Distribution and Progression of Chondrocyte Damage in Human Ankle Intraarticular Fractures

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PURPOSE: Intraarticular fractures (IAFs) are a leading cause of post-traumatic osteoarthritis (OA). Typically, at the instant of injury event, a joint surface is subject to a force pulse that fractures the juxtaarticular bone structure and articular cartilage. Recently, chondrocyte damage involved in human IAFs has been receiving increasing attention [1, 2, 3]. Death or dysfunction of chondrocytes necessarily affects the cartilage metabolism in fractured joints, presumably triggering a pathological cascade that eventually leads to OA. Unfortunately, information about acute chondrocyte damage involved with IAFs, particularly in the early acute phase, is still limited. Determining the distribution and progression of chondrocyte damage could lead to new treatments of intraarticular fractures that prevent or decrease the risk of osteoarthritis. For this purpose, site-specific, time-dependent changes in cell viability in fractured articular surfaces were studied using a quasi-in-vivo model of human ankle intraarticular fracture.

METHODS: Six normal human ankles immediately (< 4 hours) following amputation for treatment of lower extremity malignant tumors were subjected to a transarticular compressive impaction insult that mimicked the typical injury mechanism of clinical tibial plafond fractures. Each ankle, dissected at the middle of tibial shaft and the subtalar joint, with both ends potted into separated PMMA blocks, was mounted onto a drop-tower device up-side down. A mass with 60 joules of potential energy was then dropped onto an impact interface secured to the talar block. Chondrocyte viability in the fractured cartilage was studied by means of live/dead assay, using a confocal laser-scanning microscope. We measured chondrocyte viability in the superficial zone of the cartilage, within 100-150 microns from the surface, at several sites per joint along the primary fracture lines (within 1 mm of the fragment edges) and in the “non-fracture” area more than 3 mm centrally away from the fragment edges. The first two ankles were scanned for cell viability immediately post-impact, and the third scanned after 48 hours of culture. For the remaining three, scans were repeated at three time points, immediately (< 6 hours), 24 hours, and 48 hours post-impact.

RESULTS: All fractures created (Figure 1) were morphologically similar to clinical tibial plafond fractures. Chondrocyte viability immediately after fracture impaction was assessed in five ankles, at 20 near-fracture sites and at 37 non-fracture sites. Fractional cell death (dead cell count / total cell count) in the near-fracture region ranged from 0.0% to 29.6%, variable across sites/an ankles. However, the mean fraction 8.6% was significantly higher than in the non-fracture region (p = .004, Figure 2). Chondrocyte viability at 48 hours post-impact was assessed at 21 near-fracture sites and 39 non-fracture sites across four ankles. Again, fractional cell death in the near-fracture region (28.7%, 2.8 – 62.4%) was significantly higher than in the central region (p < .001). Three-time-point cell viability analysis for the latter three ankles was performed at 16 near-fracture and 33 non-fracture sites. Fractional cell death in the near-fracture region, which averaged at 10.4% at the immediate scan, increased to 19.3% at 24 hours post-impact, and further increased to 33.4% at 48 hours post-impact (p < .001, Figures 3 and 4). Fractional cell death in the non-fracture region remained relatively low, typically within 10%, throughout the test period.

CONCLUSION: To our best knowledge, this is the first study that has addressed the whole-joint distribution of chondrocyte damage involved in intraarticular fractures. Time-dependent changes in cartilage pathology during the early acute phase, phenomena difficult to study cartilage samples from clinical cases, have also been documented. Morphologically, the fractures created were very similar to clinical pilon fractures, suggesting that the natural injury mechanism of human ankle IAFs was reasonably replicated in this quasi-in-vivo experimental model. Chondrocyte death identified along fracture lines was consistent with previous studies in which fracture-associated cartilage pathology was explored in osteoarticular segments from clinical fracture cases [1, 2, 3], supporting the pathophysiological reality of cartilage injury in this model.

The whole-joint cell death distribution data revealed that most chondrocyte damage was concentrated along fracture lines, except for sporadic high cell-death spots in the central non-fracture area, implying that chondrocyte damage in fractured joints is closely associated with structural damage of articular surface. The cell viability tracking data revealed that chondrocyte damage along fracture edges developed with time, suggesting that chondrocyte damage in clinical intraarticular fractures would propagate spontaneously with time.

Figure 1. Intraarticular fractures created at the human distal tibia.

Figure 2. Chondrocyte viability at near-edge vs. central non-fracture sites. The dispersion bars indicate the 75th- and 25th-percentile values.

Figure 3. Time-dependent changes in chondrocyte viability. The dispersion bars indicate the 75th- and 25th-percentile values.

Figure 4. Confocal microscope images in the three time-point chondrocyte viability analysis at a representative near-fracture site. Cells labeled by green fluorescence are alive, while red-labeled cells are dead. White allows indicate the edge of cartilage on the fracture line.

References:

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