

## Original Article

## CHANGES IN NUMBER OF CHONDRONS IN TANGENTIAL ZONE OF AGEING MALE HUMAN ARTICULAR CARTILAGE

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**Objective:** To study the changes in number of chondrons in tangential zone of male human articular cartilage in advancing age.

**Methods:** Forty samples of articular cartilage were collected from right knees of male dead bodies ageing between 21-60 years and placed into four groups. After tissue processing and cutting, staining with H&E was done. The number of chondrons containing chondrocytes was noted in each group.

**Results:** With advancing age the number of chondrocytes within chondrons in Tangential/superficial zone of articular cartilage were reduced.

**Conclusions:** In ageing, articular cartilage the number of chondrons in Tangential zone of articular cartilage is reduced leading to osteoarthritis. Presence of stem cells in this zone makes it an attractive target for preventive and therapeutic measures.

**Keywords:** articular cartilage, chondrons, tangential zone, osteoarthritis.

### Introduction

Articular cartilage, hyaline in nature, is a specialized type of supporting connective tissue that covers the ends of the bones in synovial joints.<sup>1</sup> It is unique in its structure which gives it particular metabolic properties such as extraordinary resilience, enabling the articular cartilage to withstand enormous pressure.<sup>2</sup> In light microscopy, the articular cartilage presents four zones. Three of these zones namely tangential, transitional and radial are non-calcified while the deepest zone is the calcified cartilage zone.<sup>3</sup> In all zones, type II collagen is most abundant and constitutes about 95% of the total collagen content of cartilage.<sup>4</sup> The chondrocytes reside in chondrons and in each zone chondrons have specific shape, size, arrangement and number. These cells are responsible for the development, maintenance as well as repair of articular cartilage and by synthesizing and turning over the extracellular matrix. They are capable of creating specific microenvironment.<sup>5</sup>

Tangential/superficial zone makes up about 10-20% of articular cartilage thickness. Collagen fibers in this zone are tightly packed and are aligned parallel to the surface. The densely packed collagen fibrils limit the access of large molecules, effectively isolating cartilage from immune system. Deep to collagen layer, this superficial layer of cartilage contains a relatively large number of flattened chondrocytes. This zone is in contact with synovial fluid and is responsible for most of the tensile properties of cartilage as well as the protection and maintenance of deeper layers.<sup>3</sup> In addition to the

chondrocytes, this layer also contains the progenitor stem cells.<sup>6</sup> The secretions of the stem cells mediate tissue regeneration and can repair tissue injuries.<sup>7</sup>

Degeneration of articular cartilage leads to osteoarthritis, a most recognized major age related joint disease causing pain and disability. The disability is progressive and becomes more evident with advancing age.<sup>8,9</sup> It affects more than 15% of the adult population, becoming the second greatest cause of disability and poor life style throughout the world.<sup>10</sup> The cellular density in osteoarthritis is reduced which leads to changes in extracellular matrix secreted by these cells, clustering of chondrocytes, fibrillation and progressive cartilage degeneration. Aging also results in decreased number of cells in articular cartilage initiating the osteoarthritis.<sup>11</sup>

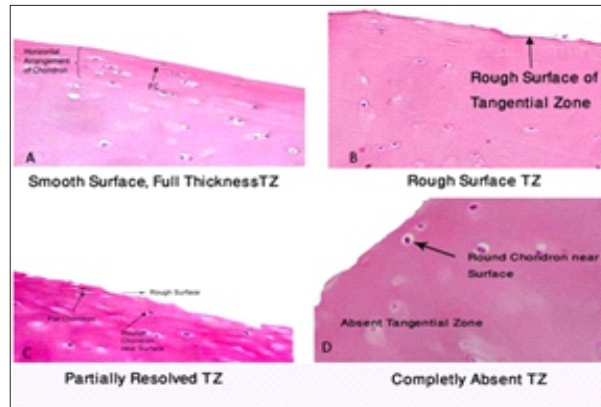
### Methods

Forty samples of articular cartilage of knee joint were collected from unknown male dead bodies in Forensic department of King Edward Medical University Lahore, brought within six hours of death. All the bodies were between 21-60 years of age. The autopsy was performed within 12 hours and till that time the temperature of bodies was maintained at 4 degree centigrade. Samples with gross abnormality or deformity and signs of surgery or trauma of the knee joints were excluded. Depending upon the age of the cadaver, the collected samples of articular cartilage were divided in four groups A, B, C and D containing 10 samples each i. e. Group A: 21-30 years Group B: 31-40 years. Group C: 41-50 years. Group D: 51-60 years. For this study articular cartilage of femoral

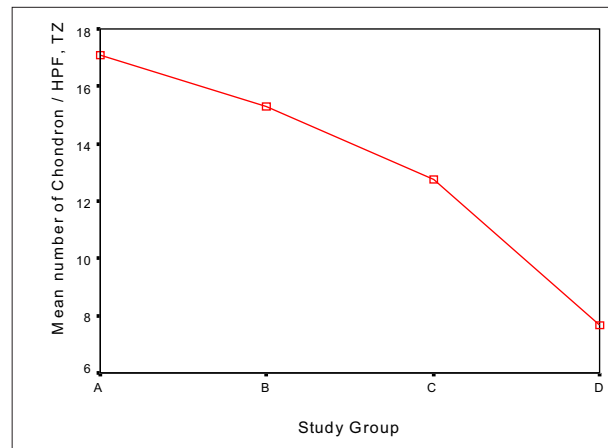
condyle of right sided knee joint was selected. Transverse incision was given on the skin extending from medial to lateral epicondyle of femur. Skin was reflected upwards and downwards to expose the quadriceps tendon. This tendon was cut by giving inverted “U” shaped incision starting above the patella and extending downwards to the tibial condyle on either side of ligamentum patellae. The cut tendon was reflected downwards along with patella to expose the articular cartilage of femoral condyle. Knee joint was flexed and 1 cm x 1 cm full thickness piece of articular cartilage was removed with the chisel from the tibial surface of femoral condyle, 1 cm medial to the medial margin of intercondylar fossa. The specimens were immediately placed in 10% neutral buffered formalin for 48 hour, processed for paraffin embedding. Five micrometer (5µm) thick sections were made on rotary microtome and mounted on clear albumin coated slides. H & E staining was done and mean number of chondrons/HPF (mean of three non overlapping fields) in tangential zone was noted in all groups.

**Results**

In this study it was observed that in tangential zone the mean number of chondrons was  $17.06 \pm 1.67$ /HPF in group A,  $15.3 \pm 1.62$ /HPF in group B,  $12.74 \pm 1.15$ /HPF in group C and  $7.66 \pm 1.52$ /HPF in group D. The mean number of chondrons was statistically significant in all study groups (p-value=0.000). The decrease in the number of chondrons with advancing age was very obvious (Fig-1-2). Using multiple comparison test it was observed that the mean number of chondrons was maximum in group A. Number of chondrons gradually decreased from A to D. The difference in



**Fig-1:** Histomicrograph showing decreasing number of chondrons in tangential zone of articular cartilage with advancing age.



**Fig-2:** Graphical presentation of mean number of chondrons in tangential zone of articular cartilage in different study groups.

number in each group was statistically significant (p-value < 0.05).

**Table-1:** Descriptive analysis of mean number of chondrons in tangential zone per hpf and multiple comparison test of number of chondrons in different study groups .

	Groups	n	Mean	Std. Deviation	Mininum	Maximum
Study Groups	A	10	17.067	1.6764	15.33	20.00
	B	10	15.300	1.6212	13.00	18.33
	C	10	12.741	1.1520	11.00	14.67
	D	10	7.6667	1.5275	5.00	9.33
	Total	40	13.667	3.6861	5.00	20.00
<i>P-value over all</i>						
	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D
Pair Wise	0.014	0.000	0.000	0.001	0.000	0.000

## Discussion

This study described that the total number of chondrons in the tangential zone of the articular cartilage is decreased with the advancing age. The findings were similar to Lotz and Loeser (2012) who observed that the cellular density of articular cartilage is reduced profoundly in tangential/superficial zone and the secretory properties of chondrocytes became abnormal with advancing age. Maintenance of normal extracellular matrix and functioning of articular cartilage is dependent on adequate number of chondrocytes. Superficial zone is unique in having large number of chondrocytes as well as progenitor stem cells which are capable of replacing chondrocytes after their destruction<sup>11</sup>. Chondrocytes are particularly prone to develop age changes affecting the mechanical properties of articular cartilage.<sup>12</sup> Main hindrance in the repair of articular cartilage is the limited intrinsic repair capacity of this avascular tissue.<sup>13</sup> The presence of large number of chondrocytes as well as stem cells in tangential zone and the fact that the cellularity of articular cartilage particularly in the tangential zone decreases with advancing age strongly indicates that this zone may play a critical

role in the initiation of osteoarthritis.<sup>14</sup> Decreased cell count of surface layer during ageing results not only in thinning of articular cartilage due to less extracellular matrix but it also deprived the articular cartilage of the cells that might play a vital role in its regeneration by combating with the degenerative changes in the old age.<sup>11,14</sup> This might explain the failure of regeneration of articular cartilage after destruction. Tangential zone is one of the areas that should be focused upon for the attractive therapeutic measures to slow down or arrest the degenerative process.<sup>15</sup>

## Conclusion

In ageing articular cartilage the number of chondrocytes in Tangential zone decreases which results in disturbance of normal orientation and composition of articular cartilage that leads to osteoarthritis. As this zone also contains the stem cells, reduction in the number of cells in tangential zone will further limit the repair of the cartilage.

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