in orbit and for ground controls. We expect LIV to increase anabolic activity of bone marrow stromal cells (BMSCs).

Methods: BMAs consist of hydrogel-encapsulated BMSCs (5 million cells/mL) within 3D-printed resin scaffolds representing young (25%) or old (15%) trabecular architecture [%: bone volume/total volume]. Controlled and consistent osteogenic factor delivery within this closed system requires StemBeads®. Studies were conducted to determine the effectiveness of StemBead-delivered osteogenic factors compared to a soluble factor control group. BMAs were prepared for RNA extraction, Live/Dead Assays, and mineralization quantification.

Results: The RNA yield from BMAs was in the acceptable range of ~ 280 ng/µL from 4 pooled BMAs. Live/Dead imaging showed stellate morphology and nodule formation in StemBead groups at D28. Nodules 100 µm in diameter formed on the surfaces of the scaffold and within the hydrogel as well on the surfaces of the hydrogel.

Conclusions: We established a 3D approach to evaluate BMSC viability, morphology, and differentiation to enhance mineralization on scaffold surfaces and within the bone marrow-like environment. The BMAs fit into the CubeWell chamber, which fastens into the flight-ready and fully automated CubeLab. Results from these studies will reveal how LIV may serve as an effective countermeasure to alter bone anabolism in the presence of microgravity, leading to age-related bone adaptation. Patients experiencing age- or disease-related physiological changes may also benefit from interventions using LIV, leading to improved clinical outcomes.

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