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Effect of aging on the toughness of human cortical bone: evaluation by R-curves

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Abstract

Age-related deterioration of the fracture properties of bone, coupled with increased life expectancy, is responsible for increasing incidence of bone fracture in the elderly, and hence, an understanding of how its fracture properties degrade with age is essential. The present study describes ex vivo fracture experiments to quantitatively assess the effect of aging on the fracture toughness properties of human cortical bone in the longitudinal direction. Because cortical bone exhibits rising crack-growth resistance with crack extension, unlike most previous studies, the toughness is evaluated in terms of resistance-curve (R-curve) behavior, measured for bone taken from wide range of age groups (34–99 years). Using this approach, both the ex vivo crack-initiation and crack-growth toughness are determined and are found to deteriorate with age; the initiation toughness decreases some 40% over 6 decades from 40 to 100 years, while the growth toughness is effectively eliminated over the same age range. The reduction in crack-growth toughness is considered to be associated primarily with a degradation in the degree of extrinsic toughening, in particular, involving crack bridging in the wake of the crack.
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Keywords: Cortical bone; Aging; Fracture toughness; R-curve

Introduction

Aging-related changes to the musculoskeletal system are known to increase the susceptibility of bone fracture [15], and in the case of the very elderly, consequent fractures can lead to mortality [16]. Traditional thinking concerning "bone quality" has focused on bone mass or bone mineral density (BMD) as a predictor of such fracture risk. However, there is mounting evidence that BMD alone may not be the sole factor responsible for the aging-induced fracture risk [4,14,15]. This has led to a renewed interest into how aging can alter the various mechanical properties of bone and, in particular, the fracture resistance. Indeed, several studies that have looked at age-related issues in the mechanical properties of bone have shown a significant deterioration in the fracture toughness with age [2,7–12,29,39,40,44–46]. To characterize the deterioration of bone with age, most studies have utilized the fracture toughness, K_c, or the strain-energy release rate, G_c, as a single-parameter approach to characterize the resistance to fracture. However, in many materials including cortical bone, so-called extrinsic toughening mechanisms[1], such as

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[1] Crack propagation can be considered as a mutual competition between two classes of mechanisms: intrinsic mechanisms that operate ahead of the crack tip and affect the material's inherent resistance to fracture and damage, and extrinsic mechanisms that principally operate in the wake of the crack tip, and "shield" the crack from the applied driving force [13,30,31]. Whereas intrinsic mechanisms primarily govern the crack-initiation toughness, extrinsic mechanisms, specifically crack bridging in bone [25], operate in the crack wake and govern the crack-growth toughness. As the effect of extrinsic mechanisms is dependent on the size of the crack, this leads to rising R-curve behavior.

constrained microcracking or crack bridging [24,26], are active. For these materials, the fracture resistance increases with crack extension and stable crack growth can occur before unstable fracture. Although this necessitates a "resistance-curve" (R-curve) approach to evaluate the fracture toughness [20], such R-curves have only been utilized formally in relatively few studies [22,25,26,28,35–38,41] to characterize bone fracture.

An early application of the R-curve approach for bone was presented by Vashishth et al. [36] for studies on cracking in human and bovine tibia in the longitudinal (anatomically proximal–distal) orientation. They reported rising R-curves for both cases, with steeper curves in bovine samples, reflecting the higher crack-growth toughness of the bovine bone. They later showed similar R-curve toughening in red deer antler [38]. Another study by Pezzotti and Sakakura [28] reported a rising R-curve in bovine bone (specimen orientation unclear); however, after an initial rising portion, a steady-state "plateau" toughness was achieved, as seen in a number of materials that exhibit R-curve behavior [19,20]. Malik et al. [22] showed rising R-curve behavior which displayed such a plateau (and in some cases subsequently decreased) for transverse crack growth in equine bone. The most recent work on R-curve behavior in human bone, by the present authors, investigated ex vivo longitudinal (proximal–distal) crack growth in the humerus; linear rising R-curves were observed in that study [25,26]. In addition, this work provided definitive evidence that crack bridging by uncracked ligaments, rather than a mechanism involving constrained microcracking which had been previously suggested [36–38], is the dominant extrinsic toughening mechanism responsible for the toughening and rising R-curve behavior in bone.

While it is now well established that the fracture toughness of bone must be characterized in terms of rising R-curves, there is a paucity of relevant data on how such R-curve behavior changes with aging. Very limited data (only five total R-curves) on the R-curve behavior of human femoral bone demonstrated a decrease in both initiation and growth toughness with age [41], although no mention of mechanisms was made. Accordingly, in the present paper, we seek to investigate the ex vivo R-curve fracture toughness properties of bone as a function of age to (1) provide additional data to confirm this aging effect and (2) to elucidate the mechanisms responsible for any age-related changes.

Materials and methods

Fresh frozen human cadaveric humeral cortical bone was used in this study from nine donors. The age of these donors varied from 34 to 99 years old (cause of donor death unrelated to skeletal state); the gender of the donors together with anatomical location is given in Table 1. Blocks of bone were obtained by carefully sectioning the medial cortices of the middiaphyses of the humeri. Seventeen (N= 17) compact–tension, C(T), specimens with specimen thicknesses[2] B = 1.2–3.3 mm, widths W = 13–18.3 mm, and initial crack lengths a = 3.0–5.5 mm were machined from these blocks and divided into three age groups—arbitrarily named *Young*, *Middle-aged*, and *Aged* (see Table 1 for details). The samples were all orientated with the starter notch and the nominal crack-growth direction along the proximal–distal direction of the humerus (in the longitudinal–radial plane), that is, parallel to the long axis of the osteons and hence long axis of the humerus. This orientation is designated C-L according to ASTM Standard E399 for fracture toughness testing [1], where the first letter of the designation refers to the direction normal to the crack plane (circumferential) and the second refers to the cracking direction (longitudinal). Although based on expected physiological loading conditions, the transverse, and not longitudinal, cracking direction is most relevant, cracks loaded so as to cause growth in the transverse direction ex vivo have been found to deflect towards and along the longitudinal direction (e.g., [6]). Accordingly, to gain a

Table 1
Resistance-curve behavior of human cortical bone with age

Donor information[a]	Initiation toughness K_o (MPa $\sqrt{}$m)	Slope (MPa $\sqrt{}$m/mm)	Coefficient of determination (R^2)
Young (34–41 years)			
34FL	2.12	0.31	0.98
37ML	1.69	0.50	0.88
37ML	2.20	0.28	0.97
37MR	2.07	0.49	0.97
37MR	1.85	0.41	0.94
41FL	2.07	0.41	0.97
41FL	2.23	0.34	0.96
Middle-aged (61–69 years)			
61ML	2.00	0.16	0.80
69FLa	2.09	0.16	0.49
69FLa	2.09	0.18	0.37
69FRb	1.66	0.23	0.91
69FRb	1.94	0.06	0.60
Aged (85–99 years)			
85FRa	1.44	0.02	0.40
85FRb	1.32	0.07	0.56
85FRb	1.30	0.08	0.73
99MR	1.11	0.07	0.65
99MR	0.92	0.11	0.47

[a] The notation reads as follows: age (years), sex (M = Male, F = Female), arm (L = Left, R = Right), with any subsequent letter being a unique identifier when more than one donor was of the same age (69 and 85 years). Data for 34- to 41-year group from Ref. [25].

[2] Variations in sample thickness were related to variations in the cortex thickness for the various donors. They are not expected to influence the measured toughness; indeed Norman et al. reported no effect of specimen thickness on the toughness of human bone C(T) specimens of a 2- to 3-mm range [27].

mechanistic understanding of cortical bone fracture, cracking in the longitudinal orientation is also considered to be physiologically relevant; in addition, the larger amount of crack extension that is possible in this orientation is useful experimentally.

R-curves were measured to evaluate the resistance to fracture in terms of the stress intensity, K, as a function of crack extension, Δa, under a monotonically increasing driving force. The C(T) specimens were thawed and thoroughly hydrated before testing by soaking in Hanks' balanced salt solution (HBSS) for at least 40 h at room temperature in airtight containers. Tests were then conducted in ambient air (25°C, 20–40% relative humidity) with the specimens being continuously irrigated with HBSS. The specimens were loaded in displacement control using standard servohydraulic testing machines (MTS 810, MTS Systems Corporation, Eden Prairie, MN) with a loading rate of 0.015 mm/s until the onset of cracking, which was determined by a drop in load or nonlinearity in the load–displacement curve. At this point, the sample was manually unloaded by 10–20% of the peak load to record the sample load-line compliance at the new crack length using a linear variable-displacement transducer (LVDT) mounted in the load frame. This process was repeated at regular intervals until the end of the test (arbitrarily chosen when data for at least 4 mm of crack growth were obtained), at which point the compliance and loading data were analyzed to determine fracture resistance, K_R, as a function of crack extension, Δa. Crack lengths, a, were calculated from the compliance data obtained during the test using standard C(T) load-line compliance calibrations [32]. Such calibrations are valid for homogeneous, isotropic and anisotropic, linear-elastic solids, in the latter case provided an effective elastic modulus is used for the particular specimen orientation. For crack length monitoring, however, the modulus need not be known a priori, as this value may be grouped into a calibration constant which is determined at the beginning of each individual test by choosing a value which best correlates the sample compliance with the initial crack/notch length. Further details of the testing procedures are provided elsewhere [25,26]. Statistical analysis of the data was conducted using the nonparametric Kruskal-Wallis test. The data were also subjected to linear regression analysis against age.

To observe crack–microstructure interactions, synchrotron X-ray computed tomography (SRCT) was performed on two specimens each of the *Young* (data reported in Ref. [25]) and *Aged* groups. This work was performed in part at the Stanford Synchrotron Radiation Laboratory (SSRL), Menlo Park, CA, and at the Advanced Light Source (ALS), Berkeley, CA. Imaging was performed with monochromatic X-rays (25 keV at SSRL and 18 keV at ALS), with a voxel size (spatial resolution) of 5 μm. The tomography data were reconstructed using a Fourier-filtered back-projection algorithm; further details of this technique are described elsewhere [17,18].

Results

As described above, the ex vivo load–displacement data obtained were analyzed to evaluate the resistance to fracture in terms of the stress intensity, K, as a function of crack extension, Δa. The resulting monotonically rising R-curves for hydrated cortical bone are shown in Fig. 1. The crack-initiation toughness, K_o, was obtained by extrapolating a linear fit of the data for each sample to $\Delta a = 0$, while the (linear) slope of the R-curve gave a measure of the crack-growth toughness. Mean (nonweighted) K_o values of 2.07 (SD = 0.11), 1.96 (SD = 0.15), and 1.26 (SD = 0.22) MPa$\sqrt{m}$ and mean slopes of 0.37 (SD = 0.06), 0.16 (SD = 0.01), and 0.06 (SD = 0.04) MPa$\sqrt{m}$/mm were thus obtained for the *Young*, *Middle-aged*, and *Aged* groups, respectively; individual values are listed in Table 1. Statistical analysis using the Kruskal-Wallis test of the data indicated that, for the three age groups, variation among group medians was significant ($P = 0.025$ and 0.0036 for the initiation and the growth toughness, respectively). Post hoc analysis was not performed in view of the small sample sizes. The data in Table 1 are plotted in Fig. 2 as variations of the crack-initiation and growth toughnesses as a function of age. While the initiation toughness decreases with age, the effect of aging is more evident on the growth toughness which is essentially eliminated in the *Aged* group.

Figs. 3a and b show typical two-dimensional through-thickness "slices" obtained by SRCT for specimens belonging to the *Young* and *Aged* groups at various distances behind the crack tip. There is evidence of "crack bridging" in both cases from the formation of uncracked ligaments in

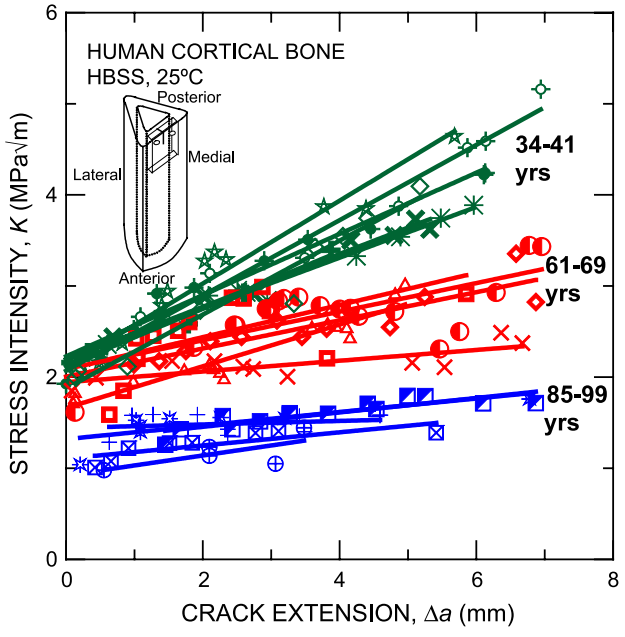

Fig. 1. $K_R(\Delta a)$ resistance curves for stable ex vivo crack extension in human cortical bone as a function of age. Note the linearly rising R-curve behavior. The inset schematically shows the anatomical orientation that the specimens were taken from the humeri.

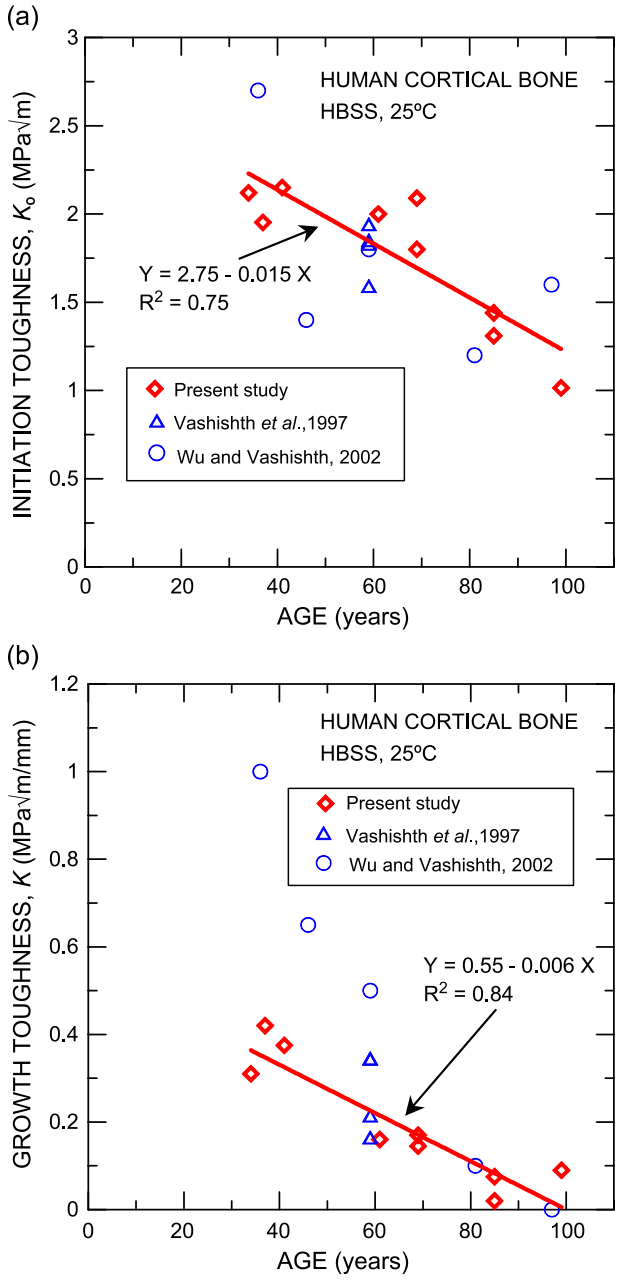

Fig. 2. Variation in the (a) crack-initiation toughness (K_o), and (b) crack-growth toughness (slope of the R-curve) with age for human cortical bone. A linear regression of the data is shown in each case (fit equation and coefficient of determination, R^2, is also included). Data from Vashishth et al. [36] and Wu and Vashishth [41] are also plotted for comparison (not included in regression).

the crack wake; these are intact regions, often tens of micrometers in size (i.e., substantially larger than individual collagen fibers), which form along the crack path, either by the nonuniform advance of the crack front and/or by the imperfect linking with the main crack of microcracks that initiated ahead of the crack tip. It has been previously shown that such bridging is the primary mechanism of toughening for cracking in the longitudinal orientation in bone and is responsible for the rising R-curve behavior [25,26]. Further examination of the tomographic slices revealed that there is a definitive decrease in the size and number of these bridges with age. Fig. 3c shows the variation in the area fraction of such bridges with distance from the crack tip for *Young* and *Aged* bone. It is apparent that the bridging zones are larger in *Young* bone (roughly 5.5 vs. 3.5 mm), and within the zone, the area fractions are in general larger for that group. Such observations are consistent with the reduction in the growth toughness with age, as discussed below.

Discussion

The data in Table 1 are plotted in Fig. 2 as variations of the crack-initiation and growth toughnesses as a function of age. The only other R-curve data available for human cortical bone from Vashishth et al. [36] and from Wu and Vashishth [41] are also included. While the initiation toughness data from these studies agrees well with the trend suggested by the linear regressions in Fig. 2a, there is a stronger effect of age on the growth toughness in Ref. [41] as compared to the present study. It should be noted that the bones used in those studies were from a different anatomical location (tibia in Ref. [36] and femur in Ref. [41]). There is a clear, observable trend of decreasing toughness with age in the present study; specifically, the crack-initiation toughness decreases by approximately 40% over 6 decades from 40 to 100 years, while the growth toughness is essentially eliminated over the same age range. Such deterioration in the fracture resistance with age is consistent with the trend observed in studies that report single-value toughnesses (e.g., [2,7–12,29,39,40,44–46]). What is important about these results, together with those of Wu and Vashishth [41], is that they clearly show that not only the intrinsic resistance to fracture (as reflected by the crack-initiation toughness), but also the increasing resistance to crack propagation (as reflected by the crack-growth toughness), decreases with age (Figs. 1 and 2b). Indeed, the age-related deterioration in the crack-growth toughness is clearly the more dominant effect.

As noted above, the crack-growth toughness is reflective of the contribution from extrinsic toughening mechanisms, which in bone are principally associated with crack bridging [25,26]. The prime source of such bridging in human bone appears to be from the formation of uncracked ligaments in the crack wake (Fig. 3). The results in Fig. 2b strongly imply that the contribution from such a mechanism is markedly reduced with age. The magnitude of this contribution is dictated by the size of the bridging zone, the area fraction of the bridges in the zone, and their load-bearing capacity. All of these factors may change with aging; indeed, Fig. 3 shows that there is a lower density of such bridges in older bone. A more detailed quantitative assessment of these parameters is currently being undertaken.

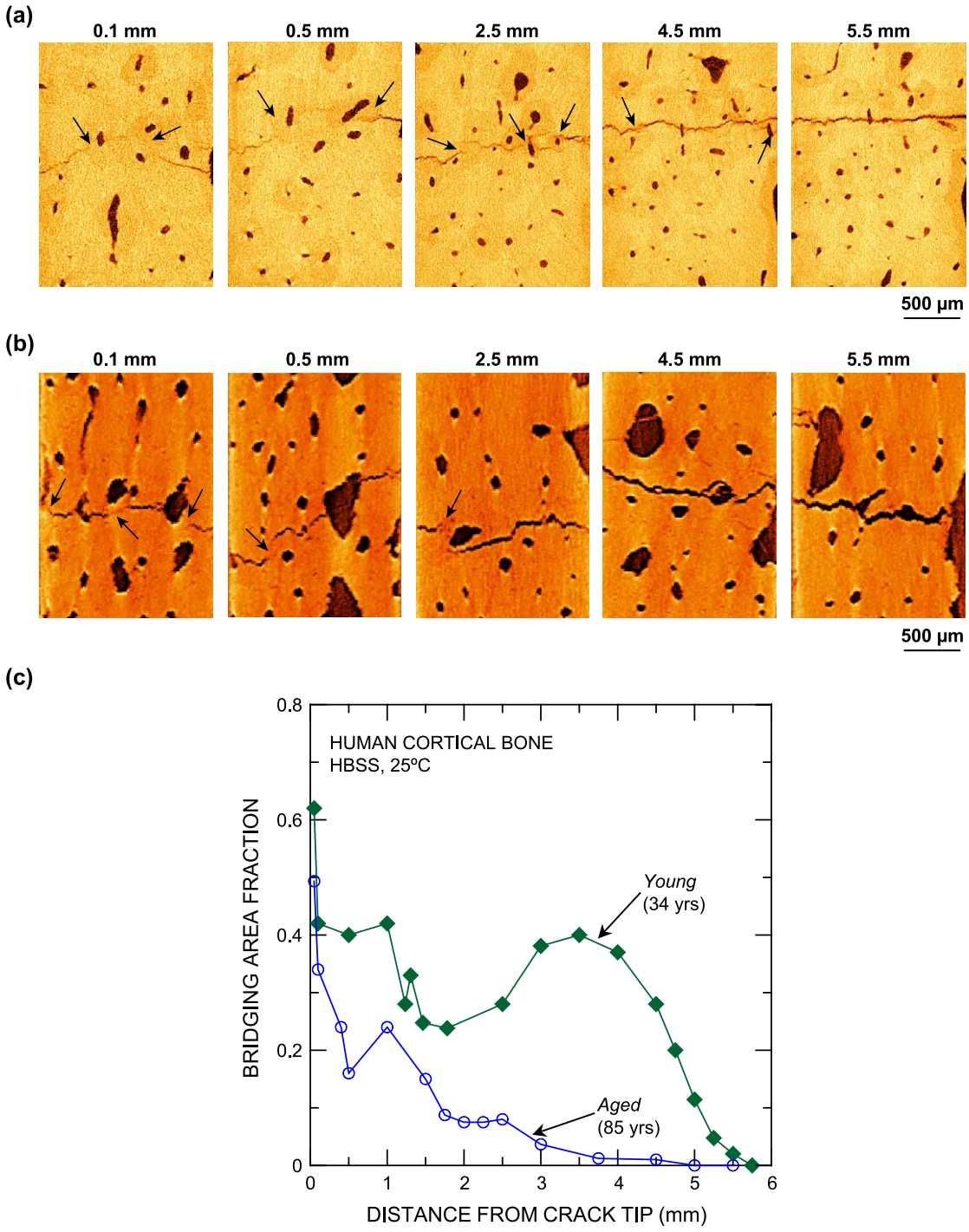

Fig. 3. Two-dimensional computed X-ray tomographic reconstruction slices showing typical cracks in specimens taken from the (a) *Young* (34FL) and (b) *Aged* (85FR) groups. The numbers on top of each figure indicate the distance from the (nominal) crack tip, and the black arrows indicate uncracked-ligament bridges. (c) The fraction of such bridges, with distance from the crack tip, indicating smaller area fractions and bridging-zone size in the older bone.

Many effects of aging on bone have been studied, in particular, in association with the micro/ultrastructural changes (i.e., at micron- and nano-scale dimensions) induced by a number of parameters, including increased mineralization [3], increased microdamage [33], lowered collagen quality [39], and increased bone turnover [23]. However, the underlying mechanisms that result in age-related changes in the fracture resistance are poorly understood. The increased mineralization has been implicated in reducing elastic deformability [2] and the (single-value) fracture toughness [12]. Increased levels of microdamage (microcracking) have been shown to lower the

fracture resistance [42], presumably by lowering the intrinsic toughness. Possible changes in collagen network integrity with age [39] could result in weaker bridges and hence a lower growth toughness in older bone. More specifically, age is known to increase nonenzymatic cross-linking in the collagen [39]; as this reduces the postyield deformation of the collagen, this also has been used to explain the age-induced reduction in growth toughness via a microcracking model [36], although recent studies have cast doubt on the significance of microcracking in affecting the toughness of bone [25,26]. Finally, it has been suggested that elevated bone turnover in older bone [21], although beneficial in repairing damage, may have a deleterious effect on the toughness due to the formation of resorption cavities and hence increased porosity. Elevated turnover also results in a higher density of secondary osteons [23] and associated cement lines which are known to provide weak interfaces, and hence preferred (weaker) paths, for cracking [5,24,25,34,43]. In fact, a recent study has concluded that elevated turnover is a risk factor in its own right, independent of its actions on BMD [14].

Thus, although the age-induced decrease in the fracture toughness of bone has been clearly quantified, specifically in terms of resistance to both crack initiation and more importantly crack growth, the mechanistic reasons for this deterioration are as yet unclear. As the microstructural factors affecting crack initiation and growth in most materials are invariably quite distinct [13,30,31], the challenge is to identify and quantify the specific mechanisms affecting each process in terms of the changes that occur in the micro/ultrastructure of bone with age. Furthermore, other factors (e.g., gender, race, pathology, genetic reasons, etc.) that might have an effect on the micro/ultrastructure and consequently the fracture behavior, which could not be studied here owing to the somewhat small sample sizes (three donors per group), need to be investigated.

In summary, the fracture toughness of cortical bone, expressed in terms of rising R-curve behavior, shows significant deterioration with aging. In quantitative terms, the ex vivo crack-initiation toughness was reduced by approximately 40%, whereas the crack-growth toughness was effectively eliminated, as age increased from 34 to 99 years. These results demonstrate the need to interpret this deterioration in bone quality in terms of specific age-related changes in the micro/ultrastructure of bone that separately affect the crack initiation and growth stages of fracture, both for the purpose of fully characterizing the aging properties of bone and for identifying the actual mechanisms that ultimately increase its fragility and fracture susceptibility. In this regard, the present results have clearly identified that a primary mechanistic factor in the deterioration in the toughness of bone with age can be associated with a degradation in the crack bridging that is developed in the crack wake.

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