

## The Effect of Sliding Velocity on Chondrocytes Activity in 3D Scaffolds

S.Grad<sup>1</sup>, M.A.Wimmer<sup>2</sup>, M.Alini<sup>1</sup>

<sup>1</sup>*AO Research Institute, AO Foundation, Davos, CH,* <sup>2</sup>*Department of Orthopedic Surgery, Rush University Medical Center, Chicago (IL), USA*

**INTRODUCTION:** Sliding motion and shear have widely been recognized as important mediators for the synthesis of cartilage matrix and surface molecules. The specific contribution of the sliding velocity vector, however, has not been systematically addressed. This study investigated the effect of (i) the velocity magnitude and (ii) the motion shape on the response of bovine chondrocytes cultured in polyurethane scaffolds and subjected to oscillation of a ceramic ball over the scaffold surface or oscillation of the scaffold against the ball.

**METHODS:** A ceramic hip ball was pressed onto the cell-seeded cylindrical scaffold. Interface motion was generated either by reciprocating rotation of the ball about an axis perpendicular to the scaffold axis or by oscillation of the scaffold around its cylinder axis. The ball oscillated  $\pm 25^\circ$  at 0.01, 0.1, or 1 Hz, resulting in surface velocity magnitudes of 0.28, 2.8, or 28 mm/s, respectively. To test the influence of the motion shape, these ‘open’ motion trajectories were tested against ‘closed’ trajectories in that the scaffold oscillated  $\pm 20^\circ$  against the ball at 1 Hz, reaching the median velocity of 2.8 mm/s.

Constructs were loaded twice a day for one hour over 5 days. Unloaded constructs and constructs exposed to the static preload only served as controls. Gene expression of cartilage oligomeric matrix protein (COMP), proteoglycan 4 (PRG4, or lubricin) and hyaluronan synthase 1 (HAS1) and release of COMP, PRG4, and hyaluronan (HA) were analyzed.

**RESULTS:** Compared with statically loaded samples, COMP mRNA was increased already at 0.28 mm/s (Figure 1). At 2.8 mm/s, PRG4 and COMP release were also enhanced, while all measured parameters were significantly up-regulated at 28 mm/s. Using linear regression models, the magnitude of sliding velocity determined both gene expression and release of all target molecules.

Motion shape characteristics affected COMP, but not PRG4 and HAS1/HA. COMP mRNA expression was higher in constructs subjected to

‘closed’ motion trajectories, while the opposite was found regarding COMP release. \*

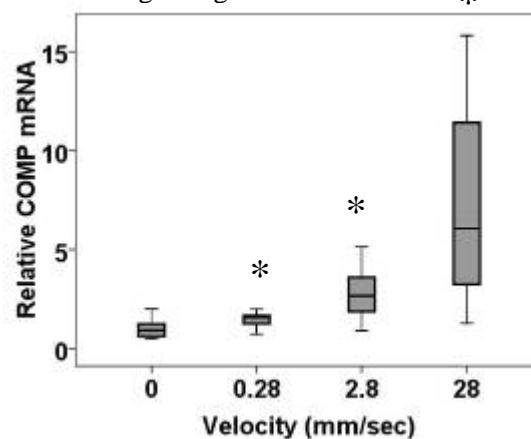


Fig. 1. Relative mRNA expression of COMP in chondrocytes cultured in 3D scaffolds and subjected to different surface velocities. Expression normalized to unloaded controls. \* $p < 0.05$  vs. statically loaded constructs.

**DISCUSSION & CONCLUSIONS:** Velocity magnitude is a critical determinant for cellular responses in tissue engineered cartilage constructs. Furthermore, the type of motion plays a role, too. However, these observations cannot be generalized, and there is a difference in the behavior of different molecules. The matrix protein COMP was most affected by both velocity magnitude and velocity profile. The apparent paradox regarding COMP gene expression and protein release can be explained as follows: The closed circular motion of the rotating scaffold induces pure shear without volume dilation to the surface. In addition, due to the closed trajectory shape, media is not exchanged with its environment. This disallows the transport of freshly synthesized molecules out of the contact area. Overall, for all investigated molecules, a certain velocity threshold appears to be necessary to induce a significant response. The specific motion type is of secondary importance. This should be considered in further studies investigating the effects of continuous or intermittent motion.

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