

We discuss the rationale for adopting Eq. [1] to estimate forearm DXA aBMD (units: g/cm^2) from digitized X-ray measurements of attenuation in regions of interest (ROIs) in the radius and ulna and an adjacent soft tissue ROI between the radius and ulna (*Figure 2A*). The digitized X-ray measurements were converted into measurements of equivalent step phantom thickness (Eq. SPT; units: mm) using the calibration provided by the step phantom (*Figure 3A*).

$$\text{DXA aBMD} = A * \text{Bone ROI Eq. SPT} + B * \text{Soft tissue ROI Eq. SPT} + C \quad [1]$$

The digitized pixel measurements provided by the Xbone device scale with the logarithm of X-ray intensity. Hence the digitized X-ray measurements of the step phantom have a linear relationship with the thickness of each step (or equivalently with their areal density in units of g/cm^2) provided confounding technical issues such as the polychromatic X-ray spectrum, beam hardening and scatter are ignored (*Figure 3A*). To justify Eq. [1], as a first step we represent the attenuation by soft tissue in the bone ROI in the digital X-ray image by its equivalent aBMD (i.e., the areal density of bone mineral that attenuates the X-ray beam to the same degree as the soft tissue). With this understanding we write the digital X-ray equivalent forearm aBMD in the bone ROI due to the combined attenuation by bone and soft tissue as:

$$\text{Bone ROI digital X-ray equivalent aBMD} = P * \text{Bone ROI Eq. SPT} \quad [2]$$

In Eq. [2], P is the constant that relates equivalent step phantom thickness measured in mm to its equivalent areal bone mineral density measured in g/cm^2 . To convert from equivalent aBMD due to the combined attenuation by bone and soft tissue and estimate the true bone aBMD that would be measured by DXA we need to subtract the soft tissue contribution from the total digital X-ray attenuation in the bone ROI. To do this we subtracted a fraction Q of the equivalent step phantom thickness measured in the soft tissue ROI between the radius and ulna (*Figure 2A*):

$$\text{Bone ROI DXA aBMD} = P * (\text{Bone ROI Eq. SPT} - Q * \text{Soft tissue ROI Eq. SPT}) \quad [3]$$

Given that there is less soft tissue in the bone ROI than the adjacent soft tissue ROI due to the replacement of some soft tissue by bone, we expect $Q < 1$. Multivariate regression fits of the training set data to Eq. [3] gave $Q = 0.6$. In reality, Eq. [3] is a simplification of a complex problem and we expect values of Q to vary between individuals depending on bone size and soft tissue thickness through the forearm. As a generalization of Eq. [3] we also examined linear equations that allowed a constant term, R, which gave a better fit to the data:

$$\text{Bone ROI DXA aBMD} = P * (\text{Bone ROI Eq. SPT} - Q * \text{Soft tissue ROI Eq. SPT}) + R \quad [4]$$

We therefore arrive at Eq. [1] as providing a suitable fit to the data where A, B and C in Eq. [1] are respectively P, $-P * Q$ and R in Eq. [4].

As emphasized in the Discussion, Eq. [1] is a simplified approximation to a complex problem. Values of the three coefficients A, B and C in Eq. [1] derived here represent a linear approximation to a more complex solution with values that are valid for the mean forearm aBMD and forearm thickness of the study population.