

# EFFECTS OF EXERCISE ON CARTILAGE STATUS

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## INTRODUCTION

The primary function of articular cartilage consists of stress dissipation, providing a frictionless surface during joint motion and improving joint surface congruence<sup>1</sup>. To fulfil these tasks, articular cartilage presents as a highly organised and complex tissue. Being an avascular, aneural and alymphatic tissue, it is the cartilage matrix and its compounds that are of utmost importance for load transmission. This interstitial matrix consists for 70% of fluid and for 30% of structural compounds of which collagen fibrils and proteoglycan molecules are the main components. Although matrix composition varies throughout the depth of the tissue and collagens are prone to structural variation, the collagen fibrils (mainly type II) constitute a three-dimensional network that provides the tissue with

tensile strength. Through linking proteins (e.g. cartilage oligomeric protein, decorin), the collagen network is attached to the proteoglycan macromolecules. The latter, in particular aggrecan, contains highly negatively charged glycosaminoglycan side chains (mainly keratan sulphate and chondroitin sulphate) that attract water molecules. Consequently, osmotic swelling pressures are created enabling cartilage to encounter compression stress<sup>1</sup>.

In general, cartilage in vitro deformational behaviour is illustrated using the linear biphasic theory. This well-known theory postulates that loading the tissue leads to an instantaneous hydraulic pressurisation allowing only little deformation during dynamic loading conditions. In the case of static loading conditions (and over longer periods of time), fluids gradually leak from the tissue, decreasing hydraulic pressures

resulting in more deformation<sup>7</sup>. This in vitro deformational behaviour is confirmed by recent in vitro studies which revealed that static loading is characterised by more deformation than dynamic loading<sup>2,3</sup>.

From a theoretical perspective, one may reason that, as intermittent dynamic loading is required for cartilage health, exercise and physical activity should be beneficial in view of structural longevity of the knee joint. However, in the context of sports medicine, there are several unanswered questions:

- What exactly is the relationship between exercise and cartilage status?
- Can cartilage still be changed or influenced in adults?
- Is running chondroprotective or harmful for the cartilage?
- When athletes return to sport, how do we know if their cartilage is ready?



- Should we prescribe exercise therapy in the healthy and injured athletes?

This review article attempts to answer these questions based on the currently available scientific knowledge in the literature.

#### EFFECTS OF IN VIVO EXERCISE ON CARTILAGE STATUS

Unloading of the knee during 6 to 8 weeks immobilisation, non-weight-bearing after surgical interventions or 6° head-down tilt bed rest can lead to decreases in thickness and changes in biochemical composition of the cartilage<sup>4,5</sup>. General remobilisation or whole-body vibration training affected the thickness and biochemical composition of the cartilage<sup>4</sup>. As patients with spinal cord injuries showed gradual decrease in cartilage thickness, repetitive in vivo loading cycles appear necessary for articular cartilage to maintain its ultra-structure and gross morphology over time<sup>6</sup>. However, it has also been shown that cartilage does not appear to functionally adapt to exercise in the same way or at the same rate as muscles or bones do<sup>4</sup>.

In terms of cartilage volume growth, children who undertake more vigorous sports demonstrate substantially higher growth rates than those who do not<sup>7,8</sup>. In young adult professional athletes (i.e. 20 to 30 years of age), joint surface areas are larger but cartilage plates were not significantly thicker when compared to untrained persons<sup>7,8</sup>. At an ultra-structural level, comparison between sedentary and recreational or elite runners showed increasing biochemical activity in the latter, suggesting adaptive capacity of knee cartilage to some extent<sup>9</sup>. A 10-year follow-up study showed that long-distance runners who had no damage at baseline did sustain considerable permanent lesions to the internal knee structures in the longer-term<sup>10</sup>. In adults (i.e. 26 to 62 years of age) without clinical osteoarthritis (OA) but with potential underlying radiographic signs of OA or at risk for OA development, a 2-year longitudinal study showed that strenuous exercise was associated with a decreased risk of progressing cartilage defects. Additionally, changes in muscle strength were positively associated with cartilage

volumes and a 4-month structured exercise programme encompassing neuromotor control, strength and aerobic exercise was suggested to induce a chondroprotective effect in the articular cartilage of the femoral condyle<sup>11</sup>.

In middle-aged adults (i.e. approximately 45 to 55 years of age) without clinical or radiographic OA (i.e. K/L [Kellgren-Lawrence] grade  $\leq 1$ ), exercise level (i.e. sedentary, light, moderate to strenuous) did not influence cartilage qualitative status in subjects without risk factors for knee OA. In those at risk for radiographic OA progression (e.g. previous knee injury or surgery, family history of total knee replacement, Heberden's nodes and/or occasional knee symptoms), light exercise was associated with better qualitative function, suggesting its beneficial effect. In addition, participation in fortnightly exercise (causing tachypnea and increased pulse rates for at least 20 minutes) was positively associated with cartilage volume or reduced rates of volume loss and was not associated with the presence of cartilage defects<sup>12,13</sup>.





In older adults (i.e. 50 to 80 years of age) without clinical OA but with uncertain status of radiographic OA, a 2-year follow-up study in more than 100 subjects showed that participation in vigorous physical activity (e.g. jogging, swimming, cycling, singles tennis, aerobic dance, skiing or other similar activities) was associated with reduced rates of cartilage volume loss with a trend towards decreased risks for worsening cartilage defects. In the case of no baseline cartilage defects combined with reduced rates of volume loss, a trend for fewer newly developed defects was observed<sup>14,15</sup>. Additionally, regular walking was associated with a reduced risk of bone marrow lesion development<sup>14</sup>. Follow-up after 3 years, however, documented that persistent participation in vigorous activity was associated with decreased cartilage volumes<sup>16</sup>.

In older adults with potential clinical and radiographic signs of OA disease, a 3-year follow-up study showed physical activity (expressed as step count per day)

as protective against cartilage volume loss in those with higher baseline volume. Additionally, excessive physical activity (i.e.  $\geq 10,000$  steps/day) increased the risk of worsening of meniscal pathology scores especially in the case of the presence of baseline meniscal damage, and also increased the risk of cartilage damage progression in those with who had baseline bone marrow lesions. Authors concluded that more than 10,000 steps/day can aggravate knee structural deterioration especially in persons with pre-existing internal knee abnormalities<sup>17</sup>.

Summarising the above, it can be said that the adaptive functional capacity of human cartilage to exercise does not appear to be straightforward. However, depending on age, type or level of exercise and baseline joint status, it has been suggested that exercise can potentially be protective against MRI-detected cartilage damage progression. In young healthy adults, exercise appears to exert beneficial influence on cartilage ultra-structure. With

increasing age, protective effects persist in the case of light-to-moderate exercise in those individuals without radiographic signs of OA or at risk for progressive radiographic OA (e.g. post meniscectomy status). One needs to stress that in the case of pre-existing internal knee derangements (i.e. cartilage defects, meniscal pathology, bone marrow lesions presence), prolonged and excessive physical activity is suggested to accelerate deterioration of joint structures. Thus, while dedicated exercise programmes seem to have the potential to alleviate symptoms and improve function, the relationship between increased loading of cartilage (e.g. running) and the quality of cartilage still needs to be explained.

#### EFFECTS OF RUNNING ON THE QUALITY OF CARTILAGE IN ADULTS

Worldwide, running is gaining popularity because of its benefits on cardiorespiratory fitness, weight control and psychosocial health<sup>18</sup>. Additionally, an athletic lifestyle has been associated with a reduced risk of type II diabetes mellitus and of cancer to the reproductive system, breast and colon<sup>18</sup>. As well as possible increases in bone density<sup>18</sup>, it was generally thought that highly repetitive loading can, in time, deplete the joint of lubricating glycoproteins, disrupt the collagen network and slowly break down the cartilage causing microfractures in the underlying bones<sup>19</sup>. However, several studies have investigated the association in prolonged running and OA of the knee and hip, showing conflicting results<sup>20,21</sup>. While some studies show no association between running and an increased prevalence of OA<sup>20,22</sup>, others indicate an increased risk for knee and hip OA<sup>21,23</sup>. Furthermore, a large cohort of community-dwelling older adults did not demonstrate association between recreational physical activity (e.g. walking, jogging) and increased or decreased risk of OA<sup>24</sup>. This disparity in outcomes can be attributed to mixed subject characteristics or analytic methods that are dependent on an imaging modality insensitive to changes of cartilage tissue itself (e.g. X-ray).

Nevertheless, since OA is the leading cause of disability in adults world-wide, strategies to preserve joint health have been desired over the years, of which exercise (and running) has been one of the proposed means<sup>11,25</sup>.

One might suggest that the possible benefits of exercise occur at an ultra-structural, qualitative level within the cartilage itself, namely the glycosaminoglycan content. In this respect, one study investigated the functional adaptation of human knee cartilage due to running, by measuring the quality of the cartilage itself (measuring the GAG content with MRI)<sup>26</sup>. In this study, the quality of the knee cartilage was measured in asymptomatic female novice runners prior to and after a 10-week start-to-run programme. The authors showed a significant increase in the quality of the knee cartilage after a 10 week running programme that built up progressively. These results suggest that even in adults, the quality of the cartilage can be changed, and that a gradually built up running scheme exerts a chondroprotective effect on the knee when compared to a sedentary lifestyle. Thus, such a moderate running scheme might be a valuable proposition in OA prevention strategies.

#### CARTILAGE STATUS IN PATIENTS AFTER ACL RECONSTRUCTION AND CONSEQUENCES FOR RETURN TO SPORT

Anterior cruciate ligament (ACL) reconstruction is offered to those patients actively engaged in cutting, jumping or pivoting sports and/or other functionally demanding activities. The purpose is to safeguard a mechanically stable knee and to reduce the risk of subsequent meniscal or chondral damage<sup>27</sup>. Long-term radiographic studies, however, suggest that ACL reconstruction may not protect against the development of post-traumatic OA<sup>28</sup>.

In view of OA prevention, careful attention should be paid to the rehabilitation process and to the decision of when to allow return to sport<sup>27</sup>. In view of cartilage deterioration due to (accidental or surgical) trauma and/or biomechanical disturbances (e.g. excessive anterior/lateral tibial translation and rotation, decreased knee extension)<sup>29</sup>, one of the key components to guide these decisions, after graft fixation and functional improvement, should also be the course of cartilage adaptation after surgery.

To evaluate this, a comprehensive evaluation of cartilage status was undertaken 6 months post ACL-reconstruction. Post ACL reconstruction patients were

compared with healthy matched control patients<sup>29-31</sup>, using 3-T MRI to evaluate the cartilage in vivo quantitative morphological characteristics, biochemical composition (T2 mapping) and function. These studies revealed that although no differences in cartilage volume and thickness were shown between ACL-reconstructed knees and healthy matched controls, differences in biochemical composition were apparent at 6 months after surgery. At 6 months after surgery, cartilage in patients with ACL reconstruction showed diminished quality and a significantly slower recovery of cartilage deformation after a 30-minute run. Hence, these signs depict precarious joint conditions that might not be able to counter the excessive torsional loads that the knee would be subjected to when returning to strenuous activities<sup>32</sup>. Moreover, studies showed the presence of cartilage macroscopic changes at approximately 2 years follow-up after ACL reconstruction. The absence of substantial baseline cartilaginous injury did not seem protective against progressive degeneration at or after 2-year follow-up<sup>32,33</sup>. In this respect, the first years following surgery seem to be of paramount importance for prevention or treatment strategies that aim at limiting



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further matrix deterioration. Finally, during a full weight-bearing single-leg lunge, ACL-deficient and reconstructed knees exhibited shifts in cartilage-cartilage contact points towards regions of thinner cartilage on the tibial plateaus accompanied by increased contact-deformation when compared to the contralateral knee. This alteration of contact points may be one of the reasons why macroscopic cartilage deterioration occurs in ACL reconstructed knees.

Increased deformational responses as noted in the radiographic OA and ACL-reconstructed patients are most likely a result from disruption of the collagen network and/or proteoglycan loss resulting in increased tissue permeability, bulk water accumulation and decreased compressive stiffness<sup>4</sup>. Collagen disruption causes loss of collagen tensile strength, which possibly accounts for the delayed recovery observed. Delayed recovery might induce a state of maintained deformation and dehydration compared with healthy joints. Enduring dehydration may have deleterious effects on chondrocyte metabolism<sup>34</sup>. In this respect, because of the fast and repetitive impact loads to be encountered during sports, delayed cartilage recovery may be potentially deleterious, eliciting a negative vicious circle toward degeneration.

Caution is advised in an early return to sport, especially when dealing with patients who have received prompt surgery. It is possible that high impacts on this qualitatively-diminished cartilage might play a role in the development of OA following ACL reconstruction. In fact, the current notion of cartilage fragility supports the advice to consider a delayed return to sports<sup>34</sup>. As such, postponing sports this far may be more suitable for knee cartilage to counter excessive repetitive loads.

#### CONCLUSION

Articular cartilage, like all structures in the human body, has an adaptive capacity to some extent. Exercise exerts a chondroprotective effect when compared to a sedentary lifestyle if the exercise programme is gradually built up and aspects such as age, type and level of exercise, and baseline joint status are taken into account.

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