The Role of Glucose on Cartilage Health in a Novel Osteoarthritis Model System

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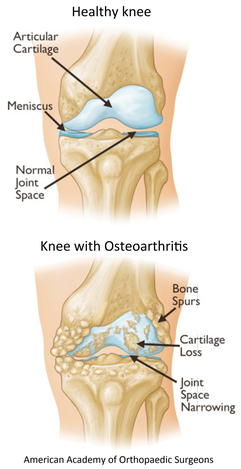
Introduction

Osteoarthritis (OA) is a degenerative joint disease caused by the wear and tear of cartilage, a material at the end of bones that allows for smooth, shock-absorbing movement. OA is an age-related disease, but other risk factors are obesity, joint injuries, gender, and the repetitive use of a joint. The most commonly affected joints are the thumb, hip, knee, and spine, and the symptoms involve pain, stiffness, and swelling in the joint. OA is one of the leading causes of disability. As there is no cure, treatment addresses ways to reduce pain and ultimately results in a total joint replacement.

While there are established chemical and surgical models for studying osteoarthritis, they have limitations. *In vivo* models, or models in live animals, are difficult to execute and don't mimic the normal wear and tear that is the main cause of OA in the human population. *In vitro* models, or models "in glass," only study one joint tissue at a time and do not mimic the normal movement of a joint. A newly developed study model uses ex-vivo culturing of a knee joint to develop osteoarthritis through normal wear and tear.

A liquid medium in this model keeps the joint tissue biologically active during the culturing process. Glucose, which is needed for energy, is one of the ingredients in this medium. Too much or too little glucose can compromise the integrity of cartilage, so this experiment tested varying glucose levels to find the optimal level for joint survival.



Objective

The objective of this study was to determine the optimal glucose concentration for cartilage and joint tissue survival.

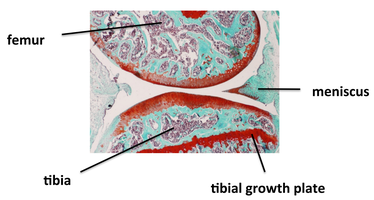
Joint-in-Motion Device

The Joint-in-Motion device cultures a mouse knee joint in a liquid medium. The knee joint is anchored at the femur and tibia, and a motor moves the top anchor to bend and extend the joint in a normal pattern of walking or biking. Over time, the cartilage in the knee wears down, resulting in osteoarthritis-like symptoms.

This device addresses the concerns of *in vivo* and *in vitro* models. The model uses a whole joint, which undergoes programmable regular movement. The system is cheaper than many models, and is more ethical.

Reference Safranin O Staining

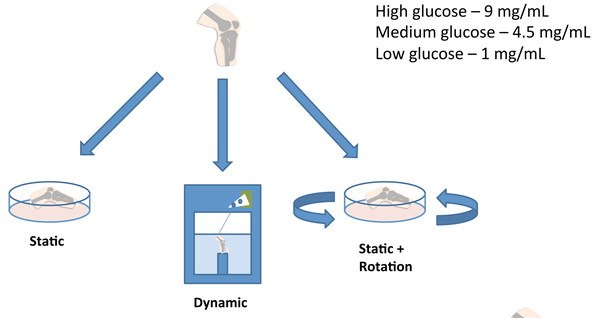
Safranin O is a red stain that shows a component of healthy cartilage. A healthy knee joint should stain red on the tibial growth plate and the articular surface. Light or no staining indicates a joint that is not optimally healthy.



Experimental Design

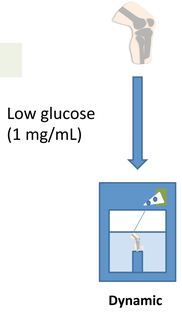
Part 1

This project used three different experimental setups – dynamic, static, and static + rotation. Additionally, it used three different glucose concentrations – low (1 mg/mL), medium (4.5 mg/mL), and high (9 mg/mL). The experiment was run for 7 days, after which the knee joints were processed and stained with Safranin O and Fast Green.



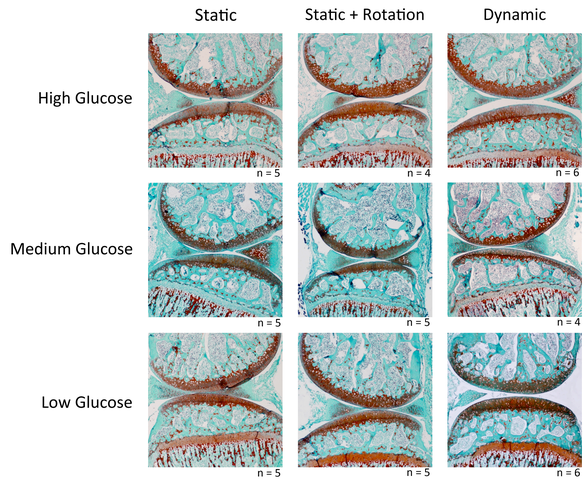
Part 2

This experiment tested long-term culturing of the joint in the machine. Guided by the results of Part 1 of the experiment, the low glucose dynamic setup was used. The experiment was run for 7 days, after which the knee joints were processed and stained with Safranin O and Fast Green.



Results

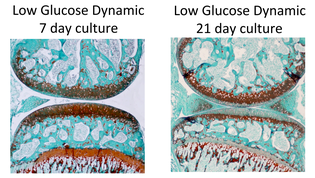
Part 1



The tibial growth plate and articular surfaces for the medium and high glucose conditions were poorly stained. The growth plate and articular surface in the low glucose condition were more stained, but not as fully or as darkly as the reference sample. For the movement conditions, static was the least stained and dynamic was the most.

Results

Part 2



Compared to those of the 7 day culture, the growth plate and articular surface of the 21 day culture were very minimally stained.

Conclusions

The low glucose concentration (1 mg/mL) is better for cartilage health than the medium or high glucose concentrations. The dynamic condition is the best movement condition, suggesting that the movement of the joint, not the movement of the liquid, was beneficial to the joint. Overall, the low glucose dynamic condition is the best condition for joint health.

The long term culture suggested that 21 days is too long to culture the joint in the low glucose dynamic condition. However, the degraded joint health could also indicate the efficacy of the Joint-in-Motion device to develop osteoarthritis-symptoms.

Future Directions

For future experiments, a glucose concentration even lower than 1 mg/mL will be tried. Additionally, the liquid medium within the device will be further improved by supplementation with growth hormones.

To test the feasibility of a long term culture, an experiment will be run for 14 days in the low glucose dynamic condition.

An improved second generation of the Joint-in-Motion device, which allows for adjustable load bearing and speed, is already undergoing testing.

Once the Joint-in-Motion device and liquid medium are optimized, this study model will serve as a platform for research across the osteoarthritis field.

Acknowledgements

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Resources

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