Predictors of Femoral Neck Bone Fracture Toughness and Strength Under High-Rate Impact Loading

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ABSTRACT

Hip fractures are one of the most common and costly type of fall-related injury, and the associated consequences highlight the importance of preventing these injuries. Previous methods established to predict hip fracture risk have focused on the relationship between macro-scale whole bone strength and femoral neck bone mineral density (BMD). Despite their strong positive relationship, most people who suffer hip fractures don't have critically low BMD, suggesting other aspects are involved in determining bone strength. One understudied aspect is the role of micro-scale level material behavior of cortical bone, such as fracture toughness, on the macro-scale level strength of bone. However, the relationship between micro-scale fracture toughness and macro-scale bone strength has yet to be investigated in the context of fall-related hip fractures. The goal of this study was to quantify this relationship, evaluating both critical elastic and elastic plastic fracture toughness (K_q and J_{IC}, respectively). Using a sample of 5 matched pairs of fresh frozen cadaveric femurs, bone strength of the proximal femur (quantified via simulated lateral impacts until failure), and fracture toughness of the inferior femoral neck (quantified by high-rate three point bending of single edge notched bending specimens) was compared within pairs. A significant strong positive relationship was observed between bone strength and critical elastic fracture toughness (K_q) (R^2=0.828, $p<0.05$). While our findings reiterate the strong relationship between bone strength and femoral neck BMD (R^2 = 835, $p<0.05$), the model combining K_q and BMD to predict bone strength yielded the strongest relationship (R^2=994, $p<0.01$) with both factors having similar β coefficients (K_q=0.528, BMD=0.539). These findings provide the first insight into the relationship between fracture toughness and femoral neck bone strength under high-rate loading, and suggest that fracture toughness may be complementary predictor of hip fractures to BMD.

INTRODUCTION

Major osteoporotic fractures, such as fall-related hip fractures, are common and costly traumatic injuries. As a fracture in one of the major load-bearing bones of the body, hip fractures can severely impede mobility and limit independence, which can greatly decrease quality of life. Hip fractures are the most debilitating and costly types of major osteoporotic fractures, accounting for approximately 70% of the 17 billion total cost associated with osteoporotic fractures in the United States (Burge et al, 2007). Additionally, these injuries can place a large burden on the healthcare system, as hip fractures account for over one third of all fall-related hospitalization in Canada (Billette & Janz, 2011). Lastly, there is an elevated risk of mortality associated with hip fractures, with death occurring within 1 year of injury in 20-25% of older adult case (Brown et al., 2021; Ioannidis et al., 2009; Jiang et al., 2005). The severe consequences of these injuries have driven efforts into identifying at-risk individuals as part of prevention efforts.

A fundamental component of current prevention efforts includes fracture risk prediction models that, in many cases, focus on estimating tissue tolerance (e.g. femoral bone strength). Various models have been developed to estimate femoral bones strength and ultimately predict hip fracture risk, with these methods almost exclusively relying on measures of femoral neck bone mineral density (BMD) (Cheng et al., 1997; Roberts et al., 2010). While previous studies have established a relationship between BMD and femoral bone strength in simulated hip fractures, the strength of the association can vary greatly between studies (R^2 ranging from 0.42-0.92) (Dall'Ara et al., 2013). As bone strength estimates and injury risk prediction models are based on this relationship, our ability to accurately identify high-risk individuals can vary just as greatly. While the T-score, the current clinical standard for identifying osteoporosis and osteoporotic fracture risk, is based on BMD, the three categories (normal BMD, osteopenia, osteoporosis) used still lack sensitivity, as approximately 70% of fall-related hip fracture cases occur in people who are not classified as osteoporotic, the category associated with the lowest measures of BMD (Schuit et al., 2004; Siris et al., 2004; Stone et al., 2003). Though BMD does explain a large part of the variance related to femoral bone strength, our current lack of precision in identifying high-risk individuals and preventing hip fractures suggests that other currently uninvestigated factors may also contribute to bone strength.

One aspect that has been understudied is the role of micro-scale level material behavior of cortical bone on the macro-scale level strength of whole bone. Previous work has established that, at the micro-scale, the material property of fracture toughness dictates the resilience of cortical bone and quantifies its ability resist crack growth (Gauthier et al., 2017; Vashishth et al., 1997; Yan et al., 2007; Zioupos et al., 1999). This property is thought to be particularly relevant to the development of fractures in the context of fall-related hip fractures, especially in cases where a greater degree of micro-damage or a greater number of bone defects are expected, such as in old age (Granke et al., 2015; Uppuganti et al., 2016; Zioupos et al., 2020). Additionally, previous work has identified a strong positive relationship between the fracture toughness of cortical bone and its organic phase, specifically the content and quality of the organic network (Willett et al., 2019; Woodside and Willett, 2016; Zioupos et al., 1999). This evidence provides a physical explanation for how the organic phase of bone, mediated via fracture toughness, may contribute to bone strength on the macro-scale level. Despite this, the relationship between micro-scale level fracture toughness and macro-scale level bone strength has yet to be investigated in the context of fall-related hip fractures. Investigating this relationship via multi-scale level testing would not only allow us to gain a deeper understanding of the mechanical behavior of bone during fall-related hip fractures, filling a clear gap in literature.

Therefore, the goal of this study was to use a novel whole-femur impact test paradigm and three-point bending tests of single edge notched beam (SENB) specimens to investigate the relationship between femoral neck bone strength and femoral neck fracture toughness when tested under high-rate loading. We hypothesized that fracture toughness results from high-rate loading tests of inferior femoral neck samples would be significantly associated with femoral neck bone strength. More specifically, as bone is expected to exhibit more elastic behavior during high-rate loading, we hypothesized that critical elastic fracture toughness (K_q) would be more strongly associated with bone strength than critical elastic-plastic fracture toughness (J_{IC}).

METHODS

Specimen acquisition

Complete femur pairs were acquired from five fresh-frozen male human donors (mean(SD) age = 57.6(20.5) years; range = 27-80) were obtained from the Innoved Institute (Elk Grove Village, IL) for a total of 10 femurs. High-quality dual-energy X-ray absorptiometry (DXA) tests were performed on each specimen to determine femoral neck BMD (Hologic Discovery W fan-beam bone densitometer, Hologic, Inc. Bedford, MA, USA). Each femur pair was split between the two experimental paradigms (whole bone strength and fracture toughness testing). This was done due to destructive nature of both paradigms and our focus on the inferior femoral neck, preventing any one specimen to be subjected to both paradigms.

Specimen Preparation and Experimental Protocol

Bone Strength/Simulated Hip Fracture Experiments. The proximal portion of the femur was isolated by transecting the specimens across the diaphysis 20 cm distal to greatest lateral protrusion of the greater trochanter. The distal end of the proximal femur was placed in a section of ABS pipe (10 cm length, 5.08 cm inner diameter) and fixed using dental stone. A custom designed mounting jig was placed on top of a force plate (AMTI OR3-6-2000, AMIT, Watertown, MA, USA) located at the base of a vertical drop tower hip impact simulator (HIS) (Figure 1). The HIS included a surrogate pelvis leaf spring system to emulate the stiffness of the hip-pelvis complex (k = 34 000 N/m), and the load carriage had a total mass of 36 kg. The potted specimen was placed in the mounting jig and oriented in a standard femur fracture testing orientation with a 10-degree abduction angle and 15 degrees of internal rotation (Courtney et al. 1994,1995). This mounting jig was affixed to the surface of an AMTI OR3-6-2000 force plate (AMTI, Watertown, MA, USA) sampled at 20 000 Hz. Specimens were subjected to repeated simulated lateral impacts at increasing impact velocities from 0.5 m/s to 4.5 m/s, increasing by 0.5 m/s increments, until specimen failure. Time-varying force data was filtered with a single pass 2^{nd} order low pass Butterworth filter with a 20 Hz cutoff frequency was applied to the force data. Bone strength was quantified as the peak force measured during the impact wherein fracture occurred.

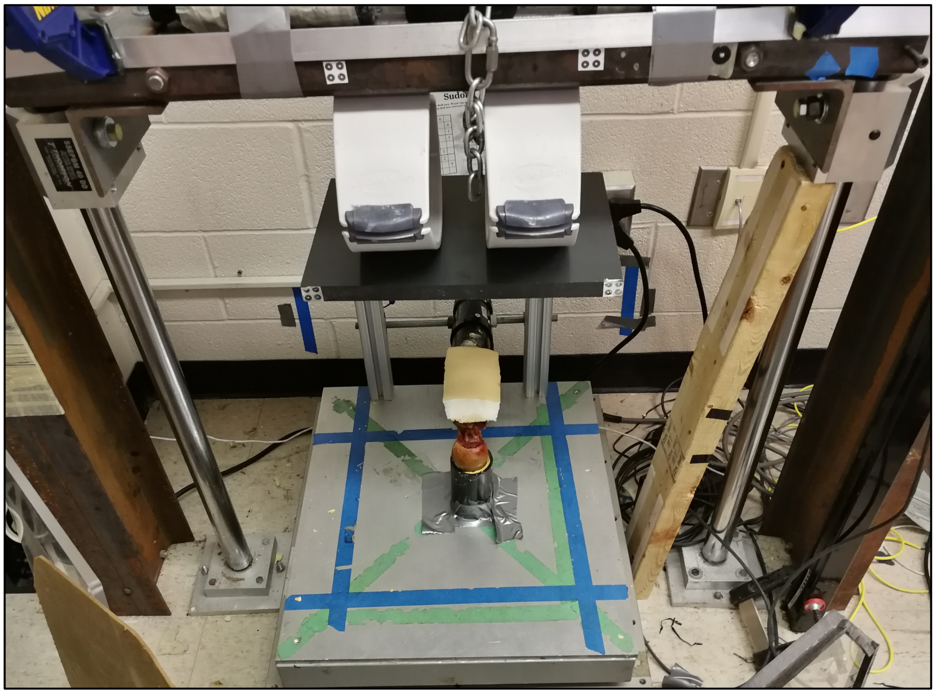

Figure 1: Vertical drop tower hip impact simulator (HIS) with specimen in place.

Fracture toughness SENB testing. Rectangular beams of cortical bone were extracted from the inferior femoral neck of the fresh frozen femur specimens. Single edge notched bending (SENB) specimens were cut to the target dimensions of 30 mm length x 4 mm width x 2 mm thickness, with a 1 mm notch cut midway along the length of the beam (Figure 2). The crack tip of the SENB was sharpened to a 10-micron width with a razor blade before undergoing three-point bending using micro material testing system (MMTS) (μTS, Psylotech Inc, Evanston, IL, USA). Fracture toughness tests were conducted in accordance with ASTM E1820-20 procedures (ASTM E1820-20a, 2020). Specimens were loaded using a displacement rate of 40 mm/s to emulate impact like loading, and a high-speed video enabled microscope system (HSV, AOS Technologies, Cheshire, CT) was used to track crack growth throughout the experiments. Load and displacement data from the MMTS was sampled at 3000 Hz, while the crack length data from the high-speed video-enabled microscopy was sampled at 1000 Hz. As the load data of some trials violated the data smoothness criteria outlined in ASTM E1820-20, a dual pass 2nd order (4th order equivalent) low pass Butterworth filter with a 750 Hz cutoff frequency was applied to mitigate the high frequency oscillations seen in the raw data (Figure 3).

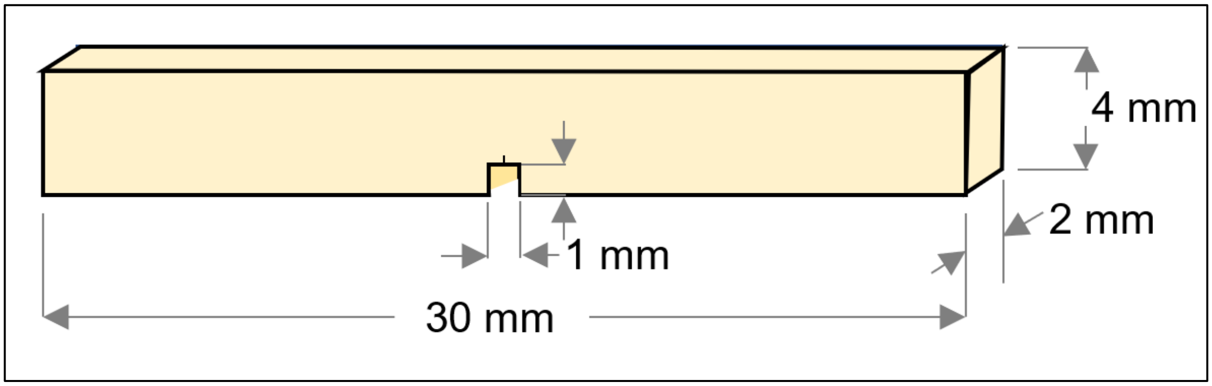

Figure 2: Femoral neck single edge notched bending (SENB) sample dimensions

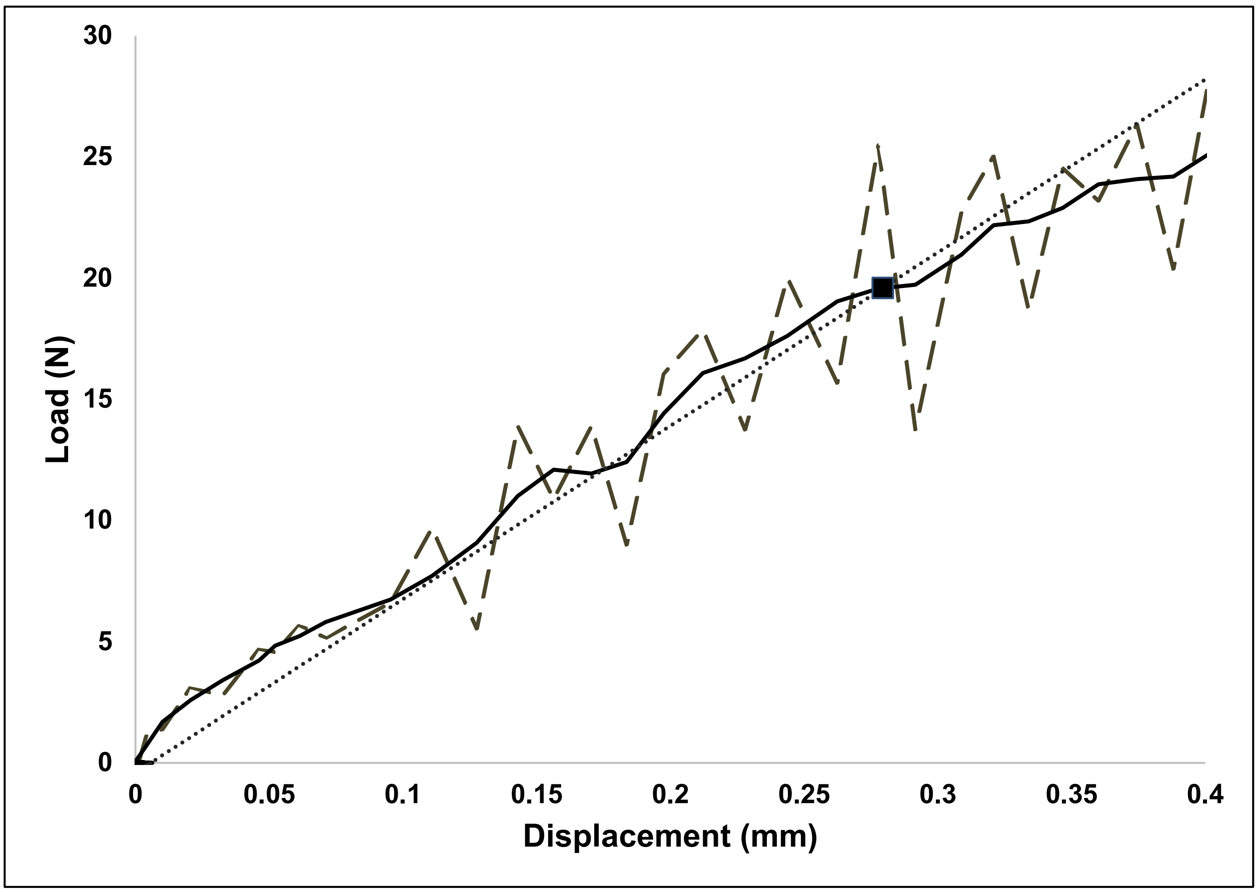

Figure 3: Comparing raw (gray dashed line) to filtered (solid black line) load and displacement observed during a three-point bending fracture toughness; 95% secant line (gray dotted line) used to find P_q (black square) at the intersection with the filtered load line.

Data Analysis

All data was processed using custom developed MATLAB (MATLAB R2020a, Mathworks, Natick, Massachusetts, USA) scripts. Two separate fracture toughness values were computed: critical elastic-plastic fracture toughness (J_{IC}), and critical elastic fracture toughness

(K_q). While both metrics attempt to quantify the fracture behavior of a material, the use of any specific metric depends on the degree of plastic deformation anticipated prior to crack growth. While previous work has shown J_{IC} is an appropriate metric of fracture toughness at the micro-scale (Willett et al., 2019), particularly during quasi-static three-point bending of SENB specimens, less plastic deformation is anticipated prior to crack growth (and ultimate fracture) during the high-rate loading experiments of this study. Therefore, both J_{IC} and K_q were computed in this study in order to identify the most appropriate fracture toughness metric to compare to macro-scale femoral neck bone strength. More specifically, J_{IC} was computed at the onset of crack extension (ASTM E1820-20a, 2020; Willett et al., 2019; Yan et al., 2007), whereas K_q (ASTM E399-20, 2020) was computed at the point where the load displacement line crosses the 95% secant modulus line (P_q). Due to the high-rate nature of the experiment, there was no "clear linear portion" that could be used to determine the secant modulus line. Therefore, a combined approach was used, using the line of best fit defined by the smoothness criteria outlined in ASTME E1820 to determine the secant modulus, and ultimately define the 95% secant modulus line as outlined in ASTM E399.

Multiple linear regression analyses were conducted to investigate the relationship between bone strength and fracture toughness. Multiple models were considered which also considered femoral neck BMD and age. More specifically, a total of 11 multiple linear regression models were generated, which can be generally separated into 3 separate groups of models, which are: 1) models without fracture toughness metrics, 2) models with J_{IC}, and 3) models with K_q. For significance tests an α level of 0.05 was employed, while model strength was evaluated via adjusted R^2.

RESULTS

We observed a significant association between femoral neck BMD and bone strength (Adjusted $R^2 = 0.835$, $\beta = 0.936$, $F(1, 3) = 21.27$, $p < 0.05$), despite the large variance observed in both bone strength (mean [SD] = 4190.2 [1273.6] N) and BMD (mean [SD] = 0.655 [0.099] g/cm^2). It should be noted that the large variance was driven by one sample, which had the lowest bone strength (2030 N) and BMD (0.513 g/cm^2); these values also likely contribute to the strong positive relationship observed. There was, however, no significant relationship between bone strength and age (Adjusted $R^2 = 0.200$, $\beta = 0.632$, $F(1, 3) = 2.00$, $p = 0.252$). The combination of age and femoral neck BMD resulted in a non-significant but strong positive relationship (Adjusted $R^2 = 0.866$, age $\beta = 0.266$, BMD $\beta = 0.817$, $F(2,2) = 13.94$, $p = 0.07$).

Overall, there were strong positive relationships between bone strength and fracture toughness, yet only models with critical elastic fracture toughness (K_q) were significant (Table 1). More specifically, there was a significant strong positive relationship between bone strength and K_q (Adjusted $R^2 = 0.828$, $\beta = 0.933$, $F(1, 3) = 20.32$, $p < 0.05$), as well as between bone strength and combination of K_q and femoral neck BMD (Adjusted $R^2 = 0.997$, K_q $\beta = 0.528$, BMD $\beta = 0.539$, $F(2, 2) = 349.6$, $p < 0.01$). While both factors have relatively similar β coefficients, it should be noted that a moderate-to-strong correlation was observed between K_q and femoral neck BMD, although the correlation was not significant (r = 0.753, n = 5, p = 0.142). Models combining age and K_q, as well as age, K_q and BMD, all had strong positive, yet non-significant relationships ($p > 0.05$). While not significant, some of the models with critical elastic-plastic fracture toughness revealed strong positive relationships with bone strength. Most notable were the models combining J_{IC} with age (Adjusted $R^2 = 0.869$, J_{IC} $\beta = 0.732$, age $\beta = 0.601$, $F(2, 2) = 14.25$, p = 0.07), and J_{IC} and femoral neck BMD (Adjusted $R^2 = 0.806$, J_{IC} $\beta = -0.356$, age $\beta = 1.253$, $F(2, 2) = 9.31$, p = 0.10). When comparing the two fracture toughness metrics, a weak-to-moderate correlation was observed ($R^2 = 0.285$).

Table 1: Multiple linear regression model for predicting femoral bone strength.

Fracture Toughness	Standardized Regression Coefficients (*β*)			Adjusted R^2	*p*
	Age	BMD (g/cm²)	Fracture Toughness		
K_q (MPa√mm)	0.05	0.547	0.487	0.994	0.051
	-0.027	-	0.952	0.743	0.128
	-	0.539	0.528	0.994	0.003**
	-	-	0.933	0.828	0.020*
J_{IC} (N/mm)	0.439	0.394	0.388	0.763	0.307
	0.601	-	0.731	0.869	0.066
	-	1.253	-0.356	0.806	0.097
	-	-	0.757	0.431	0.138

* denotes significance at an α level of 0.05
** denotes significance at an α level of 0.01

DISCUSSION

In this study, a sample of five matched pairs of male femurs from fresh frozen donors were included in this study, with one femur from each pair undergoing either simulated lateral impacts to emulate fall-related hip fractures or having a rectangular SENB subjected to three-point bending under impact like loading until failure. In addition to observing the significant relationships between BMD, age, and bone strength that are commonly reported (Courtney et al., 1995; Dall'Ara et al., 2013; Roberts et al., 2010), fracture toughness, quantified during high-rate loading experiments was found to be significantly related to bone strength, supporting the general hypothesis of this study. In terms of comparing between fracture toughness metrics, the only significant models observed in this study were those that included K_q. Additionally, most models including K_q yielded larger R^2 values than those that used J_{IC} as the fracture toughness metric, which supports the more specific hypothesis of this study. The only exception to this was the model that included J_{IC} and age, which outperformed its K_q counterpart, however, neither model reached significance.

While our results confirm the strong relationship between femoral bone strength and femoral neck BMD, our findings also suggest that fracture toughness, particularly critical elastic fracture toughness K_q, may play an equal or complementary role to femoral neck BMD in dictating bone strength. When compared to the values reported by of previous investigations for the relationship between femoral bone strength and BMD (R^2 ranging from 0.64-0.92), the R^2 value observed in this work ($R^2 = 0.835$) falls well within that range (Dall'Ara et al., 2013). On par with the relationship, we observed a significant strong positive the relationship between bone strength and K_q with an R^2 value of 0.828, and when K_q was combined with femoral neck BMD, an even stronger relationship was observed ($R^2 = 0.994$). This latter model had relatively similar standardized β coefficients for K_q and femoral neck BMD (0.528 and 0.539, respectively), which suggests relatively equal contributions to bone strength. While the potential interdependence between bone strength (the materials ultimate strength) and fracture toughness is not in itself surprising, as such a relationship is expected in common engineering materials (Alexopoulos and Tiryakioğlu, 2009; Ritchie et al., 1973), the relationship between these factors has yet to be fully characterized or investigated in complex nanocomposite materials, such as cortical bone. Furthermore, these results indicate that fracture toughness, or a related factor, may be the missing piece that could account for the unexplained variance present in femoral strength models based on BMD alone. However, it should be noted that there was a moderate relationship between femoral neck BMD and K_q ($r = 0.753$), which suggests that these factors may not be entirely independent from each other. While BMD represents a quantitative estimate of the degree of mineralization over a given area, fracture toughness metrics themselves do not necessarily represent any direct physical element of a tissue or a material, but rather represent a material property. Therefore, further research is required to explore the physical characteristics of material that contribute to fracture toughness.

At the micro-scale level, the content and quality of the organic phase of bone, namely type I collagen, have been shown to relate significantly to the fracture toughness of cortical bone (Granke et al., 2015; Poundarik et al., 2015; Willett et al., 2019; Zioupos et al., 1999), and could therefore be the underlying physical elements that dictate fracture toughness, and ultimately contribute to femoral bone strength. In the context of fall-related hip fractures, our results indicate that critical elastic fracture toughness K_q is the more relevant of the two fracture toughness metrics investigated in this study. When comparing the two fracture toughness metrics K_q and J_{IC}, our results indicate that K_q is more strongly related to bone strength than critical elastic-plastic fracture toughness J_{IC}. This might be due to the high loading rate of the simulated hip impacts, and of the high-rate three-point bending experiments, driving a more elastic behavior in the bone samples; K_q likely captures more of this elastic behavior. It is possible that slower rate loading would result in a greater degree of plastic deformation prior to fracture, and thus result in a stronger relationship between J_{IC} and bone strength. However, loading rate, driven largely by impact velocity in the context of fall-related hip fractures, has been found to significantly affect femoral bone strength (Courtney et al., 1994; Dragomir-Daescu et al., 2018; Gilchrist et al., 2014). Therefore, high-rate or impact-like loading experiments to quantify fracture toughness are likely more clinically and mechanically relevant for investigations relating to fall-related hip fractures. While the results of this study point to some degree of non-linear or plastic behavior being captured by J_{IC}, K_q appears to be the more appropriate fracture toughness metric in this case, as it captures more of the predominantly elastic nature of this tissue loading. It should be noted that J_{IC} and K_q differ not only in how they are calculated, but more specifically at which point in time, or data point, these values are calculated (ASTM E1820-20a, 2020; ASTM E399-20, 2020). As detailed in the methods section, J_{IC} was calculated at the point at which the crack began to grow (as determined through the high-speed microscopy-enabled videography), whereas K_q was computed at the point P_q as determined by the load-displacement data. Future work will investigate critical elastic plastic fracture toughness at this same point, resulting in a value that could be labeled J_q.

The observed relationship between fracture toughness and bone strength opens the door to investigating the factors that contribute to ,or dictate, fracture toughness towards ultimately investigating how these underlying factors may influence bone strength, either directly or indirectly. The unique structure of cortical bone results in the material having multiple inherent toughening mechanisms that span from the macroscale, such as crack deflection from osteon orientation, down to the nanoscale with the uncoiling of tropocollagen molecules (Buehler, 2007; Gautieri et al., 2009; Launey et al., 2010; Nalla et al., 2003). In fact, many of these toughening mechanisms relate to the organic phase of bone, specifically pertaining to the state of the collagen. Previous work in this domain has established that both the quantity and the quality of the collagen network in cortical bone are significantly and positively associated with the fracture toughness of the material (Granke et al., 2015; Poundarik et al., 2015; Willett et al., 2015; Zioupos et al., 1999). More specifically, metrics of collagen network connectivity, representative of the quality of the collagen, have been shown to be significant predictors of both critical elastic and elastic plastic fracture toughness during low-rate three-point bending tests of femoral diaphysis SENB (Willett et al., 2019). Though these experiments were performed on a different aspect of the femur and subjected to a much lower loading rate (applied through a 5 mm/s displacement rate) than what was used in this study, their findings demonstrate the key role that organic phase of bone plays in the fracture behavior of cortical bone. Therefore, the strong relationship between fracture toughness and bone strength observed in this study suggests that both the organic of bone contributes to its strength. However, further research is needed to more directly investigate the relationship between bone strength and the organic phase of bone.

CONCLUSION

To the author's knowledge, this is the first study in which multi-scale level testing, including both macro-scale bone strength and micro-scale fracture toughness experiments, was utilized to investigate the underlying mechanics of fall-related hip fractures. Our results suggest that not only is critical elastic fracture toughness strongly and significantly related to bone strength, it may very well explain an equivalent amount of variance as does femoral neck BMD. This study demonstrates the value of multi-scale or multi-level experimentation and modeling, as it may provide a more fulsome understanding of the underlying mechanics of fractures. When combined with findings of previous studies that have shown a link between fracture toughness and the collagen network of cortical bone, our results indirectly support the notion that, mediated via fracture toughness, bone collagen contributes to femoral bone strength.

ACKNOWLEDGEMENTS

This research was funded in part by a catalyst grant from the University of Waterloo Network for Aging Research, with additional support from the Natural Sciences and Engineering

Research Council of Canada under Grant RGPIN-2015-03636 and the Alexander Graham Bell Canada Graduate Scholarship – Doctoral program.

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