e-Incubator: MRI Compatible Mini-Incubator

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Introduction

Modern medicine is expected to greatly benefit from the development of instruments that enable non-invasive *ex vivo* testing and *in vitro* imaging during tissue culture procedures. For example, such an instrument can potentially visualize the activity of incubated brain slices from different disease models, such as for multiple sclerosis and Alzheimer's, for which these models are widely used by drug companies as screening platforms for the identification of novel therapeutics(*1*). Another example is tissue engineering. The concept of tissue engineering was introduced over 25 years ago, but a limited number of products have been approved for clinical application (*2*). The tissue engineering community has been vocal in seeking a non-invasive instrument to assess the development of engineered tissue constructs. Introducing a non-invasive visualization capability to the community is expected to expedite the translation of tissue engineered (TE) products to clinical settings.

Medical imaging technologies have proved their superiority in clinical settings for the diagnosis of various diseases, and these imaging technologies can play a major role in tissue culture applications. However, one major problem is that a specimen allocated in a test tube for imaging cannot be tested for a prolonged period of time nor can it be returned to the incubator. In turn, the sample is wasted due to potential contamination and transfer incubation in a sub-optimal growth environment. To address these problems, we present a miniature magnetic resonance imaging (MRI)-compatible incubator, termed the *e*-incubator, which enables real-time, on-board imaging for tissue specimen testing and development in clinical applications. The e-incubator is a standalone unit that is controlled via a microcontroller (MCU). The MCU acts as a central control unit to automatically sense and regulate physiological conditions, including temperature, CO_2, and pH, and to perform media exchange for cultured constructs.

Material and Methods

The *e*-incubator (Fig. 1) featured a microcontroller unit (MCU) that initiated the media to the chamber and heating element as well as monitored the temperature, CO_2, and pH. Human MSCs (Lonza) were expanded in media composed of DMEM with 10% FBS and 0.5% antibiotic/antimycotic. Porous silk scaffolds (TERC) were seeded at 2.0 x 10^6 cells/ml with osteogenic media (*3*) added at 24 hrs. The e-incubator was loaded and inserted in a 9.4T vertical bore MR (Varian) at 48hrs. MR images were acquired daily for the duration of 4 weeks. Axial fast spin-echo (TR, 2000 ms; ESP, 20 ms; in-plane square resolution, 109 µm; slice thickness, 1 mm). After 4 wks, the *e*-incubator construct was evaluated using Live/Dead Assay (Invitrogen) and comparisons made to a standard incubator grown osteogenic construct.

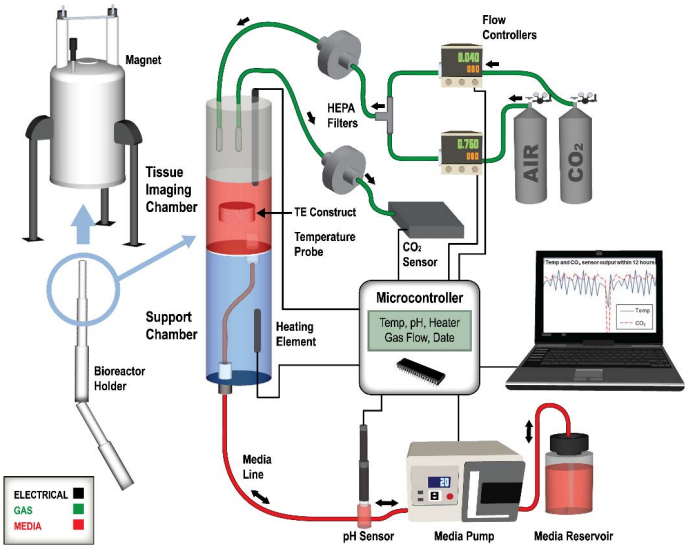

Figure 1. *e*-Incubator Design Schematic.

Results

MR images showed progressive darkening of the construct indicating mineralization (Fig. 2). The Live/Dead assay showed similar amount and growth of live to dead cells between constructs cultured in a conventional incubator and the *e*-incubator. Areas without the silk scaffold were evaluated and a similar amount of dead cells were in both samples (Fig 3).

Discussion and Conclusions

This study demonstrated an e-incubator that allowed for continuous monitoring of tissue growth while in culture. The MR images verified our design by showing positive changes to the tissue as well as similar growth between the e-incubator and standard incubator constructs.

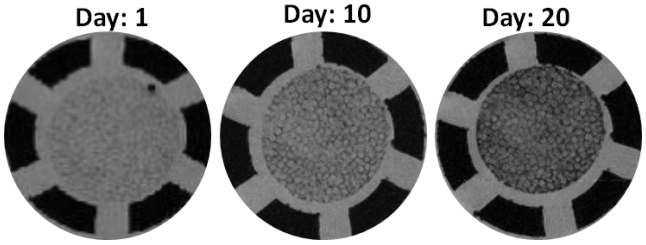

Figure 2 . Axial MRI of TE bone hMSC silk based construct at days 1 , 10, and 20. MR images were acquired by a fast spin-echo sequence.

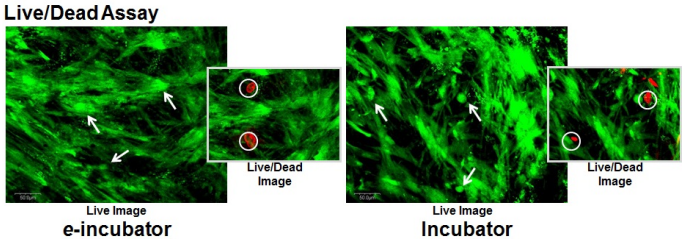

Figure 3.Confocal images of Live/Dead staining for the e-incubator and the standard incubator grown osteogenic constructs. Arrows indicate live cells and circles indicate dead.

References

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