respectively. The discrete variables of right knee from each trial were used for inter-trial reliability. The mean of five trials were used for inter-session reliability. ICC were used to examine inter-trial (ICC (3, k)) and inter-session (ICC (3, 1)) reliability of discrete variables [18]. The absolute measures of measurements error was accessed by standard error of measurement (SEM) and MDC. Statistical analysis was performed in SPSS 21 (SPSS Inc., Chicago, IL, USA).

Results: According to the ICC classifications (greater than 0.75 is excellent) of Fleiss [8], all the discrete variables were excellent in inter-trial reliability. For the knee kinematics, the inter-trial reliability was generally better than the inter-session reliability. The knee flexion angles had higher SEM and MDC than valgus and internal rotation angles. For knee kinetics and peak vertical GRF, the peak knee abduction moment had a larger MDC compared to other moment variables. The peak vertical GRF and the peak knee flexion moment showed an excellent rank correlation between sessions.

Discussion: In the present study, the results showed that inter-trial reliability is higher than the inter-session reliability. The possible sources of variability include skin marker placement, body position of the standing static calibration and task difficulty. Among all the discrete variables, peak vertical GRF got the higher value in reliability and rank correlation. It implies that vertical GRF is the most reliable and repeatable variables over time. However, the MDC of the peak vertical GRF is 89.7N, which is large for clinical practice. It implies a difference smaller than 89.7N cannot be regarded as a true difference between two sessions.

The reliability of peak knee valgus angle and moment are of great interest because they have been suggested to be able to predict ACL injury [3]. Both of them achieved an excellent inter-trial reliability. The MDC of peak valgus angle and moment were 2.2° (39% of SD) and 23.1Nm (59% of SD). Although peak knee abduction moment had a high inter-session reliability, the peak knee valgus angle demonstrated a promising MDC with smaller percentage of SD.

Conclusion: Among all the discrete variables, the peak vertical ground reaction force is the most reliable variables. Although peak knee abduction moment had a high inter-session reliability, the peak knee valgus angle demonstrated a promising minimum detectable change with smaller percentage of standard deviation.

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3D printing and characterization of bioactive scaffold potential for reconstructing calcified cartilage zone

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Background: The osteochondral injury is a common disease in clinic, which is a huge burden on society and economy, but the treatment has always been a problem. In view of the importance of the zone of calcified cartilage in maintaining the stable microenvironment of bone and cartilage respectively and promoting osteochondral healing and stress conduction, an organic-inorganic composite tissue engineering scaffolds used to reconstruct calcified cartilage layer were built, and the relationship between calcium magnesium silicate content and the compressive properties of the scaffolds was investigated systematically.

Materials: Hyaluronic acid sodium, sodium alginate, collagen type I, $CaCl_2$, $Ca(NO_3)_2 \cdot 4H_2O$, $Mg(NO_3)_2 \cdot 6H_2O$, $Na_2SiO_3 \cdot 9H_2O$, ammonia, anhydrous alcohol, polyvinyl alcohol.

Methods: Three-dimensional (3D) printing technique was used to build the scaffolds with highly bioactive calcium-magnesium silicate ultrafine particles of 1%, 3%, or 5% of mass fraction, in which the organic phases were composed of type I collagen and sodium hyaluronate. The as-printed scaffolds were then crosslinked and solidified by alginate/$CaCl_2$ aerosol. Scanning electron microscope (SEM) was used to observe the pore size and distribution of inorganic phase, universal material testing machine to test mechanical properties, and the porosity of scaffolds was also measured.

Results: Pore size is approximately (212.3 ± 34.2) μm with a porosity of (50.1 ± 3.1)%, the compressive modulus of the scaffolds is (7.2 ± 1.2) MPa on the average, which is irrelevant to the percentage changes of calcium-magnesium silicate.

Discussion: Cartilage tissue engineering research lacking in understanding of the integration and isolation effect of calcified cartilage layer uesd to simply focus on cartilage repair. The damage repair of subchondral bone and calcified cartilage layer is often ignored. With the deepening of researches in interfacial tissue, the importance of these three different soft/hard tissue interfaces between ligament-bone, tendon-bone and cartilage-bone has caught increased attention, and breakthrough discovery in osteochondral tissue engineering will be likely made in future and applied in clinic. 3D printing is one of the most commonly used methods in building tissue engineered scaffolds. 3D printing, without any mold or mechanical processing, is very suitable for personalized manufacturing compared with other manufacturing methods, which saves a lot of time and costs. A wide range of material sources can be used in 3D printing, such as natural and synthetic polymers, bio ceramics and composite, which results in good biocompatibility and controllable pore size and shape for cell migration, proliferation and differentiation for the repair of osteochondral defects providing excellent environment. The scaffold for reconstruction of calcified cartilage layer in this experiment is of moderate size, which is bionic to compression performance and composition of calcified cartilage layer to a certain degree. The compressive modulus of the scaffold is irrelevant to the percentage changes of magnesium doped calcium silicate, which is between that of cartilage and subchondral bone.

Conclusion: A porous scaffold featuring reconstruction of calcified cartilage layer was successfully fabricated for the first time and compressive modulus of the scaffold is irrelevant to the percentage changes of calcium-magnesium silicate, which lays foundation for building multi-layered composite scaffolds for osteochondral injury in future.

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Human mesenchymal stem cell-derived exosomes promote orderly cartilage regeneration in an immunocompetent rat osteochondral defect model

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Background: Mesenchymal stem cell (MSC) therapy is currently evaluated in clinical trials for treatment of cartilage injuries. While cell therapy has demonstrated therapeutic efficacy, logistical and operational challenges associated with shipping constraint, storage and proper handling remain. Exosomes are nano-sized, cell-secreted bi-lipid membrane vesicles present in MSC secretome that have been found to mediate the regenerative and immunomodulatory functions of MSCs in treatment of various diseases in animal models. Here, we hypothesize that human MSC exosomes may represent a novel cell-free therapeutic to promote cartilage regeneration.

Materials and methods: Accordingly, exosomes were purified from conditioned medium of human embryonic MSCs and evaluated in their ability to heal a critical-sized osteochondral defect in an immunocompetent rat model over a 12-week period.

Results: Our results showed that weekly intra-articular injections of MSC exosomes promoted early cellular infiltration and proliferation that facilitated orderly cartilage and subchondral bone regeneration. Analysis of proliferative cell nuclear antigen (PCNA) immunoreactivity showed significantly higher numbers of PCNA positive cells in both the synovium and reparative tissue in animals treated with MSC exosomes than in animals treated with saline ($P<0.001$). Concomitantly, we detected reduced numbers of apoptotic cells in the reparative tissue in animals treated with MSC exosomes. By end of 12 weeks, MSC exosome-treated rats showed a smooth continuous hyaline neocartilage layer and regenerated subchondral bone. On contrary, saline-treated defects showed severe surface irregularity and mostly fibrous/non-cartilaginous tissues with minimal matrix deposition. We also demonstrated that MSC exosomes induced polarization of the synovial macrophages with a regenerative M2 phenotype. Importantly, no adverse reactions were observed in all animals.

Conclusion: Taken together, our results show that MSC exosomes are safe and effective, and likely mediate cartilage regeneration through multiple mechanisms. This study provides the basis for future use of human MSC exosomes as a novel off-the-shelf and cell-free therapeutic for cartilage repair in patients.

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