Magnetoelastic Materials as Novel Bioactive Coatings for Control of Cell Adhesion
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INTRODUCTION:
In order to develop a better method to prevent uncontrolled fibrosis, the novel approach addressed in this work has been developed with the ultimate goal to mitigate fibrous overgrowth at the surface of implantable biomaterials. Specifically, we have developed a bioactive vibrational coating to modulate local cell adhesion to control tissue overgrowth. The vibrational coating is based upon a magnetoelastic (ME) material that, when subjected to an applied magnetic AC field, can be remotely set to vibrate at a predetermined amplitude and frequency. When placed inside a magnetic AC field, the ME material changes dimensions ultimately converting magnetic energy into mechanical energy in the form of vibrations. Although ME materials have shown great potential as biological sensors, the aim of this work was to determine if sub-micron mechanical vibrations produced by the ME material could be used as a therapeutic tool to control cell adhesion. We hypothesize that small local vibrations can be used to selectively modulate cell adhesion to minimize fibrosis and promote proper integration at the soft tissue-implant interface.

METHODS:
Cell adhesion to bio-activated ME material surface. L929 fibroblasts were cultured at 2x10^4 cells/cm^2 onto ME material materials coated with polyurethane and chitosan for 2, 4, and 6 days followed by the application of a vibrational load to experimental groups. Vibrations were applied for two hours at 170-176 Hz. Cell response to vibrations was assessed qualitatively with fluorescence imaging to directly view fibroblast adhesion as well as quantitatively by counting and normalizing to static controls.

Cell viability after vibration induced detachment. Cell survival (attached and detached cells) was determined after direct culture and vibrational loading. Detached and adherent (removed with Trypsin) cells were re-seeded together in 2 ml of media and further cultured for 24 hours followed by cell viability assessment at hour 72. Percent cell survival was determined for fibroblasts (including adherent and detached cells) cultured directly on vibrated ME materials relative to static controls.

Cell adhesion to ME material with altered polymer coating. The effect of the polymer substrate on the adhesion response to sub-micron vibrations was determined by comparing chitosan with poly-L-lactic acid (PLLA). Fibroblast attachment was assessed after direct culture for two days on ME materials spin-coated with chitosan or PLLA (initial polyurethane layer used for both samples) followed by vibration and imaging.

Cell adhesion to ME material with altered vibrational profile. ME vibrational parameters (strain amplitude and interval delay) were altered to determine if fibroblast adhesion was sensitive to specific loading conditions. Vibrations with strains at amplitudes of 0.117 µm and 0.1542 µm (Fig.4A) or interval delays (period between vibrational loading) of 1 and 10 seconds (Fig.4C) were applied after direct culture of fibroblasts for 2 days followed by fluorescence imaging and quantification of cell attachment.

Statistics. Comparisons were made using ANOVA with a standard t-test, p-values of <0.05 were considered significant.

RESULTS:
The results clearly indicate that controlled vibrations can induce cell detachment from the ME material compared to static controls (Fig.1 A and B). Cells detached via applied vibrations were immediately re-suspended and cultured to assess viability. No significant decrease in cell viability was seen compared to non-vibrated controls (Fig.1C).

DISCUSSION:
In this work, we show that active vibrations induced in the ME material are capable of attenuating cell attachment without inducing an appreciable apoptotic response (Fig.1). Results suggest the ME material may be used to mitigate fibrous overgrowth at a biomaterial interface and that the polymer substrate (Fig.2) and vibrational profile (Fig.3) has a significant effect on the response to vibrational loading.

This work demonstrates the potential of a novel ME-based biomaterial. One major benefit of the ME coating is the site specificity of the applied therapy. The vibrational ME materials are remotely tunable, meaning the affects can be controlled even after in situ delivery of an implanted biomaterial. Additionally, the secondary magnetic field created while vibrating allows substrate adhesions to be monitored in real time, allowing therapy to be delivered on an as needed basis via a wireless activation coil for the life of the implant.

The results of this work provide the basis for future ME experiments and, ultimately, a novel approach to combat the fibrous overgrowth associated with biomedical implants including bone anchored prosthetics. Current work is underway to test the ability of the ME material vibrations to minimize fibrous capsule formation in vivo. Overall, this work demonstrates the development of a novel biomaterial that, through remotely applied sub-micron vibrations, can prevent cell adhesion without inducing cell death.