



Letter to the Editor

An agreed statement on calculating lead concentration and uncertainty in XRF in vivo bone lead analysis

The *Journal of Applied Radiation and Isotopes* has provided a platform for a lively exchange of views amongst some of us, who develop and use X-ray fluorescence for in vivo measurement of bone lead concentration. We appreciate the opportunity to challenge each other and to air our differences in public. However, we are concerned that the vigour of these exchanges may have given the impression of a fundamental difference of approach or interpretation. This is not in fact the case and we should greatly appreciate the courtesy of being allowed the opportunity to provide a statement laying out matters pertaining to the recent debate on which we are all agreed.

(1) Bone lead concentrations are evaluated from in vivo spectra using a calibration line derived from standard addition plaster of Paris phantoms. The lead concentration generally has been calculated using

$$\text{Pb} = (k(R - c))/m, \quad (1)$$

where k is the ratio of the coherent scattering cross sections for the two different media, bone mineral and plaster of Paris, at a particular energy, 88 keV and at the range of angles subtended in in vivo bone measurements (130–170°). R is the ratio of X-ray peak amplitude (or area) to coherent scattering peak amplitude (or area), c is the intercept of the calibration line and m is the slope of the calibration line. The above equation is incorrect and the correct equation in this context (Kondrashov and Rothenberg, 2001) is

$$\text{Pb} = (kR - c)/m. \quad (2)$$

(2) The intercept in the calibration line can arise for more than one reason. (i) There is commonly a trace level of lead in the plaster of Paris. (ii) There can be external lead contamination of the phantom. (iii) There can be lead present in the environment in which measurements are being conducted, for example, on a carpet or other flooring, in painted walls or in the chair in which a subject sits. (iv) The peak extraction algorithm can, in principle, produce an artifactual signal when no lead is present. (v) There can be materials, other than plaster of Paris and lead, present in the phantoms, which can cause a positive or negative offset in the assessment of lead. Of these factors, the first

virtually always occurs, others can also be present in some circumstances. If there is good reason to suppose that trace lead contamination in the plaster of Paris used to construct the calibration phantoms is the only, or dominant factor contributing to a calibration line intercept, then the intercept should not be used in evaluating bone lead concentration and the following equation (Todd, 2000) should be used

$$\text{Pb} = (kR)/m. \quad (3)$$

(3) (i) Uncertainties in in vivo bone lead measurements are dominated by the uncertainty in X-ray peak amplitude. There are contributions to the overall lead uncertainty from uncertainties in the coherent peak amplitude, from the calibration line and from the fact that lead estimates based on PbK_α and PbK_β X-rays are largely statistically independent, but they do share common information from the coherent peak. (ii) Statements in the paper by Kondrashov and Rothenberg (2001) addressing crude uncertainty estimates and the table, which appeared to show much lower uncertainties than had previously been reported, arose from a misunderstanding of data reported by Gordon et al. (1994). This part of Kondrashov and Rothenberg's paper should be disregarded. A crude estimate of uncertainty can be derived from the expression

$$\sigma_{\text{Pb}} \simeq (k(\sigma_x/\text{coh}))/m. \quad (4)$$

Although not suitable for formal reporting of results, this expression can be useful as a quick check of performance, particularly when setting a measurement system up. (iii) In practice, the uncertainty in repeated measurements in human subjects is observed to be 20–50% higher than that accounted for by estimates of uncertainty in a single measurement. This increase in uncertainty is less apparent in phantom reproducibility. Changes in measurement geometry, sometimes accompanied by non-uniform lead distribution, even in phantoms, are amongst the reasons for this increased uncertainty.

(4) The fact that an incorrect algorithm has been used to evaluate bone lead data in the past (point 1, above) requires consideration of whether such data should now be re-evaluated. Comparing Eqs. (1) and (2), it can be

seen that, for a given calibration line, the use of the wrong equation results in a fixed offset. The difference (Δ) is given by

$$\Delta = (c(1 - k))/m \quad (5)$$

If the intercept is dropped from the evaluation altogether, which is frequently going to be the case, then the difference, Δ' , is larger in magnitude

$$\Delta = -(ck)/m. \quad (6)$$

In both cases, this difference is negative; i.e., the true bone lead concentration will have been underestimated.

The size of this fixed offset will, of course vary somewhat from calibration set to calibration set. For a given group of standard phantoms the variation in size of offset should not vary very greatly from one data set to another. If one is comparing between data derived from different sets of phantoms, then the differences in offset could be larger, probably stretching to being as large as the offset itself. The data shown for illustrative purposes in Gordon et al. (1994) have larger intercepts on the calibration lines than are commonly observed. Amongst these data, the largest intercept is for the α_2 calibration line. In this case, c is 0.0134, m is 1.87×10^{-3} and k is usually taken to be 1.46. This produces an absolute value for Δ' of 10.5 $\mu\text{g Pb/g}$ bone mineral. This represents a realistic upper bound estimate for Δ' .

If one is using bone lead data to derive some sort of absolute interpretation, for example, extrapolating to estimate mass of lead in the body, or in a particular compartment of the body, such as cortical bone, then correction should be made for previously incorrectly estimated data.

If one is comparing data collected under different sets of calibration standard data (this would commonly be the case if one were comparing a person with her/himself say 6 months previously), then both sets of data should be corrected. In this case, the difference in the calculated change in bone lead would be expected to be minor, probably 1–3 $\mu\text{g Pb/g}$ bone mineral or less. Nevertheless, correction is warranted. If one were making the same sort of comparison using calibration data derived from different sets of phantoms (not just different measurements on the same phantoms) then the impact could be larger.

If one is comparing data evaluated using the “correct” formula, either Eq. (2) or Eq. (3) (this still begs the question of whether or not to retain the intercept at all) with data previously analysed using the incorrect formula, then the previous data should certainly be re-evaluated.

The time when one does not need to re-evaluate data, because interpretation and conclusions would not be affected, is when exposed and referent data are collected under the same set of calibration phantom measurements and one is primarily interested in comparing

exposed with referent. In this case the absolute values will change, but the difference between groups will not change at all, because the correction is a fixed offset within a given set of calibration standard measurements.

To conclude, an expression involving erroneous treatment of calibration line intercepts had been used. This has now been corrected. Indeed, in many circumstances such an intercept derives from trace lead contamination in the calibration phantom material and is better set to zero in evaluating lead concentration in bone. There are a number of studies, particularly those involving repeated measurements of subjects with bone lead concentrations below about 40 $\mu\text{g Pb/g}$ bone mineral, for which the bone lead data should be re-evaluated.

References

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