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Bone lead variability in bone repository skeletal samples measured with portable x-ray fluorescence

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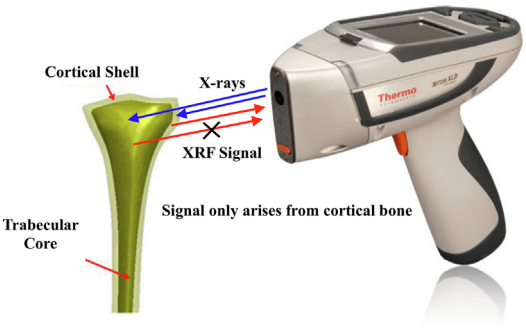
HIGHLIGHTS

- Portable XRF is only able to measure cortical bone metal biomarkers.
- Skull and tibia are optimal sites for portable XRF bone measurements.
- Portable XRF bone measurements should be comparable regardless of measurement site.

GRAPHICAL ABSTRACT



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ABSTRACT

Bone lead serves as a better, more accessible biomarker to many communities experiencing chronic exposure to lead. A new method using low energy x-ray fluorescence in a handheld device (portable XRF) allows us to measure this chronic biomarker in only a few minutes. However, many unknowns remain about this biomarker measured using a new low energy x-ray technique. The low energy of the new method was theorized to measure a slightly different portion of the bone than previous techniques, which could influence measurements at different bone sites and types. We tested how bone measurements varied across five bone sites: mid-tibial shaft, proximal tibia, distal tibia (ankle), ilium, and cranium. We found bone lead measurements are not significantly different between skeletal elements when measured using a portable XRF. On average, bone lead in the repository samples was measured to be 21.6 ± 21.3 μg/g with an XRF detection limit of 2.1 ± 0.5 μg/g. Cumulative lead exposure can be effectively measured using the portable XRF on a variety of bone types, but the tibia should be preferentially measured to compare between studies and individuals.

1. Introduction

Lead continues to be a pervasive toxicant in many communities due to legacy exposures, aging building infrastructure, and emerging industries (Lanphear et al., 2005, 2018; Pirkle et al., 1994). Recent exposure to lead can be assessed by whole blood measurement Nilsson et al., 1991). However, bone serves as the best marker of cumulative lead exposure, as >90 % of lead is stored in bone and the slow turnover rate of lead in bone allows for one bone measurement to represent up to decades worth of lead exposure for an individual (Rabinowitz, 1991). Previous research using K-shell X-Ray Fluorescence (KXRF) to measure *in vivo* bone lead typically measured either the tibia or patella because these bones are largely

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comprised of cortical and trabecular bone, respectively, which reflect different time windows of exposure related to the different turnover rates in those bone types (Aro et al., 1994; Chettle et al., 1991). In general, cortical bone reflects long-term storage of lead over decades, and trabecular bone reflects lead exposure over the past several years (Rabinowitz, 1991; Wilker et al., 2011).

We recently reported on a lower energy portable bone measurement system (portable L-shell XRF, or pXRF) and found good agreement between pXRF and KXRF measurements of tibia lead (Specht et al., 2016, 2014, 2018; Zhang et al., 2021). Traditional KXRF uses a radioisotope source, a 30 min measurement time, and requires liquid nitrogen cooling, whereas pXRF is handheld, uses a three minute measurement, and an x-ray tube source. Thus, pXRF measurements are dramatically easier for traveling for field measurements, registration with regulatory bodies in the US, and conserving time during measurements. However, there are some differences between the pXRF and KXRF. One is that the lower energy excitation of the pXRF only penetrates roughly a half millimeter into bone while the K-shell lead excitation penetrates deeper (Specht et al., 2019a). The outer shell of most bones is comprised largely of cortical bone (Gray et al., 2005). Therefore, measurements with the pXRF may be similar regardless of the specific bone analyzed, whereas for KXRF oftentimes both cortical and trabecular bone were measured. In a previous report we found that for both predominantly trabecular and cortical bones, the pXRF appeared to only measure cortical bone, but the analysis was complicated by overlying soft tissue for that study (Specht et al., 2019a). The lower energy of the pXRF, compared with the KXRF, renders it susceptible to some interference from overlying tissue that can be statistically accounted for, but adds uncertainty to the measurements and reduces sensitivity, which would decrease correlations in measurements across different bones and different sites on the same bone. In order to more directly assess the within-person variability in bone lead concentration across different bones and sites on the same bones—without additional measurement error from soft tissue—in the present study we measured human bone samples without overlying soft tissue. Without the complications of overlying soft tissue, our accuracy for each measurement improved by a factor of 6. Thus, creating a dataset with much greater specificity for the actual measured bone lead value in each bone site allowing us to precisely define the limitations of the pXRF bone lead measurement technique. We measured bone lead at five sites on three different bones from the same individual, with two primarily trabecular and three primarily cortical. We also compared values across three different sites on the tibia. All measurements were taken on dry human bones, which allowed us to achieve a negligible uncertainty and low minimum detection limit on all samples. Thus, this study aims to provide greater context on the limitations of measurement across different bones with the pXRF device.

2. Methods

2.1. Bone samples

Bone samples were from the Forensic Anthropology Center of Tennessee University in Knoxville, USA and are part of the University of Tennessee, Knoxville (UTK) Donated Skeletal Collection obtained *via* the Body Donation Program with a total of >2000 donors. Among 22 of these donors, we measured lead at the mid-tibial shaft, proximal tibia, distal tibia (ankle), ilium, and cranium. These measurement locations are identified in Figs. 1, 2, and 3. The mid-tibia, cranium, and ilium have relatively thick cortical bone, while the proximal and distal tibia have a thin layer of cortical bone such that trabecular bone is closer to the surface (Eswaran et al., 2006; Gray et al., 2005; Todd et al., 2001). The bones analyzed had been stored in the collection for an average of 8 years. Demographic and age characteristics of the donors are shown in Table 1. The sample in our data was skewed towards including older individuals.

2.2. Portable X-ray fluorescence lead measurements

Lead was measured using the Thermo Fisher Niton XL3t GOLDD+ portable x-ray fluorescence (XRF) device (Thermo Fisher, Billerica, MA, USA). The device utilized custom calibration and settings using a 50 kV and 40 μA x-ray tube and a silver and iron filter. Calibration was done using plaster-of-Paris samples ranging from 0 to 100 μg lead/g dry bone. Corrections were made based on size of the bone by normalizing to the silver anode Compton

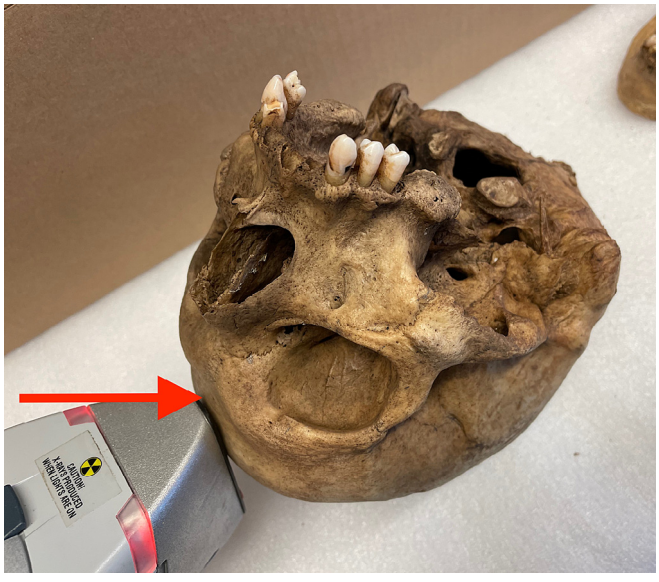

Fig. 1. Measurement location on the cranium (red arrow points to measurement location).

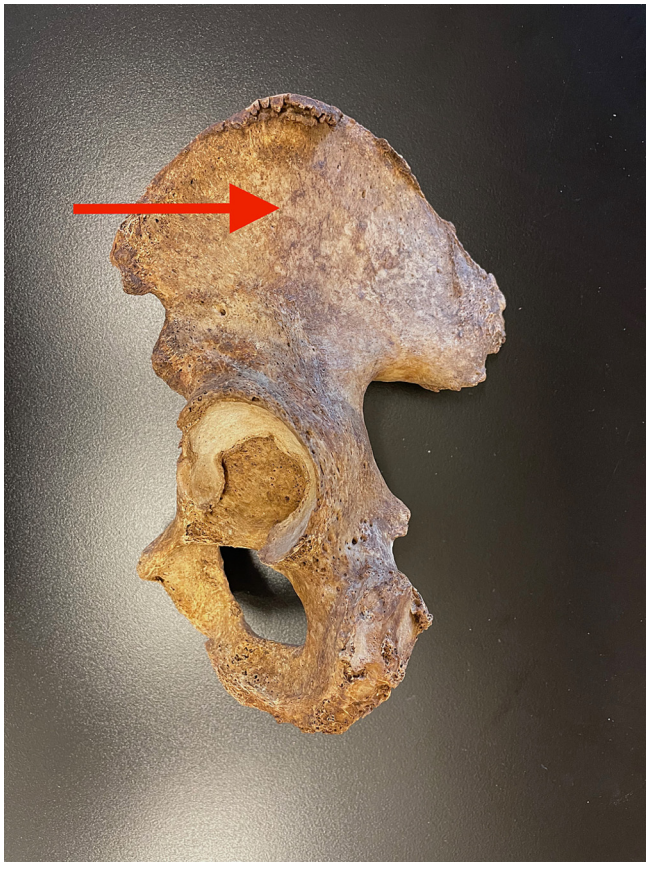

Fig. 2. Measurement location on the ilium (red arrow points to measurement location).

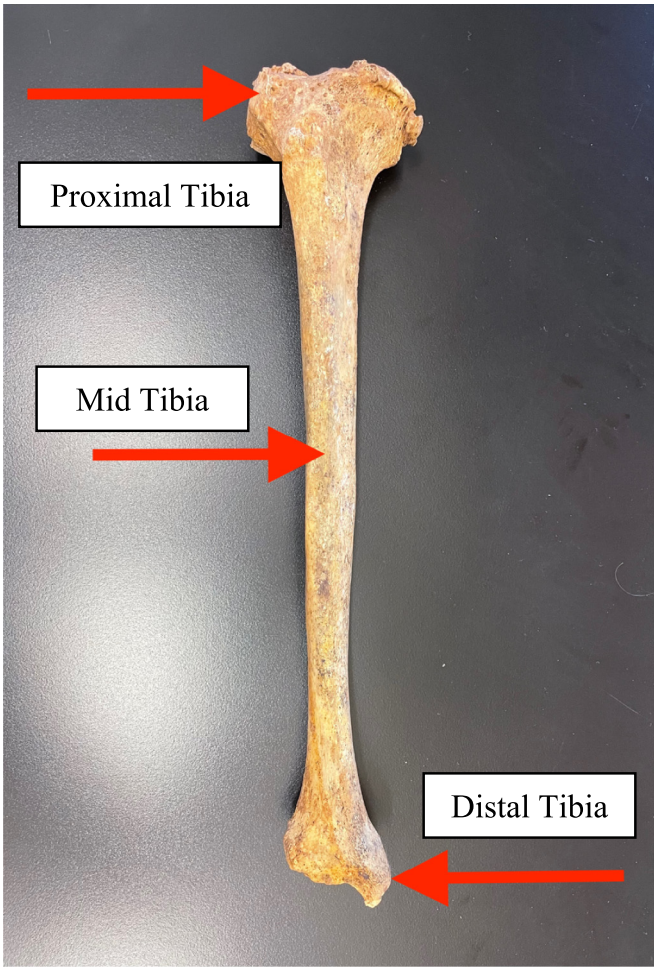

Fig. 3. Measurement locations on the tibia (red arrows points to measurement location for proximal, mid, and distal tibia measurements).

Table 1
Age and death information on donors measured in our study (n = 22).

	Average	Median	Standard Deviation	Quartile 1	Quartile 3
Age	81.0	82	10.9	71	89
Year of birth	1933.0	1934	10.3	1924	1944
Year of death	2013.9	2014	1.6	2013	2015
Years of education	13.7	13	2.3	12	14
Sex	67 % Female 33 % Male				

Scattering peak. Bone measurements were all made on bare bone; thus, skin thickness correction was unnecessary. An example full spectral image is included in Fig. 4 below.

Although calibration is done using units of μg/g dry bone, we were able to convert this to μg/g bone mineral using the equation

$$B_{Mineral} = 1.5\, B_{Dry} \quad (1)$$

As is shown, a multiplicative factor of 1.5 is used with the dry bone results to achieve the bone mineral normalized result as reported in previous works (Specht et al., 2019b, 2018). This factor and unit originates from previous measurements of bone lead using K-shell XRF in the 1980's (Chettle et al., 1991; LK et al., 1985). Bone mineral, as reported in the units, should be proportional mainly to the calcium in the bone, but can also be related to phosphorus and strontium based on the coherent scattering at the K-shell energy. For portable XRF, this value is based on our Compton scattering normalization, which similarly has a proportional dependence on the calcium content of the bone. The detection limit for the measurements in this study were on average 2.1 ± 0.5 μg/g bone mineral. This detection limit is markedly lower than previous studies that had measurements through soft tissue with slightly different procedures average detection limit of 12.6 μg/g (Specht et al., 2019a, 2019c). The primary reason for the difference in detection limit between this and the previous study is the lack of soft tissue thickness in the current study.

The raw XRF spectra were quantified using the lead beta peak (12.6 keV), as the alpha peak (10.55 keV) has significant overlay with other elemental peaks and background, such as arsenic (10.5 keV), as has been noted in previous works (Specht et al., 2018, 2016). The peak was fitted using a Gaussian function with an exponential background to identify net counts. We used the net counts of lead along with a function of the silver Compton Scattering peak to obtain quantified lead in μg/g dry bone, which was finally converted to μg/g bone mineral. As in our previous work, the uncertainty (σ) of each measurement was calculated using the following equation,

$$\sigma = \frac{C \times \sqrt{\frac{BKG+Gross}{t}}}{Net} \quad (2)$$

where c is the concentration, *BKG* is the background count rate as estimated by our fitting, *Gross* is gross count rate over the area of the fitted peak, t is measurement time, and *Net* is the net Pb count rate from the Gaussian function in our fitting (Nie et al., 2011; Specht et al., 2016, 2014, 2017).

2.3. Statistical analysis

Statistical analyses were completed using R version 3.03 (Foundation for Statistical Computing, Vienna, Austria). For determining whether there were significant differences by bone and measurement site, we used

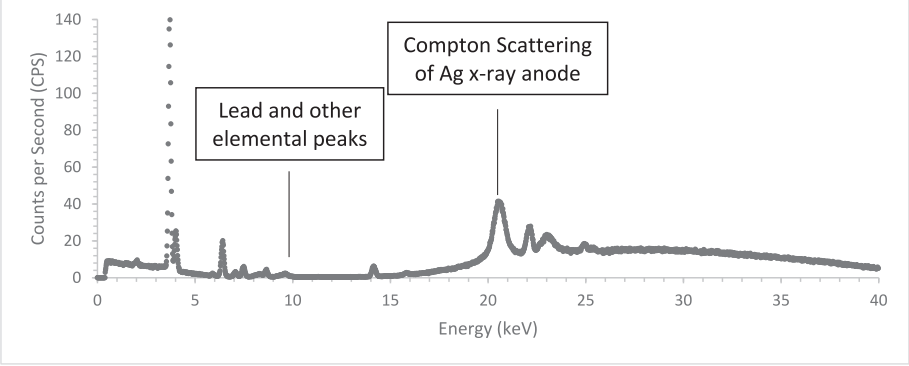

Fig. 4. Example XRF spectra from a donor bone.

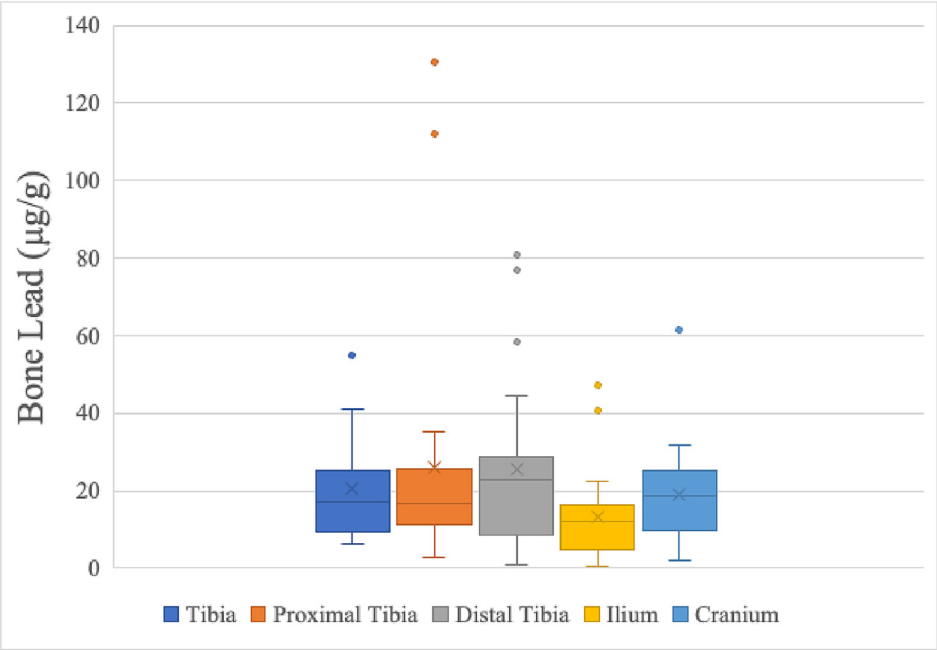

Fig. 5. Box and whisker plot of bone lead measurements by bone site in the 22 donor skeletal samples (box represents quartile 1 to quartile 3; Horizontal line is median; X is average; Range is vertical line between minimum and maximum; Outside of the range is potential outlying points).

linear mixed models with a random intercept to account for correlations within participants (Bates, n.d.). Linear mixed effects models are generally found to be robust when used with non-normal data (Schielzeth et al., 2020). We used pairwise correlations to assess an association between measurements of different bone sites. Pearson correlations do not depend on normality assumptions and might be more appropriate than Spearman rank correlations when the measured values are meaningful in context. In addition, the context of the differences for individual measurements matters so that we can effectively demonstrate that within individuals the bone sites do or do not differ in lead accumulation. Log transforming this would reduce any potential differences found and the potential applicability of data to only group analyses rather than potentially evaluating individual level measures as well. 22 subjects is much more than several previous studies with similar levels of certainty for individual measurements, which had as little as 10 subjects (Specht et al., 2019a; Todd et al., 2001). One previous study had 31 subjects (Specht et al., 2019a), but the bone lead uncertainty was on average 6 times greater than ours; thus, we should have proportionally more power given our greater measurements precision (Fig. 5).

3. Results

3.1. Bone lead measurements

Table 2 shows the results for the bone measurements of lead in each of the different measurement locations. The average lead reading across all bone sites was 21.6 ± 21.3 µg/g with an average detection limit across all bone sites of 2.1 ± 0.5 µg/g. The individual bone site measurements and uncertainties are reported in Figure 5 and Table 2. The average result for the tibia bone is higher than that of general population studies from the 1990's and early 2000's looking at bone lead in elderly populations (Gerhardsson et al., 1993; Hu et al., 2007; McNeill et al., 2017).

Table 2
Lead measurements and uncertainty (σ) for each bone measurement.

	N	Lead result (µg/g)			Uncertainty (µg/g)	
		Median	Mean	Standard deviation	Mean	Standard deviation
Tibia	22	17.11	20.47	14.41	2.05	0.51
Proximal tibia	22	16.87	26.04	32.16	1.99	0.73
Distal tibia	22	22.94	25.64	22.08	2.03	0.76
Ilium	22	12.00	13.34	11.38	1.97	0.73
Cranium	22	18.85	19.13	12.50	2.26	0.62

3.2. Correlation matrix of bone measurements

Table 3 shows the correlation matrix of all bone measurements. The highest correlations were seen between the different sites on the tibia, while correlation between the cranium and other sites were notably lower although not statistically significant. One cranial vault measurement was outlying (Grubb's test p-value = 0.0005) and when removed changed the cranium Pearson correlations in the last column of Table 3 to 0.44, 0.34, 0.32, and 0.31 for tibia, proximal tibia, distal tibia, and ilium correlated to cranium respectively.

3.3. Linear mixed effects model

We utilized a linear mixed effects model to determine whether the measurements on different bone sites for the same individual differed between any of the bone sites in comparison to tibia bone. Table 4 shows computed 95 % confidence intervals for the estimated true differences from tibia for each bone site predicted from our model. Ilium lead concentration is shown to have a non-zero (between −15.2 and − 0.5 µg/g) difference from tibia lead using this model. The standard deviation of the variance between individuals was 16.77 and the standard deviation of the variance for

Table 3
Pearson correlation (Spearman in parentheses) matrix of all bone measurements.

	Tibia	Proximal tibia	Distal tibia	Ilium	Cranium
Tibia	1.00	0.83 (0.70)	0.85 (0.75)	0.71 (0.36)	0.51 (0.53)
Proximal tibia		1.00	0.87 (0.70)	0.91 (0.64)	0.18 (0.43)
Distal tibia			1.00	0.86 (0.62)	0.21 (0.19)
Ilium				1.00	0.07 (0.04)
Cranium					1.00

Table 4
Differences and 95 % confidence intervals in bone lead observed between each bone site and tibia bone (reference).

	Point estimate	95 % CI lower bound	95 % CI upper bound
Tibia	(Reference)	(Reference)	(Reference)
Proximal tibia	4.82	−2.52	12.16
Distal tibia	4.42	−2.92	11.76
Ilium	−7.88	−15.22	−0.54
Cranium	−2.09	−9.43	5.25

the residual was 13.74 showing that variation between individuals accounted for 60 % of the variation in the model. The model had an intraclass correlation coefficient of 0.56. Indicating the agreement between bones within an individual is greater than between individuals.

4. Discussion

The results from this study suggest that bone lead measured with a pXRF varies little across bone sites. We found the ilium lead concentration in our data was the only bone measurement to show differences from the mid-tibia. We did not find any other statistically significant differences between bone sites measured, and we found high correlations (average Pearson r = 0.6 including all correlations from Table 3 and $r = 0.84$ excluding cranium) for the $n = 22$ individuals measured across bone sites.

The results from this study had very low pXRF measurement uncertainty across all measurements (2.1 μg/g), much lower than the pXRF measurement uncertainty (12.6 μg/g) found in our previous study that measured bone lead concentration through overlying soft tissue (Specht et al., 2019a). This improved the power we had in detecting the difference between bones significantly. We only found the ilium to be significantly lower than the mid-tibia. The lower results could be explained by: 1) geometry issues with the pXRF measurement (further explained below); or 2) due to degradation of the surrounding cortical bone of the ilium, revealing the trabecular bone more clearly to the lower energies of the pXRF. However, for *in vivo* measurements, due to the low energy of the newer device, it is typically impossible for it to penetrate through the cortical shell in trabecular bone. The cortical shell surrounding the trabecular bone sites would need to be <0.5 mm for any potential signal impact, and, as indicated by this and the previous study, the cortical shell for most intact bone is all that is measured for these individuals. Many previous studies of bone lead measured by KXRF, which measured both cortical and trabecular found variations of health outcome associations between both (Shih et al., 2007; Weisskopf et al., 2004). Neurodegeneration was found to be more associated with trabecular KXRF bone lead biomarkers, whereas cardiovascular outcomes were found to have a greater association with KXRF cortical bone lead measurements (Shih et al., 2007; Weisskopf et al., 2009, 2004). This likely derives from the differing biomarkers and accumulation of lead over time in trabecular or cortical bone respectively for adults. Importantly, the KXRF studies on neurological or cardiovascular deficit were not definitive in the relationships with trabecular *versus* cortical bone, as these were limited to only select cohorts. Thus, the potential measurement of cortical bone *via* pXRF may have differing impacts on health outcomes than previous works with KXRF. More study is needed with the pXRF in relation to health outcomes to understand these relationships to bone lead and the cortical bone measured by pXRF.

The bone lead measurements found here were slightly higher than that of populations from the 1990's and early 2000's in general population (Gerhardsson et al., 1993; Hu et al., 2007; McNeill et al., 2017). The levels were less than many occupational studies of the time with mean bone lead of >25 μg/g (about 30 % of studies were above this 25 μg/g cutoff) (Shih et al., 2007). An elderly population from Boston identified a median tibial lead level of 21 μg/g, which is similar to bone lead levels identified here (Weisskopf et al., 2004). Importantly, age is a primary predictor of bone lead, and the donors measured were older than most from previous studies, which may lead to higher values. In addition, the relatively more rural geography of the Tennessee donors may be very different from the areas surveilled in previous studies in the 1990's, and may have a slightly higher exposure than those from the more urban environments (Kamai et al., n.d.). Lead has been linked with occupations in agriculture and has agricultural legacy exposures through pesticides in addition to its well-known additives in gasoline and paint, which may lead to higher rural exposures (Dickerson et al., 2019). However, the exact source of exposure in these cases remain unknown.

The agreement between bones was identified as much greater in this study (Pearson $r = 0.6$) *versus* the previous (Pearson $r = 0.4$) (Specht et al., 2019a). The cranium had the worst correlation with the other bone measurements, but with removal of one outlier this correlation increased to slightly higher levels (Pearson $r = 0.25$ to $r = 0.35$). A potential explanation is the difficulty in measuring a purely convex surface over the cranium, which can result in less signal from geometrical differences that vary in each measurement (Specht et al., 2014). A similar problem existed in measurements of donor samples in a previous study (Specht et al., 2014). This would change the distribution of bone lead preferentially. For example, a more planar geometry would give a consistently lower measurement than a convex sample with signal arising closer to the detector. This effect can clearly be identified in the ilium measurements, which are consistently lower than all other bones. Since the ilium was measured on a flat surface and no convex locations could increase distance to the detector, it consistently recorded less signal. This consistency can then be seen in the correlations, which are still high, even though the measurements themselves were lower on average. Alternatively, as stated above, this could be the result of exposed trabecular bone, rather than the measurements being dominated by cortical bone. The ilium, as measured in our study within the center of the bone, is unlikely to be the target for *in vivo* study, as the overlying tissue would be substantial and could influence the results (Specht et al., 2016). The measurements for the other bones, which are primarily cortical, were not significantly different from tibia in our linear mixed effects model, and could all be reasonable targets for *in vivo* pXRF bone lead measurements.

Since we have lower pXRF measurement uncertainty in this study, the standard deviation of the measurements was more reflective of actual differences in cumulative lead exposure between individuals, resulting in higher correlations between bones. This is reflected in the intraclass correlation coefficient of 0.56, which is reasonably high for our measurements. Measured differences better reflected the true spread of exposures, rather than an artificial spread affected by added uncertainty in the pXRF measurement. The higher correlations also bring us in line with the expectations from previous studies of bone lead, where the correlation values were typically higher between bones with an expected Pearson correlation ~0.7 between patella and tibia in previous studies using KXRF (Kim et al., 1997; Weisskopf et al., 2004).

In summary, bone lead measurements do not change significantly from bone to bone in cortical bone sites or across the tibia when measured using a portable XRF. Our more accurate data, collected in the absence of soft tissue, indicates that cumulative lead exposure from cortical bone can be effectively measured *in vivo* or *via* stored samples using the portable XRF on a variety of bone types. Importantly, the pXRF cannot be used to determine trabecular bone lead as a biomarker. Ideally, the tibia bone should be used to compare to studies using tibia with KXRF or pXRF previously.

CRediT authorship contribution statement

Aaron J Specht.
Writing, analysis, review, edit.
Dawnie W Steadman.
Review, Edit, Conceptualization.
Mary Davis.
Review, Edit, Conceptualization.
Scott Bartell.
Statistical Analysis, Review, Edit.
Marc Weisskopf.
Analysis, review, edit.

Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Aro, A.C.A., Todd, A.C., Amarasiriwardena, C., Hu, H., 1994. Improvements in the calibration of 109-cd K x-ray fluorescence systems for measuring bone lead in vivo. Phys. Med. Biol. 39.

Bates,n.d., D.M. Bates , n.d. Mixcd-Effects Models in S and S-PLUS 8.

Chettle, D.R., Scott, M.C., Somervaille, L.J., 1991. Lead in bone: sampling and quantitation using K X-rays excited by 109Cd. Env. Health Perspect 91, 49–55.

Dickerson, A.S., Hansen, J., Specht, A.J., Gredal, O., Weisskopf, M.G., 2019. Population-based study of amyotrophic lateral sclerosis and occupational lead exposure in Denmark. Occup. Environ. Med. 76, 208–214. https://doi.org/10.1136/oemed-2018-105469.

Eswaran, S.K., Gupta, A., Adams, M.F., Keaveny, T.M., 2006. Cortical and trabecular load sharing in the human vertebral body. J. Bone Miner. Res. 21, 307–314. https://doi.org/10.1359/jbmr.2006.21.2.307.

Gerhardsson, L., Attewell, R., Chettle, D.R., Englyst, V., Lundstrom, N.G., Nordberg, G.F., Nyhlin, H., Scott, M.C., Todd, A.C., 1993. In vivo measurements of lead in bone in long-term exposed lead smelter workers. Arch. Environ. Health 48, 147–156. https://doi.org/10.1080/00039896.1993.9940813.

Gray, H., Standring, S., Ellis, H., Berkovitz, B.K.B., 2005. Gray's Anatomy : The Anatomical Basis of Clinical Practice. 39th ed. Elsevier Churchill Livingstone, Edinburgh ; New York.

Hu, H., Shih, R., Rothenberg, S., Schwartz, B.S., 2007. The epidemiology of lead toxicity in adults: measuring dose and consideration of other methodologic issues. Environ. Health Perspect. 115, 455–462. https://doi.org/10.1289/ehp.9783.

Kamaietal.,n.d., E.M. Kamai J.L. Daniels P.L. Delamater B.P. Lanphear G.J. MacDonald D.B. Richardson , n.d. Patterns of children's blood lead screening and blood lead levels in North Carolina, 2011–2018—who is tested, who is missed? Environ. Health Perspect. 130, 067002. 10.1289/EHP10335

Kim, R., Landrigan, C., Mossmann, P., Sparrow, D., Hu, H., 1997. Age and secular trends in bone lead levels in middle-aged and elderly men: three-year longitudinal follow-up in the normative aging study. Am. J. Epidemiol. 146, 586–591.

Lanphear, B.P., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D.C., Canfield, R.L., Dietrich, K.N., Bornschein, R., Greene, T., Rothenberg, S.J., Needleman, H.L., Schnaas, L., Wasserman, G., Graziano, J., Roberts, R., 2005. Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. Environ. Health Perspect. 113, 894–899.

Lanphear, B.P., Rauch, S., Auinger, P., Allen, R.W., Hornung, R.W., 2018. Low-level lead exposure and mortality in US adults: a population-based cohort study. Lancet Public Health 3, e177–e184. https://doi.org/10.1016/S2468-2667(18)30025-2.

Lk, S., Dr, C., Mc, S., 1985. In vivo measurement of lead in bone using X-ray fluorescence. Phys. Med. Biol. 30, 14.

McNeill, F.E., Fisher, M., Chettle, D.R., Inskip, M., Healey, N., Bray, R., Webber, C.E., Manton, W.I., Marro, L., Arbuckle, T.E., 2017. The decrease in population bone lead levels in Canada between 1993 and 2010 as assessed by in vivo XRF. Physiol. Meas. 39, 015005. https://doi.org/10.1088/1361-6579/aa904f.

Nie, H., Sanchez, S., Newton, K., Grodzins, L., Cleveland, R.O., Weisskopf, M.G., 2011. In vivo quantification of lead in bone with a portable x-ray fluorescence system–methodology and feasibility. Phys. Med. Biol. 56, N39–N51. https://doi.org/10.1088/0031-9155/56/3/N01.

Nilsson, U., Attewell, R., Christoffersson, J.O., Schutz, A., Ahlgren, L., Skerfving, S., Mattsson, S., 1991. Kinetics of lead in bone and blood after end of occupational exposure. Pharmacol. Toxicol. 68, 477–484.

Pirkle, J.L., Brody, D.J., Gunter, E.W., Kramer, R.A., Paschal, D.C., Flegal, K.M., Matte, T.D., 1994. The decline in blood lead levels in the United States. The National Health and nutrition examination surveys (NHANES). JAMA 272, 284–291.

Rabinowitz, M.B., 1991. Toxicokinetics of bone lead. Environ. Health Perspect. 91, 4.

Schielzeth, H., Dingemanse, N.J., Nakagawa, S., Westneat, D.F., Allegue, H., Teplitsky, C., Réale, D., Dochtermann, N.A., Garamszegi, L.Z., Araya-Ajoy, Y.G., 2020. Robustness of linear mixed-effects models to violations of distributional assumptions. Methods Ecol. Evol. 11, 1141–1152. https://doi.org/10.1111/2041-210X.13434.

Shih, R.A., Hu, H., Weisskopf, M.G., Schwartz, B.S., 2007. Cumulative lead dose and cognitive function in adults: a review of studies that measured both blood lead and bone lead. Environ. Health Perspect. 115, 483–492. https://doi.org/10.1289/ehp.9786.

Specht, A.J., Dickerson, A.S., Weisskopf, M.G., 2019a. Comparison of bone lead measured via portable x-ray fluorescence across and within bones. Environ. Res. 172, 273–278. https://doi.org/10.1016/j.envres.2019.02.031.

Specht, A.J., Kirchner, K.E., Weisskopf, M.G., Pokras, M.A., 2019b. Lead exposure biomarkers in the common loon. Sci. Total Environ. 647, 639–644. https://doi.org/10.1016/j.scitotenv.2018.08.043.

Specht, A.J., Lin, Y., Weisskopf, M., Yan, C., Hu, H., Xu, J., Nie, L.H., 2016. XRF-measured bone lead (Pb) as a biomarker for pb exposure and toxicity among children diagnosed with pb poisoning. Biomarkers 21, 347–352. https://doi.org/10.3109/1354750X.2016.1139183.

Specht, A.J., Mostafaei, F., Lin, Y., Xu, J., Nie, L.H., 2017. Measurements of strontium levels in human bone in vivo using portable X-ray fluorescence (XRF). Appl. Spectrosc. 71, 1962–1968. https://doi.org/10.1177/0003702817694383.

Specht, A.J., Parish, C.N., Wallens, E.K., Watson, R.T., Nie, L.H., Weisskopf, M.G., 2018. Feasibility of a portable X-ray fluorescence device for bone lead measurements of condor bones. Sci. Total Environ. 615, 398–403. https://doi.org/10.1016/j.scitotenv.2017.09.123.

Specht, A.J., Weisskopf, M., Nie, L.H., 2014. Portable XRF technology to quantify pb in bone in vivo. J. Biomark. 2014, 9.

Specht, A.J., Zhang, X., Goodman, B.D., Maher, E., Weisskopf, M.G., Nie, L.H., 2019c. A dosimetry study of portable X-ray fluorescence in vivo metal measurements. Health Phys. 116, 590–598. https://doi.org/10.1097/HP.0000000000000971.

Todd, A.C., Parsons, P.J., Tang, S., Moshier, E.L., 2001. Individual variability in human tibia lead concentration. Environ. Health Perspect. 109, 1139–1143.

Weisskopf, M.G., Jain, N., Nie, H., Sparrow, D., Vokonas, P., Schwartz, J., Hu, H., 2009. A prospective study of bone lead concentration and death from all causes, cardiovascular diseases, and cancer in the department of veterans affairs normative aging study. Circulation 120, 8. https://doi.org/10.1161/CIRCULATIONAHA.108.827121.

Weisskopf, M.G., Wright, R.O., Schwartz, J., Spiro, A., Sparrow, D., Aro, A., Hu, H., 2004. Cumulative lead exposure and prospective change in cognition among elderly men: the VA normative aging study. Am. J. Epidemiol. 160, 1184–1193. https://doi.org/10.1093/aje/.

Wilker, E., Korrick, S., Nie, L.H., Sparrow, D., Vokonas, P., Coull, B., Wright, R.O., Schwartz, J., Hu, H., 2011. Longitudinal changes in bone lead levels: the VA normative aging study. J. Occup. Environ. Med. 53, 850–855. https://doi.org/10.1097/JOM.0b013e31822589a9.

Zhang, X., Specht, A.J., Wells, E., Weisskopf, M.G., Weuve, J., Nie, L.H., 2021. Evaluation of a portable XRF device for in vivo quantification of lead in bone among a US population. Sci. Total Environ. 753, 142351. https://doi.org/10.1016/j.scitotenv.2020.142351.