A three dimensional rotating bioreactor for the production of micro engineered bone tissue in large scale-feasibility study

Andrew B Grottkau[1], Yonggang Pang[2] MD, PhD, Brian E. Grottkau[2] MD

1 Phillips Academy Andover, 2 Department of Orthopaedics, MassGeneral Hospital for Children, Harvard Medical School

Engineering micro scale tissue is an emerging and promising technology that can be applied to tissue regeneration in orthopaedics through a minimally invasive approach. These micro tissues can self-assembly in vivo to form macro tissues. Previous studies have demonstrated that micro tissues require in vitro culture before implantation for improved viability in vivo and better ultimate therapeutic outcomes. However, larger numbers of micro tissues, usually several hundred micro meters in size, prematurely condense in conventional static culture conditions limiting the nutrition and waste transportation of the micro tissues. Previously developed one-axis rotating culture systems have drawbacks such as uneven culture conditions, overloaded shear forces and complicated operation. In order to solve these problems, we developed a novel three dimensional rotating bioreactor that rotates in three axes. The bioreactor was manufactured in our laboratory using 3D printing technology. The constructed bioreactor has variable rotating speed and can be place directly in a regular incubator. The CO_2 permeable container for the micro tissues was designed and manufactured for easy manipulation, rendering the operation of loading micro tissues and changing media as simple as using a regular laboratory test tube. Multiple containers can be mounted in the bioreactor simultaneously for large scale micro tissue production. We generated micro bone tissue using alginate hydrogel and MC-3T3 osteoblasts. Compared to conventional one axis rotating bioreactors, our newly developed bioreactor requires lower RPM to suspend the micro tissues, thus reducing the shear forces. The micro tissues were evenly distributed within the 3D space in the container within a few minutes of starting rotation. This evenly-suspending condition was maintained for days. The cells had good viability in our rotating bioreactor, which we evaluated by live-dead cell staining. We have developed a novel three dimensional rotating bioreactor, which proves good feasibility in micro bone tissue development. It also has the potential for broad application in other micro tissue developments.