Universität Basel

Research Project

The effect of high tibial osteotomy on in vivo cartilage mechanobiology in patients with knee osteoarthritis

Third-party funded project

Project title The effect of high tibial osteotomy on in vivo cartilage mechanobiology in patients with knee osteoarthritis
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Department
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Although osteoarthritis (OA) is the most common degenerative joint disease and despite international research efforts, to date the factors involved in the initiation and progression of this debilitating disease are poorly understood, diagnostic markers are lacking and there is no cure. High tibial osteotomy (HTO) is a well-accepted therapy for patients with knee OA and varus alignment aimed at re-establishing a more even distribution of ambulatory load between the affected medial knee compartment and the lateral knee compartment. However, the survival rate of HTO is only around 75% after 5 years. There is some evidence that the change in ambulatory load after HTO may be more relevant than the post-operative static alignment although this relationship has not yet been investigated. Because of the large changes in ambulatory load with HTO, we propose that HTO may serve as a valuable model for studying the effect of changes in ambulatory load on in vivo cartilage mechanobiology in patients with knee osteoarthritis. Our previous work has shown that serum biomarkers for cartilage increase after a 30-minute walking exercise (termed 'walking stress test') and indicated that these changes may be associated with the accumulated ambulatory load during the test. Our overall hypothesis is that a sudden ambulatory load reduction (caused by HTO) leads to changes in cartilage biology that delay or reverse osteoarthritic processes determining the clinical outcome and representing an in vivo model for assessing cartilage mechanosensitivity. We will address the following specific aims:
Specific Aim 1: To test the relationship between changes in ambulatory load pre-HTO to 6 months post-HTO, static alignment 6 months post-HTO and changes in clinical scores pre-HTO to 12 months post-HTO.
Specific Aim 2: To test the relationship between magnitude of ambulatory load (modified by HTO) during a walking stress test and the change in serum concentrations of cartilage biomarkers.
Specific Aim 3: To test the relationship between changes in cartilage biomarkers during a walking stress test 6 months after HTO and functional outcome 12 months post-HTO.
Patients with medial compartment knee OA and varus alignment will be clinically assessed (including mechanical axis measurement from radiographs) and complete questionnaires on physical function prior to medial opening wedge HTO. Patients will complete a walking stress test with blood sampling (30 minutes walking, 5.5 hours sitting) to assess load-induced changes in serum biomarker concentrations (COMP, MMP-1, MMP-3, MMP-9, C2C/CPII), and undergo gait analysis to assess the external knee adduction moment. Once full load bearing is achieved (6 weeks after HTO), the mechanical axis will be

measured from radiographs. Patients will complete the questionnaires and a second walking stress test with blood sampling and undergo gait analysis 6 months after HTO. At the 12-month follow-up, subjects will complete the questionnaires.
The results of this study can be considered as proof-of-concept of a potential prognostic test (walking stress test) for cartilage degeneration. To date, the use of cartilage biomarkers for OA diagnostics and prognostics is limited in part because of the large inter-subject variation in serum markers. A direct relationship between ambulatory load and cartilage metabolism assessed as degradation to synthesis ratio would allow developing novel load-modifying interventions and evaluating the efficacy of existing interventions. Moreover, a predictive relationship between load-induced changes in cartilage biomarkers 6 months post-HTO and functional outcome another 6 months later would suggest that the stress test may be a promising prognostic tool for detecting degenerative cartilage processes. Overall, a model for measuring in vivo mechanosensitivity may also provide unique insights into in vivo cartilage degeneration and regeneration processes in healthy subjects, after injuries or in patients with musculoskeletal disease.

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Add publication

Published results

4508175, Herger, S.; Vach, W.; Liphardt, A.-M.; Egloff, C.; Nüesch, C.; Mündermann, A., Dose-response relationship between ambulatory load magnitude and load-induced changes in COMP in young healthy adults, 1063-4584 ; 1522-9653, Osteoarthritis and cartilage, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

4179939, Donath, Lars; Faude, Oliver; Lichtenstein, Eric; Pagenstert, Geert; Nüesch, Corina; Mündermann, Annegret, Mobile inertial sensor based gait analysis: Validity and reliability of spatiotemporal gait characteristics in healthy seniors, 1879-2219, Gait & Posture, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

4179944, Donath, Lars; Faude, Oliver; Lichtenstein, Eric; Nüesch, Corina; Mündermann, Annegret, Validity and reliability of a portable gait analysis system for measuring spatiotemporal gait characteristics: comparison to an instrumented treadmill, 1743-0003, Journal of neuroengineering and rehabilitation, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

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Specify cooperation partners

ID	Kreditinhaber	Kooperationspartner	Institution	Laufzeit - von	Laufzeit - bis
4508182	Mündermann, Annegret	Liphardt, Anna-Maria, Advisor biomarkers	Universitätsklinikum Erlangen	01.01.2016	31.12.2023