Supplementary Table 1. Calculation of collagen half-life for OA knee and hip cartilage.

Racemization rates are affected by temperature. Haimovici suggests that the intra-articular temperature of hips and knees may differ, estimated at ~37°C for hips and ~33°C for knees [1]. We therefore performed half-life calculations based on previously published methods [2] with temperature adjusted ki values. To calculate protein half-life we calculated the protein turnover constant (k_T) using the following equation:

Equation 1

$$d(D/(D+L)/dt = K_i - K_T(D/(D+L)$$

where:

d(D/(D+L)/dt is the rate of change of racemization with time. This was determined by calculating the slopes of a linear regression analysis for Asp-RR (i.e. D/D+L) for OA hips (slope = 0.00089, r^2=0.371, p=0.007) and OA knees (slope =0.0003, r^2=0.157, p=0.093) using data presented in Figure 1B. Our determined slopes/accumulation rates were similar to previously published rates for articular cartilage and disc cartilages (2.58×10^{-4}/yr and 5.18-6.74×10^{-4}/yr respectively [3].

(D/(D+L) is the racemization ratio previously calculated and used in Figures 1-3;

K_T is the protein turnover constant;

K_i is the racemization rate constant (derivation explained below).

Derivation of K_i for collagen at 33°C and 37°C.

As with the earlier work, we based our calculation of K_i on the value determined for collagen from tooth dentin, which has no or minimal turnover throughout life. The k_i for dentin collagen has been estimated previously to be 7.6×10^{-4} and the enamel temperature is estimated to be 33°C, which is proposed to be the intraarticular knee temperature [1]. However, the hip intraarticular temperature is possibly higher and much nearer core body temperature of 37°C so the K_i value would need to be adjusted for temperature using the following equation originally derived by Bada 1981 [4];

Equation 2

$$K_{i2}(T_2) = K_{i1}(T_1) \times \exp(-(16{,}890 \times (T_1 - T_2)/(T_2 \times T_1))$$

Where:

K_{i2} = the temperature adjusted Ki constant to be calculated;

T_2 = the new temperature in Kelvin (37°C = 310.15°K);

K_{i1} = the original Ki calculated for dentin collagen (7.6×10^{-4});

T_1 = the original Ki temperature for dentin collagen (33°C = 306.15°K).

16,890 = activation energy (Ea)/the gas constant (R), originally determined by Bada [4].

Using the above equation, a Ki for collagen racemization of 0.00152 at 37°C can be determined and used as the K_i for the hip turnover rate calculation.

Calculation of half-life for collagen.

Using equation 1 and the Ki values determined from equation 2 we calculated KT for both OA knee and OA hip assuming the same intra-articular temperature of 37°C and dissimilar temperatures of 33°C and 37°C, respectively (see Supplementary Table 1 below). The KT value was converted into a collagen half-life using the following equation:

Equation 3

$$t_{1/2} = \ln(2)/K_T$$

Supplementary Table 1. Collagen turnover (half-life) in OA hip and knee cartilages of individual patients based on different estimations of intra-articular temperatures.

OA Knee collagen $t_{1/2}$ at 33°C and 37°C						OA Hip collagen $t_{1/2}$ at 37°C			
Age	d/(d+L)	K_T (33°C)	$t_{1/2}$ (33°C) years	KT (37°C)	$t_{1/2}$ (37°C) years	Age	d/(d+L)	KT (37°C)	$t_{1/2}$ (37°C) years
67	0.03765	0.01291	53.7	0.03450	20.1	71	0.08086	0.00777	89.2
69	0.05766	0.00843	82.2	0.02253	30.8	83	0.08011	0.00784	88.4
87	0.05493	0.00885	78.3	0.02365	29.3	76	0.07295	0.00861	80.5
66	0.04745	0.01024	67.7	0.02738	25.3	83	0.08253	0.00761	91.1
88	0.06366	0.00763	90.8	0.02041	34.0	69	0.06369	0.00986	70.3
56	0.04215	0.01153	60.1	0.03082	22.5	69	0.06530	0.00962	72.0
76	0.06273	0.00775	89.5	0.02071	33.5	81	0.10012	0.00628	110.5
69	0.04977	0.00976	71.0	0.02610	26.6	90	0.09937	0.00632	109.6
77	0.06253	0.00777	89.2	0.02077	33.4	79	0.07074	0.00888	78.0
59	0.06116	0.00795	87.2	0.02124	32.6	76	0.07193	0.00873	79.4
54	0.04883	0.00995	69.6	0.02660	26.1	65	0.05979	0.01051	66.0
79	0.04903	0.00991	69.9	0.02650	26.2	57	0.06954	0.00903	76.7
75	0.04396	0.01106	62.7	0.02955	23.5	79	0.08235	0.00763	90.9
62	0.05671	0.00857	80.9	0.02290	30.3	76	0.06055	0.01038	66.8
65	0.05291	0.00919	75.5	0.02455	28.2	92	0.08023	0.00783	88.5
59	0.04975	0.00977	71.0	0.02611	26.5	89	0.07861	0.00799	86.7
60	0.05081	0.00957	72.5	0.02557	27.1	72	0.09211	0.0068	101.6
64	0.05382	0.00903	76.8	0.02414	28.7	90	0.10671	0.00589	117.7
74	0.06152	0.0079	87.7	0.02111	32.8				
mean			**75.6**		**28.3**				**86.9**
SD			**10.6**		**4.0**				**15.2**

Based on our racemization data, the calculated mean $t_{1/2}$ (half-life) of collagen turnover was 28.3±4.0 years for OA knees at 37°C and 86.9±15.2 years for OA hips at 37°C ($p<0.0001$). Since racemization is a physical process, physical factors, such as pH or temperature can impact rates of racemization. We therefore considered the possibility that temperature differences in knees and hips might account, at least in part, for different amounts of racemized amino acids in cartilages from these different joints. We therefore re-estimated the half-life of collagen turnover based on a conservative assumption of an intra-articular temperature of 33°C in knees, representing a 4°C lower intra-articular temperature than for hips. The calculated mean $t_{1/2}$ of collagen turnover for OA knee at 33°C was 75.6±10.6; this was still significantly shorter than the mean $t_{1/2}$ for OA hip collagen ($p=0.012$).

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