Preliminary investigation of bone mineral density differences between female and male post-mortem human subjects

Randee L. Hunter, Zachary A. Haverfield, Lauren Hayden, Zhaonan Sun, Amanda M. Agnew

Abstract

To address persisting sex-based injury risk inequities during motor vehicle crashes, investigations into the underlying physiological components of skeletal fracture resistance could be beneficial. Due to fundamental biological differences between males and females, it cannot be assumed that scaled male volumetric bone mineral density (vBMD) would be accurate for females. Thus, the objective of this study was to quantify intra-skeletal variation and the effects of demographic variables on female post-mortem human subjects (PMHS) vBMD and compare to previously reported male data. vBMD was calculated from quantitative computed tomography (QCT) for 70 female PMHS (29-98 years) in the lumbar spine and the left femoral neck, distal radius, and distal tibia. Nuanced patterns of intra-skeletal variation in vBMD were found in females compared to males. Femoral neck vBMD was significantly higher than other sites within their bone type ($p<0.01$) in both sexes. Effects of age and body size on vBMD were inconsistent across sites in females. Although males had larger radius and tibia vBMD, females had larger femoral neck total and inferior cortex vBMD ($p<0.001$). These results suggest both anatomical specificity in assessing bone quality as well as fundamental differences in female PMHS vBMD compared to males that could be considered in occupant safety research.

Keywords: BMD, bone quality, intra-skeletal variation, injury risk, sex differences

I. INTRODUCTION

Addressing injury risk disparities between males and females in motor vehicle crashes is a universally important initiative for the field of injury biomechanics. Recent work has highlighted the inequitable reduction in risk between sexes despite comprehensive improvements in survivability in newer model year vehicles [1-3]. While the overall number of male fatalities in crashes are higher than females due to behavioral factors and historically higher exposure levels, the relative risk of sustaining serious injury or fatalities for females remains higher than males even after controlling for crash severity [2][4-6]. However, it has recently been suggested that some of these risk disparities may be attributed to confounding conditions not captured by crash severity metrics used in these studies [4]. Reference [4] found a reduction in relative risk for females when controlling for airbag deployment and vehicle compatibility, yet the higher risk of lower extremity injury noted by others [7][8] seems to persist at 3x that of males [4]. Addressing the underlying causes of sex-based inequities in vehicle occupants may require a multi-tiered approach that considers not only the structure of the vehicle and its occupant safety mechanisms but also the physiological differences in injury tolerance between females and males [9]. In order to promote more equitable protection for a wide range of occupants, a panel of experts has recommended a series of initiatives for the field [9] which includes a better understanding of sex-based variability in human injury tolerances. Although factors such as size, body proportions, and body mass influence the effectiveness of passive safety mechanisms across a diverse population, inherent physiological differences between males and females could also be incorporated. Despite the inclusion of the 5th percentile female ATD, a scaled down version of the HIII- 50M, in some regulatory tests, this evaluation tool only accounts for size-based differences between sexes and does not address physiological differences in tissues. The difficulty is that inherent variability among the female population currently makes it unrealistic to establish objective criteria. Additionally, it is premature to consider transferring findings into a test device that could be used to better analyze this widely varied injury risk.

R.L. Hunter (Randee.Hunter@osumc.edu) is an Associate Professor, Z.A. Haverfield and L. Hayden are PhD students, and A.M. Agnew is a Professor in the Injury Biomechanics Research Center at The Ohio State University, Columbus, OH, USA. Z. Sun is a principal scientist at the Collaborative Safety Research Center, Toyota Motor North America, Ann Arbor, MI, USA.

Moving the field closer to this goal requires a better understanding of variability between and within sexes and its expression in bone.

Sex-based differences in the physiology of bone have long been studied particularly due to age-related hormonal changes (i.e., menopause) that influence fracture risk. Bone mineral density (BMD) is a relatively accessible and commonly utilized skeletal trait for characterizing probability of fracture [10]. Although only a single component that could contribute to injury tolerance, improvements in BMD have been associated with decreased injury risk (see [11] for a review). Utilizing volumetric BMD (vBMD) which allows for 3-dimensional analysis of bone and corrects for some of the pitfalls associated with dual x-ray absorptiometry (DXA) improves predictive capabilities for fractures [12] in clinical populations. For example, vBMD in the distal tibia and radius in conjunction with microarchitecture influenced fracture risk at all ages in both sexes [13]. However, there is evidence that males and females do not build or maintain bone by similar mechanisms [14-17] in a complex relationship between bone size and underlying physiological sex-based differences. Previous work has identified a pattern of substantial variability in vBMD within male post-mortem human subjects (PMHS) across the skeleton [18]. It is currently unclear if female PMHS experience similar patterns of variation in vBMD which would suggest site-specific assessment of injury tolerance (i.e., not all bone is the same) is necessary. It is often commonly assumed that males will demonstrate larger values of vBMD than females due to their overall larger skeletons; however, due to non-standardized acquisition, limited anatomical sites, and conflicting evidence [19], this assumption needs further exploration. Thus, the purpose of this study is to characterize female PMHS variation in vBMD across the skeleton as a measure of bone quality, the effects of age and body size on female PMHS vBMD, and lastly, to compare male and female PMHS vBMD.

II. MATERIALS AND METHODS

Retrospective analyses of 70 female PMHS whole-body CT scans, curated by the Injury Biomechanics Research Center (Columbus, OH, USA), were performed. Female PMHS represented a wide range of ages and body sizes (Table I), were predominantly white, and met scan-specific acquisition inclusion criteria. PMHS were only excluded for specific anatomical site issues including pathological changes of the bone noted in the field of view (FOV), surgical hardware, artifacts or beam-hardening, evidence of previous fracture or infection, or any portion of the bone outside the usable FOV. Clinical CT scanners (Siemens Definition Edge and Siemens Force) with a combined coefficient of variation (CV) of 1.92% were used to acquire all whole-body scans under consistent acquisition parameters (0.6 mm slice thickness, 120 kVp, and a reference 250 mA). To facilitate the standardized phantom-based vBMD calculation from specific anatomical regions of interest, an INTable^{TM} phantom with rods of known densities (0, 75, and 150 mg/cm^3) was included in each scan. Site-specific density calibration of Hounsfield units (HU) to vBMD values minimizes the inherent effects of x-ray tube fluctuations between scans as well as accounts for differential x-ray attenuation due to varying densities of tissue within a scan. Data collection for female PMHS was performed using methods reported in detail in [18] for direct comparisons between datasets and are described below.

TABLE I
SAMPLE DEMOGRAPHICS

		Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m^2)
Female (n=70)	*Mean±SD*	67.7±16.1	162.3±7.0	54.9±11.7	20.7±3.3
	Range	29-98	134.6-190.5	38.1-95.5	13.5-28.9
Male* (n=76)	*Mean±SD*	62.0±14.5	176.2±7.1	73.4±10.6	23.7±3.4
	Range	24-102	160.0-190.5	52.2-96.2	17.0-32.7

**Male data reported in [18]*

Osirix MD software (v.12.0) was used to create volumes of interest (VOIs) in the lumbar spine (L2-L4), left femoral neck, left distal tibia, and left distal radius (Fig. 1). These sites were chosen for their relevance to the typically measured locations for bone quality assessment (femoral neck, lumbar spine, and radius) as well as a

representative lower extremity anatomical location (distal tibia) where disparities in injury risk between sexes appears to persist in real-world crash data [4][20]. A combination of blunt (manual; Fig. 1) and Hounsfield unit (HU) threshold segmentations isolated only bone voxels for vBMD analysis. Previously reported HU threshold ranges [18] were utilized in this study for comparability and resulted in bone type specific (i.e., trabecular [Tb] 150-660 HU; cortical [Ct] 661-3000 HU; and total 150-3000 HU) VOIs at each site. Lumbar spine VOIs at each level (L2-L4) were collected at 50% of the total vertebral height and included 5 axial slices (3mm of bone in z-direction). To properly capture the inferior (Inf) and superior (Sup) cortices, the femoral neck (Fem-N) VOIs were identified in the coronal plane and also included Fem-N Tb and Fem-N Total. Radius and tibia VOIs were defined as 4% of the total length of each bone (Rad-4 and Tib-4) relative to the distal end and included 5 axial slices for analyses (Table II). Site-specific calibration curves from the INTable™ phantom were used to convert mean HU values from each bone type VOI into vBMD values.

TABLE II
vBMD VOLUMES OF INTEREST

Anatomical site	Abbreviation	Tissue type
Lumbar spine	L2, L3, L4	Tb, Total
Femoral Neck	Fem-N	Ct (Inf, Sup), Tb, Total
Radius	Rad-4	Tb, Total
Tibia	Tib-4	Tb, Total

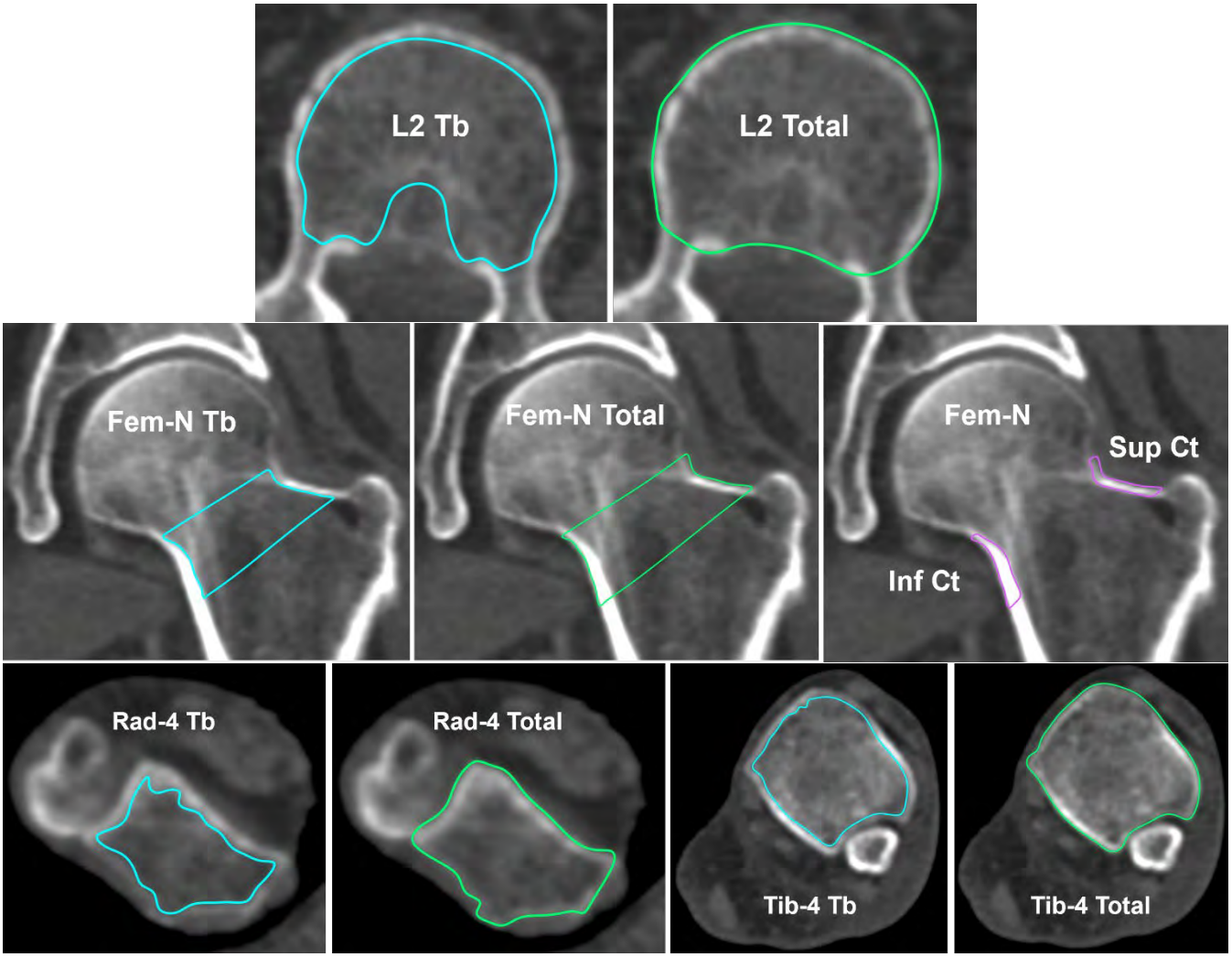


Fig. 1. Representative manual VOIs (without threshold applied) for each anatomcial location and bone type. The lumbar spine VOIs are collected for each vertebra (L2, L3, and L4). The femoral neck (Fem-N), distal radius (Rad-4), and distal tibia (Tib-4) VOIs were collected on left elements only.

Data Analysis

All statistical tests were performed using Minitab 21 statistical software with an *a priori* α=0.05. vBMD normality for each VOI was assessed using Kolmogorov-Smirnoff tests. Repeated measures mixed model ANOVAs were used to quantify the variation in vBMD across sites in female PMHS for trabecular and total bone. Fem-N Inf and Sup cortical sites were compared using a paired t-test. Investigations into the relationship between vBMD at each anatomical location were conducted using univariate linear regressions. The effects of female PMHS demographics (i.e., age, height, weight, BMI) on vBMD were investigated using univariate linear regressions. Lastly, comparisons between previously reported male data [18] and female vBMD from comparable sites were conducted using two-sample t-tests.

III. RESULTS

Female variation in vBMD

All vBMD values were normally distributed ($p>0.05$). Descriptive statistics for female vBMD are provided in Table III. Repeated measures mixed model ANOVA results for trabecular and total vBMD indicated significant variation in vBMD across anatomical sites (Table IV). When comparing the pattern of inter-site variation between sexes, dissimilar to trends observed in males [18], females did not demonstrate any differences in either Tb or total vBMD across the lumbar spine ($p>0.143$). In general, Fem-N Tb and total vBMD values were higher than any other anatomical site in both sexes (Fig. 2). Additionally, Fem-N Inf Ct vBMD was significantly higher than Fem-N Sup Ct vBMD (paired t-test; $p<0.01$) in female PMHS. This pattern was also noted in male PMHS [18] and reflects the compressive loading environment of the inferior cortex of the femoral neck stimulating greater accumulation of bone mineral than the superior cortex experiencing mainly tensile loads. With the exception of L2 and Rad-4, Tb vBMD appeared to be more consistent between the lumbar spine and the distal appendices (Rad-4 and Tib-4; $p>0.205$; Table IV). However, this was not the case for Total vBMD perhaps due to the inclusion of cortical bone within the segmentation of the Total VOI ($p<0.001$) with the exception of the Tib-4 and Rad-4 ($p=0.168$) sites (Table IV). Despite the widely different loading environments of these sites where the Tib-4 is considered weight-bearing and Rad-4 is non-weight-bearing and under the influence of complex muscle effects for precise hand and wrist movements, their resulting Tb and Total vBMD values do not vary. These similarities were also reported for male PMHS [18].

TABLE III
SITE-SPECIFIC FEMALE vBMD DESCRIPTIVE STATISTICS (N=70)

Site	Bone Type	Mean ± SD (mg/cm^3)	Min (mg/cm^3)	Max (mg/cm^3)
L2†	Tb	210.5 ± 29.2	147.4	308.5
	Total	293.8 ± 42.0	211.3	395.2
L3	Tb	214.8 ± 34.3	161.2	335.6
	Total	303.4 ± 44.3	222.8	438.7
L4	Tb	221.7 ± 34.3	138.6	337.0
	Total	306.4 ± 43.3	233.6	412.0
Fem-N*	Tb	299.2 ± 38.2	218.6	372.0
	Total	469.2 ± 72.3	339.6	714.0
	Inf Ct	1085.3 ± 82.5	818.4	1267.7
	Sup Ct	800.1 ± 85.5	611.7	1039.2
Tib-4*†	Tb	215.8 ± 39.7	156.6	370.5
	Total	242.9 ± 38.8	189.8	391.8
Rad-4*	Tb	225.2 ± 36.2	145.4	314.4
	Total	260.5 ± 48.3	148.1	409.5

**Left element only Tb= trabecular; Ct= cortical. †n=69 (PMHS removed for preexisting fracture callus)*

TABLE IV
INTER-SITE COMPARISONS FOR FEMALE TRABECULAR AND TOTAL vBMD

Skeletal Sites		*Post-hoc* Tukey		Linear Regression			
		Trabecular	Total	Trabecular		Total	
		p-value	p-value	p-value	R^2 (%)	p-value	R^2 (%)
L2	*Fem-N*	**<0.001**	**<0.001**	**<0.001**	19.3	0.406	1.03
L3	*Fem-N*	**<0.001**	**<0.001**	**<0.001**	31.8	0.868	0.04
L4	*Fem-N*	**<0.001**	**<0.001**	**<0.001**	29.6	0.880	0.03
Rad-4	*Fem-N*	**<0.001**	**<0.001**	**<0.001**	24.9	0.519	0.61
Tib-4	*Fem-N*	**<0.001**	**<0.001**	**<0.001**	28.2	0.615	0.38
L2	*L3*	0.976	0.818	**<0.001**	52.6	**<0.001**	72.3
L2	*L4*	0.143	0.562	**<0.001**	54.0	**<0.001**	47.5
L3	*L4*	0.532	0.998	**<0.001**	67.1	**<0.001**	49.5
L2	*Rad-4*	**0.013**	**<0.001**	**<0.001**	18.2	0.052	5.5
L2	*Tib-4*	0.912	**<0.001**	**0.001**	14.7	0.059	5.3
L3	*Rad-4*	0.107	**<0.001**	**<0.001**	34.0	**<0.001**	19.7
L3	*Tib-4*	1.000	**<0.001**	**<0.001**	20.3	**0.009**	9.7
L4	*Rad-4*	0.956	**<0.001**	**<0.001**	39.5	**<0.001**	29.0
L4	*Tib-4*	0.717	**<0.001**	**0.001**	15.2	**0.001**	16.0
Tib-4	*Rad-4*	0.205	0.168	**<0.001**	26.1	**<0.001**	36.5

***Bold** = statistically significant*

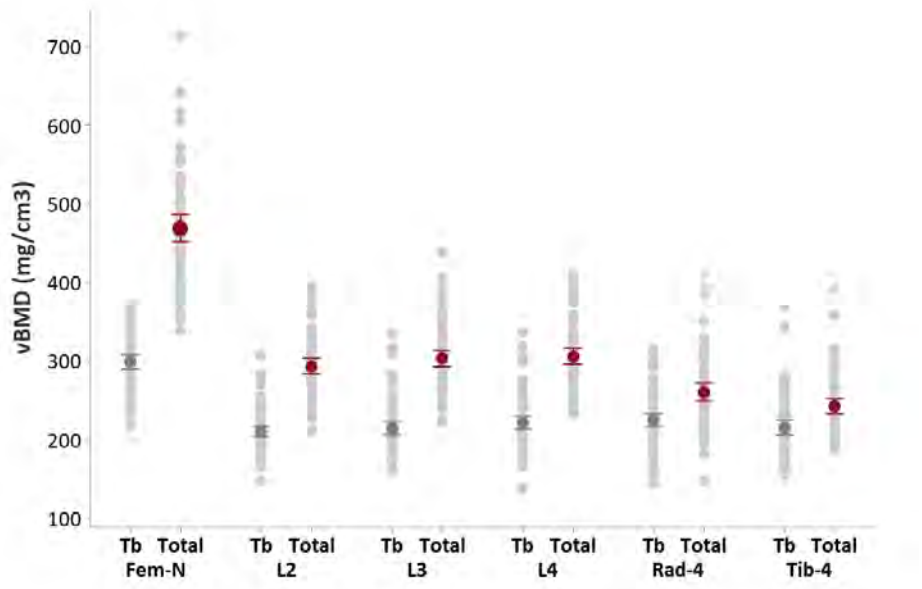


Fig.2. Interval plot (95% CI for mean) of Tb (gray) and Total (red) vBMD across sites for female PMHS. Individual data points for each site are shown in light gray.

Despite significant differences in magnitude across anatomical sites that represent the axial (lumbar spine) and appendicular (femoral neck, radius, and tibia) skeleton, linear regressions suggested some level of systemic influences on vBMD across the female skeleton. The strongest relationships were between lumbar vertebrae in both Tb and Total vBMD with R^2 values ranging from 52.6-67.1% and 49.5-72.3%, respectively (Table IV; Fig. A1). The relationship between femoral neck cortices (Inf and Sup) was significant ($p<0.001$) but less strong (R^2=35.6%) than those in the anatomical region of the lumbar spine. Overall, in female PMHS, trabecular vBMD from any site was able to predict trabecular vBMD from another site ($p<0.01$); however, the strength of these relationships varied with R^2 values ranging from 14.7-67.1% (Table IV). Total vBMD demonstrated fewer predictable relationships between sites (Table IV) which were generally weaker than the Tb comparisons (e.g., for the L4 and Rad-4 relationship, Tb R^2=39.5 whereas Total R^2=29.0) (Fig. 3). When comparing across sites outside of the lumbar spine, Tib-4 Total vBMD explained the most variation in vBMD at the Rad-4 site (R^2=36.5) despite their differences

in loading environment (Table IV, Fig. 3). In the weight-bearing lower extremity, Fem-N Tb vBMD predicted Tib-4 Tb vBMD ($p<0.001$; $R^2=28.2$); however, with the addition of cortical bone in the VOI, there was no relationship between Total vBMD at these sites suggesting cortical bone may be adapting to load using different mechanisms (Table IV; Fig. 4). All remaining regressions can be found in Fig. A1 through Fig. A5.

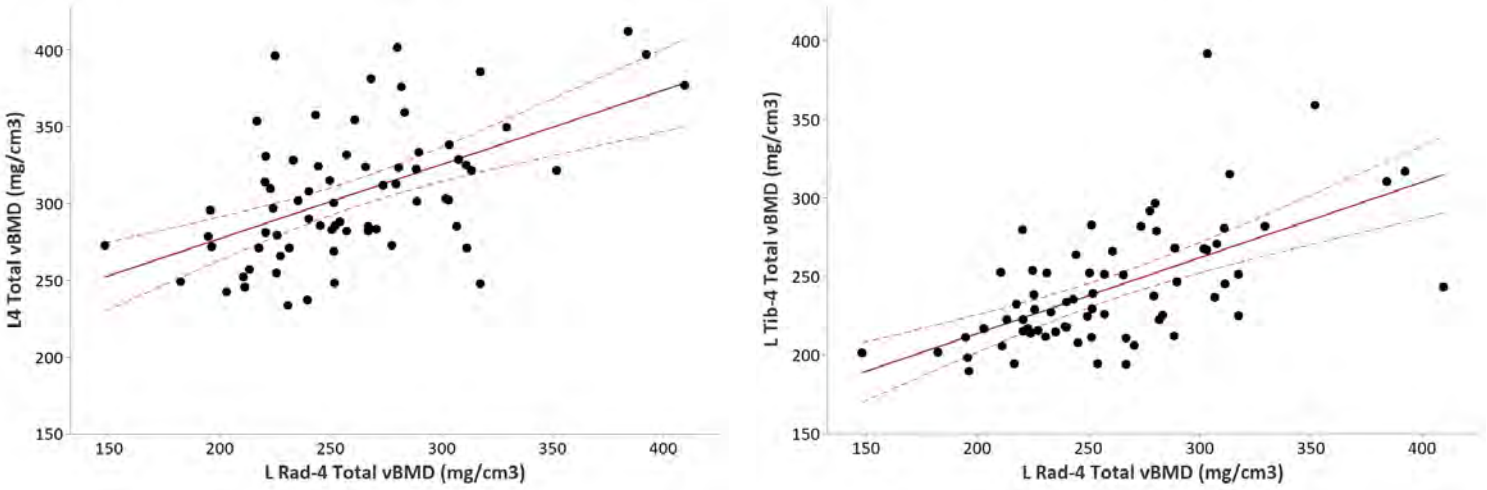


Fig. 3. Total vBMD linear regressions for the strongest relationships between sites that are not considered part of the same anatomical region (i.e., lumbar spine). Left: L4 and Rad-4 ($p<0.001$; $R^2=29.0$). Right: Tib-4 and Rad-4 ($p<0.001$; $R^2=36.5$). Regression lines (red) with 95% confidence interval (dotted red lines).

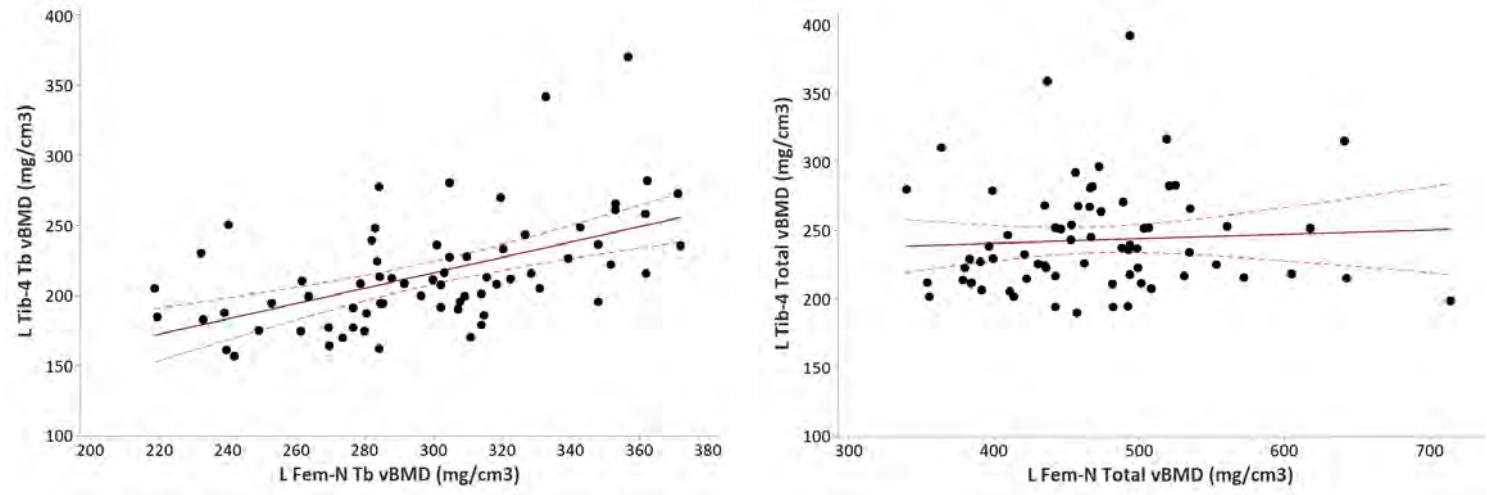


Fig. 4. Linear regressions between the weight-bearing lower extremity sites Tib-4 and Fem-N. Left: Tb vBMD ($p<0.001$; $R^2=28.2$). Right: Total vBMD ($p=0.615$). Regression lines (red) with 95% confidence interval (dotted red lines).

Female vBMD and demographic variables

Relationships between vBMD and demographics commonly used to categorize PMHS based on body size (i.e., height, weight, BMI) or make assumptions about bone quality status (i.e., age) are reported in Table V. For female PMHS, there was no biologically relevant relationship between age and BMI ($p=0.03$; $R^2=5.5\%$); thus, for a parsimonious approach, only univariate regressions were performed. Age demonstrated some effect on vBMD but inconsistently throughout the sites. In the lumbar spine, only Tb vBMD significantly declined with age ($p<0.04$) but with weak relationships ($R^2=6.36$-29.19%) across all vertebrae; whereas, only L4 Total vBMD weakly declined with age ($p=0.002$; $R^2=13.07$) (Table V; Fig. 5). Femoral neck vBMD was inconsistently predicted by age and contrary to typical aging assumptions, demonstrated a significant, albeit weak increase in Total vBMD (Table V; Fig. 6). At the distal appendicular sites, Rad-4 consistently declined with age in both Tb and Total vBMD ($p<0.009$); however, only Total vBMD at the Tib-4 site demonstrated a weak relationship with age ($p=0.02$) (Table V; Fig. 7).

TABLE V

FEMALE VBMD LINEAR REGRESSIONS WITH DEMOGRAPHIC VARIABLES

Skeletal Site	Tissue Type	Age		Height		Weight		BMI	
		p-value	R^2 (%)	p-value	R^2 (%)	p-value	R^2 (%)	p-value	R^2 (%)
L2	Tb	**0.04**	6.36	0.32	1.49	0.57	0.48	0.80	0.09
	Total	0.47	0.78	0.29	1.65	0.40	1.08	0.53	0.59
L3	Tb	**0.004**	11.37	0.49	0.70	0.20	2.40	0.17	2.74
	Total	0.21	2.26	0.56	0.50	0.47	0.78	0.45	0.84
L4	Tb	**<0.001**	26.19	0.25	1.99	0.06	5.30	0.052	5.42
	Total	**0.002**	13.07	0.53	0.57	0.18	2.67	0.14	3.21
Fem-N	Tb	0.57	0.47	0.12	3.53	**0.03**	6.62	**0.04**	6.30
	Total	**0.02**	7.86	0.82	0.08	0.22	2.25	0.08	4.53
	Inf Ct	0.24	2.02	0.08	4.40	0.14	3.18	0.29	1.64
	Sup Ct	0.07	4.69	0.13	3.41	0.08	4.44	0.13	3.37
Tib-4	Tb	0.79	0.11	0.88	0.03	0.48	0.74	0.28	1.75
	Total	**0.02**	7.82	0.75	0.15	0.32	1.49	0.22	2.27
Rad-4	Tb	**0.009**	9.73	**0.008**	9.95	**0.01**	9.09	0.07	4.77
	Total	**0.001**	16.34	0.11	3.75	**0.009**	9.69	**0.01**	9.27

***Bold** = statistically significant*

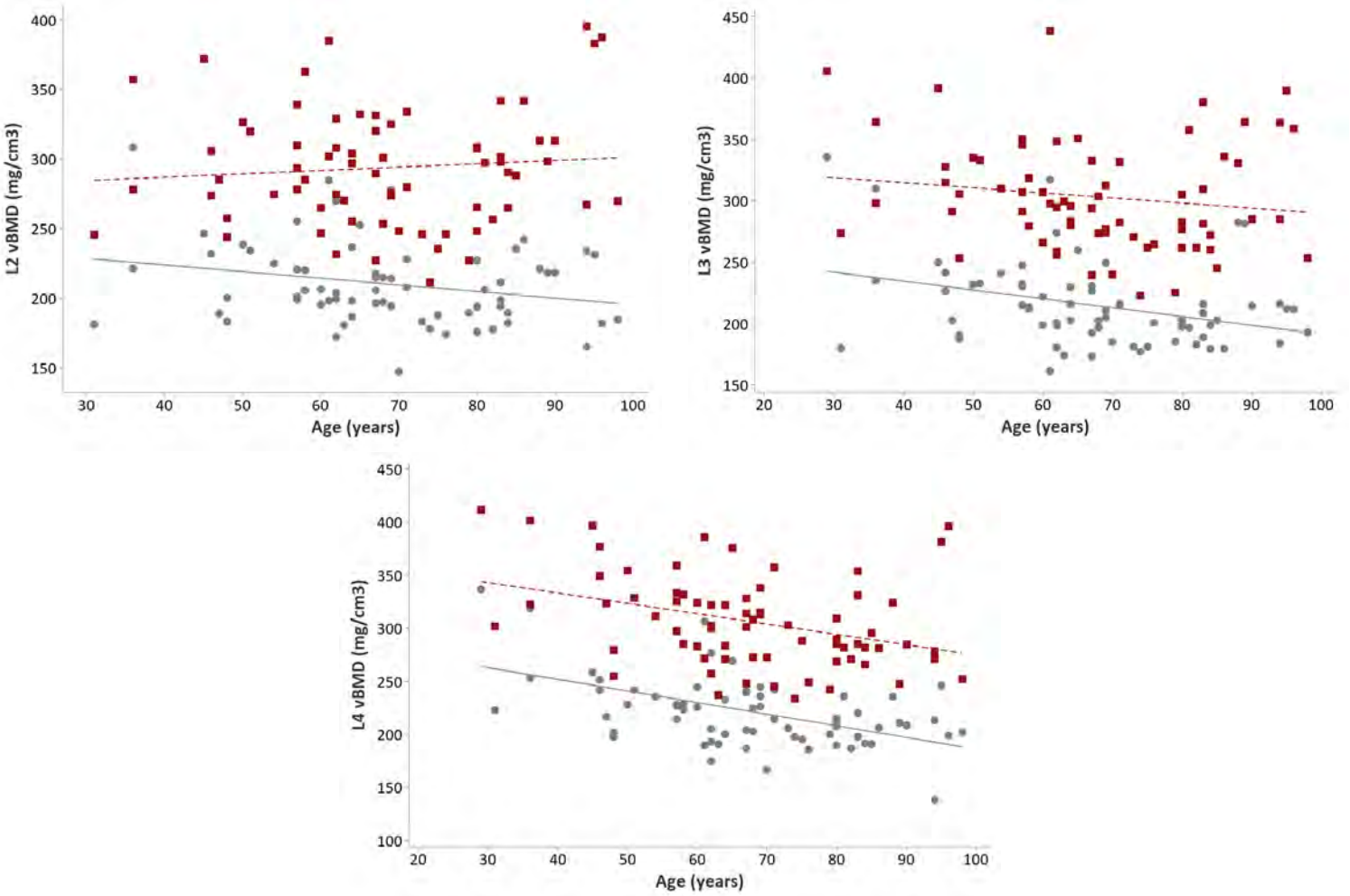


Fig. 5. Lumbar spine linear regressions with age for Tb (gray) and Total (red) vBMD. Top left: L2 Tb vBMD (0.04; R^2=6.36) and Total vBMD (p=0.47). Top right: L3 Tb vBMD (p=0.004, R^2=11.37%) and Total vBMD (p=0.21). Bottom center: L4 Tb vBMD (<0.001; R^2=26.19%) and Total vBMD (p=0.002, R^2=13.07).

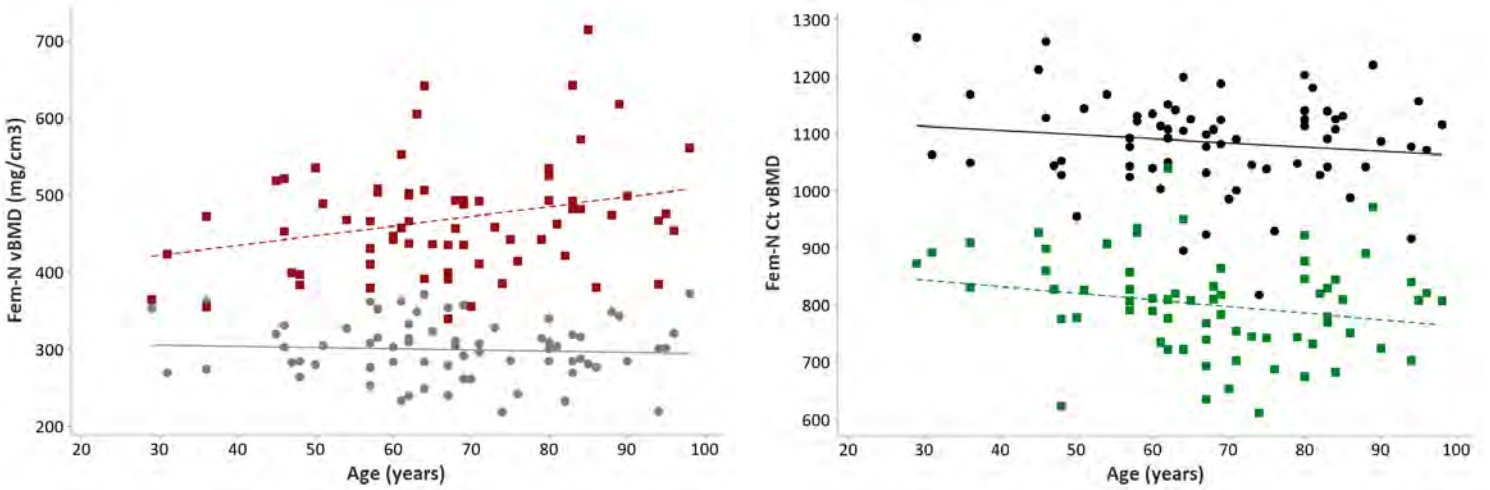


Fig. 6. Femoral neck linear regressions with age. Left: Tb vBMD in gray ($p<0.57$) and Total vBMD in red ($p=0.02$; $R^2=7.86$). Right: Inf Ct vBMD in black ($p=0.24$) and Sup Ct vBMD in green ($p=0.07$).

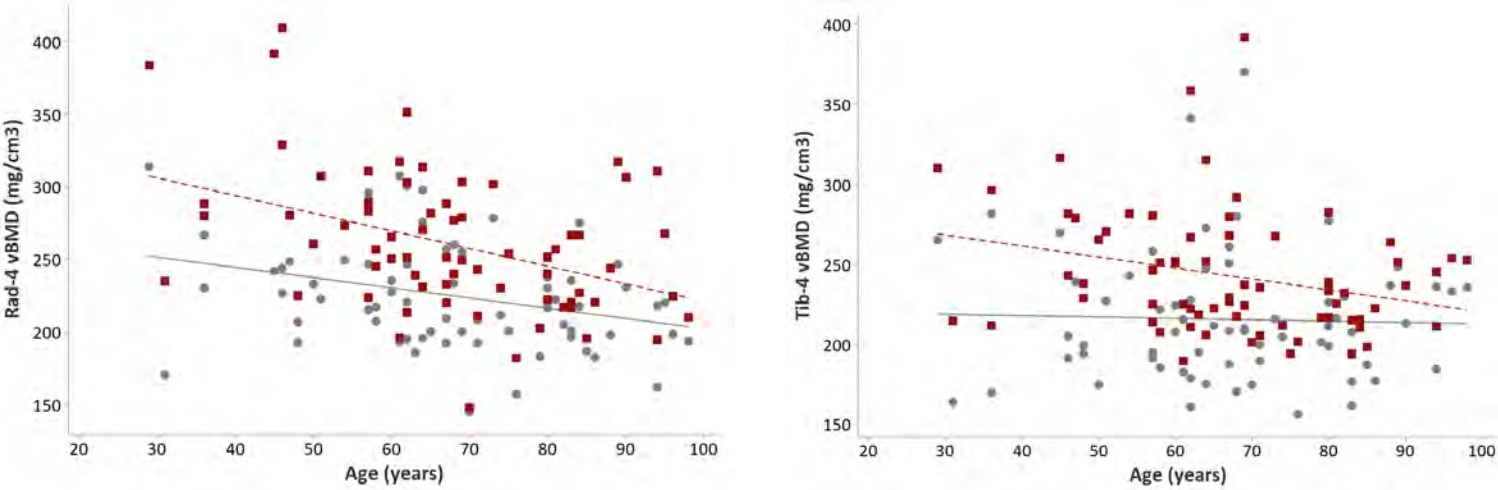


Fig. 7. Rad-4 and Tib-4 linear regressions with age. Left: Rad-4 Tb vBMD in gray ($p=0.009$; $R^2=9.73$) and Total vBMD in red ($p=0.001$; $R^2=16.34$). Right: Tib-4 Tb vBMD in gray ($p=0.079$) and Total vBMD in red ($p=0.02$; $R^2=7.82$).

The distal radius site was the only anatomical location where body size variables demonstrated multiple significant, albeit weak, relationships with vBMD (Table V; Fig. 8). Rad-4 Tb and Total vBMD R^2 values from regressions with body size were consistently less than 10% which indicated a large amount of variation in vBMD was unexplained by height, weight, or BMI. The only weight-bearing site that reflected a significant increase in vBMD with weight and BMI was Fem-N Tb ($p=0.03$ and 0.04, respectively) but with non-biologically relevant R^2 values of 6.62% and 6.30%, respectively (Fig. 9). Any Fem-N VOI that included cortex (Total, Inf Ct, and Sup Ct) had no relationship with body size in this female PMHS sample (Table V). The distal weight-bearing site, Tib-4, demonstrated no relationships with body size ($p>0.22$) (Table V; Fig. 10). See Figs. A6 through A8 for linear regressions between body size and vBMD not depicted here.

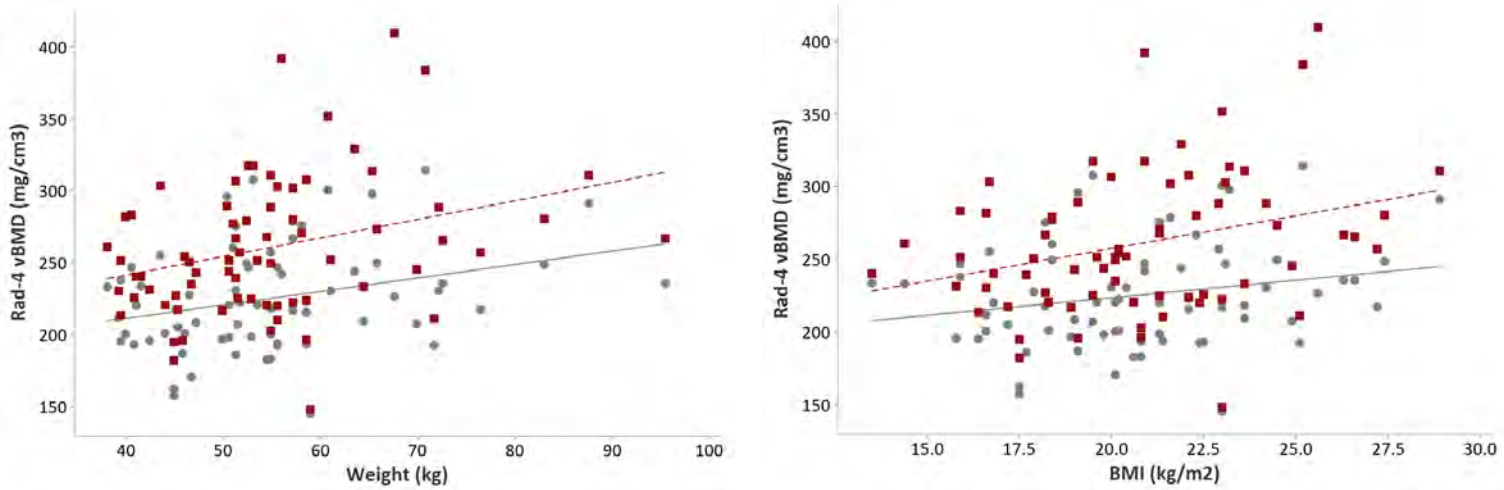


Fig. 8. Rad-4 linear regression with body size variables. Left: Rad-4 Tb vBMD in gray (p=0.01; R^2=9.09) and Total vBMD in red (p=0.009; R^2=9.69) with weight. Right: Rad-4 Tb vBMD in gray (p=0.07) and Total vBMD in red (p=0.01; R^2=9.27) with BMI.

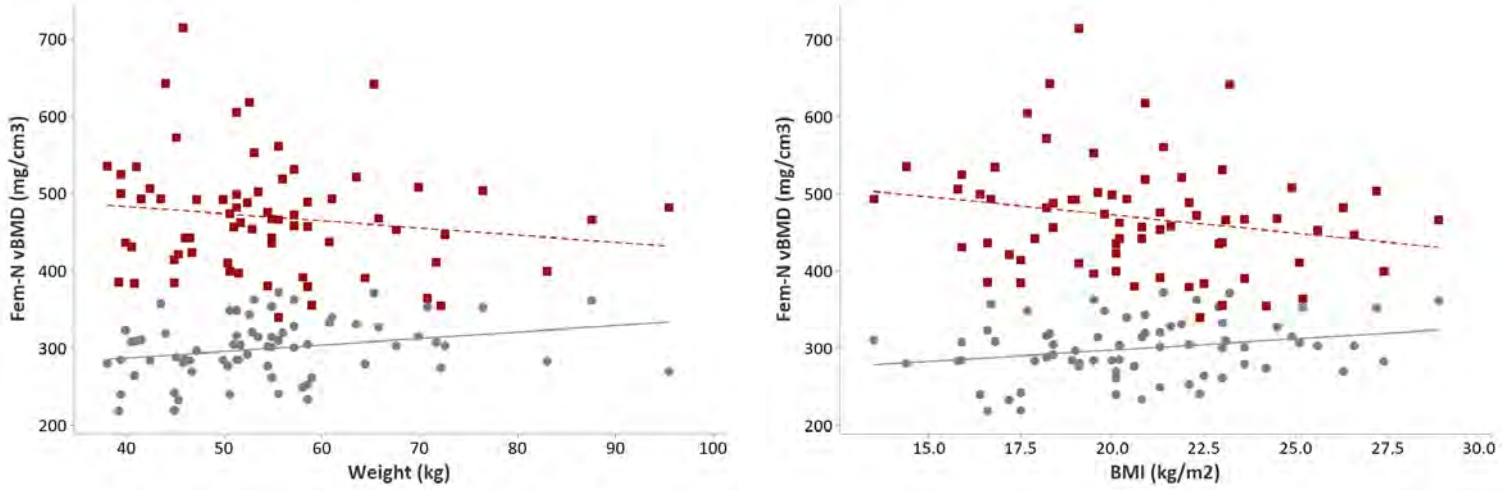


Fig. 9. Fem-N linear regression with body size variables. Left: Fem-N Tb vBMD in gray (p=0.01; R^2=9.09) and Total vBMD in red (p=0.009; R^2=9.69) with weight. Right: Fem-N Tb vBMD in gray (p=0.07) and Total vBMD in red (p=0.01; R^2=9.27) with BMI.

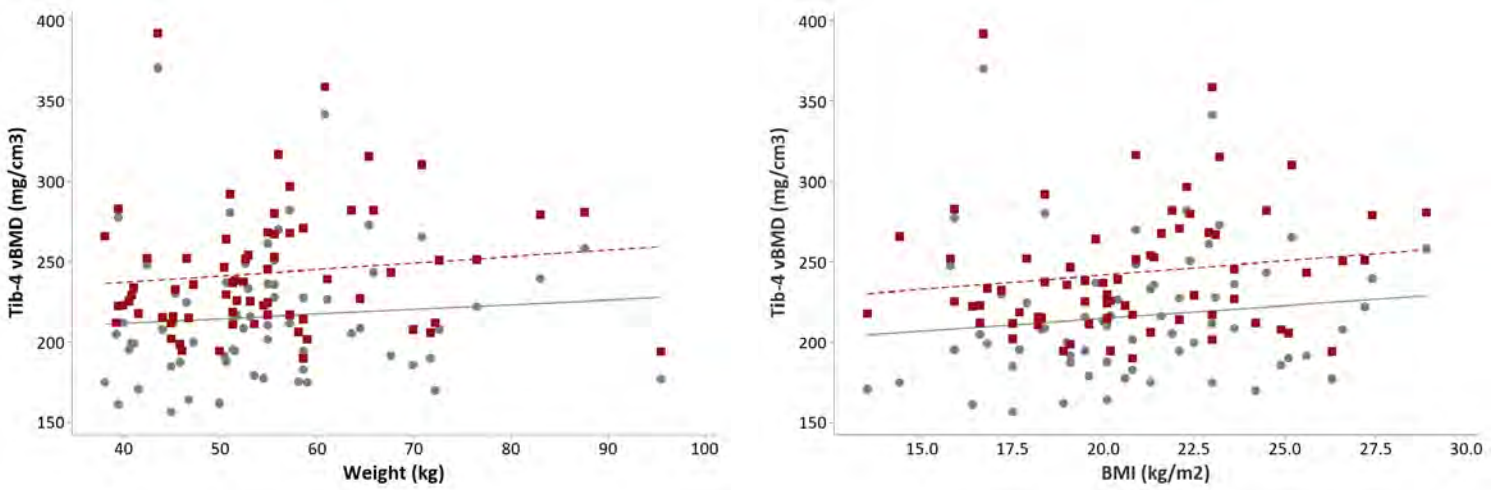


Fig. 10. Tib-4 linear regression with body size variables. Left: Rib-4 Tb vBMD in gray (p=0.48) and Total vBMD in red (p=0.32) with weight. Right: Tib-4 Tb vBMD in gray (p=0.28) and Total vBMD in red (p=0.22) with BMI.

Female vs. male vBMD comparisons

The previously reported male PMHS sample [18] was significantly younger (62.0 ± 14.5 years) than the female (67.7 ± 16.1) PMHS sample (p=0.03) utilized in this study; however, their distribution and range of ages (Fig. 11) permitted direct comparisons between sexes. As expected, males were significantly heavier (weight: p<0.01), taller (height: p<0.01), and had larger BMIs (p<0.01; Fig. 11) than females.

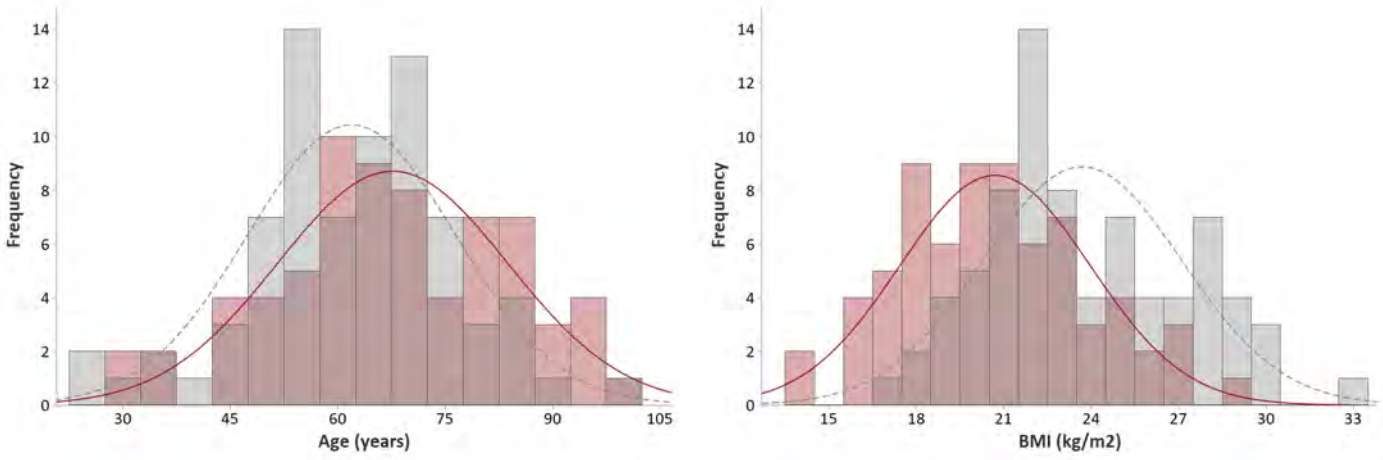


Fig. 11. Histogram of female (red; n=70) and male (gray; n=76 reported in [18]) age distribution (left) and BMI (right).

Two-sample t-tests showed no significant differences in vBMD between males and females at L3 (p>0.24) for either tissue type, L2 Total (p=0.46), or L4 Tb (0.06) (Table VI; Fig. 12). Males had higher vBMD values in the distal appendicular sites (Tib-4 and Rad-4) in both tissue types (Fig. 12). Conflicting patterns in sex differences in vBMD across tissue types occurred in the femoral neck. Males and females were most similar in Tb vBMD (p=0.15) with females on average demonstrating larger values than males (Table VI; Fig. 12). Females were significantly larger than males in both Total vBMD (p<0.001) and in the Inf Ct vBMD (p<0.001) with average magnitude differences of 63.4 mg/cm^3 and 86.4 mg/cm^3, respectively (Table VI; Fig. 13). Conversely, male Fem-N Sup Ct was significantly larger than females (p<0.001) by an average of 42.5 mg/cm^3 (Table VI; Fig. 13).

TABLE VI
FEMALE VS. MALE VBMD COMPARISONS

Skeletal Site	Tissue Type	Two-sample T-test	
		T-value*	p-value
L2	Tb	-2.2	**0.03**
	Total	-5.2	0.46
L3	Tb	-6.5	0.24
	Total	-4.2	0.54
L4	Tb	-10.52	0.06
	Total	-16.43	**0.02**
Fem-N	Tb	9.8	0.15
	Total	63.4	**<0.001**
	Inf Ct	86.4	**<0.001**
	Sup Ct	-42.5	**0.001**
Tib-4	Tb	-30.8	**<0.001**
	Total	-50.9	**<0.001**
Rad-4	Tb	-15.3	**0.02**
	Total	-44.3	**<0.001**

***Bold** = statistically significant*
**Positive T-values: females>males*

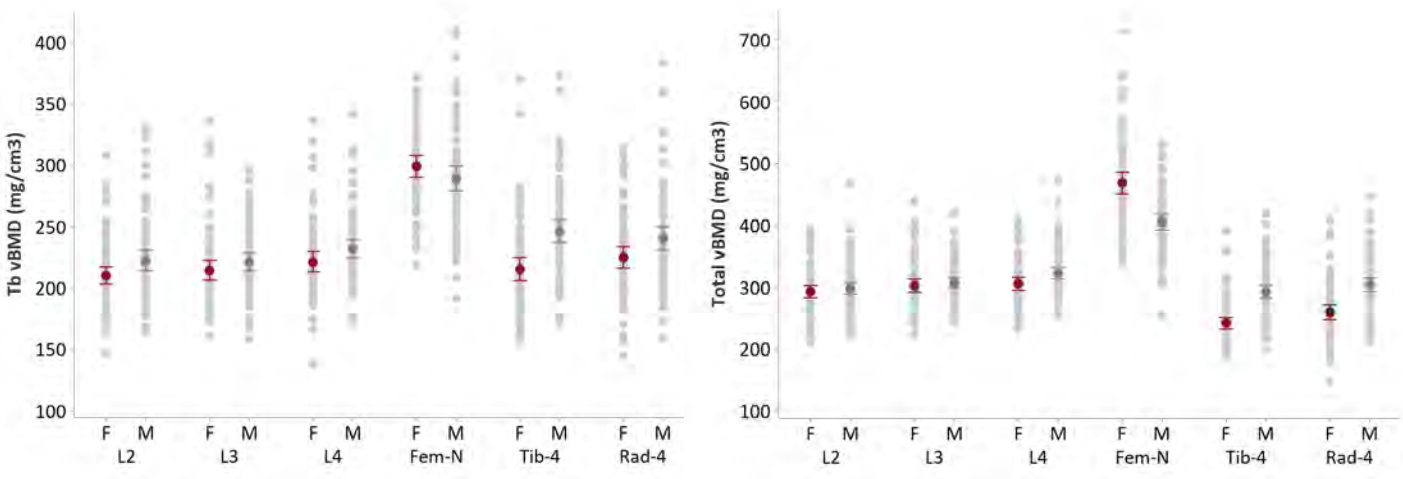


Fig. 12. Interval plots (95% CI for mean) for Tb (left) and total (right) vBMD for females (red) and males (gray). Individual data points for each site are shown in light gray.

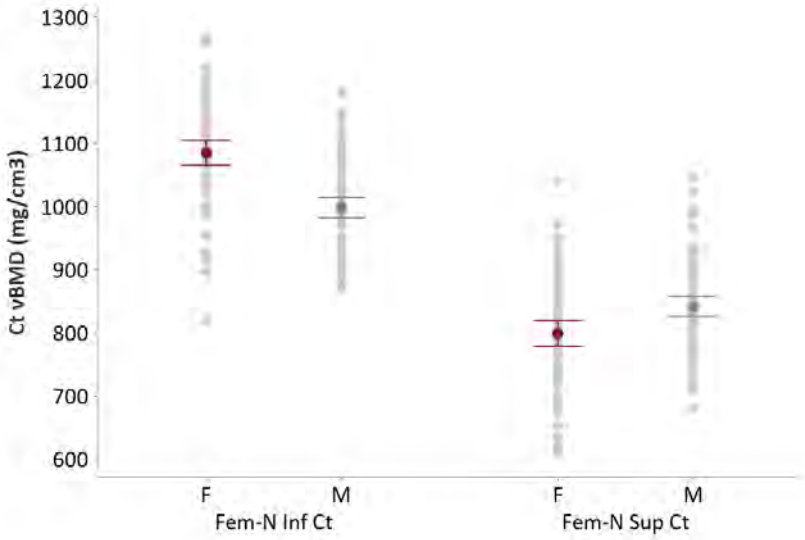


Fig. 13. Interval plots (95% CI for mean) for Ct vBMD for females (red) and males (gray). Individual data points for each site are shown in light gray.

IV. Discussion

Before successful amelioration of injury risk inequities between sexes can be accomplished, it is crucial to quantify the sex-based differences in skeletal physiological traits including vBMD in PMHS used for developing and evaluating safety tools. In this study, intra-skeletal variation in vBMD was identified in female PMHS and compared to male PMHS patterns reported in [18]. Both male and female PMHS samples represented a large range of variation in individuals that may be selected for experimental testing in the field of injury biomechanics. In general, female PMHS demonstrated similar variation across anatomical regions as male PMHS; however, these varied by tissue type. Female lumbar spine vBMD values were more similar than in males where L4 was reported as significantly greater than L2 in Total vBMD but not Tb vBMD [18]. Comparisons between the lumbar spine and the distal extremities (Rad-4 and Tib-4) demonstrated more similar Tb but not Total vBMD for females suggesting the inclusion of cortical bone in the Total VOI overshadowed the similarities in the Tb bone across sites (Table IV). Dissimilarly in males, there appear to be more differences between both tissue types (Tb and Total) when comparing these body regions [18]. The femoral neck (Tb and Total) vBMD were consistently higher than any axial or appendicular site in females (Fig. 2) which was also the case in males [18]. Additionally, both sexes

demonstrated a higher Inf Ct than Sup Ct vBMD which aligns with the localized compressive load experienced by the inferior cortex in contrast to the tensile loading of the superior cortex characteristic of bipedalism [21-23]. Although a large body of vBMD literature exists for each anatomical site analyzed in this study, few studies incorporate all sites into their analyses due to the nature of radiation exposure in living populations. Often these studies employ non-comparable thresholding vs. non-thresholding methods, particularly for trabecular and total VOIs, which can influence results. For example, [24] demonstrated significant differences in Tb vBMD across a small sample of female PMHS but did not utilize thresholding techniques so that bone marrow and adiposity were included in their vBMD values. Thus, the heterogeneity of Tb vBMD across the skeleton in their study, where the femoral neck region was not significantly higher than other sites, does not match the intra-skeletal variation found here where methods intentionally isolate only bone voxels. Regardless, heterogeneity in vBMD appears to persist across sexes. Given that recent genomic work has found that the heritability of BMD varies across anatomical locations within individuals and are differentially affected by genetic and environmental (e.g., mechanical loading) factors [25], the intra-individual variation found here and in [18] is unsurprising, though some of the differences in trends observed between sexes may indicate key sex hormone effects on BMD that may impact differential injury risk.

Epidemiological studies using dual x-ray absorptiometry (DXA) areal BMD (aBMD) to predict low-energy fractures suggest that the relative risk of fracture can be inferred from non-site specific values of BMD due to intra-skeletal correlations [26]. As vBMD has been shown to outperform aBMD in characterizing bone quality [27] and predicting fragility fractures [28] in addition to characterizing different aspects of bone than DXA [29], the role of vBMD variability and the predictive relationships between sites needs further investigation. The results presented here for females suggest weakly related vBMD across the lumbar spine, femoral neck, distal radius, and distal tibia. Similar to males [18], female vertebral levels (L2-L4) have the strongest relationships in both Tb (R^2=52.6-67.1%) and Total (R^2=49.5-72.3%) vBMD which is to be expected given the consistent mechanical loading environment of the spine bearing the weight of the torso, upper extremities, and head/neck. However, whereas males demonstrated significant relationships between the femoral neck and all other sites in Total vBMD [18], female Fem-N Total vBMD was not predictive of vBMD in the lumbar spine, radius, or tibia (Table IV; Fig. AII). Again, this suggests a female-specific sensitivity to localized mechanical loading by cortical bone included in the Total vBMD VOI. Trabecular bone demonstrated more inter-site relationships potentially due to its higher sensitivity to systemic influences (e.g., circulating hormones, inflammatory status, aging processes, etc.) with evidence suggesting early-onset loss in trabecular but not cortical bone in both sexes [30]. In almost all relationships (Table IV), trabecular R^2 values were higher than Total vBMD in females further supporting the similar role of systemic factors, regardless of localized mechanical loading, on Tb bone. Importantly, these physiologic processes have sex-based hormonally driven differences which reinforces the need to characterize bone quality and injury risk with respect to sex and in a site-specific manner when evaluating safety tools using PMHS.

Common assumptions concerning the effects of demographic variables on bone include losses or decreasing values with increasing age, and that larger body sizes would be associated with “stronger” bones to support the increased mass. However, the results reported here suggest these assumptions, often used to predict injury outcomes, should be investigated more carefully in PMHS. Increasing age did not consistently predict decreasing vBMD across sites (Table V; Figs. 4-6); in fact, Fem-N Total vBMD significantly increased with age in this sample. Due to the nature of a PMHS sample, this study was unable to assess the effects of increasing age in the same individuals which is quantifiable in a living population through longitudinal data collection. Previous work has highlighted the age-related decline in vBMD in the radius, tibia, and lumbar spine [31], but it is suggested this pattern is not consistent across sites nor does it follow similar trajectories in males [32]. Longitudinal studies on older, postmenopausal females found a 1.8- and 6-fold greater loss in Total and Tb vBMD, respectively, at the distal radius compared to the distal tibia [33]. Although rates of loss with age could not be directly assessed in this PMHS sample, the Rad-4 site did demonstrate stronger relationships with age than the Tib-4 site (Table V). However, previous experimental PMHS testing has questioned the importance of chronological age in assumptions about bone strength in the human rib [34]. In this study (Table V), the highest R^2 value was only 29.2% (L4 Total vBMD) indicating a large amount of the variation in vBMD between individuals was not explained by chronological age. Meanwhile, despite known increases in intracortical porosity with age, neither the Inf Ct nor the Sup Ct vBMD values were predicted by age ($p>0.07$) perhaps suggesting a compensatory mechanism of

maintaining mineralization to offset increased porosity. Supporting earlier discussions of the differential response of trabecular and cortical bone mentioned above, evidence suggests age-related declines in Tb vBMD varied from Ct vBMD in their age-at-onset, severity, and interactions with hormonal changes between sexes [31].

Meanwhile, the role of body size in predicting vBMD was underwhelming in almost all sites in this study (Table V). The current sample, although spanning a large range of body sizes (Fig. 11) did not include a large representation of obese individuals where effects on vBMD have been previously demonstrated [35] which may be the source of the observed weak relationships. The increased fracture risk associated with females of very low or very high body weight or BMI classification has been demonstrated with respect to low-energy fragility fractures [36]. Although there is a positive association between bone quality and lean muscle mass [37], the relationship between mass and BMD is complicated including an interaction with race [38] as well as the role of tissue type constituting the mass (lean vs. fat) neither of which were investigated here. Recently, it was suggested that rather than BMI or weight alone, an appropriate ratio of lean mass (i.e., skeletal muscle) to visceral fat mass positively influences BMD in both sexes [39]. In this study, body size parameters were restricted to those simply obtained and often used to categorize safety tools (height and weight) and the popular combination of these variables, BMI. The overall lack of relationships between these variables and vBMD in the female PMHS sample supports the assertion that more discriminate assessment of body size is likely needed to identify relationships with bone quality. The distal radius (Rad-4) seems to be the only region analyzed that was sensitive to the influence of body size variables suggesting future work could leverage this site for correlations between body size and physiologic causes of injury risk. Reference [18] did not report the male relationships between multi-site vBMD and age or body size for comparison. These are necessary to address recent work by [6] suggesting the increased female lower extremity injury risk relative to males may be complicated by BMI rather than only physiologic reasons. There is likely a complex relationship between body size and overall bone quality that is influenced by sex hormones and tissue type (lean vs. fat mass) which further contributes to the elevated injury risk of higher BMI individuals due to increased mass interacting with the vehicle interior during crash scenarios. These differences should be investigated in future work that can include more PMHS in the obese body size classification and a more discriminate measure of body mass by tissue type to quantify sex-mediated effects of demographic variables on vBMD in PMHS and elucidate the biological role of body size on injury risk.

Sex differences in vBMD were inconsistent across the skeleton. The male PMHS sample from [18] was significantly larger in body size than the females in this study. Despite differences in body size, the lumbar spine vBMD were similar between sexes in both tissue types with the exception of L2 Tb vBMD and L4 Total vBMD (Table VI; Fig. 12). It may be that mineralization is relatively conserved despite differences in magnitudes of weight-bearing across individuals possibly due to the immobile and supportive function of the lumbar spine. Conversely, males had consistently larger vBMD at the non-weight-bearing Rad-4 and the weight-bearing Tib-4 sites (Table VI; Fig. 12). The magnitude of differences between sexes were larger in the Total vBMD with males on average 44.3 mg/cm^3 and 50.9 mg/cm^3 larger than females at Rad-4 and Tib-4, respectively, than in the trabecular tissue type (15.3 mg/cm^3 and 30.8 mg/cm^3, respectively). As mentioned above in the intra-skeletal variation patterns between males and females, these results suggest that cortical bone may be driving these differences as it is included in the Total VOI, and trabecular bone may be more similar between sexes as evidenced by the Fem-N Tb vBMD ($p=0.15$). The differences in cortical bone are inconsistent in the femoral neck. Interestingly, females had significantly higher values of Total and Inf Ct vBMD but lower values of Sup Ct vBMD than males (Table VI; Fig. 12). Higher Total vBMD in the femoral neck of females has been previously reported [40] and persists across races [41]. Unlike the results reported here, [40] found higher Tb and Ct vBMD in females in a sample with a more restricted age range (40-90 years) than included in this study (29-98 years). The differences in findings between studies may be due to the more discriminant method utilized here that isolates the inferior cortex (higher in females) and superior cortex (higher in males) which may be obfuscated in [40] due to their combined Ct VOI selection. The bone functional adaptation processes that result in higher mineralization in the inferior cortex in females compared to males is not fully understood. Recent work has found that external geometry at the femoral neck results in different compensatory mechanisms in narrow compared to wide bones with varying effects on strength [14][42][43] which may contribute to the observed differences here. Although, the role of geometry was not explored in this study, future work should include sub-sampling sex-based external geometry groups to explore differences in vBMD.

Since vBMD has performed as well as finite element models for predicting clinical fragility fracture [44], it could

be used for exploring sex-specific injury risks in human body models (HBM). However, much of the evidence associated with the role of vBMD in resistance to fracture is concentrated on aging, clinical populations sustaining low-energy fragility fractures. It is unknown how intra-skeletal variation in vBMD, and the sex differences identified in this study, will affect site-specific injury tolerances in dynamic loading scenarios that are more representative of motor vehicle crashes. Future work must contextualize the biological relevance of vBMD in fracture resistance through experimental whole-body and component PMHS testing. The data provided here and in [18] will provide a PMHS specific vBMD dataset in which these experimental results could be contextualized. This was preliminarily explored in [29] for male PMHS on a small, whole-body experimental sample with respect to number of rib fractures, but investigations should be expanded to varied loading scenarios and inclusive of female PMHS. Additionally, despite significant differences in vBMD between sexes at some anatomical sites, there is a substantial amount of overlap in the data (Figs. 12-13) suggesting complementary variables quantifying other aspects of bone quality (e.g., cross-sectional geometry) may be necessary to include when investigating injury risk disparities between male and female PMHS particularly in HBMs. When predicting injury outcomes from experimental testing, future work should investigate the inclusion of morphological data with vBMD when performing QCT analyses of PMHS. Furthermore, although the male [18] and female PMHS samples in this study included a wide range of ages and body sizes, they were opportunistic samples with more mid-size males and small females than other body size categories. Results from this study should be further explored within a larger PMHS sample that is more inclusive of a diverse occupant population, particularly in body size measures. This study supports the previously reported importance of considering site-specific analyses of skeletal injury risk [18][45] but was limited to only four anatomical sites. To further pursue this area of study, female vBMD should be collected for additional body regions where real-world crash data indicate persistent injuries such as the thorax, and in recent experimental work highlighting alternative seating arrangements associated with automated driving systems, the pelvis [46][47].

V. CONCLUSIONS

These results continue to support the necessity for utilizing anatomical specificity in assessing aspects of bone quality that are often used to characterize injury risk. Differences in vBMD across the body in female PMHS are not identical to previously reported male PMHS intra-skeletal variation which may have implications for interpreting injury outcomes in experimental testing or validating HBMs. Disparate effects of demographic variables such as age and body size on vBMD in the females of this PMHS sample challenge commonly held assumptions of bone. The lack of sex differences in vBMD in the lumbar spine and femoral neck (trabecular) suggests similar mechanisms of maintaining structural integrity in these regions. The higher vBMD values in female PMHS for some of the VOIs in the femoral neck portend a more discriminate approach to understanding PMHS sex differences in fracture resistance that should be combined with experimental loading mechanisms. Importantly, these results suggest that sex-based assumptions concerning the physiological underpinnings of skeletal injury risk could be expanded to include additional metrics of bone as well as additional anatomical locations such as the thorax and pelvis. Results from this study contribute to a growing body of sex-specific PMHS data in the field of injury biomechanics generated to potentially improve vehicle occupant protection by quantifying a physiologic component, vBMD, of skeletal fracture resistance.

VI. ACKNOWLEDGEMENT

The authors would like to thank the anatomical donors and the faculty, staff, and students of the Injury Biomechanics Research Center, Columbus, OH, USA. The funding for female vBMD data collection was provided by Toyota Collaborative Safety Research Center (CSRC), Ann Arbor, MI, USA.

VII. REFERENCES

[1] Atwood, J., Noh, E.Y., and Craig, M.J. Female crash fatality risk relative to males for similar physical impacts. *Traffic Injury Prevention*, 2023. 24: p. S1-S8

[2] Forman, J., Poplin, G.S., et al. Automobile injury trends in the contemporary fleet: Belted occupants in frontal collisions. *Traffic Injury Prevention*, 2019. 20(6): p. 607-612

[3] Abrams, M.Z. and Bass, C.R. Female vs. male relative fatality risk in fatal motor vehicle crashes in the US, 1975–2020. *PLoS ONE*, 2024.

[4] Brumbelow, M.L. and Jermakian, J.S. Injury risks and crashworthiness benefits for females and males: Which differences are physiological? *Traffic Injury Prevention*, 2022. 23(1): p. 11-16

[5] Kahane C. Injury vulnerability and effectiveness of occupant protection technologies for older occupants and women. *NHTSA Technical Report. Office of Vehicle Safety: National Highway Safety Association*, 2013

[6] Brumbelow, M.L. Female Driver Lower Extremity Injury: Contributing Factors and Crash Test Relevance. *Proceedings of International Research Council on the Biomechanics of Injury (IRCOBI 2023)*, 2023.

[7] Crandall, J. and Martin, P.G. Lower injuries sustained in crashes and corresponding biomechanical research. *Proceedings of International Symposium on Real World Crash Injury Research, Leicestershire, England*, 1997.

[8] Dischinger, P.C., Kerns, T.J., and Kufera, J.A. Lower extremity fractures in motor vehicle collisions: The role of driver gender and height. *Accident Analysis & Prevention*, 1995. 27(4): p. 601-606

[9] Jermakian, J.S., Arbelaez, R.A., and Brumbelow, M.L. Mapping the Path Forward Toward Equity in Crash Safety: Recommendations From an Expert Workshop. *Proceedings of 27th International Technical Conference on the Enhanced Safety of Vehicles (ESV) National Highway Traffic Safety Administration*, 2023.

[10] WHO. WHO scientific group on the assessment of osteoporosis at primary health care level. *Proceedings* 2004. Brussels, Belgium

[11] Bouxsein, M.L., Eastell, R., et al. Change in Bone Density and Reduction in Fracture Risk: A Meta-Regression of Published Trials. *Journal of Bone and Mineral Research*, 2019. 34(4): p. 632-642

[12] Whittier, D.E., Bevers, M.S.A.M., Geusens, P.P.M.M., van den Bergh, J.P., and Gabel, L. Characterizing Bone Phenotypes Related to Skeletal Fragility Using Advanced Medical Imaging. *Current Osteoporosis Reports*, 2023

[13] Szulc, P., Dufour, A.B., et al. Fracture risk based on HR-pQCT measures does not vary with age in older adults – the bone microarchitecture international consortium (BoMIC) prospective cohort study. *Journal of Bone and Mineral Research*, 2024: in press

[14] Jepsen, K.J., Bigelow, E.M.R., et al. Structural differences contributing to sex-specific associations between femoral neck bone mineral density and whole bone strength for adult white women and men. *JBMR Plus*, 2024: in press

[15] Jepsen, K.J. and Andarawis-Puri, N. The amount of periosteal apposition required to maintain bone strength during aging depends on adult bone morphology and tissue-modulus degradation rate. *Journal of Bone and Mineral Research*, 2012. 27(9): p. 1916-1926

[16] Jepsen, K.J., Bigelow, E., and Schlecht, S. Women build long bones with less cortical mass relative to body size and bone size compared with men. *Clinical Orthopaedics and Related Research*, 2015. 473(8): p. 2530-2539

[17] Hunter, R.L., Haverfield, Z., and Agnew, A.M. Investigation of Sex-specific Effects on Variation in Cortical Bone Morphometrics of the Radius. *Proceedings of Conference proceedings International Research Council on the Biomechanics of Injury, IRCOBI*, 2021.

[18] Haverfield, Z.A., Hunter, R.L., Loftis, K.L., and Agnew, A.M. Skeletal Site and Method-dependent Variability of Bone Mineral Density in Injury Biomechanics Research. *Proceedings of Conference proceedings International Research Council on the Biomechanics of Injury, IRCOBI*, 2022.

[19] Naganathan, V. and Sambrook, P. Gender differences in volumetric bone density: a study of opposite-sex twins. *Osteoporosis International*, 2003. 14(7): p. 564-569

[20] Bose, D., Maria Segui-Gomez, S., and Crandall, J.R. Vulnerability of Female Drivers Involved in Motor Vehicle Crashes: An Analysis of US Population at Risk. *American Journal of Public Health*, 2011. 101(12): p. 2368-2373

[21] Lovejoy, C.O. Evolution of Human Walking. *Scientific American*, 1988. 259(5): p. 118-125

[22] Kersh, M.E., Martelli, S., Zebaze, R., Seeman, E., and Pandy, M.G. Mechanical Loading of the Femoral Neck in Human Locomotion. *Journal of Bone and Mineral Research*, 2018. 33(11): p. 1999-2006
[23] Machado, M.M., Fernandes, P.R., Cardadeiro, G., and Baptista, F. Femoral neck bone adaptation to weight-bearing physical activity by computational analysis. *J Biomech*, 2013. 46(13): p. 2179-85
[24] Arentsen, L., Hansen, K.E., et al. Use of dual-energy computed tomography to measure skeletal-wide marrow composition and cancellous bone mineral density. *J Bone Miner Metab*, 2017. 35(4): p. 428-436
[25] Kemp, J.P., Medina-Gomez, C., et al. Phenotypic Dissection of Bone Mineral Density Reveals Skeletal Site Specificity and Facilitates the Identification of Novel Loci in the Genetic Regulation of Bone Mass Attainment. *PLOS Genetics*, 2014. 10(6)
[26] Blake, G., Knapp, K., Spector, T., and Fogelman, I. Predicting the risk of fracture at any site in the skeleton: Are all bone mineral density measurement sites equally effective? *Calcified Tissue International*, 2006. 78: p. 9-17
[27] Engelke, K., Libanati, C., Fuerst, T., Zysset, P., and Genant, H.K. Advanced CT based In Vivo Methods for the Assessment of Bone Density, Structure, and Strength. *Current Osteoporosis Reports*, 2013. 11(3): p. 246-255
[28] Gruenewald, L.D., Koch, V., et al. Diagnostic accuracy of quantitative dual-energy CT-based volumetric bone mineral density assessment for the prediction of osteoporosis-associated fractures. *Eur Radiol*, 2022. 32(5): p. 3076-3084
[29] Hunter, R.L., Haverfield, Z.A., Kang, Y.S., and Agnew, A.M. Potential Consequences of Contradictions in Bone Mineral Density Assessments in Injury Biomechanics. *Proceedings of Conference proceedings International Research Council on the Biomechanics of Injury, IRCOBI*, 2023.
[30] Riggs, B.L., Melton Iii, L.J., et al. A Population-Based Assessment of Rates of Bone Loss at Multiple Skeletal Sites: Evidence for Substantial Trabecular Bone Loss in Young Adult Women and Men. *Journal of Bone and Mineral Research*, 2008. 23(2): p. 205-214
[31] Riggs, B.L., Melton, L.J., et al. Population-based study of age and sex differences in bone volumetric density, size, geometry and structure at different skeletal sites. *Journal of Bone and Mineral Research*, 2004. 19(12): p. 1945-1954
[32] Riggs, B.L., Wahner, H.W., et al. Differential changes in bone mineral density of the appendicular and axial skeleton with aging: relationship to spinal osteoporosis. *Journal of Clinical Investigation*, 1981. 67(2): p. 328-335
[33] Johannesdottir, F., Putman, M.S., et al. Age-Related Changes in Bone Density, Microarchitecture, and Strength in Postmenopausal Black and White Women: The SWAN Longitudinal HR-pQCT Study. *Journal Bone and Mineral Research*, 2022. 37(1): p. 41-51
[34] Schafman, M., Kang, Y., et al. Age and sex alone are insufficient to predict human rib structural response to dynamic A-P loading. *Journal of Biomechanics*, 2016. 49: p. 3516-3522
[35] Cherukuri, L., Kinninger, A., et al. Effect of body mass index on bone mineral density is age-specific. *Nutrition, Metabolism and Cardiovascular Diseases*, 2021. 31(6): p. 1767-1773
[36] Johansson, H., Kanis, J.A., et al. A meta-analysis of the association of fracture risk and body mass index in women. *Journal Bone and Mineral Research*, 2014. 29(1): p. 223-33
[37] Sutter, T., Toumi, H., et al. Relationships between muscle mass, strength and regional bone mineral density in young men. *PLoS One*, 2019. 14(3): p. e0213681
[38] Johannesdottir, F., Putman, M.S., et al. Age-Related Changes in Bone Density, Microarchitecture, and Strength in Postmenopausal Black and White Women: The SWAN Longitudinal HR-pQCT Study. *Journal of Bone and Mineral Research*, 2021. n/a(n/a)
[39] Li, L., Zhong, H., et al. Association between lean body mass to visceral fat mass ratio and bone mineral density in United States population: a cross-sectional study. *Archives of Public Health*, 2023. 81(1): p. 180
[40] Srinivasan, B., Kopperdahl, D., et al. Relationship of femoral neck areal bone mineral density to volumetric bone mineral density, bone size, and femoral strength in men and women. *Osteoporosis International*, 2012. 23(1): p. 155-162
[41] Peacock, M., Buckwalter, K.A., et al. Race and sex differences in bone mineral density and geometry at the femur. *Bone*, 2009. 45(2): p. 218-225
[42] Jepsen, K.J., Kozminski, A., et al. Femoral Neck External Size but not aBMD Predicts Structural and Mass Changes for Women Transitioning Through Menopause. *Journal Bone and Mineral Research*, 2017. 32(6): p. 1218-1228

[43] Jepsen, K.J., Bigelow, E.M.R., et al. Associations Among Hip Structure, Bone Mineral Density, and Strength Vary With External Bone Size in White Women. *JBMR Plus*, 2023. 7(3): p. e10715

[44] Praveen, A.D., Sollmann, N., Baum, T., Ferguson, S.J., and Benedikt, H. CT image-based biomarkers for opportunistic screening of osteoporotic fractures: a systematic review and meta-analysis. *Osteoporosis International*, 2024

[45] Hunter , R., Haverfield, Z., Kang, Y.-S., and Agnew, A.M. Potential Consequences of Contradictions in Bone Mineral Density Assessments in Injury Biomechanics. *International Research Council on the Biomechanics of Injury Conference Proceedings*, 2023. IRC-23-131: p. 1031-1047

[46] Kang, Y.S., Stammen, J., et al. Biomechanical Responses and Injury Assessment of Post Mortem Human Subjects in Various Rear-facing Seating Configurations. *Stapp Car Crash J*, 2020. 64: p. 155-212

[47] Kang, Y.-S., Stammen, J., et al. Effects of Seatback Recline and Belt Restraint Type on PMHS Responses and Injuries in Rear-Facing Frontal Impacts. *SAE International Journal of Transportation Safety*, 2022. 10(2): p. 235-289

VIII. APPENDIX

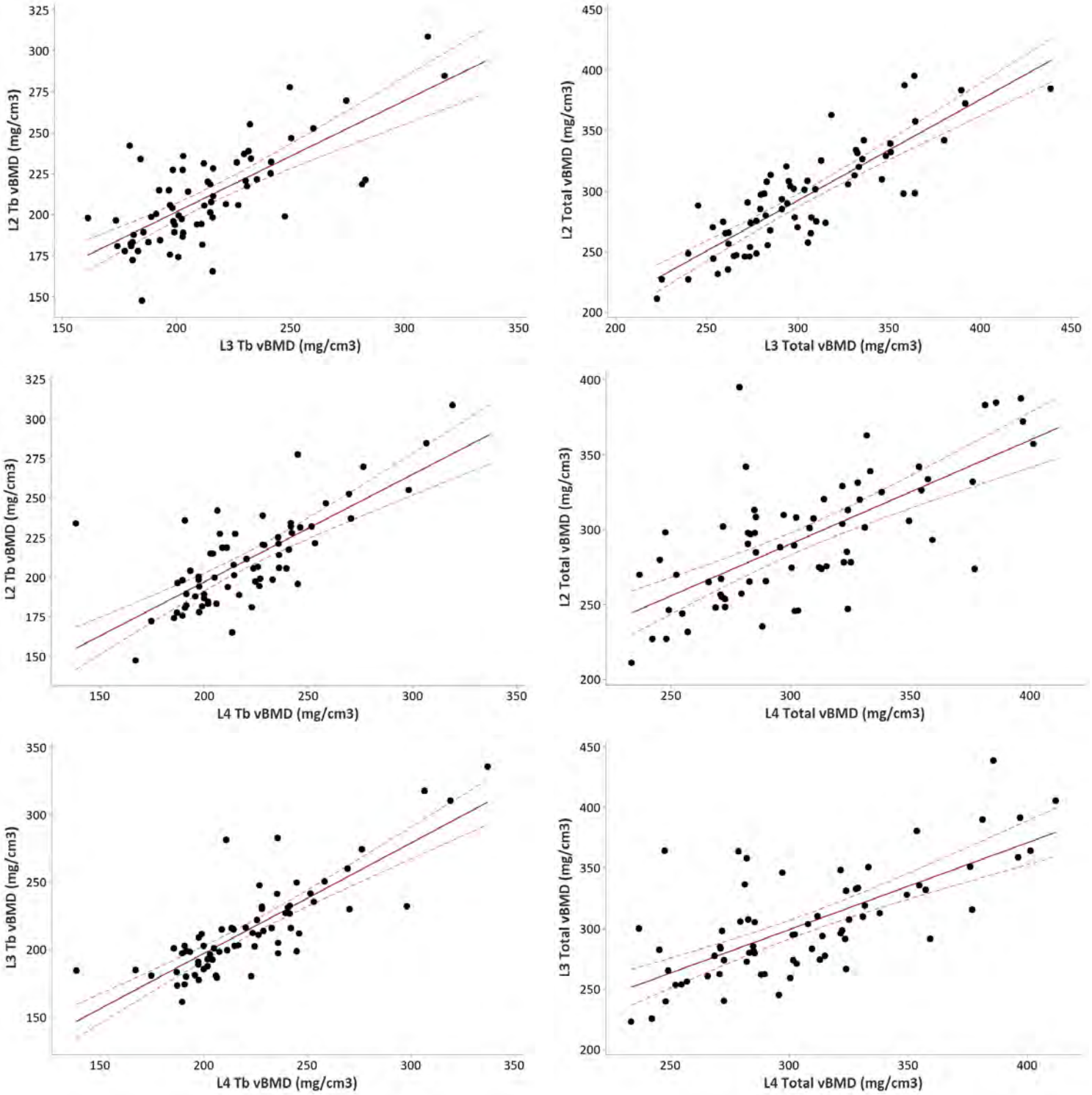


Fig. A1. Linear regressions between female lumbar spine sites vBMD (left: Tb; right: Total). Regression lines (red) with 95% confidence interval (dotted red lines).

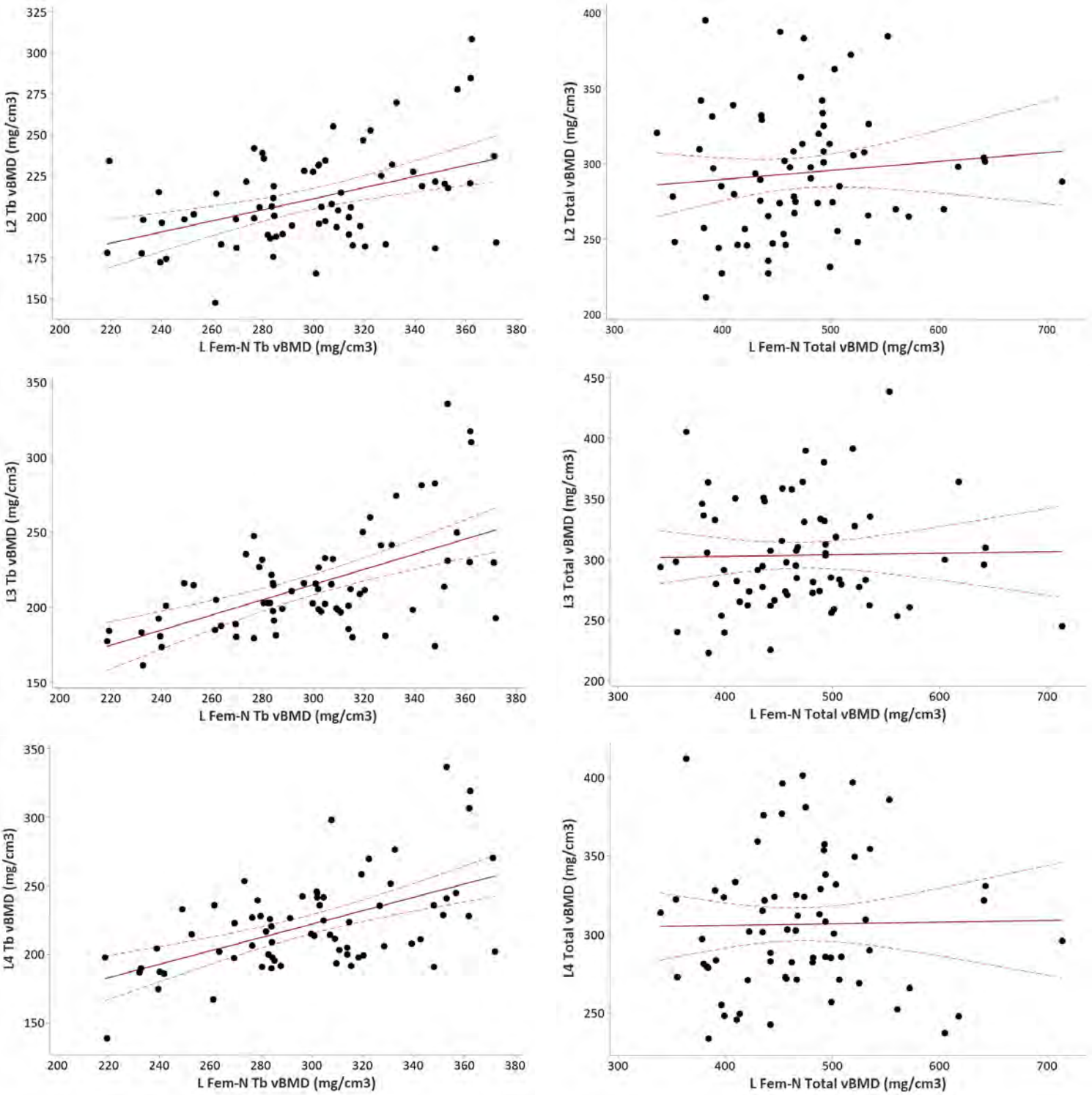


Fig. A2. Linear regressions between female lumbar spine vBMD (left: Tb; right: Total) and Fem-N. Regression lines (red) with 95% confidence interval (dotted red lines).

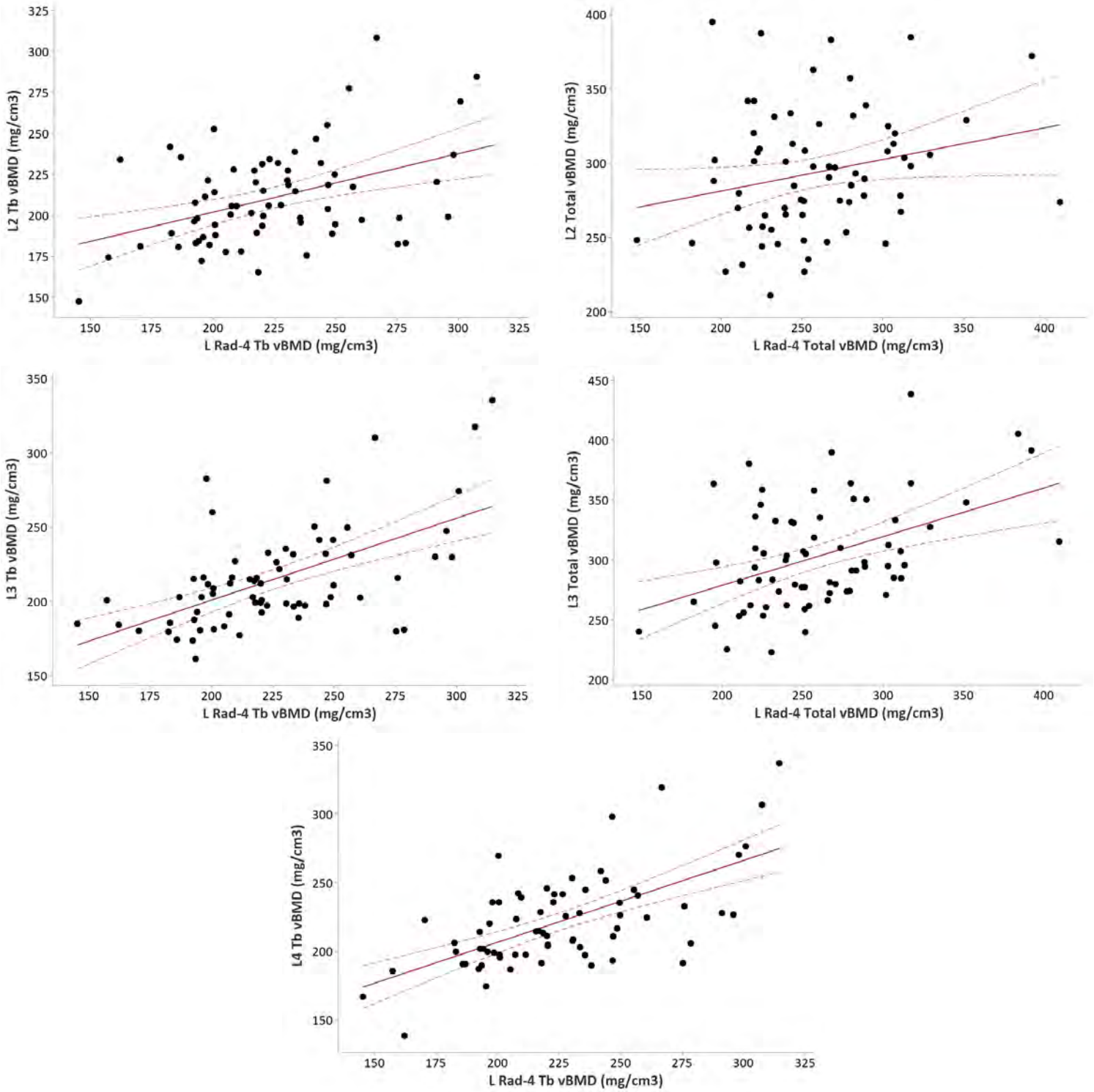


Fig. A3. Linear regressions between female lumbar spine vBMD (left: Tb; right: Total) and Rad-4. Regression lines (red) with 95% confidence interval (dotted red lines). Note: Rad-4 Total vs. L4 Total vBMD located in Fig. .

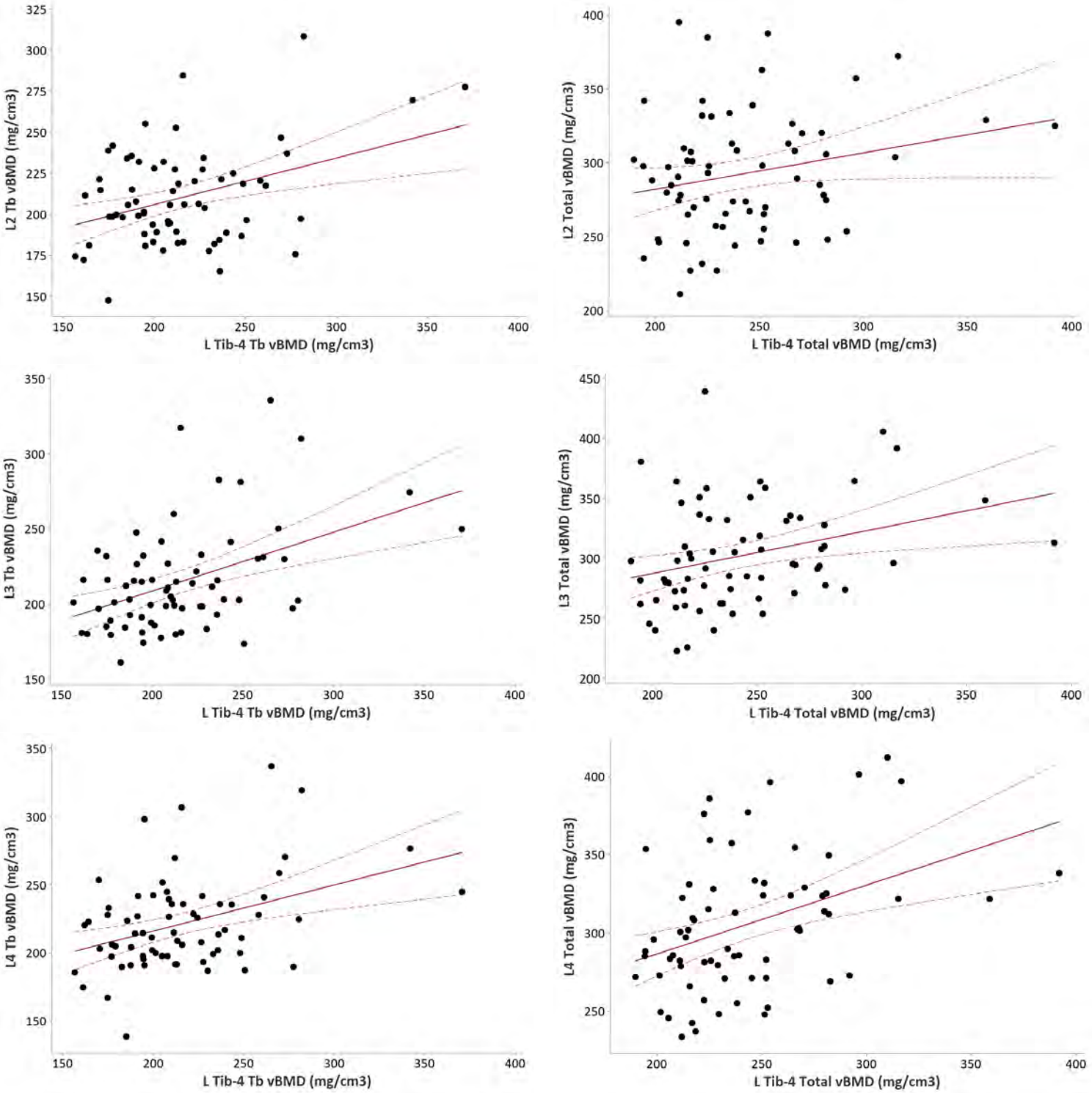


Fig. A4. Linear regressions between female lumbar spine vBMD (left: Tb; right: Total) and Tib-4. Regression lines (red) with 95% confidence interval (dotted red lines).

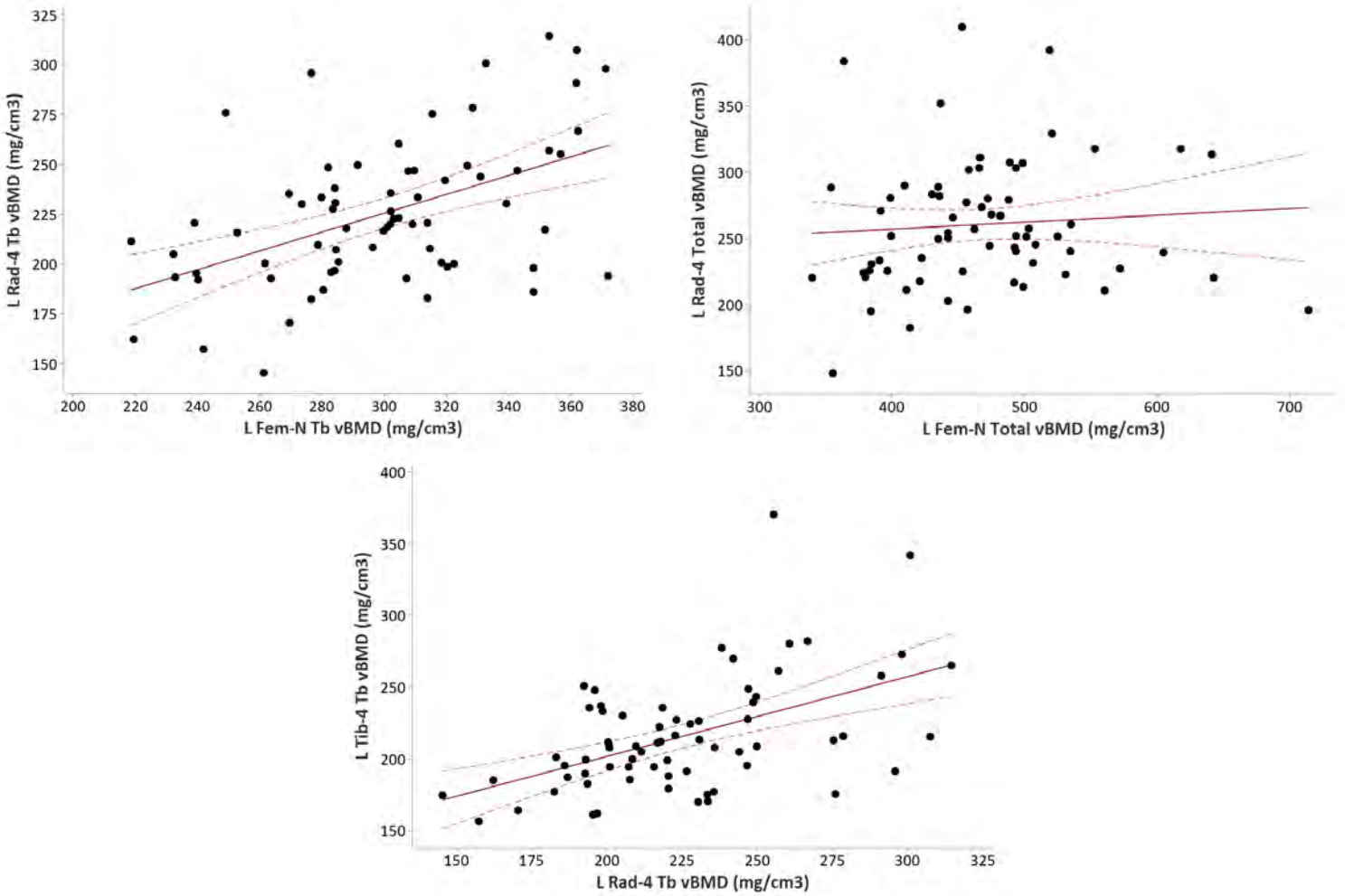
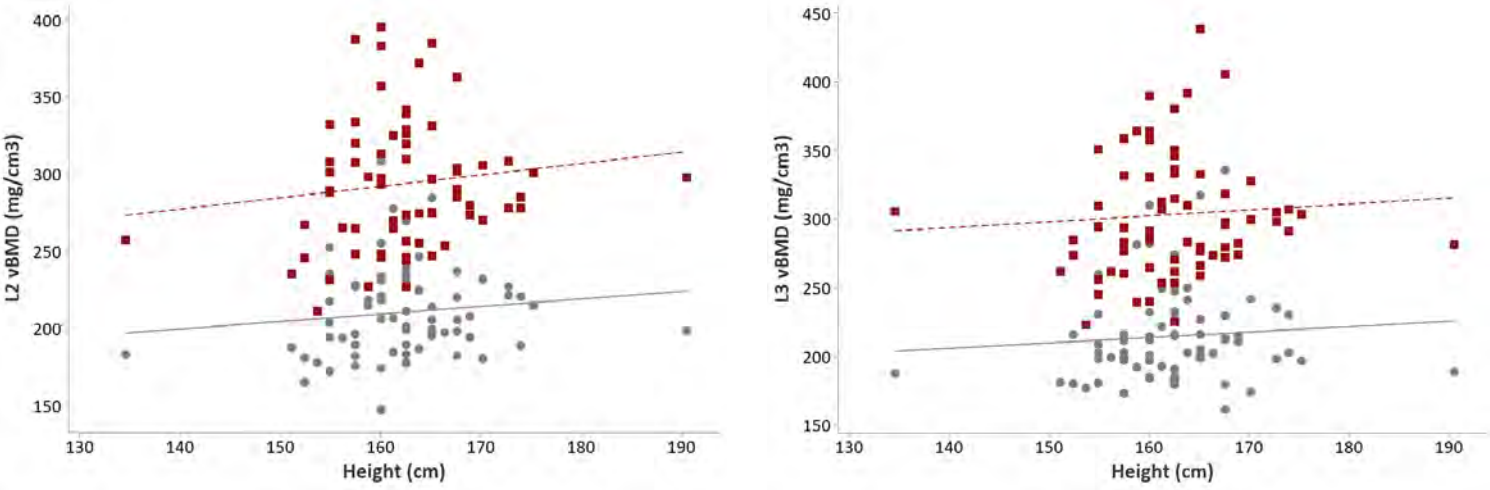


Fig. A5. Linear regressions between female extremity vBMD (left: Tb; right: Total). Regression lines (red) with 95% confidence interval (dotted red lines). Note Rad-4 Total vs. Tib-4 Total vBMD located in Fig. 3; Fem-N vs. Tib-4 (Tb and Total vBMD) located in Fig. 4.



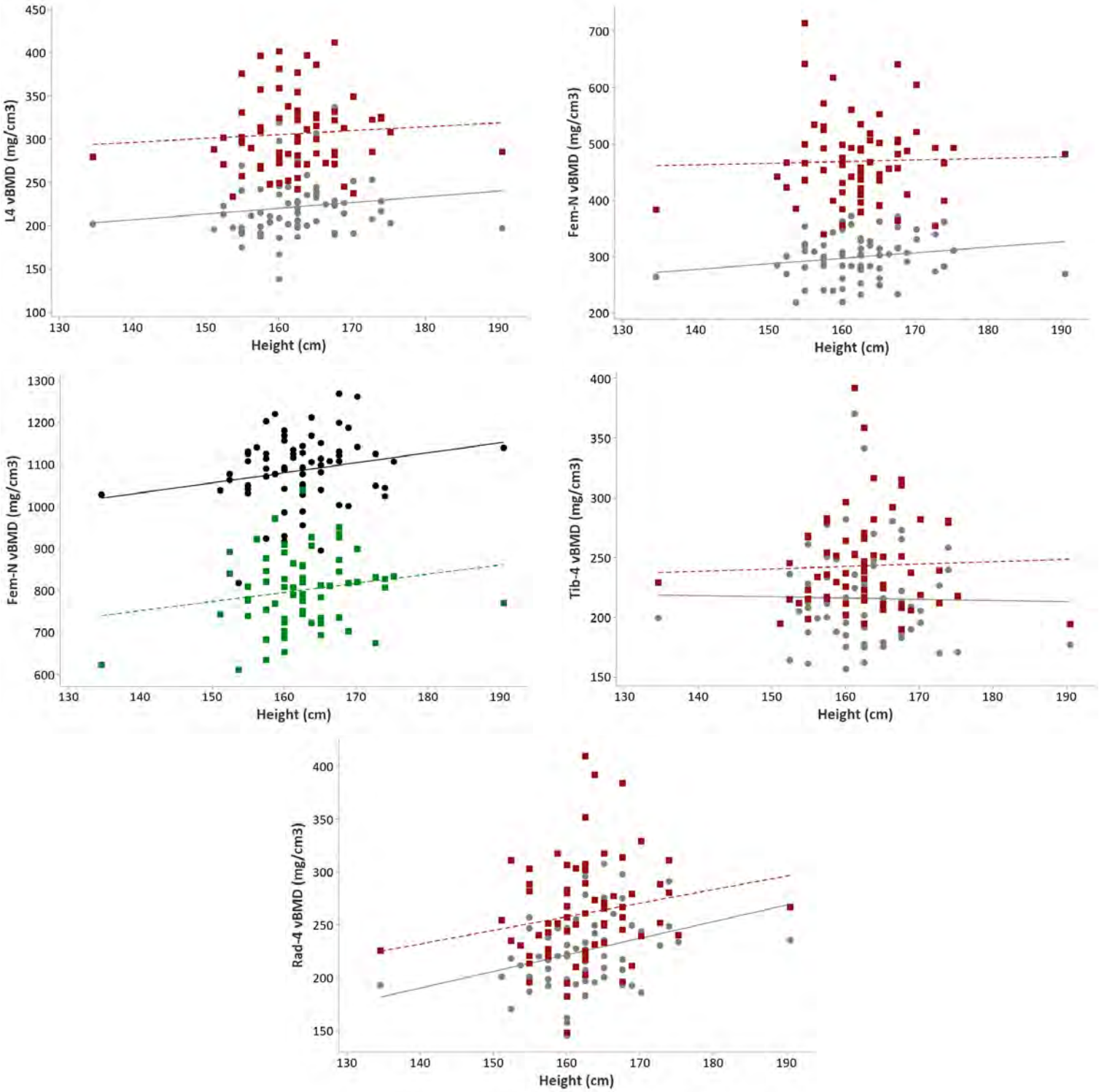


Fig. A6. Linear regressions between female vBMD and height (cm). Trabecular (gray), Total (red), Inf Ct (black), Sup Ct (green) with regression lines.

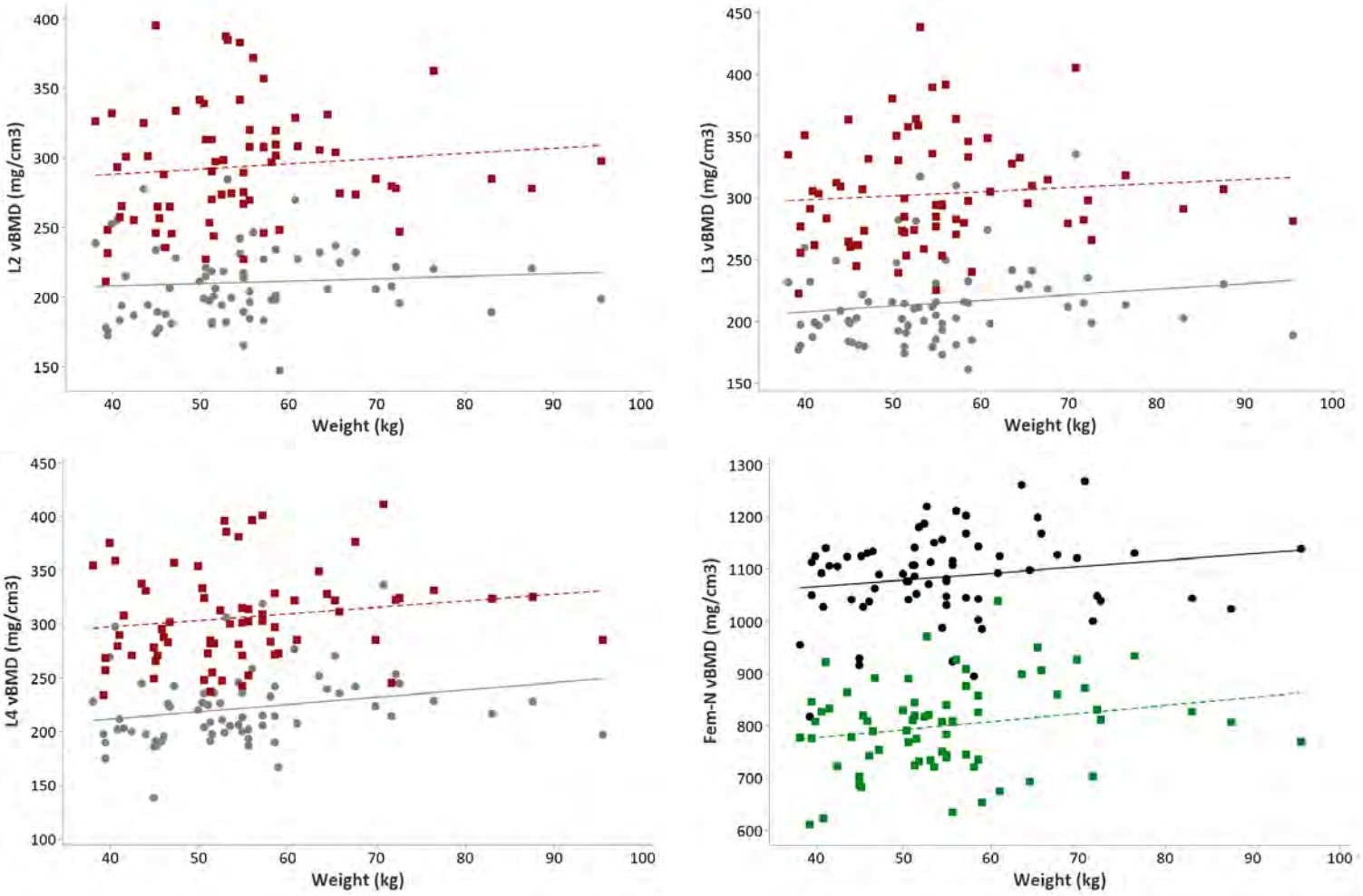
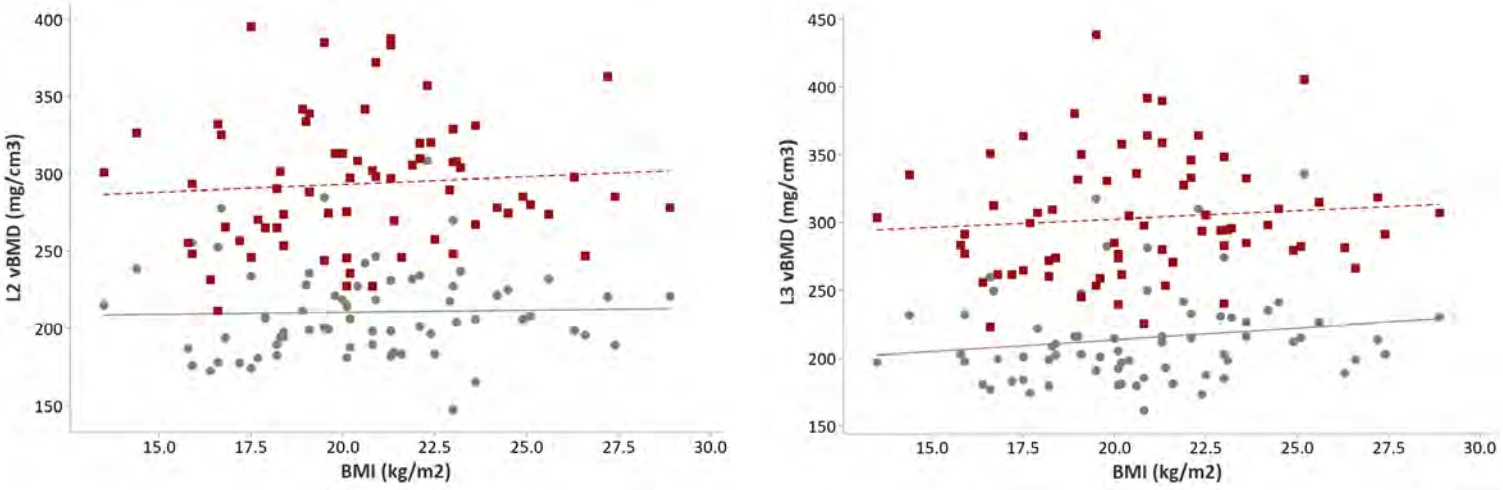


Fig. A7. Linear regressions between female vBMD and weight (kg). Trabecular (gray), Total (red), Inf Ct (black), Sup Ct (green) with regression lines. Note Rad-4 vBMD vs. weight is located in Fig. 8; Fem-N vBMD (Tb and Total) vs. weight is located in Fig. 9; Tib-4 vBMD vs. weight is located in Fig. 10.



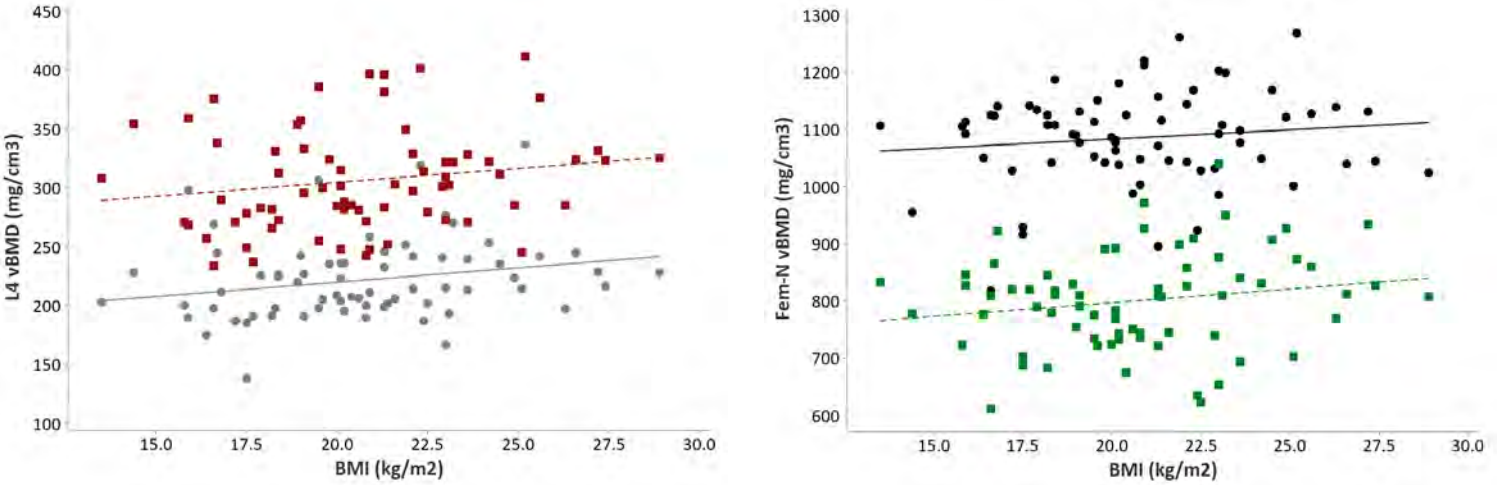


Fig. A8. Linear regressions between female vBMD and BMI (kg/m^2). Trabecular (gray), Total (red), Inf Ct (black), Sup Ct (green) with regression lines. Note: Rad-4 vBMD vs. BMI is located in Fig. 8; Fem-N vBMD (Tb and Total) vs. BMI is located in Fig. 9; Tib-4 vBMD vs. BMI is located in Fig. 10.