INTRODUCTION:
Post-traumatic arthritis is one of the most common causes of secondary osteoarthritis (OA). Damage initiation and its progression has been investigated using ex vivo cultures of articular cartilage [1]. However, most of these models are lacking the possibility to apply physical stimuli expected in vivo. In particular, joint movement, which affects the nutrition and metabolic activity of damaged cartilage [2], has not been included. Using young healthy bovine cartilage, it has been recently demonstrated, that "natural" articular motion stimulates the synthesis of lubricin [3] while maintaining a low coefficient friction [4]. The purpose of this study is to directly evaluate the biosynthetic effects of interface motion (e.g. gross sliding) on traumatized human cartilage explants. We hypothesized that articular motion will augment the intrinsic tissue repair thereby influencing the biosynthetic and functional response.

MATERIALS AND METHODS:
Adult human cartilage was obtained from ankle talus pairs of tissue donors (4M/2F aged 80 ± 7 years), within 24 hours of death through the Gift of Hope Organ and Tissue Donor Network (Elmhurst, IL). Only normal tissue (Collins grade 0) without prior fibrillation/erosion was chosen for the study. Four circles (ø 10 mm) were outlined on the central region of each talus and randomized into two 'damaged' and one 'undamaged' groups. Damage was initiated centrally within the circles on the intact talar cartilage. The flat end of a cylindrical indentor (ø 4 mm) was accelerated onto the joint surface by a pneumatically controlled impactor. A single impact with an impulse of 1 Ns, generating a peak contact force of up to 600 N, was applied to initiate (partial) damage to the cartilage surface. Full thickness cartilage explants (ø 10 mm, 4 per ankle), outlined by the circles, were then removed from the talar regions, and organized into their previously assigned groups. These groups were: traumatized cartilage explant with applied articular motion (damaged + motion, DM), traumatized cartilage explant without articular motion (damaged only, DO), and cartilage explant without trauma or articular motion (undamaged control, UC). All explants were cultured in DMEM-F12 and 1 ml of the medium was collected and replaced daily. The explants from DM group were subjected to two 1-hour long motion cycles per day from Day 1 to 5 after damage initiation. A ceramic ball was pressed against the cartilage and oscillated in a sine-wave at 1 Hz ± 30°. The compression at the ball apex was 10% of explant thickness and migrated across the explant surface (±2.5 mm; 0.1 Hz). Explants were evaluated on Days 0 and 6 for cell viability and also histologically using Safranin O/fast green, TUNEL staining (apoptotic cell death). The functional response was examined on day 6 by measuring the compressive stiffness (at strain rate of 1.5 mm/s), and coefficient of friction on the stations of the cartilage testing apparatus. The metabolic response was evaluated by sulphate incorporation (%S) in explants on Day 6, and proteoglycan (PG) content in the daily collections of conditioned media was evaluated using DMMB Statistical analyses were performed using one way ANOVA, for a significance level of 0.05.

RESULTS:
**Structural:** Surface fissures and cracks were observed during visual inspection of damaged explants immediately after impaction (Day 0). Both on Day 0 and Day 6 (after testing), the damaged explants had significantly higher histological grades, higher apoptotic cell death, and lower cell viability in the superficial zone, compared with undamaged control explants (p<0.05).

**Functional:** Applied motion had no influence on the structural response and there was no difference between the DM and the DO groups (p=0.25). However, the DM group exhibited higher compressive stiffness (Fig.1) and lower friction compared with DO (Fig.2). Interestingly, these functional differences could not be manifested when both 'no-motion' groups, DO and UC, were compared (p=0.3).

**Biosynthesis:** The DM group had a significantly higher PG/sGAG release into the media (p<0.05) from Day 1 to 5, but significantly lower PG synthesis on Day 6 (p < 0.01) compared to DO. There was no difference between DO and UC regarding biosynthetic activity (p=0.7).

DISCUSSION:
The results support our hypothesis that articular motion augments the intrinsic tissue repair by influencing the biosynthetic and functional response of damaged cartilage. The uniqueness of this approach was the study of human adult articular cartilage from organ donors using an incubator-housed joint motion simulator. Thereby, the structural integrity of the tissue was not affected. Hence, taking the results together, the joint motion simulator was successful in mimicking the contact kinematics and loading kinetics of articular joints in the presence of damage. This in vitro study provides additional proof to an already existing in vivo literature body that articular motion alters the functional and biosynthetic response of damaged articular cartilage. An ex vivo study has the advantage that the actual treatment can be tailored towards human tissue. The ankle joint has a low risk of primary OA and a relatively high risk of post-traumatic secondary OA and is therefore ideally suited. The single impact resulted in cell death by necrosis and apoptosis, cartilage degeneration, and progression of cell death. In the presence of articular motion, early intervention with anti-catabolic and pro-anabolic agents may open doors for new treatment strategies. In conclusion, this study strongly suggests that application of articular motion influences the functional and biosynthetic response of damaged explants, while not altering the structural response. It provides an opportunity to systematically document the catabolic and anabolic response of damaged cartilage under the presence of joint articulation.

ACKNOWLEDGEMENTS: This study was financed in part by the Alternatives Research & Development Foundation (ARDF).