LONG-TERM CYCLIC SUBMAXIMAL JOINT LOADING BY IN VIVO MUSCLE STIMULATION LEADS TO CHONDROCYTE DEATH AND ACCELERATES CARTILAGE DEGENERATION IN A RABBIT MODEL

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SUMMARY
Excessive chronic mechanical loading is thought to be responsible for the onset of osteoarthrosis (OA). The aim of this study was to evaluate the effects of long-term cyclic application of joint loading using physiologic and known amplitudes of loading, but excessive duration.

METHODS
Institutional Review Board approval was obtained from the Life and Environmental Sciences Animal Care Committee at our institution. Twenty-three New Zealand White rabbits underwent implantation of a nerve cuff electrode on the right femoral nerve and were divided into three groups (50 mins of unilateral knee joint loading by cyclic submaximal (i) eccentric, (ii) concentric or (iii) isometric quadriceps stimulation three times a week for four weeks =19500 cycles). All knee joint surfaces were analyzed for cell death and histologically using Mankin scores and cartilage thickness. All groups showed significantly higher cell death (p=0.001-0.141) and higher Mankin Scores for the loaded joints compared to the contralateral joints (p=0.017-0.042) with the highest Mankin scores observed for eccentric loading. Cartilage thickness was not significantly different between loaded and non-loaded joints. This is the first study to show a link between a known physiologic amount and type of joint loading and cell viability as well as cartilage degeneration. Our findings may help explain the increased OA incidence observed in endurance athletes and heavy labourers.

RESULTS AND DISCUSSION
All loading groups showed significantly higher chondrocyte death rates than controls (0.8-1.4% vs. 0.2%; p<0.001; figure 1). Cell death was highest for the inferior femoral groove, patella, and the tibial plateaus. Eccentric and isometric joint loading resulted in the highest cell death rate while concentric loading produced the lowest percentage of cell death among the loaded joints. All loaded joints had significantly higher Mankin scores than the contralateral non-loaded joints (p=0.017-0.042; figure 2 and 3) with a tendency for the highest scores for the eccentric loading conditions. Cartilage thickness was not significantly different between loaded and non-loaded joints. This is the first study to show that long-term cyclic application of muscle-induced joint loading of physiologic amplitude and...
loading parameters, but excessive duration, leads to chondrocyte death and cartilage degeneration. The results further suggest a regional distribution and dependence of cell death on the type of loading. Surprisingly, cell death rate for isometric loading was similar to that obtained for the eccentric loading despite much lower absolute loads for the isometric compared to the eccentric contractions. The percent cell death was also much higher for the isometric compared to the concentric conditions, despite very similar loading amplitudes. This result suggests that cell death for the isometric conditions is higher than expected based on joint loading, compared to the dynamic (eccentric and concentric) conditions, which might be explained with the lack (or at least largely reduced) articular motion in the isometric compared to the dynamic conditions. Therefore, a given articular surface area, and associated chondrocytes, might be loaded for longer periods of time during each loading cycle and the entire loading protocol in the isometric compared to the dynamic conditions, suggesting that not only the magnitude, but also the amount of time of loading might be important in the occurrence of cell death. Also, the dynamic loading conditions would be expected to produce different internal tissue stresses (for example, greater shear stresses) than isometric loading, and these differences might explain the relatively high percentage of cell death in isometric compared to the dynamic conditions.

Mankin-Scores were increased for all loading conditions after the four week experimental period compared to control, but there was only a tendency towards increased joint degeneration for the eccentric condition. Possibly, Mankin scores are not sensitive enough to detect subtle differences in cartilage degeneration that may have occurred in the short experimental period. Nevertheless our findings may help explain the increased OA incidence in endurance athletes and heavy labourers [2-4]. The high Mankin scores for the eccentric conditions may provide a hint as to the increased OA incidence in workers subjected to continuous eccentric muscle work. Our work further underlines the link between chondrocyte death in early OA and histological changes in articular cartilage. More studies are needed to evaluate the detailed relationship between joint loading and cartilage degeneration.

CONCLUSIONS
This is the first study to demonstrate a link between physiologically relevant joint loading conditions of long duration and articular cartilage degeneration. Long-term application of perfectly normal joint loading can lead to chondrocyte death and cartilage degeneration after as little as four weeks in a rabbit model.

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REFERENCES