

Multi-Scale Mapping of Diaphyseal Strains Across Gait Modalities Using Femoral Digital Twins

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Abstract

Bone health decreases with age and can culminate in fractures with particularly devastating consequences in the femur. Exercise-induced mechanical loading can be prescribed as preventative care, but clinical recommendations are hindered by a lack of clarity regarding the mechanical strains experienced during habitual locomotive tasks such as walking, stair descent, and stair ascent. We used subject-specific, muscle-driven finite element *digital twins* of post-menopausal women to conduct a multi-scale analysis of the spatiotemporal distribution of femoral principal strains during each task. At the macroscopic level, strains peaked during both the early and late stance phases of the gait cycle and the femur was subjected to a combination of bending and torsional loads for all tasks. Mesoscale analyses revealed a noticeable regional partition: strain distributions were highly consistent across tasks and timepoints in the proximal and mid-diaphysis, but deviated in the distal diaphysis. At the tissue level, peak strains during stair ascent were lower in the proximal region but higher in the distal region compared to walking and stair descent; meanwhile, in the mid-diaphysis, peak strains during stair descent exceeded those during walking. Together, these findings indicate that while the global femoral loading environments were similar across tasks, there was heterogeneity in the spatial and temporal mechanical response. Incorporating stair activity into daily routines can diversify bone remodeling stimulation throughout the diaphysis.

Keywords: Bone, Strain, Exercise, Walking, Stair use, Femur, Finite element

1. Introduction

Maintaining bone health is essential for quality of life and becomes particularly salient with aging when the risk of fracture increases [1]. Mechanical loading is critical for bone quality with the potential for stimulating bone adaptation as described by Frost's mechanostat theory [2]. There are numerous examples demonstrating the net forma-

tive response of bone to increased [3–5] mechanical stimulation beyond habitual activity.

In human adults, the use of walking as a form of exercise-based stimuli for bone has produced modest positive adaptations dependent on the distance walked per week [6, 7]. When comparing individuals who walk regularly to those with a sedentary lifestyle, regular walking lowers hip fracture incidence [8]. Coupling walking with other exercise or pharmacological treatments can further increase bone adaptation [9–12]. Thus, while the evidence basis supporting the use of ex-

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ercise for bone health is emerging [13], it would be bolstered by a clearer understanding of the homeostatic range of mechanical stimuli bone is subjected to during habitual locomotion.

Understanding these physiological limits is particularly critical because when pre-existing microdamage alters bone structural capacity, loads within the homeostatic range can trigger failure. A prime example is in the case of atypical femoral fractures (AFF), which initiate as a silent crack on the lateral cortex that propagates medially leading to catastrophic failure in the absence of trauma [14, 15]. Although nearly non-existent prior to the widespread adoption of bisphosphonates, AFFs have emerged as a complication of long-term antiresorptive therapy [16, 17], whose relative risk rises exponentially with duration [17, 18]. Notably, bisphosphonates successfully reduce primary osteoporotic fracture risk by 25–77% [19, 20], and the incidence rate of AFFs remains low compared to untreated osteoporotic fractures (11 vs. 750 per 100,000/person-years) [18]. Yet, because AFFs begin in thick cortical bone, their underlying initiation mechanism remains unclear [21]. While, prior work has focused on the effect of whole-bone geometry [22], we hypothesize that the local strain state induced by habitual locomotion [23, 24] may also contribute to the risk of AFF.

Because long-term antiresorptive therapy suppresses remodeling and alters matrix quality over time, defining the baseline diaphyseal strain state in healthy postmenopausal bone is a critical first step toward understanding why specific anatomical regions become vulnerable to failure during habitual locomotion. Computational modeling allows for the non-invasive estimation of in vivo strains across a variety of physical activities. Most prior studies mapping the diaphysis have focused primarily on methodological development of finite element (FE) models using generic literature-derived loading [25–29], simulated walking loads [30, 31], or subject-specific walking muscle forces [32]. To date, only a few studies have compared diaphyseal strain fields across different locomotive tasks [24, 33]. While Martelli et al. compared a broad range of activities, their analysis was lim-

ited to a single subject ($n = 1$) using muscle forces derived from a 25-year-old motion capture subject applied to an 81-year-old cadaveric femur [24]. Similarly, Deng et al. incorporated subject-specific loading for seven older males and ten older females, but relied on non-subject-specific imaging and restricted their comparison to stair use [33]. To our knowledge, full-diaphyseal principal strains during habitual locomotion (walking and stair use) have not been statistically evaluated in healthy postmenopausal women using fully subject-specific (imaging and muscle-driven kinematics) FE models.

Therefore, the aim of this study was to assess the bulk macroscopic loading and tissue-level strain state of the femoral diaphysis during walking, stair ascent, and stair descent. We performed a multi-scale analysis using subject-specific, muscle-driven digital twins of healthy post-menopausal women to assess the spatiotemporal evolution of strains during the stance phases of these common locomotive tasks. Quantifying the in vivo strains during habitual locomotive tasks would elucidate the homeostatic mechanical stimuli relevant to the design of exercise interventions as well as clinical scenarios involving diaphyseal fractures.

2. Methods

2.1. Subjects

The absolute maximum principal strains in the femoral diaphysis during walking, stair ascent, and stair descent were analyzed using previously developed [34], subject-specific, muscle-driven FE models of postmenopausal women ($n=18$, age range: 60 to 74 years) with no history of bone disease. Unrecoverable errors in data collection prevented analyses of one subject’s stair usage data resulting in $n=17$ models for both stair ascent and stair descent. The stance phase of each task was discretized into 20 timepoints and normalized between 0 and 100%. These data were further separated into five intervals: heel strike (0 – 20%), early stance (21 – 40%), mid stance (41 – 70%), late stance (71 – 85%), and toe off (86 – 100%).

2.2. Model registration

The diaphysis was defined as the region spanning from the lesser trochanter (identified within the computed tomography-based computer-aided design models) to 120 mm above the proximal end of the condyles. Elements corresponding to bone marrow (Young’s modulus, $E < 1000 \text{ MPa}$) were removed, and all models were co-registered using the linea aspera within the distal diaphysis (Python 3.12.7). For each task, the absolute maximum principal strains (herein referred to as principal strain) during the stance phase were calculated.

2.3. Whole-bone macroscopic analysis

To visually characterize the bulk deformation of the femur during locomotion, the displacements were scaled by a factor of 15. The displacements were compared to the femur location before joint and muscle reaction forces were applied (unloaded). The resulting visualizations were used to assess the loading of the femur in the frontal and sagittal anatomical planes.

2.4. Meso-scale analysis during discrete stance intervals

We characterized the meso-scale strain state of the femur by dividing the diaphysis into five equidistant sections (Fig. 1A) and first assessing when the strain was maximum within each section. For each element, we identified the stance interval corresponding to when principal strain was highest during stance (Fig. 1B,C). We then calculated the proportion of each section under maximum strain during each stance interval. Initial analyses revealed that peak strains occurred during early and late stance for walking and stair descent, and during early stance for stair ascent (Table 1, Fig. 2A). Thus, the meso-scale strain state was characterized during these two timepoints for all activities.

The element centroids of each diaphyseal section were projected onto 2D cross-sections (Fig. 1D) to map principal strains during early and late stance. From these profiles, we measured the neutral axis orientation relative to the medial-lateral

axis (0° – 180° , ImageJ 1.52p), the sectional percentage under tension, and the maximum tensile and compressive principal strains. While the neutral axis angles were bounded within $[0^\circ, 180^\circ]$, progressive cross-sectional rotation under torsion caused the tension–compression boundary to continuously pass 180° across consecutive spatial levels. To prevent artificial phase-wrapping artifacts and track this continuous rotation, neutral axis orientations were unwrapped past 180° for torsion-dominant conditions, whereas bending-dominant conditions were maintained in the original $[0^\circ, 180^\circ]$ domain.

2.5. Tissue-level peak strain analysis

To compare the peak principal strains between tasks (independent of stance time), each projected cross-section was divided into 360 radial sections (Fig. 1E). For each radial section, the 90th percentile principal strain was calculated and visualized at the geometric centroid of each radial section (Fig. 1F). The peak principal strain data were filtered using a low-pass Butterworth filter with the cut-off frequency determined using spectral analysis (power threshold=90%) as a function of radial location.

2.6. Statistical analysis

Normality of the neutral axis measurements and the percent of the projected cross-section under tensile loads were confirmed using a Shapiro-Wilk test. Both measures were analyzed using one-way repeated measures ANOVA followed by a post-hoc analysis with a paired t-test and Bonferroni correction (R Studio, Boston, MA, USA).

Stance phase strains were not normally distributed (D’Agostino-Pearson K2) and comparisons between activities were performed using Statistical non-Parametric Mapping (SnPM; spm1d v.0.4.18) with one-way ANOVA [35]. Post-hoc analysis was performed with a two-sample t-test and Bonferroni correction. In significant regions, the average percent difference of the peak strain magnitude was calculated. When the peak strain direction differed in significant regions, SnPM was performed on the magnitudes to confirm significance. Significance was set at $\alpha = 0.05$.

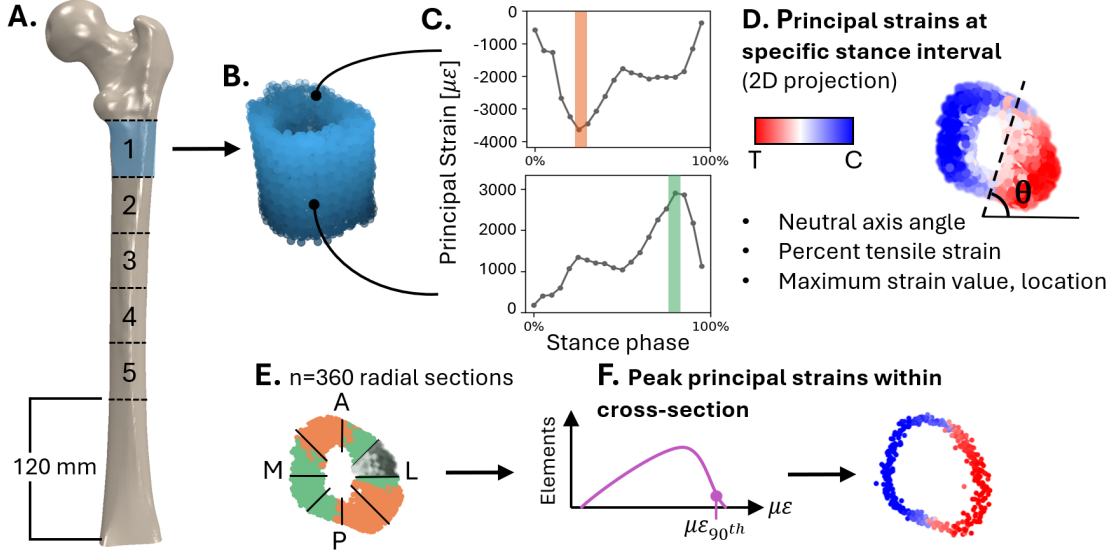


Figure 1: Data processing of (A) five equidistant sections of the femoral diaphysis. (B,C) The highest principal strains and corresponding timing during stance was identified. (D) Principal strains during the times of maximum strain was analyzed using 2D projections. (E,F) The 90th percentile principal strain within each radial section was also calculated. Methods presented are for a representative subject.

Table 1: Spatial distribution of peak principal strain timing across femoral diaphyseal regions. Values represent the percentage of the total cross-sectional area reaching peak strain during each stance interval.

Diaphysis section	Walking					Stair descent					Stair ascent				
	HS	ES	MS	LS	TO	HS	ES	MS	LS	TO	HS	ES	MS	LS	TO
Prox: S1	-	45.0	-	55.0	-	-	72.5	-	27.5	-	-	97.5	-	-	2.5
S2	-	37.5	-	62.5	-	-	77.5	-	22.5	-	-	100.0	-	-	-
S3	-	34.2	-	65.8	-	-	71.9	-	28.1	-	0.8	99.2	-	-	-
S4	-	73.3	-	26.7	-	0.3	93.6	-	6.1	-	-	100.0	-	-	-
Dist: S5	2.2	74.7	-	23.1	-	1.9	64.2	-	33.9	-	-	100.0	-	-	-

HS = Heel Strike; ES = Early Stance; MS = Mid Stance; LS = Late Stance; TO = Toe Off.

3. Results

3.1. Timing of peak strain

During walking and stair descent, the peak strains most commonly occurred during early and late stance, while the peak strains during stair ascent occurred only during early stance (Table 1). Across all three tasks, peak strains occurred at $25.3 \pm 4.0\%$ and $75.5 \pm 1.6\%$ of the stance phase of gait.

3.2. Macroscopic deformation

All three locomotive tasks exhibited similar macroscopic deformations. During early stance, the femur was under lateral S-shape bending (frontal), internal torsional rotation (frontal), and

posterior cantilever bending (sagittal)(Fig. 2A). Late stance resulted in medial S-shaped bending and a tendency towards anterior buckling (Fig. 2B).

3.3. Strain distributions during early and late stance

Our qualitative observations of the macroscopic deformations of the femoral diaphysis were confirmed by the quantitative tissue-level analyses of strains. Specifically, there was a clear distinction in strain distributions between the proximal/mid diaphyseal regions (S1-S3) and the distal diaphysis (S4-S5, Fig. 3A).

Proximal and mid-diaphysis (S1-S3): For all three activities, the neutral axis was aligned near

the anterior-posterior axis ($81.3 \pm 15.0^\circ$, Fig. 3A₂₆₅ dashed lines, Fig. 3B). There was a modest medial rotation of the neutral axis at the mid-diaphysis ($\Delta 12.6^\circ$, $p = 0.026$ to < 0.001) during the early stance phase of stair ascent. In contrast, the neutral axis orientation was relatively₂₇₀ constant during the late stance phase of all three locomotive tasks with the exception of stair descent (S1-S2: $p = 0.018$).

In all tasks, the lateral half of the proximal diaphyseal sections were in tension during both early₂₇₅ and late stance (S1,S2: $45.1 \pm 3.5\%$; Fig. 3A red regions; Fig. 3C). The percent of each cross-section in tension decreased by 19.0% in the mid diaphysis ($p < 0.001$). The strains were highest₂₈₅ in the most proximal section (S1), and the maximum compressive strain was 14% higher than the maximum tensile strain (C: $-2380 \mu\epsilon$, T: $2065 \mu\epsilon$; Fig. 3D). In the subsequent two sections (S2 and S3), the maximum strain values decreased by 32% relative to the previous section.

Lower-middle diaphysis (S4): Compared to the mid-diaphysis, torsion during the early stance phase of walking and stair ascent resulted in a pronounced medial rotation of the neutral axis in the₂₉₀ lower-middle diaphysis ($\Delta 78.0^\circ$; $p < 0.001$; Fig. 3A,B). A less pronounced rotation occurred during the late stance phase of stair activity ($\Delta 34.8^\circ$; $p = 0.02$, $p = 0.008$). Additionally, the percent under tension decreased by 18.09% for all tasks₂₉₅ ($p = 0.002$ to $p < 0.001$) except for the early stance phase of stair ascent. Compared to all other sections, the strains in the lower-middle diaphysis were the lowest (C: $-975 \mu\epsilon$, T: $309 \mu\epsilon$).

Distal diaphysis (S5): Compared to the lower-

middle diaphysis, the neutral axis during the early stance phase of stair ascent continued to rotate medially from the torsional load ($\Delta 16.1^\circ$; $p < 0.001$). In contrast, the neutral axis rotated by 26.4° laterally during the late stance phase of stair ascent and the medial aspect was under tension. For the early stance phase of stair descent and the late stance of the other tasks, the neutral axis angle did not rotate but instead shifted medially. The medial aspect was in tension as a result of the macroscopic bending inflection point. During the early stance phase of walking and stair descent, the amount of the cross-section in tension increased by 19.7%. The maximum strain values in section 5 were similar to the mid-diaphysis (C: $-1281 \mu\epsilon$, T: $700 \mu\epsilon$). We note that for early stance of stair descent and the late stance of all tasks, the strain state (bending with a neutral axis oriented along the anterior-poster direction) in the distal diaphysis (S5) was nearly equal to the mid-diaphysis (S3) with the primary difference being the location of the region under tension.

3.4. Peak local strains due to locomotion

Our last analysis involved local comparisons of peak strains within each femoral cross-section between the different tasks. In general, peak strains during walking and stair descent were similar. Compared to walking and stair descent, the strains during stair ascent were lower in the proximal diaphysis and higher in the distal diaphysis.

Within the two most proximal regions, stair ascent resulted in lower strains in the anterolateral and posteromedial quadrants (Fig. 4A,B). In the

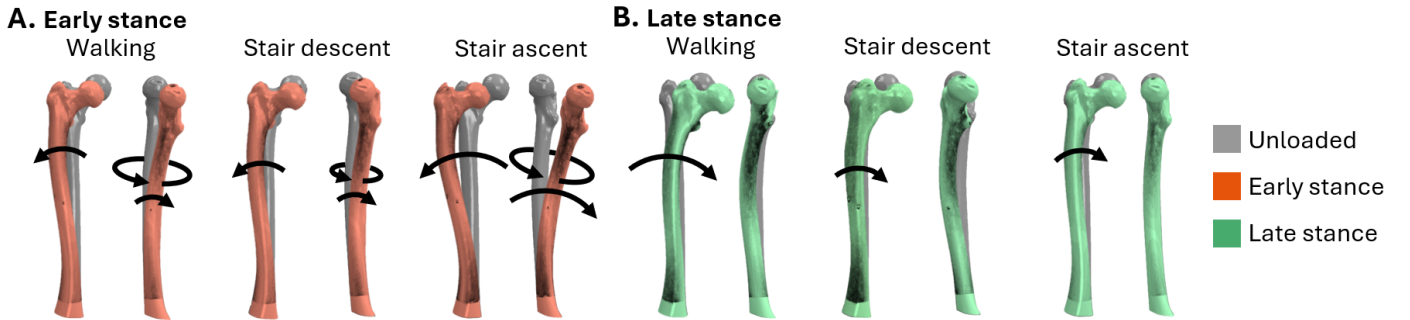


Figure 2: Whole bone, macroscopic, load condition in the frontal (left) and sagittal (right) views for each task during (A) early and (B) late stance. Results presented are for a representative subject.

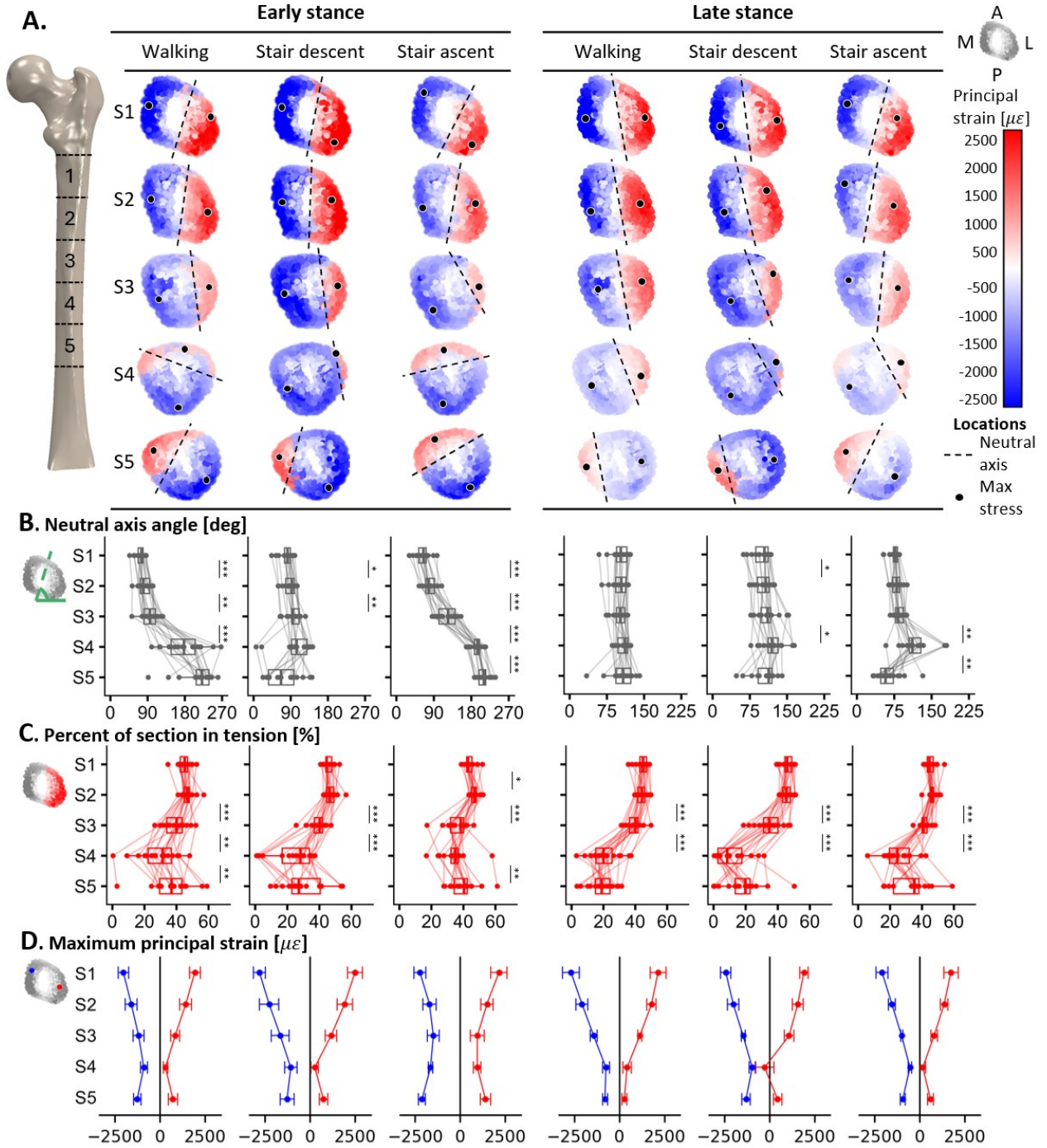


Figure 3: (A) Principal strain distribution for each task during early stance and late stance. (B) Neutral axis orientation. (C) Portion of each section under tensile strain. (D) Maximum principal compressive and tensile strain. * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

most proximal region (S1), the strains during stair ascent were $80.2 \pm 30.9\%$ lower than those during walking and stair descent ($p = 0.0036$). In S2, strains were $57.5 \pm 15.6\%$ lower than the strains during walking and stair descent ($p = 0.024$). In the mid-diaphysis, the peak strains on the posterior aspect during walking were $66.4 \pm 26.9\%$ lower

than the strains during stair descent ($p = 0.036$; Fig. 4C). This trend continued into the distal diaphysis (S4,S5) and shifted to the lateral cortex ($p = 0.026$; Fig. 4D,E).

In the distal regions, the loading mode during stair ascent shifted from compression to tension in the anterior quadrants (Fig. 4D,E). Upon com-

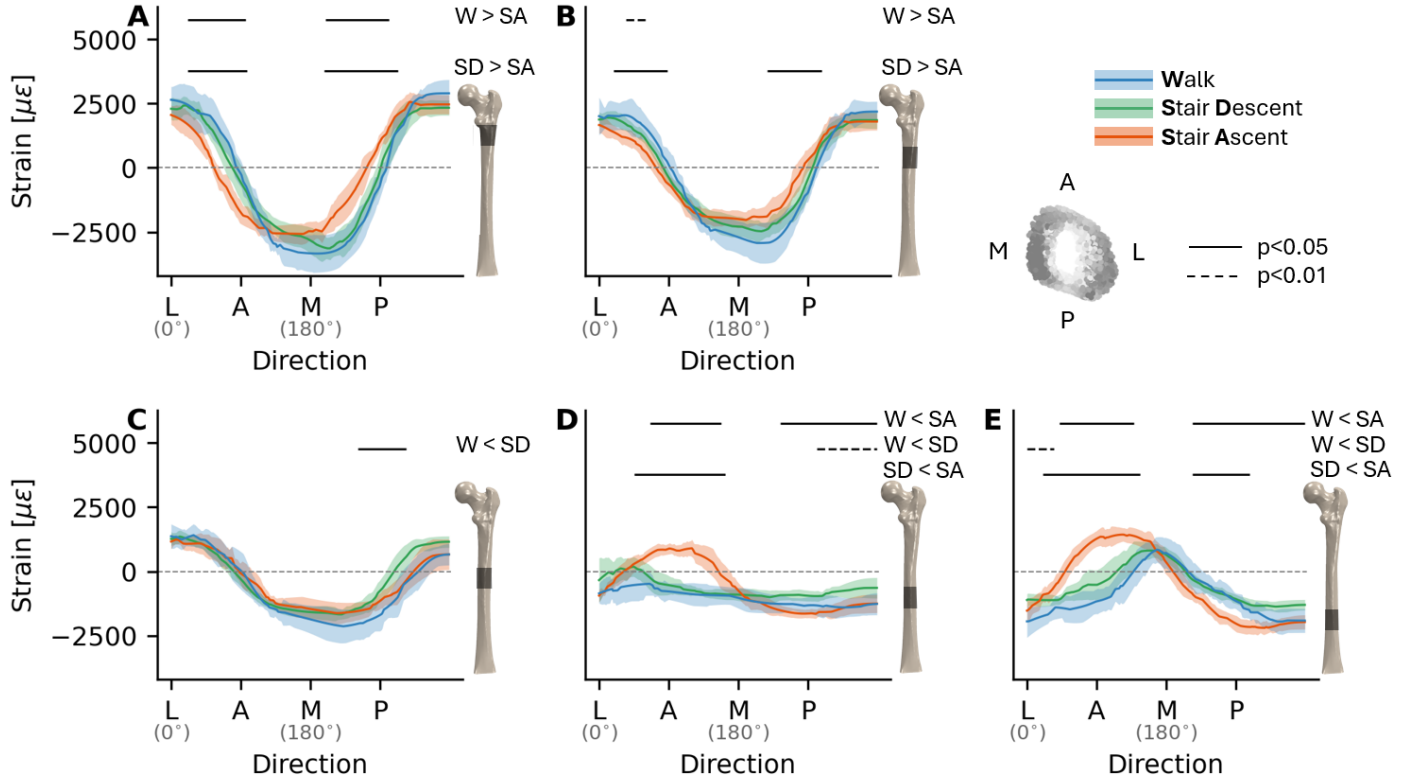


Figure 4: SnPM results for strains in each (A-E) vertical section during all three locomotions. Solid lines indicate the mean, and shaded regions represent the standard deviation. (W, walking; SA, stair ascent; SD, stair descent) — $p < 0.05$ ---- $p < 0.01$

paring the magnitudes, there was only a small anteriolateral region in section 5 where the strains during stair descent were higher than the strains during stair ascent. In the posterior regions, the peak strains for all tasks were compressive. In sections 4, the strains during stair ascent were $42.2 \pm 14.3\%$ higher than walking and stair descent ($p = 0.0012$), and in section 5 they were $74.8 \pm 26.3\%$ higher ($p = 0.0012$).

4. Discussion

Spatiotemporal variations in diaphyseal strains were observed during habitual locomotion using subject-specific, muscle-driven femoral digital twins of healthy post-menopausal women. To our knowledge, this study provides the first comprehensive, multi-scale mapping of diaphyseal strain mechanics across three distinct structural scales: macro-level bulk loading, meso-level strain state, and localized peak principal strains. Overall, strains were highest within the proximal diaph-

ysis, with peak magnitudes occurring during early and late stance. The peak strains throughout the diaphysis were similar between walking and stair descent, but differed during stair ascent, reflecting shifts in the multi-axial loading regimes between tasks.

Our peak diaphyseal strains across all three tasks (C: -2237 to $-2689 \mu\epsilon$; T: 2153 to $2491 \mu\epsilon$) closely matched the magnitude range reported by Martelli et al. [24] (C: -1162 to $-2059 \mu\epsilon$; T: 871 to $2000 \mu\epsilon$). However, our spatial strain distribution within each task, as well as the relative spatial shifts between tasks, diverged from their predictions, likely driven by our introduction of axial springs simulating hip capsule constraints. Conversely, our calculated peak strains during stair use was 2.7–5.5 times higher than those reported by Deng et al. [33] (C: -484 to $-890 \mu\epsilon$; T: 399 to $754 \mu\epsilon$), but our spatial distributions were similar. When directly comparing the stair-based tasks, Deng et al.[33] observed

consistently higher strains during stair descent than ascent along the entire diaphysis, our models revealed a regional reversal in the distal diaphysis, where stair descent induced lower strains than ascent. These differences may stem from our use of subject-specific imaging and inhomogeneous material properties, which retain localized strain concentrations caused by regional variations. Crucially, our observed spatial distributions agree with Speirs et al. [28], who similarly demonstrated that stair ascent reduces proximal strains but elevates distal strains relative to walking. Finally, our meso-scale neutral axis orientations during early stance align within one standard deviation of the neutral axis predicted by Polgar et al. at heel strike [27].

We found that the peak principal strains during walking and stair descent were similar in the diaphysis. Both walking and stair descent gait patterns can be characterized as a controlled series of forward falling and recovery, with stair descent having a farther distance to fall. In contrast, stair ascent requires a pushing action early in the stance phase to enable upward movement to the next step. As expected, these two gait styles require different muscles and is most clearly seen in the gluteus maximus force profiles [34]. During stair ascent, gluteus maximus force was approximately double that of the force during walking and stair descent. Curiously, despite this increase in muscle force, principal strains in the proximal diaphysis were lower during stair ascent suggesting that either co-contraction of opposing muscles (or the hip joint reaction force vector) may offset the effects of increased gluteus medius muscle force. Given that the principal strains in the femur are a result of over twenty temporally and spatially varying muscle forces culminating in a complex, multi-modal strain state there is a desire for proxy measurements of the local mechanical environment. Using the ground reaction force as a proxy for the femoral diaphysis strain state may not provide enough information. For example, during stair ascent, the GRF was higher during late stance [34], but our results show the diaphyseal strains were primarily higher during early stance. Similar conclusions have also been made

regarding the femoral neck and tibia [34, 36].

Nonetheless, the strains were consistently higher in the proximal diaphysis, nearest to the hip joint reaction force and most muscle insertion points. The three highest muscle forces - gluteus medius, gluteus maximus, and iliopsoas [34] - insert into the greater trochanter, proximal diaphysis, and lesser trochanter, respectively. This high-strain region corresponds to where half of reported atypical femoral fractures (AFF) occur [22]. An AFF typically begins on the lateral aspect, where the tensile stresses were concentrated, and perpetuates as a stress fracture due to fatigue [21]. The combination of bone being mechanically weaker in tension [37] and the lack of remodeling from bisphosphonates could be a potential mechanism driving these fractures. We attribute the tensile versus compressive distributions to longitudinal bending of the femur as a result of the muscle insertion locations relative to the joint reaction force. However, whole bone geometry, including the bicondylar angle of the femur, may also contribute to femoral bending [38–42]. More work is needed to understand the relative contribution of femoral geometry and muscle forces to the meso- and tissue level strain state during locomotion.

The current study has several strengths, including being the first to employ a multi-scale strain analysis in the femoral diaphysis to compare the spatial and temporal shifts during three common locomotive tasks that represent the homeostatic mechanical stimuli using muscle-driven finite element models of healthy post-menopausal women. However, this study also has several limitations. Our study is limited to one specific population. Locomotion style, and therefore muscle forces, may differ by age and sex [43, 44]. Our models used an isotropic Young’s moduli. While an orthotropic Young’s moduli would be more accurate, the resulting strains when using isotropic or orthotropic material properties have been found to be only marginally different [45]. The use of a fixed boundary condition at the distal diaphysis may result in an overestimation of strains [28]. Additionally, errors due to anatomical scaling of a generic model induce larger errors in the distal

regions. [32]. However, our regions of interest followed and exceeded Saint-Venant’s principle and⁴⁹⁰ were applied systematically to all models. For this reason, we did not include the gastrocnemius muscles as they overlap spatially with our fixed constraints [46]. Future studies could extend this framework to other activities, such as running, that cause higher bone loads and are more likely⁴⁹⁵ to stimulate bone adaptation [47–49].

Overall, our results reveal that diaphyseal loading is similar during walking and stair descent, but distinct from stair ascent. We found spatial and temporal differences in the mechanical response of bone to the locomotive forces. Crucially, the elevated tensile strains observed in the proximal lateral diaphysis offer a mechanical basis for where atypical femoral fractures initiate, demonstrating how habitual loading can drive microdamage when remodeling is suppressed. While walking remains the primary recommended habitual activity, incorporating stair ascent may serve as a targeted stimulus for bone maintenance. Ultimately, this anatomical mechanical atlas of normative strains during locomotion establishes a necessary baseline for future work evaluating bone quality, adaptation, and localized fracture risk.⁵¹⁰

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6. Conflict of Interest

Declarations of interest: none.

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