X-Ray Spectra Optimization for the Hydroxyapatite/Collagen Ratio Determination - A New Approach in Osteoporosis Diagnosis

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Abstract

The Dual energy method, using two different energies generated by an X-ray tube, has been applied in the diagnosis of osteoporosis by determining bone mass or bone density. By measuring parameters that characterize bone quality, such as the Ca/P or Hydroxyapatite/Collagen (HAp/Col) ratios, a potential bone fracture can be predicted more efficiently. The aim of this study was the optimization of dual energy X-ray spectra through the estimation of the Coefficient of Variation (CV) in HAp/Col ratio determination. The upper limit of CVHAp/Col value was set to ≤ 3%. Single and double exposure methods were used in order to obtain polyenergetic spectra. Unfiltered spectra were obtained from Boone et al (1997 Med. Phys. 24 1661–70) for Tungsten (W) anode. For the implementation of the low and high energy beams, several filters were applied to the spectra, based on their K-edges, so as to provide quasi-monochromatic beams. The optimum results, for the single exposure method, were obtained for a 120kVp spectrum with added beam filtration of 800um Ce (CVHAp/Col=1.88%). For the double exposure technique, a CVHAp/Col value of 2.23% was obtained using 40 and 120kVp with added filtration of 250um Cd and 1150um Yb, respectively.

Key words: Osteoporosis, CV, HAp/Col ratio

Introduction

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially of the hip, spine, and wrist [1]. A number of noninvasive techniques are available for measuring bone mass at multiple sites of the skeleton as X-ray and photon absorptiometry, quantitative computed tomography and ultrasound measurements [2]. Dual energy methods have also been used for osteoporosis diagnosis [3].

In conventional methods the measurement of bone does not give information about the bone quality but for the bone quantity. A non -invasive method that will have the ability to determine the bone quality is of interest. Such a method will contribute to the prediction or even the prevention of bone malfunction. A parameter that can be used in terms of bone quality assessment is Hydroxyapatite/Collagen ratio [4-7].

The aim of this study is to obtain narrower energy band of X-ray spectra using K-edge filtering technique in both single and double exposure techniques [8-12]. Optimization of these Dual-Energy X-ray spectra will be accomplished for the estimation of Coefficient of Variation (CV) in HAp/Col ratio determination [13-18].

Materials and Methods

Considering a three component attenuating system consisted of HAp, Col and Water, a statistical model was developed in order to obtain the energy pair (Low Energy-LE, High Energy-HE) which corresponds to ratios with minimum CVHAp/Col. Based on error analysis and assuming that radiation intensity follows Poisson distribution, CVHAp/Col was calculated with the following formula [10,11]:

$$
\begin{aligned}
CV^2_{\frac{HAp}{Col}} &= \left(\ln\frac{1}{I_{b(E_1)}} + \ln\frac{1}{I_{w(E_1)}}\right) \\
&\cdot\left(\frac{\left(\left(\frac{\mu_{Col}}{\rho}(E_2)d_{Col} - \frac{\mu_w}{\rho}(E_2)d_w\right)d_{HAp}\right)^2}{\left(\ln\frac{I_{w(E_1)}}{I_{b(E_1)}}\left(\frac{\mu_{Col}}{\rho}(E_2)d_{Col} - \frac{\mu_w}{\rho}(E_2)d_w\right)d_{HAp} - \ln\frac{I_{w(E_2)}}{I_{b(E_2)}}\left(\frac{\mu_{Col}}{\rho}d_{Col}(E_1) - \frac{\mu_w}{\rho}(E_1)d_w\right)d_{HAp}\right)^2}\right. \\
&\left.+\frac{\left(\left(\frac{\mu_{HAp}}{\rho}(E_2)d_{HAp} - \frac{\mu_w}{\rho}(E_2)d_w\right)d_{Col}\right)^2}{\left(-\ln\frac{I_{w(E_1)}}{I_{b(E_1)}}\left(\frac{\mu_{HAp}}{\rho}(E_2)d_{Hap} - \frac{\mu_w}{\rho}(E_2)d_w\right)d_{Col} + \ln\frac{I_{w(E_2)}}{I_{b(E_2)}}\left(\frac{\mu_{HAp}}{\rho}(E_1)d_{HAp} - \frac{\mu_w}{\rho}(E_1)d_w\right)d_{Col}\right)^2}\right)\cdot 100^2 \\
&+ \left(\ln\frac{1}{I_{b(E_2)}} + \ln\frac{1}{I_{w(E_2)}}\right) \\
&\cdot\left(\frac{\left(\left(\frac{\mu_{Col}}{\rho}d_{Col}(E_1) - \frac{\mu_w}{\rho}(E_1)d_w\right)d_{HAp}\right)^2}{\left(\ln\frac{I_{w(E_1)}}{I_{b(E_1)}}\left(\frac{\mu_{Col}}{\rho}(E_2)d_{Col} - \frac{\mu_w}{\rho}(E_2)d_w\right)d_{HAp} - \ln\frac{I_{w(E_2)}}{I_{b(E_2)}}\left(\frac{\mu_{Col}}{\rho}d_{Col}(E_1) - \frac{\mu_w}{\rho}(E_1)d_w\right)d_{HAp}\right)^2}\right. \\
&\left.+\frac{\left(\left(\frac{\mu_{HAp}}{\rho}(E_1)d_{HAp} - \frac{\mu_w}{\rho}(E_1)d_w\right)d_{Col}\right)^2}{\left(-\ln\frac{I_{w(E_1)}}{I_{b(E_1)}}\left(\frac{\mu_{HAp}}{\rho}(E_2)d_{HAp} - \frac{\mu_w}{\rho}(E_2)d_w\right)d_{Col} + \ln\frac{I_{w(E_2)}}{I_{b(E_2)}}\left(\frac{\mu_{HAp}}{\rho}(E_1)d_{HAp} - \frac{\mu_w}{\rho}(E_1)d_w\right)d_{Col}\right)^2}\right)\cdot 100^2
\end{aligned}
\quad (1)
$$

The mass attenuation coefficients for each pair of energies were calculated using data from Hubbell [19]. The substitution of the mass attenuation coefficients with the effective mass attenuation coefficients is essential in order to calculate the CV. The energy-dependent effective mass attenuation coefficients can be calculated as follows [20]:

$$
({}^{\mu}/_{\rho})_{eff} = \frac{\sum_{E_{min}}^{E_{max}} I_{filtered}(E)\frac{\mu}{\rho}(E)}{\sum_{E_{min}}^{E_{max}} I_{filtered}(E)} \quad (2)
$$

In order to obtain the two energies single and double exposure techniques were used. In the case of single exposure technique, one exposure is required with K-edge filtering for both energies to be present simultaneously in the radiation beam. This method requires photon counting energy dispersive detectors. In double exposure technique two sequential measurements at different kVps, typically with different beam filters, are required. In this method both photon counting and energy dispersive (imaging) detectors can be used.

In order to obtain quasi-monochromatic spectra, in single exposure technique, all the lanthanide filters were used in a kVp range from 50 to 120kVp. The thickness ranged from 100 to 2000um, in 50um increments. Filters with K-edges ranging from 25 to 33keV for the low energy, and from 70 to 83keV for the high energy were used for the double exposure technique. The thickness range was the same as in single exposure technique. The kVp range was from 40 to 50kVp for the low energy, and 100 to 120kVp for the high energy. The unfiltered spectra were obtained from Boone et al. (1997 Med. Phys. 24 1661-1670) for a Tungsten anode [21].

The optimization of the X-ray spectra was based on the minimization of (i) Root Mean Square Error (RMSE)[22] of spectral energy band, and (ii) the CV of incident photons, where CVIinc <0.3%, which corresponds to 105 incident photons after filtration.

Results and Discussion

In Table 1 the results of the single exposure technique are shown. Only two filters resulted in a $CV_{HAp/Col}$ lower than 3% which was set as the upper limit. It should be mentioned that the Cerium (Ce) filtered spectrum with 800um at 120kVp gave the lowest $CV_{HAp/Col}$ (1.88%) among all.

Table 1. Single exposure results

Filter material	Thickness (um)	kVp	Mean Energy (keV)		RMSE		$CV_{HAp/Col}$ (%)
			LE	HE	LE	HE	
Ce	900	110	36	85	0.15	1.56	2.86
	800	120	37	89	0.18	2.19	1.88
Sm	850	120	43	93	0.21	1.65	2.92
	900	120	43	94	0.19	1.57	2.97

Figure 1 shows the spectra resulted in the lowest $CV_{HAp/Col}$. In the case of Cerium filter the lowest $CV_{HAp/Col}$ value was 1.88 achieved by 800um thickness at 120kVp with mean energies 37 and 89keV for low and high energy respectively. In the case of Samarium filter the lowest $CV_{HAp/Col}$ value was 2.92 achieved by 850um thickness at 120kVp with mean energies 43 and 93keV for low and high energy respectively.

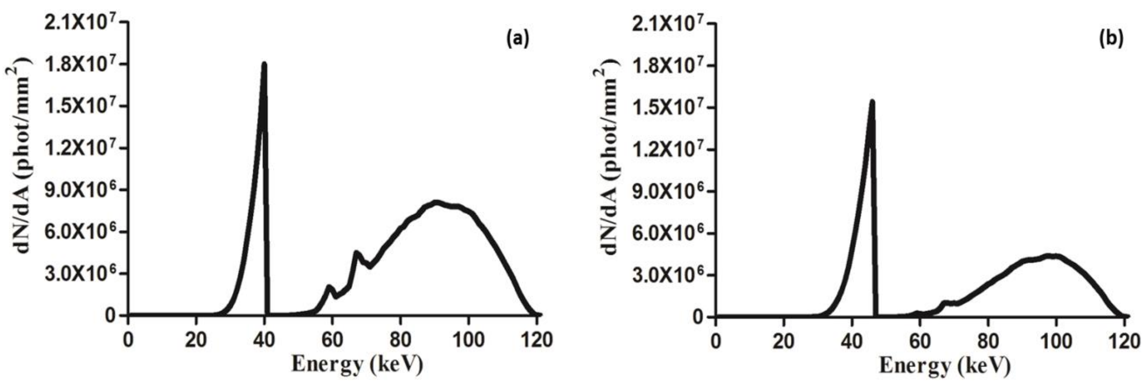

Figure 1. (a) 120kVp spectrum filtered with 800μm Ce, (b) 120kVp spectrum filtered with 850μm Sm

In Figures 2 and 3 RMSE and CV_{Iinc} plotted as a function of surface density in order to select the low energy filter are shown. In the RMSE plot it can be clearly seen that Cadmium (Cd) and Silver (Ag) are the filters with the lowest values. For the final selection of the low energy filter, these two filters were compared in the CV_{Iinc} plot, where Cd has slightly smaller values than Ag. According to these, the low energy filter that was selected is Cd.

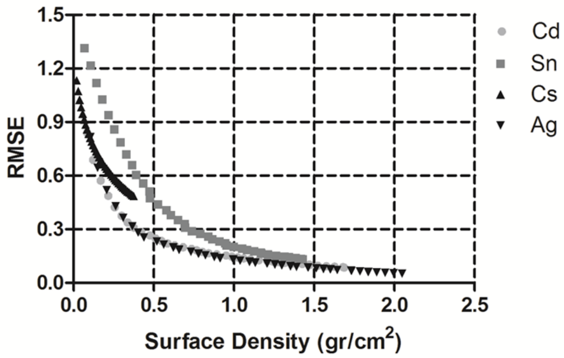

Figure 2. RMSE plots of the low energy filters as a function of surface density

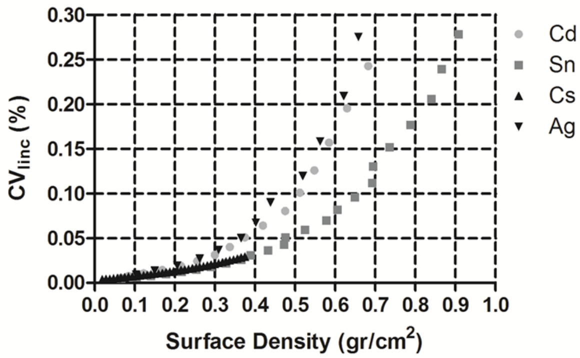

Figure 3. CV_{Iinc} plots of the low energy filters as a function of surface density

The same procedure was followed for the selection of the high energy filter. Ytterbium (Yb) and Bismuth (Bi) are the two filters with the lowest values in the RMSE plot. Yb has also the lowest values in the CV_{Iinc} plot compared to Bi. For these reasons the high energy filter that was selected is Yb. Figures 4 and 5 show the RMSE and CV_{Iinc} plots for the high energy filter selection.

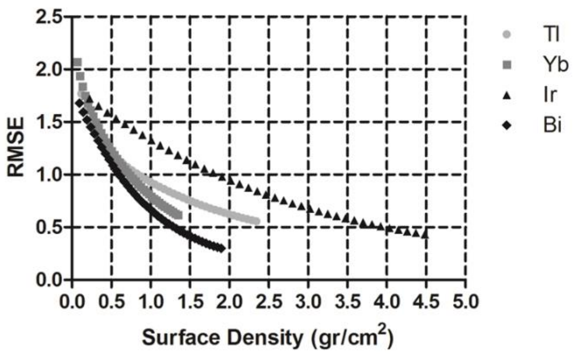

Figure 4. RMSE plots of the high energy filters as a function of surface density

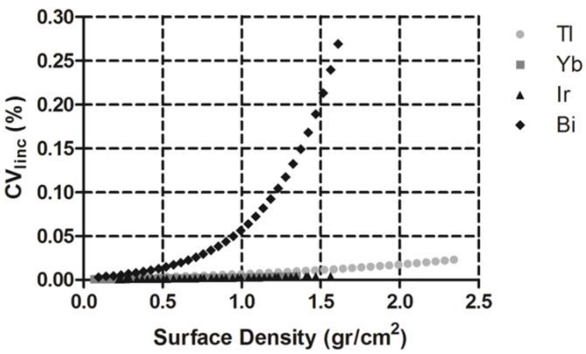

Figure 5. CV_{Iinc} plots of the high energy filters as a function of surface density

Figure 6 presents the low and high energy spectra for the double exposure technique as they were selected by the procedure described above.

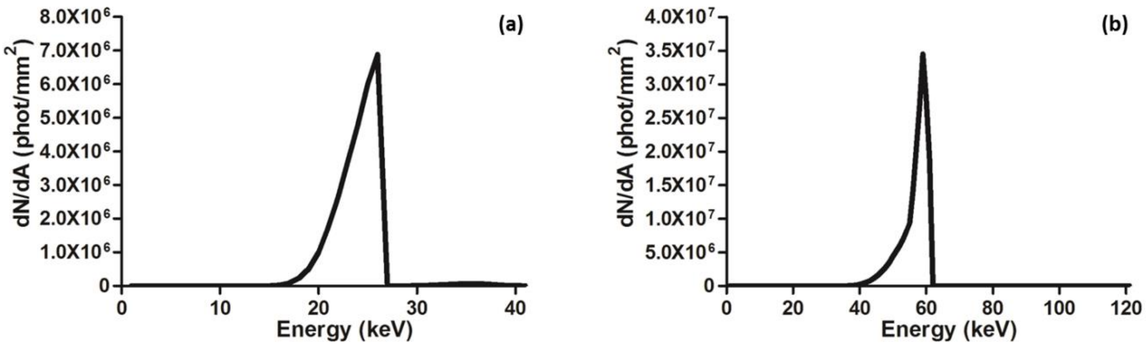

Figure 6. (a) 40kVp spectrum filtered with 250μm Cd combined with (b) 120kVp spectrum filtered with 1150μm Yb

Conclusion

In this study, optimization of dual energy X-ray spectra through the estimation of the CV was performed in order to improve the precision of HAp/Col ratio. For the single exposure method the X-ray spectrum at 120 kVp filtered with 800um Ce indicated the best performance characteristics for the determination of $CV_{HAp/Col}$. For the double exposure method the minimum $CV_{HAp/Col}$ was obtained from combination of 40kVp Cd filtered spectrum (LE) and 120kVp Yb filtered spectrum (HE), with 250 and 1150um, respectively.

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References

1. WHO scientific group on the assessment of osteoporosis at primary health care level: “Summary Meeting Report Brussels”, Belgium, 5-7 May 2004
2. Grampp S, Jergas M, Glüer C.C., Lang P., Brastow P., Genant H.K.: “Radiologic diagnosis of osteoporosis. Current methods and perspectives”, *Radiologic Clinic North America* 1993 Sep;31(5):1133-45.
3. Baltas C.S., Balanika A.P., Raptou P.D., Tournis S., Lyritis G.P. “Clinical practice guidelines proposed by the Hellenic Foundation of Osteoporosis for the management of osteoporosis based on DXA results”, *J Musculoskelet Neuronal Interact* 5(4):388-392, 2005
4. Friedman A.W. “Important determinants of bone strength: beyond bone mineral density”, *J. Clin. Rheumatol.*12, 70-77, 2006
5. Fountos G., Kounadi E., Tzaphlidou M., Yahumura S., and Glaros D. “The effects of Inflammation-mediated Osteoporosis (IMO) on the Skeletal Ca/P Ratio and on the structure of Rabbit Bone and Skin Collagen”, *Appl. Radiat. Isot*. 49, 657-659, 1998
6. Jiroušek O. “Nanoindentation of Human Trabecular Bone – Tissue Mechanical Properties Compared to Standard Engineering Test Methods,

Nanoindentation in Materials Science" Dr. Jiri Nemecek (Ed.), ISBN: 978-953-51 0802-3, InTech, DOI: 10.5772/50152, 2012
7. Isaksson H., Turunen M.J., Rieppo L., Saarakkala S., Tamminen I.S., Rieppo J. "Infrared spectroscopy indicates altered bone turnover and remodeling activity in renal osteodystrophy", *Journal of Bone and Mineral Research* 25(6), 1360-1366, 2010
8. Rutt B. "Dual-energy X-radiography with gadolinium filter", *NASA Tech. Brief 11*, *JPL Invention Report* No. NPO-16773/SC-1443 Jet Propulsion, Pasadena, CA, 1987
9. Kuhn H. "Reduktion der Patientendosis durch Vorfilterung Electrornedica" 2 41- 4-1 985 Reduktion der Patientendosis bei bestmoglicher Sicherung der Bildqualita*R*t *6ntgen-B/.* 38 224-30, 1982
10. Gustaffson L., Jacobson B., and Kusoffsky L. "X-ray spectrophotometry for bone mineral determinations", *Medical and Biological Engineering* 12,113, 1974
11. Koedooder K., and Venema H.W. "Filter materials for dose reduction in screen-film radiography", *Phys. Med. Biol.* 31,585-600, 1986
12. Nagel H.D. "Comparison of performance characteristics of conventional and K-edge filters in general diagnostic radiology", *Phys. Med. Biol.* 34, 1269-1287, 1989
13. Friedman A.W. "Important determinants of bone strength: beyond bone mineral density*", J. Clin. Rheumatol.*12, 70-77, 2006
14. Jiroušek O. "Nanoindentation of Human Trabecular Bone – Tissue Mechanical Properties Compared to Standard Engineering Test Methods, Nanoindentation in Materials Science" Dr. Jiri Nemecek (Ed.), ISBN: 978-953-51 0802-3, *InTech,* DOI: 10.5772/50152, 2012
15. Isaksson H., Turunen M.J., Rieppo L., Saarakkala S., Tamminen I.S., Rieppo J. "Infrared spectroscopy indicates altered bone turnover and remodeling activity in renal osteodystrophy", *Journal of Bone and Mineral Research* 25(6), 1360-1366, 2010
16. Tzaphlidou M., Fountos G., and Glaros D. "Bone Hydroxyapatite/Collagen ratio In vivo measurements by x-ray absorptiometry"
17. Tzaphlidou M., Speller R., Royle G., Groffiths J., Olivo A., Pani S., and Longo R. "High resolution Ca/P maps of bone architecture in 3D synchrotronradiationmicrotomograpfic images", *Appl. Radiat. Isot.* 62, 569-575, 2005
18. Fountos G., Yasumura S., and Glaros D. "The skeletal calcium/phosphorus ratio: A new in vivo method of determination", *Med. Phys.* 24, 1303-1310, 1997
19. Hubbel J and Seltzer M. "Tables of X-ray mass attenuation coefficients and mass energy absorption coefficients 1 keV to 20MeV for elements Z=1 to 92 and 48 additional substances of dosimetric interest", NISTIR 5632
20. Toutounztzis A. "Upgrading dual energy angiography algorithms", Master Thesis, 2009
21. Boone et al., "An accurate method for computer-generating tungsten anode Xray spectra from 30 to 140kV", Med. Phys., 1661-1670, 1997
22. Fountos G., Michail C., Zanglis A., Samartzis A., Martini N., Koukou V., Kalatzis I., Kandarakis I. "A novel easy-to-use phantom for the determination of MTF in SPECT scanners", *Med. Phys.*, 39, 1561-1570, 2012