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Polynomial dual energy inverse functions for bone Calcium/Phosphorus ratio determination and experimental evaluation

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HIGHLIGHTS

- Determination of bone Ca/P mass ratio using linear and nonlinear XRDE methods.
- The method was verified by measuring six test bone phantoms.
- Nonlinear quadratic function modeled calcium and phosphate thicknesses.
- Improved accuracy in the determination of the Ca/P mass ratio with nonlinear method.

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ABSTRACT

An X-ray dual energy (XRDE) method was examined, using polynomial nonlinear approximation of inverse functions for the determination of the bone Calcium-to-Phosphorus (Ca/P) mass ratio. Inverse fitting functions with the least-squares estimation were used, to determine calcium and phosphate thicknesses. The method was verified by measuring test bone phantoms with a dedicated dual energy system and compared with previously published dual energy data. The accuracy in the determination of the calcium and phosphate thicknesses improved with the polynomial nonlinear inverse function method, introduced in this work, (ranged from 1.4% to 6.2%), compared to the corresponding linear inverse function method (ranged from 1.4% to 19.5%).

1. Introduction

Crystal structure and chemical composition of biological apatite reflect bone mechanical support capabilities, which are very important to the skeletal system (Bala et al., 2013). Alterations in bone quality can be attributable to disease-related structural and chemical changes. A spectrum of methods (Bala et al., 2013; Malluche et al., 2013) is, therefore, used to measure bone tissue material properties owing to multidimensional nature of bone quality. The relative content of calcium (Ca) and phosphorus (P) acts as a regulator to maintain mineral homeostasis and bone metabolism (Moe, 2008). Since variations in the concentrations of either Ca or P are not necessarily in direct association, changes of the Ca/P ratio are crucial for the valuation of bone health. The Ca/P bone ratio, in cases of diseases, such as osteogenesis imperfecta or osteoporosis is systematically lower than that derived from normal bone samples (Fountos et al., 1998; Tzaphlidou et al., 2005; Tzaphlidou, 2008; Nakagaki et al., 2011; Hadjipanteli et al., 2014). Consequently, the determination of the Ca/P ratio as a bone quality index may add valuable information regarding bone mineralization state and bone diseases (Fountos et al., 1997; Fountos et al., 1999; Zaichick and Tzaphlidou, 2002, 2003; Zoehrer et al., 2012; Sotiropoulou et al., 2015).

Dual-energy method (XRDE) is a basis material decomposition method, firstly described by Johns and Yaffe (Johns and Yaffe, 1985; Johns et al., 1985). XRDE exploit the energy dependence of X-ray attenuation coefficients to obtain quantitative information for two or three material thicknesses in body from a pair of log-signal measurements, obtained at two different energies (Johns and Yaffe, 1985). Visualization and/or measurement of certain structures (lung nodules, calcifications and bone minerals) can be achieved due to suitable combination of the low-energy (LE) and

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the high-energy (HE) measurements (Koukou et al., in press; Kumar et al., 2015). For monoenergetic sources, the dual-energy equations are linear (Fountos et al., 1997; Lemacks et al., 2002) and can be solved for the basis-material thicknesses. However, for the broad polyenergetic spectra, obtained from X-ray tubes, dual-energy equations are nonlinear integral equations and cannot be solved analytically (Fountos et al., 1999; Lemacks et al., 2002; Sotiropoulou et al., 2015). The effective mass attenuation coefficients (Sotiropoulou et al., 2015) can be used in the linear equation system to overcome this issue. Alternatively, the dual-energy integral equations can be approximated by various nonlinear functional forms (Cardinal and Fenster, 1990; Cardinal and Fenster, 1991) for material thicknesses determination. The selected functional form is fitted to calibration data obtained by imaging or measuring a calibration phantom (Cardinal and Fenster, 1991; Kappadath and Shaw, 2004). The fitted functions are then used to decompose a pair of dual-energy log-signal images, or measurements into the corresponding material thicknesses. The accuracy of the decomposed materials depends primarily on how well the calibration data are fitted by the fitting function. When polynomial nonlinear inverse functions, for material thicknesses determination is applied, error parameters arising from beam hardening, scatter radiation and nonlinear response of the detector, can be diminished or even eliminated (Cardinal and Fenster, 1990).

The aim of this study is to investigate the use of polynomial nonlinear inverse functions for the improvement of the accuracy in the X-ray dual energy determination of the Calcium-to-Phosphorus (Ca/P) mass ratio in bones. Linear, quadratic, and cubic functional forms of inverse equations were investigated. Additionally, the presented method was compared with the dual energy X-ray method using the polynomial linear inverse functions described previously (Sotiropoulou et al., 2015). The comparison between the two dual energy methods was based on the accuracy of Ca/P mass ratio estimation.

2. Materials and methods

2.1. Ca/P mass ratio formalism

2.1.1. XRDE using linear equation system

The theory, where the in vivo determination of Ca/P mass ratio in bone parts was based, first described by Fountos et al. (Fountos et al., 1997). A bone part, of thickness T, can be considered to be composed of three materials: calcium (thickness t_{Ca}), phosphate (thickness t_{PO_4}) and water or soft tissue (thickness t_w) (Fig. 1).

The total thickness is given by:

$$T = t_{Ca} + t_{PO_4} + t_w \tag{1}$$

In Ca/P mass ratio determination the dual energy equation system is solved to obtain the thickness of each of the three materials.

Two intensity measurements (Fig. 1) are obtained for each spectrum (low and high), the I_{b,E_i} that attenuates from the three components and the I_{w,E_i} that attenuates in a bone adjacent area, which the X-ray beam was attenuated by 100% water of total thickness T, the I_{b,E_i} and I_{w,E_i} are given by:

$$I_{b,E_i} = \int I_{o,(E_i)} \cdot e^{-\frac{\mu}{\rho}(Ca,E_i)\cdot\rho_{Ca}\cdot t_{Ca} - \frac{\mu}{\rho}(PO_4,E_i)\cdot\rho_{PO_4}\cdot t_{PO_4} - \frac{\mu}{\rho}(w,E_i)\cdot\rho_w\cdot t_w} \cdot Q_{(E_i)} \cdot dE \qquad i = l, h \tag{2}$$

and

$$I_{w,E_i} = \int I_{(o,E_i)} \cdot e^{-\frac{\mu}{\rho}(w,E_i)\cdot\rho_w\cdot T} \cdot Q_{(E_i)} \cdot dE \quad i = l, h \tag{3}$$

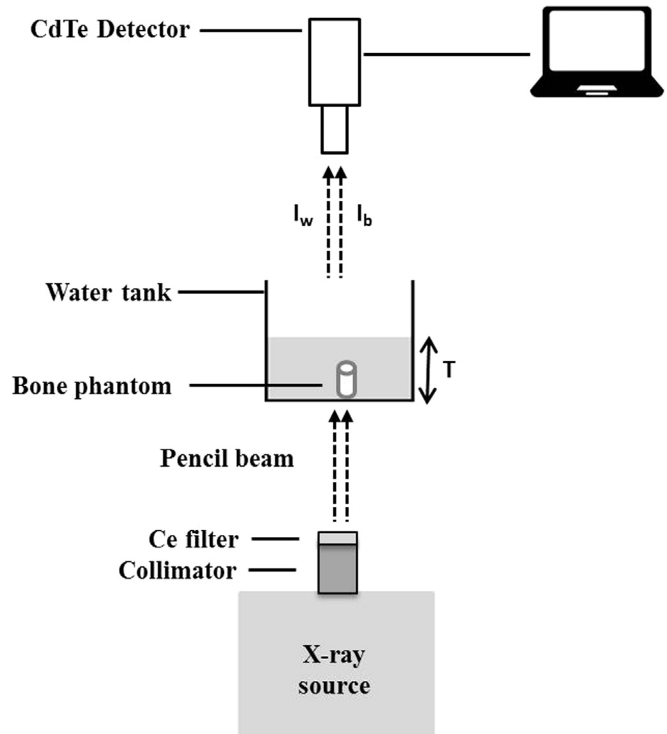

Fig. 1. Experimental set-up for measuring the Ca/P mass ratio in bone phantoms. Two irradiations (bone and adjacent area) and four measurements are obtained for each phantom, by integrated counts in two regions of interest in the energy spectrum (LE and HE).

where, I_{o,E_ℓ} and I_{o,E_h} are the unattenuated low- and high-energy photon fluence per unit energy $\left(photons/\mathrm{cm}^2\,\mathrm{keV}\right)$ at the detector input and $Q_{(E_i)}$ is the detector efficiency as a function of photons energy $E(keV)$. The mass attenuation coefficients $\left(\mathrm{cm}^2/\mathrm{g}\right)$ and density $\left(\mathrm{g}/\mathrm{cm}^3\right)$ for calcium, phosphate, and water are given by $\mu/\rho(Ca, E_i)$, $\mu/\rho(PO_4, E_i)$, $\mu/\rho(w, E_i)$ and ρ_{Ca}, ρ_{PO_4}, ρ_w, respectively.

The log-intensity function, $Y(t_{Ca}, t_{PO_4})$, defined as the logarithm of the ratio of the reference intensity, I_{w,E_i}, to the bone intensity I_{b,E_i}. The low- (Y_{E_ℓ}) and the high- (Y_{E_h}) log-intensity functions can be written as:

$$Y_{E_\ell}(t_{Ca}, t_{PO_4}) = \ln\left(\frac{I_{w,E_\ell}}{I_{b,E_\ell}}\right) \tag{4}$$

$$Y_{E_h}(t_{Ca}, t_{PO_4}) = \ln\left(\frac{I_{w,E_h}}{I_{b,E_h}}\right) \tag{5}$$

Since the X-ray spectra are polyenergetic, equation system (Eqs. (1), (4), (5)) cannot be solved analytically for t_{Ca} and t_{PO_4}. With the total thickness (T) known (Fig. 1), the two unknown parameters are the calcium thickness (t_{Ca}) and the phosphate thickness (t_{PO_4}). In order, the inverse functions, $t_{Ca}(Y_\ell, Y_h)$ and $t_{PO_4}(Y_\ell, Y_h)$, to be analytically solved, monoenergetic approach must be followed, using effective mass attenuation coefficients. According to this, the equation system (Eqs. (1), (4), (5)) becomes linear and can be solved by Cramer' method.

The two thicknesses, t_{Ca} and t_{PO_4}, are expressed by:

$$t_{Ca} = \frac{D_{Ca}}{D} = \frac{Y_\ell \cdot \Delta\mu(PO_4, E_h) - Y_h \cdot \Delta\mu(PO_4, E_l)}{\Delta\mu(Ca, E_\ell)\cdot\Delta\mu(PO_4, E_h) - \Delta\mu(Ca, E_h)\cdot\Delta\mu(PO_4, E_\ell)} \tag{6}$$