# Triple contrast method for computed tomography diagnostics of cartilage injuries

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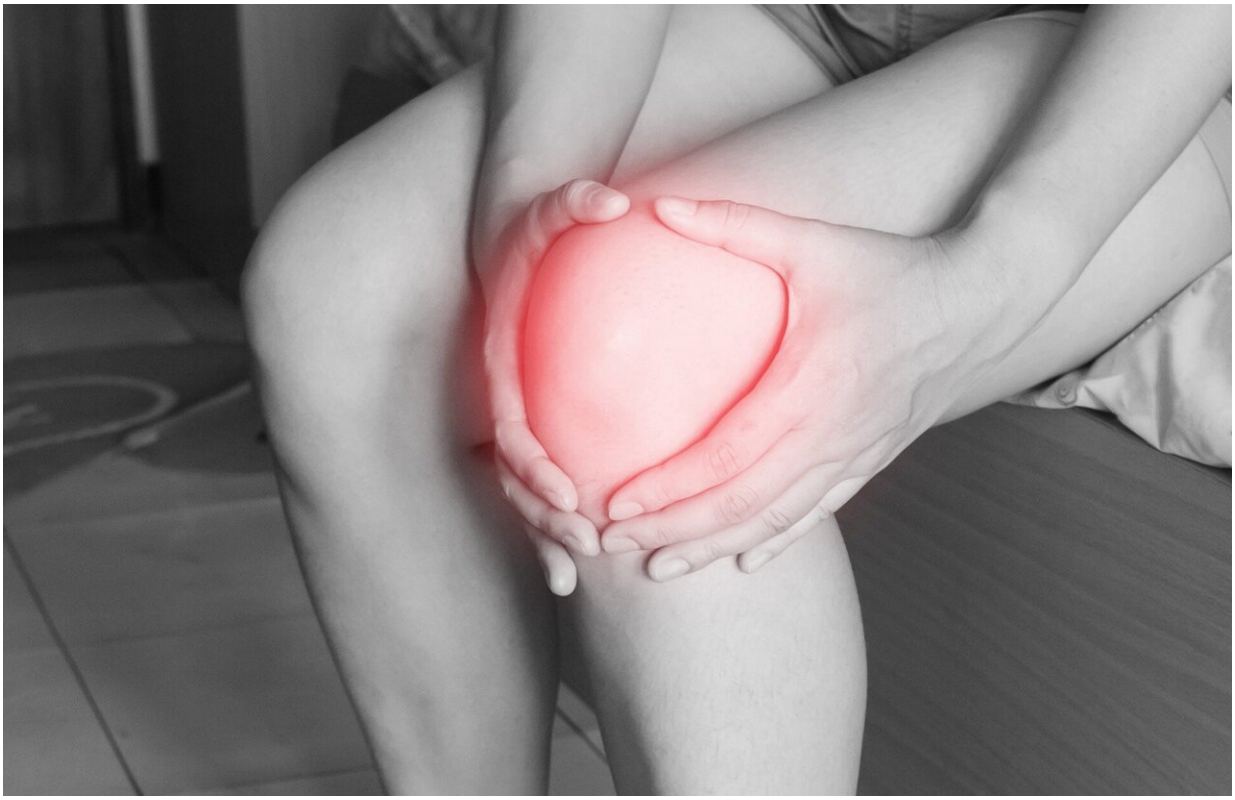

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Post-traumatic osteoarthritis (PTOA) is a joint disease associated with the gradual erosion of cartilage covering the ends of articulating joints. It can result from a single traumatic incident, repetitive injurious incidents, or due to excessive mechanical stress and strain. Resulting abnormal

mechanical function and biochemical alterations may lead to post-traumatic changes in cartilage structure and composition. In PTOA, these changes may eventually worsen and lead to a progression of osteoarthritis (OA). Identification of incipient post-traumatic changes is crucial for the selection of the optimal conservative, such as exercise, losing weight, pain relief medicines, steroid injections, non-steroidal anti-inflammatory drugs, or surgical intervention, but effective means to identify them are still limited.

Superficial collagen disruption, proteoglycan (PG) loss, and increased water content are the first signs of OA. These alterations in tissue structure and composition increase tissue permeability and decrease the fixed charge density in cartilage matrix. Contrast-enhanced computed tomography (CECT) is an imaging technique that utilizes contrast agents. With CECT, the detection of OA-related changes is possible as the degenerative changes alter the diffusion and accumulation of contrast agents in articular cartilage. Contrast agents may also be exploited for segmentation of cartilage tissue in CT images since contrast agents enhance the interface between synovial fluid and cartilage as the natural contrast at this interface is almost non-existent.

Current CECT of a knee joint includes two subsequent CT scans acquired immediately and 45 minutes after the intra-articular injection of an anionic contrast agent. The scan acquired immediately after contrast agent administration allows segmentation of the articulating surface and lesions, while the latter scan enables detection of internal cartilage changes related to the initiation of PTOA. This method includes two drawbacks. Firstly, recent studies suggest that a recently developed cationic contrast agent has a superior sensitivity for PG content at diffusion equilibrium compared with conventional anionic agents. However, a critical weakness of cationic agent occurs at clinically feasible time points (

The aim of this thesis was to introduce a triple contrast agent method that, together with a quantitative dual-energy CT (QDECT), enables simultaneous quantification of PG and water contents in articular cartilage and enables the accurate segmentation of the articulating surfaces. To this end, we first studied the suitability of two different dual contrast methods for the detection of different types of cartilage injuries. This research then led to the development of the triple contrast agent. In study I, the potential of the dual contrast agent consisting of anionic, iodinebased contrast agent and a suspension of bismuth(III) oxide nanoparticles (BiNPs) to detect different types of articular cartilage injuries was evaluated. Also, the ability to facilitate a high contrast at articular surfaces for improved segmentation was examined. The dual contrast agent consisting of cationic, iodine-based and non-ionic, gadolinium-based contrast agents was examined in study II. The ability of this dual contrast agent to allow simultaneous determination of PG and changed permeability at clinically feasible time points (i.e., 1 h and 2 h after contrast agent administration) was determined. In study III, a triple contrast agent, being a mixture of three contrast agents (cationic, iodine-based and non-ionic, gadolinium-based contrast agents together with BiNP suspension), was studied for simultaneous determination of cartilage PG content, water content, and changed permeability and segmentation of the articulating surfaces. Finally, the capability of the dual contrast agent based on cationic and non-ionic contrast agents to detect post-traumatic changes in equine cartilage tissue around the surgically-induced lesions was evaluated in study IV.

BiNPs were found to maintain a high contrast at articulating surfaces. This was shown to allow an accurate segmentation of the cartilage surfaces at the same time as anionic contrast agent enabled the detection of cartilage degeneration. Further, the cartilage lesions caused by the mechanical impact were visualized (study I). The findings of study II suggest that the simultaneous evaluation of cationic, iodinebased and non-ionic, gadolinium-based contrast agent partitions is possible with

QDECT. As the cationic contrast agent is sensitive to PG, tissue permeability as well as water content and non-ionic agent to tissue permeability and water content, their mixture allows subsequent quantitative determination of PG and water contents. As a result, a significant correlation (P contrast agents; accurate determination of articulating surface was possible with simultaneous quantification of PG and water contents. In study IV, significant differences in partition of cationic, iodine-based agent between post-traumatic and control samples were seen at 30 min (P = 0.004), 60 min (P = 0.028), and 20 h (P

In light of the findings presented in this thesis, the triple contrast method enables improved characterisation of cartilage composition, i.e., PG and water contents can be evaluated simultaneously together with accurate segmentation of the articulating surfaces. Thereby, for example, the evaluation of post-traumatic degeneration around a lesion site is possible with a single scan. These improvements in CECT may allow a more effective selection of patient-specific surgical treatment options and prevention of PTOA.

The doctoral dissertation of MSc (Tech.) Annina Saukko, titled "Triple Contrast Method for Computed Tomography Diagnostics of Cartilage Injuries," will be examined at the Faculty of Science and Forestry on the 27th of August online.

**More information:** Triple Contrast Method for Computed Tomography Diagnostics of Cartilage Injuries, erepo.uef.fi/

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contrast-method-tomography-diagnostics.html