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X-Ray Spectrom. 2008; **37**: 69–75
Published online 14 September 2007 in Wiley InterScience
(www.interscience.wiley.com) DOI: 10.1002/xrs.992

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Application and methodology of *in vivo* K x-ray fluorescence of Pb in bone (impact of KXRF data in the epidemiology of lead toxicity, and consistency of the data generated by updated systems)

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Received 11 April 2007; Revised 23 May 2007; Accepted 13 July 2007

K x-ray fluorescence (KXRF) technology has been used to make *in vivo* measurements of lead in bone for more than three decades. The data obtained are beneficial to research on lead toxicity as well as, in certain circumstances, the practice of occupational and environmental medicine. This paper reviews the impact of KXRF data on epidemiologic research involving lead toxicity and demonstrates that bone lead is and will continue to be a valuable biomarker in addressing long-term health effects related to cumulative exposure. The KXRF system has been improved and upgraded several times ever since it was first used. The consistency of the data obtained from these KXRF systems has been investigated in many studies. This paper provides an overview of the factors that will affect the data generated by the KXRF systems. A calibration problem encountered in one of the major KXRF laboratories is described, and the approach taken to solve the problem is discussed. Despite all the theoretical considerations, there are still some important practical challenges to the intercalibration of KXRF instruments both within the laboratory, and between laboratories. Copyright © 2007 John Wiley & Sons, Ltd.

INTRODUCTION

The first *in vivo* x-ray fluorescence (XRF) measurement of lead in bone was made in the 1970s.[1] The significance of this technology in lead exposure assessment was then appreciated by a group of epidemiology scientists.[2–5] Prior to the K x-ray fluorescence (KXRF) bone lead measurement, blood lead measurement was widely used to monitor lead exposure. Since bone is the primary storage organ for lead in the human body, whereas blood reflects the current or short-term exposure, there are some epidemiological studies of lead expsoure for which measurement of bone lead is preferred to that of blood lead.[6,7] Bone lead has been used to investigate the association between lead exposure and many health outcomes, such as hypertension, kidney impairment, and cognition loss.[8–10] It will continue to be important in this area.

Lead exposure has largely declined in the United States over the last two decades; however, lead exposure and toxicity in children remains a significant public health issue because of heavy environmental pollution, especially due to extensive usage of lead paint in housing, and hand-to-mouth activities of toddlers. Research shows that children are vulnerable to lead-induced subsymptomatic health effects, such as neurodevelopmental impairment and behavioral disturbances, even at very low-level lead exposures.[11,12] There are concerns regarding fetal lead exposure due to lead transfer from maternal blood and bone. In addition, lead exposure in the general population, especially in children, continues to be a serious health threat in developing countries.

Recently, gene-environmental interaction has become significant for epidemiologic studies and researchers have found that some people who carry certain types of genes may be more susceptible to lead exposure than people who do not carry these genes.[13] Both past achievements and existing issues with the epidemiology of lead toxicity render KXRF technology as a valuable exposure assessment tool for the present and for the future.

There are two types of bone lead measurement systems—the KXRF and the LXRF systems. The KXRF system, which was more widely adopted in the x-ray laboratories for bone lead measurement, is the technology that will be discussed in the paper. The KXRF system has gone through several improvements which include both hardware and software upgrades. The sensitivity of the system has been greatly improved since it was first used. On the one hand, some researchers, such as epidemiologists, require improved sensitivity, which provides an impetus towards improvement; on the other hand, the improvement of the system has made consistency of the data from the upgraded systems a

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concern for the researchers who rely on these data. There are many factors that affect the data generated by these systems. This paper summarizes most of the work published in this area, and describes an intercalibration problem encountered at the KXRF laboratory in Harvard School of Public Health (HSPH). Since its establishment in 1981, the Harvard Metals Epidemiology Research Group (MERG) has performed bone lead measurements for thousands of patients using two types of KXRF systems. A discrepancy was observed for the data obtained by these two systems. A calibration problem with one of the systems was brought to light by analyzing the calibration lines and lead concentrations of standard phantoms. An adjustment is proposed to one set of data, and this adjustment is verified by reference to a small group of data.

IMPACT OF KXRF DATA ON THE EPIDEMIOLOGY OF LEAD TOXICITY

In the United States, lead remains a highly significant environmental toxicant with regard to exposure to children as well as a persistent occupational health problem for thousands of workers. It also continues to be the focus of intensive screening in pediatric and occupational medicine clinics, and awareness, testing, and controls are increasing throughout the developing world where industrialization has occurred.

Research on lead toxicity has also intensified, in part because of continued exposures, but in large measure due to the recent insight that the full toxicologic implications of lead exposure have yet to be appreciated because of inadequate attention to long-term health effects related to cumulative exposure (as opposed to acute effects of short-term exposure). The significance of bone lead as a biological marker of lead dose for adults has been reviewed in some previous articles.[3] In a recent mini-monograph published in *Environmental Health Perspectives*, the journal of the US National Institute for Environmental Health Sciences, scientists who had participated in an expert national panel observed that major recent progress has been made in understanding the impact of cumulative lead exposure on adult toxicity.[14] It can be noted that much of this progress was attributed to epidemiologic studies using KXRF instruments to estimate cumulative lead burden in participating research subjects[15] which has allowed investigators to better detect the impact of lead exposure on the risk of cardiovascular disease[16] and the decline of cognitive function.[17]

BONE LEAD AS A BIOMARKER IN THE EPIDEMIOLOGY OF LEAD TOXICITY

In most of the epidemiologic studies of lead toxicity that use KXRF measured bone lead as a biological marker, measurements have been made on the mid-tibia bone, where the target tissue is cortical bone which is well known to accumulate lead in relation to fairly constant rates of bone deposition and mineralization and very slow rates of bone resoprtion.[15] Such measurements essentially provide a cumulative lead 'dosimeter' for each person, which, in turn, has been shown in many recent studies to be superior to blood lead levels (which mostly reflect recent exposure) in predicting the individual risk of developing chronic ailments like hypertension,[8,18–20] accelerated declines in cognition,[21] renal dysfunction,[22] and cataracts.[23]

KXRF measurements have also been taken on bone sites that are primarily of a trabecular nature, such as the patella or the calcaneus. These bones have rates of bone turnover that are much faster than that of cortical bone,[15] and evidence indicates that lead stores are much more mobilizable in trabecular bone than in cortical bone.[24]

KXRF measured bone lead levels have also proved to be of great value in understanding the potential impact on fetal development of maternal bone lead stores. In a series of studies conducted in Mexico City, investigators have found that KXRF measured maternal bone lead levels predict smaller infant weight at birth,[25] shorter head circumference and birth length,[26] lower mental development scores when offspring are at the age of two years,[27] and greater risk of maternal hypertension in the peripartum period.[28]

Although the number of laboratories with KXRF capability remains small, it seems clear that this technology is here to stay. Not only does it have superb value in the many on-going (and future) epidemiologic studies on lead toxicity, but also it has clinical value, usually through its ability to do retrospective dose assessment in individuals who are suspected of having had chronic lead over-exposure but who have lacked reliable blood lead levels in the past.

CONSISTENCY OF KXRF DATA GENERATED BY UPDATED SYSTEMS OVERVIEW

KXRF bone lead measurement systems have made great contributions to environmental epidemiologic studies of chronic lead toxicity as described above. However, consistency of the data obtained from KXRF systems is currently under greater scrutiny. There are many factors that affect the data generated by *in vivo* KXRF bone lead measurement systems. These factors can be grouped into three categories: (1) setup of the system, or the hardware, (2) analysis of the data obtained by the system, or the software, and (3) calibration of the system. The following section will provide an overview of these factors. Five versions of KXRF systems have been used worldwide to measure bone lead, with relatively slight differences between the versions amongst laboratories. The first *in vivo* XRF measurement of lead in bone was performed by Ahlgren *et al*. using a ^{57}Co source in a 90° geometry. This is the first generation measurement. Later, ^{109}Cd induced KXRF was found to yield superior results. The second generation of KXRF instruments included two types, one with an annular ^{109}Cd source mounted in front of the detector in a 150–160° backscattering geometry,[29–32] and the other one with a point ^{109}Cd source mounted above the detector in a 160–170° backscattering geometry.[33,34] The latter version was commercialized and manufactured for a limited period of time (AbioMed, Inc.; Danvers, MA, USA). The third generation has a ^{109}Cd point source mounted centrally in front of a larger detector in a 180° backscattering geometry.[35] This system uses a relatively large detector to offset the loss of signals that results from having the source holder mounted in front of the detector. This is the version that is currently used in most KXRF laboratories. The fourth generation KXRF

DOI: 10.1002/xrs

instrument has a ^{109}Cd point source mounted in front of an array of four detectors at a 180° backscattering geometry,[36,37] which affords a significant advance in sensitivity. The ^{57}Co system has only been consistently used by one laboratory because of its lower sensitivity, and most of the epidemiology and toxicology studies of the last 15 years have been carried out with ^{109}Cd systems. Thus, only the ^{109}Cd systems will be discussed further in this paper.

The spectra produced by ^{109}Cd systems have several features in common (Fig. 1). There are several lead characteristic K x-ray peaks, with a large Compton background overlapping with them. The Compton peak varies between 65.5 and 67 keV depending on the slightly different backscattering angles. There are four factors in the system setup category that will affect the precision of the calculated lead concentration results: characteristics of the detector(s), geometry of the setup, source dimension and strength, and source holder's dimension, types of electronics used and setup of the electronics. These issues have been described in many papers and will not be reviewed in detail here.[32,38–42] Two main versions of the data analysis programs for signal extraction are involved in calculating the lead concentration once the spectra are collected. The Marquardt algorithm is used by most of the uncommercialized systems whereas the commercial system (Abiomed, Inc) uses a baseline construction algorithm

The type of data analysis program can affect both the accuracy and precision of the result. This will be illustrated in some detail in the following sections. System calibration is one of the essential steps in the calculation of the lead concentration of an unknown sample. Plaster of Paris phantoms have been used as standard samples for system calibration in most of the bone lead KXRF laboratories. Three factors affect the accuracy and precision of the result in the system calibration process: matrix correction, accuracy of the lead concentration in the phantoms, and understanding and handling of the intercept of the calibration lines. The principle of matrix correction has been described in detail by Todd[43] and a calibration issue regarding this subject has been discussed by Nie *et al*.[44] This paper will concentrate on challenges relating to system calibration using phantoms, with a particular emphasis on the need to secure accurate independent analysis of the lead concentration in the phantoms in order to use these phantoms to determine absolute concentrations of lead in human subjects. There will also be a brief description of the issues involved in calculating the lead concentration, and the data analysis program (with a focus on programs using the baseline construction algorithm). The handling of the intercept of the calibration lines has been explained in detail in Todd's paper and will not be repeated in this paper.[33] In summary, the following section will be devoted to two issues regarding the methodology of the KXRF bone lead measurement systems that were not clarified in previous papers. The discussion will be based on the data that were collected in the KXRF systems at the Harvard School of Public Health.

INTERCALIBRATION OF COMMERCIAL AND NONCOMMERCIAL KXRF SYSTEMS AT THE HARVARD SCHOOL OF PUBLIC HEALTH — SPECTRAL ANALYSIS AND SYSTEM CALIBRATION

Since its establishment in 1991, the Harvard MERG (http://www.hsph.harvard.edu/merg) has performed bone lead measurements on thousands of subjects using KXRF systems. Two systems have been involved. One is a second generation commercialized AbioMed system with a ^{109}Cd source mounted above the detector, and the other is a third generation system, which is a system with a ^{109}Cd source mounted in front of the detector. The spectral analysis programs and system calibration procedures are different for these two types of systems, which are to be addressed when dealing with intercalibration between these systems.

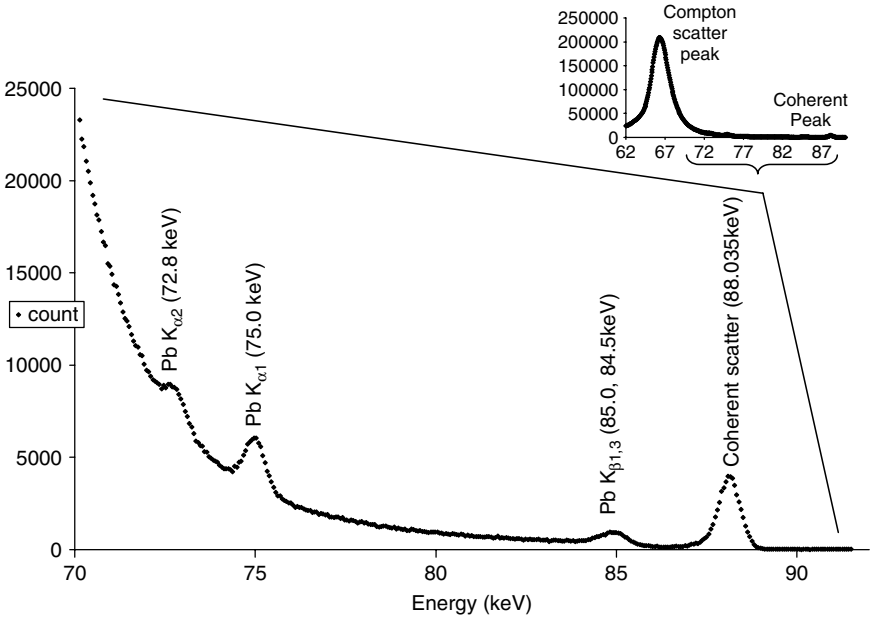

Figure 1. Spectrum for ^{109}Cd KXRF lead measurement.

DOI: 10.1002/xrs

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SPECTRAL ANALYSIS PROGRAMS

The algorithm used in the AbioMed system for peak extraction is termed the baseline construction and was developed by the ABIOMED group.[45] The idea is to construct a baseline in the full energy peak region so that the number of counts above this line (peak area) is a measure of the intensity of the peak of interest. The theory involved in this algorithm has been described in other papers.[46,47] In bone lead measurements, the peaks of interest include the coherent peak and the Kα and Kβ peaks. For the coherent peak, a linear baseline was constructed. Four channels from the left side of the peak and four channels from the right side of the peak were selected to calculate the average background counts per channel; the net peak counts are the total counts minus the total background counts. For the Kα and Kβ peaks, because of the peak being relatively small compared to the huge Compton background, a linear baseline is not accurate enough to estimate the background, hence, a nonlinear baseline was constructed. The baseline was formulated as $(a + bx + cx^2)$. The parameters a, b, and c can be calculated by fitting a certain number of channels on the left side and right side of the channels of the peak. Again, the net peak counts are the total counts minus the total background counts calculated from the nonlinear baseline. In this method, the net peak area is sensitive to the number of channels selected on the left and right side of the peak, and to where the channels are located, especially when the peak is having a large background. In addition, a variety of interferences must be dealt with in extracting the net peak area.[45]

As mentioned, the algorithm used to extract peaks for most of the uncommercialized systems is based on the Marquardt algorithm. The functions were originally developed by the Birmingham group,[48] using a published version of the Marquardt algorithm.[49] In this program, the peak is fitted to an arbitrary function, which includes all the known components in the peak. For example, the coherent peak is known to contain background, the coherent peak, Kβ_2 peaks, O, Ca, C, and P/S K and L Compton scattering edges. These edges arise from Compton scattering from bound electrons. The binding energy of the electron involved sets a maximum limit for the distribution of possible energies of the Doppler-broadened Compton-scattered continuum. Therefore, an upper limit edge arises at the energy corresponding to the full energy of the incident photon (88.025 keV) minus, for example, the K shell binding energy of oxygen (0.543 keV), that is at 87.492 keV. This cannot be resolved from the other features listed above. Thus, the function includes Gaussian peaks for coherent and Kβ_2 peaks, an exponential part for the background, and a complementary error function for the incomplete charge collection for the Gaussian peaks and all the edges. The detailed functions and components of all the peaks can be found elsewhere.[50] This algorithm describes the peaks with components that are predicted theoretically and verified by experiment; hence, the lead signal can be extracted with a higher accuracy compared to the baseline construction algorithm.

SYSTEM CALIBRATION

A unique feature of using ^{109}Cd source and backscattering geometry is that both α and β peaks can be normalized to the coherent peak; hence, it is not necessary to correct for tissue attenuation, geometry, and slight movement of the subject.[31] The calibration line is created by measuring a set of lead doped plaster of Paris phantoms, and plotting the α/coh and β/coh ratio *vs* lead concentration. The subject or patient's bone lead concentration can then be calculated from the α/coh and β/coh ratio for the bone lead spectrum of the subject and the intercept and slope of the calibration line. When the plaster of Paris matrix is solely $CaSO_4 \cdot 2H_2O$, the ratio between the coherent cross-section of the bone and that of the phantoms, i.e. the matrix correction factor, is about 1.46 at the large scattering angles for the systems involved in this paper. This has to be accounted for when calculating the subject's bone lead concentration.

There is only one calibration line for the AbioMed system, which was created at the time when the system was built. It was based on the measurements of a set of lead doped phantoms, and the $(\alpha_1 + \beta_1 + \beta_3)$/coh ratio was used instead of α_1/coh and β_1/coh. The concentration of the subject or patient's bone lead is calculated as:

$$concentration = 1.46 \times \frac{\alpha_1 + \beta_1 + \beta_3}{coh} / 0.00490$$

where 1.46 is the converting factor, and 0.00490 is the slope of the calibration line. The slope (0.00490) is fixed in the program.

For the systems other than AbioMed system (noncommercial systems), two calibration lines, one for the α_1 peak and one for the β_1 peak, were created. A set of lead doped phantoms were measured and the α_1/coh and β_1/coh ratios *vs* Pb concentrations are plotted. The slopes and intercepts of the calibration lines were used to calculate the lead concentration. The final result is the inverse variance weighted mean of the concentrations from α_1 and β_1 calibrations, where the concentrations were weighted inversely by their own variances.[51]

The phantoms used to calibrate the AbioMed system were made by the ABIOMED group.[45] These phantoms were used only once for system calibration during manufacture, as the calibration line was then fixed in the program. The phantoms used for calibrating noncommercial systems were made by the Chemistry laboratory at Harvard School of Public Health.[34] The Pb concentrations of these nine phantoms were calculated at the time of manufacture, which is known as the nominal value. The concentrations were then measured by ICP-MS (ELAN-5000) in 1993, and the calibration lines were calculated based on these values for the noncommercial systems. The average and standard deviation of the slopes are 0.00319 and 0.00003 for the α_1 peak, and 0.00069 and 0.00002 for the β_1 peak, respectively for all the calibration lines created by one of the systems. The average and standard deviation of the intercepts are 0.003 and 0.003 for the α_1 peak, and 0.0007 and 0.0006 for the β_1 peak, respectively.

In order to compare with the AbioMed system, the slope for the $\alpha_1 + \beta_1 + \beta_3$ was calculated from the intensities of these peaks for the noncommercial systems, which give a

DOI: 10.1002/xrs

slope of 0.00425. This value differs from the AbioMed value by a factor of 0.87 and this factor is significantly different to 1.0. As the intercepts of the calibration lines are close to 0 ppm, significant lead contamination of the phantoms can be ruled out. The most likely cause is that there is some problem with the lead concentrations in the phantoms. It happens that the lead concentrations in the phantoms were measured by ICP-MS (ELAN-6100) again in 2004. The nominal values and the values obtained in 1993 and 2004 by ICP-MS for lead concentrations in phantoms are listed in Table 1. A regression line was plotted for the nominal values *vs* the 1993 ICP-MS values. It has a high correlation coefficient ($1 - r^2 = 2.0 \times 10^{-4}$) and a slope of 0.885 ± 0.005 with a small intercept of 0.28. The regression line of the nominal values *vs* the 2004 ICP-MS values also has a high correlation coefficient ($1 - r^2 = 3.0 \times 10^{-4}$) and a slope close to 1 (1.030 ± 0.006) with a small intercept of 0.61. Therefore, if we use either the nominal lead concentrations, or the 2004 ICP-MS values to perform the calibration, the calibration line for the AbioMed system and the noncommercial systems will be consistent. So the AbioMed system, the nominal phantom concentrations and the 2004 ICP-MS agree with each other and differ significantly from the 1993 ICP-MS values. The high likelihood is that the factor of 0.87 is due to wrong lead concentrations in phantoms obtained by ICP-MS in 1993.

In order to verify the above argument, i.e. the calibration inconsistency is due to the wrongly measured lead concentrations in phantoms, some *in vivo* data were analyzed. Forty five people had previously been measured by both the AbioMed system and one of the noncommercial systems. The bone lead concentration from the AbioMed system were analyzed by the AbioMed program. The bone lead concentrations from the noncommercial system were analyzed by the Marquardt program, with the calibration lines calculated from the 1993 ICP-MS phantom lead concentration values. There is a marginally significant difference that cannot be explained by the statistical fluctuation between the data obtained from the AbioMed system and that from the noncommercial system. When the factor of 0.87 was applied to adjust the noncommercial system, the data show no significant difference. In addition, the inverse variance weighted (IVW) means of bone lead for this population obtained by the two systems are significantly different before the adjustment, and the difference disappeared after the adjustment. The results are listed in Table 2.

Table 1. Lead concentrations in lead doped phantoms

Nominal value (ppm)	1993 ICP-MS value (ppm)	2004 ICP-MS value (ppm)
0.00	0.30 ± 0.01	0.48 ± 0.01
5.06	5.73 ± 0.10	5.27 ± 0.05
10.12	11.57 ± 0.05	10.51 ± 0.15
15.18	17.33 ± 0.40	14.77 ± 0.26
20.24	23.27 ± 0.77	21.25 ± 0.35
30.35	34.77 ± 0.37	30.45 ± 0.42
50.59	56.60 ± 0.96	49.40 ± 0.87
75.89	83.97 ± 0.94	73.50 ± 1.12
101.18	114.07 ± 0.79	99.23 ± 1.94

CONCERNS WITH THE ABOVE CALIBRATION PROBLEM FOR EPIDEMIOLOGY STUDIES

The AbioMed system was used before 1999 and the noncommercial systems were used after 1999. As the bone lead measurement data obtained by these systems have been and will continue to be used in several large epidemiology studies, the immediate concern is how the unadjusted data obtained from the noncommercial systems will affect the conclusion from these studies. For the upcoming studies and data analysis, adjusting the post-1999 value by a factor of 0.87 will make the pre-1999 and post-1999 data consistent, hence there is no effect of unadjusted post-1999 data for these studies. As for the past studies, there are three possible circumstances. In the first circumstance, the study only involved the pre-1999 data. In this case, there is no effect to any conclusion as the post-1999 data were not included in the study. The second circumstance is that the study only involved the post-1999 data. In this case; the effect is that the absolute lead concentration of an individual would be shifted by about 10%. However, this shift makes absolutely no difference to conclusions with subjects having higher and lower lead concentrations within the study. It therefore makes no difference to the interpretation on the relationship between bone lead concentration (exposure) and a certain disease (outcome). The third circumstance is a study involving both pre-1999 and post-1999 data. In this case, if there is a true relationship between bone lead and outcome, the unadjusted post-1999 data would most likely weaken this relationship, because the data would be more scattered with a10% higher Pb concentration for some of the subjects distributed randomly with respect to outcome. In

Table 2. Lead concentration difference and *Z*-Scores with and without adjustment for the 45 subjects. The *Z*-Score is the difference divided by the uncertainty in the difference. Ideally, the *Z*-Score should be distributed with a mean of zero and a standard deviation of 1.0

	Without adjustment		With adjustment	
Average difference (ppm)	-6.8 ± 11.5		-2.9 ± 9.3	
Z-Score	-0.8 ± 1.2		-0.3 ± 1.0	
χ^2 (df = 78)	2.11 ($p = 0.0000$)		1.01 ($p = 0.4520$)	
IVW (inverse variance weighted) mean (ppm)	AbioMed	Noncommercial	AbioMed	Noncommercial
	22.3 ± 0.7	26.1 ± 0.6	22.3 ± 0.7	22.7 ± 0.5

DOI: 10.1002/xrs

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other words, if the post-1999 data is adjusted and the analysis carried out again, the relationship will be strenthened. If there is no relationship between bone lead and outcome, the unadjusted post-1999 data are unlikely to create an artificial relationship, as the randomly distributed 10% bias is only based on the exposure, i.e. bone lead, and should have no effect on the outcome.

The epidemiologic scenario most problematic with respect to a pre- and post-1999 shift would be if there were an imbalance in the distribution of the outcome with respect to pre- and post-1999, e.g. if there were a case-control design and the cases were more likely to have been measured pre-1999 and the controls were more likely to have been measured post-1999. In such an example, a difference would become apparent between the mean bone leads of the cases and controls that were based on the bias rather than on true biological differences.

COMMENTS ON THE CALIBRATION OF THE KXRF BONE LEAD SYSTEM AND THE DATA ANALYSIS PROGRAMS FOR THE SYSTEM

In principle, if there is no problem with the calibration, two different KXRF bone lead measurement systems should produce the same results within the uncertainties. Hence, when there is a problem with the data consistency between two systems, the first thing to check is the calibration of the systems. Commonly seen issues with the calibration include the inaccurate lead concentration values attributed to the phantoms, which is the case in the above investigation, unexpected compositions of the phantoms,[44] and lead contamination of the phantoms.[33] Creating calibration lines and examining the slopes and intercepts of the lines is the first step in investigating these problems.

The AbioMed system has only been calibrated once. This has an advantage in that the calibration line is not phantom dependent, i.e. as long as this calibration is fine, there will be no big problem with the results for the *in vivo* measurement if the system is stable. The disadvantage is that it cannot catch minor systematic changes in the calibration for the system, which could make a small difference for the *in vivo* results. (In practice, two noncommercial systems, which are calibrated regularly, do not show a significant variation in the calibration. So this factor is unlikely to have caused any significant problems with the data from the commercial system.) The problem will be more evident for a more sensitive system. In addition, the calibration line of the AbioMed system has no intercept. It is fine in principle; however, it is not completely practical, as there are many factors that can create an intercept. The intercept was not considered in the adjustment for the pre-1999 and post-1999 values for two reasons. Firstly, we do not really know the intercept for the calibration line for the AbioMed system; secondly, the magnitude of the difference is small, and can be neglected when compared to the relatively high uncertainties of both systems. The intercept of ~1–2 ppm is not a big problem for a system with a minimum detection limit of 6–10 ppm, but it will make some difference to the result for a system with a minimum detection limit of 2–3 ppm, which has been developed recently.[37] In that case, we may want to know more about the cause of the intercept. The possible causes of the intercept are described elsewhere.[33,52]

As for the data analysis process, the software used to analyze the data may not be the same, or people may use different versions of the same software. On the basis of the analysis of the data from the 45 subjects, the AbioMed program and the Maquardt program did not make a significant difference to the results. If the system is more sensitive than the ones used in the Harvard MERG group, different softwares may cause significant differences for the results. Even with the most updated software, there may still be some flaws.[53] Since there is no strict standard for these issues, researchers in New York State Department of Health and the Mount Sinai School of Medicine are in the process of finding a way to standardize the whole procedure by organizing a bone lead standardization program (BLSP). They sent the same set of bones from lead-fed goats to most of the KXRF laboratories around the world. These bones will be measured by a more sensitive and standardized method after they are measured in each of these KXRF laboratories. By comparing the KXRF results and the results from the more standardized method, we will find out if there is a problem with the whole procedure for all the laboratories. If it is possible, one solution for the standardization would be for all the laboratories to use the phantoms produced by the same laboratory with the same material for system calibration, use the same software to do the data analysis, and follow the same measurement protocol.

SUMMARY AND CONCLUSION

The KXRF bone lead measurement technique has made great contributions to epidemiologic studies of lead toxicity and it will continue be a valuable exposure assessment tool in this field. Driven by the requirements of its application, this technique has been and is still in the process of being improved. On the one hand, the improvement of technology will provide more valuable data for the epidemiologic studies; on the other hand, the upgraded systems have induced some problems and concerns about the consistency of the data. A great deal of work has been done in standardizing the KXRF bone lead measurement method, and more work in this area is expected.

Acknowledgements

The research described in this paper was supported primarily by NIEHS R01-ES05257, R01-ES10798, R01-ES07821, and NIEHS Center Grant P30-ES00002. Test subjects were evaluated for measurement of bone lead levels in the outpatient Clinical Research Center of the Brigham and Women's Hospital with support from NIH grant no. NCRR GCRC M01RR02635. The KXRF instrument used in some of this work was developed by ABIOMED, Inc., of Danvers, Massachusetts, with support from NIH grant no. SBIR 2R44 ES03918-02. The authors would like to thank Mr Steve Oliveira and Dr Chitra Amarasiriwardena for their assistance in acquiring the data and information involved in the project.

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