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論　文　内　容　の　要　旨
Synopsis of Thesis

氏　　名 Name	張　子陽(ZHANG ZIYANG)
論文題名 Title	Basic research on intrameniscal injection as a direct treatment for knee meniscal pathology （膝半月板病変に対する直接的治療としての半月板内注射に関する基礎研究）

論文内容の要旨

〔目　的(Objective)〕

The meniscus is an essential structure of the knee joint, performing functions such as load transmission, shock absorption, joint stability, and joint lubrication. The deterioration of meniscal function due to trauma or degenerative changes causes meniscal-related symptoms and leads to cartilage damage and osteoarthritis. Current treatments target not the meniscus itself, but the entire knee joint or intra-articular tissues, and non-surgical treatments that directly access the meniscal tissues are not widely used. This study aimed to evaluate the effects of the intrameniscal injection technique on meniscal tissue and cells.

〔方法ならびに成績(Methods/Results)〕

Methods: Four healthy porcine menisci and 10 human menisci from patients after total knee arthroplasty were injected with different solutions to investigate the required injection force, intrameniscal distribution of the injected solution, and biological effects on the meniscal cells. The initial force exerted by the syringe piston was measured by a pressure gauge. After the injection of Fast Green FCF solution, the distribution was observed, measured, and analyzed in 3 indicators: Width, Stained Area, and Calculated Volume. Other meniscal tissues were injected with recombinant interleukin-1 beta (rIL-1β), dexamethasone or papain, cultured and harvested for qRT-PCR or histology analysis.

Results: Statistically significantly greater force was required for the intrameniscal (24.9 ± 4.3 N) versus adipose (1.1 ± 0.2N) or muscle tissue (0.8 [interquartile range 0.6-1.1] N) using a 1 mL syringe ($p < 0.01$), while less force was required when using a microsyringe (0.5 [interquartile range 0.4-0.5] N) versus 1 mL syringe ($p < 0.0001$). When different injection volumes were compared, the indicators were significantly higher after a 10-μL versus 5-μL injection ($p < 0.05$). When the same amount of Fast Green FCF solution was injected, the indicators were larger in the degenerative human versus healthy porcine menisci. The injection of rIL-1β promoted inflammatory factor and matrix proteinase transcription in meniscal cells. In contrast, the injection of dexamethasone into meniscal tissue cultured in rIL-1β-containing medium suppressed this transcription. The injection of papain resulted in decreased Safranin O staining and a changed picrosirius red staining pattern.

〔総　括(Conclusion)〕

In summary, injecting solutions into porcine and human meniscal tissues requires statistically significantly greater force than injecting into subcutaneous adipose tissue or skeletal muscle tissue ($p < 0.01$). Furthermore, the distribution of the injected solution within the meniscus is influenced by the structural arrangement of meniscal fibers. Additionally, injecting solutions into ex vivo cultured meniscal tissue altered meniscal tissue structure and gene expression in meniscal cells. This study provides preliminary evidence that will serve as a foundation for further translational research.

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論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

本論文は、膝関節の機能維持に不可欠な半月板に生じた病変の治療を目的として、半月板組織内に薬剤を注入する「半月板組織内注射手技」を検証した基礎研究の報告である。健常ブタの半月板組織と人工膝関節置換術患者のヒト半月板組織を対象に、溶液注入に必要な力と溶液の組織内への分布、ならびに半月板細胞と半月板組織への生物学的効果を検討した。

半月板組織への注入には筋組織や脂肪組織と比較して有意に大きな力が必要なこと、注入溶液は半月板の線維構造に沿って拡散すること、さらに抗炎症薬の注入により炎症関連因子や組織分解酵素の遺伝子発現が抑制されることが示された。

これらの成果は、半月板病変に対する膝関節腔内投与による間接的な薬液投与とは異なる新規治療法に関する重要知見を提供するものとして、膝関節外科・スポーツ医学の国際学術誌に掲載された。

以上より、本論文は博士（医学）の学位授与に値するものと認める。