Feasibility of Radiographic Absorptiometry of the Mandible as an Osteoporosis Screening Method

Julie A. Skipper
Wright State University

Follow this and additional works at: http://corescholar.libraries.wright.edu/etd_all

Part of the Biomedical Engineering and Bioengineering Commons

Repository Citation

This Dissertation is brought to you for free and open access by the Theses and Dissertations at CORE Scholar. It has been accepted for inclusion in Browse all Theses and Dissertations by an authorized administrator of CORE Scholar. For more information, please contact corescholar@www.libraries.wright.edu.
FEASIBILITY OF RADIOGRAPHIC ABSORPTIOMETRY
OF THE MANDIBLE AS AN
OSTEOPOROSIS SCREENING METHOD

A dissertation submitted in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

By

JULIE A. SKIPPER
B.S.B.E., Wright State University, 1991

2003
Wright State University
I HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER MY SUPERVISION BY Julie A. Skipper ENTITLED Feasibility of Radiographic Absorptiometry of the Mandible as an Osteoporosis Screening Method BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF Doctor of Philosophy.

__________________________________
Thomas N. Hangartner, Ph.D.
Dissertation Director

__________________________________
Gerald M. Alter, Ph.D.
Director, Biomedical Sciences Ph.D. Program

__________________________________
Joseph F. Thomas, Jr., Ph.D.
Dean, School of Graduate Studies

Committee on Final Examination

__________________________________
Thomas N. Hangartner, Ph.D.

__________________________________
Jay B. Dean, Ph.D.

__________________________________
Ping He, Ph.D.

__________________________________
John E. Horton, D.M.D., M.S.D

__________________________________
Michele G. Wheatly, Ph.D.
ABSTRACT

Skipper, Julie A. Ph.D., Biomedical Sciences Ph.D. Program, Wright State University, 2003. Feasibility of Radiographic Absorptiometry of the Mandible as an Osteoporosis Screening Method.

The purpose of this work was to develop and evaluate single- and dual-energy radiographic absorptiometry (RA) for the measurement of mandibular bone mineral density (BMD), using standard dental equipment, that would allow for inexpensive and widespread osteoporosis screening. Accurately measured x-ray tube spectra are important for validating the simulations used in the design of the method. A constrained least-squares deconvolution technique for reducing the detector-induced blurring of the energy spectrum was developed. Application of this analytic correction to spectra acquired with a NaI-photomultiplier detector improved the measured data by 20-60%. Implementation of the screening method is accomplished by simultaneously acquiring high- and low-energy images on a single dental radiograph by appropriate filtering of the dental x-ray tube output. Computer simulations were performed to optimize the filters with respect to error in the bone measurement. A custom-designed film holder houses the beam filters and accommodates calibration wedges that allow the radiographs to be normalized for differences in exposure and developing conditions. Forty-six
male and female subjects, ages 27 to 87 years, participated in a pilot study to assess the RA techniques. Left and right vertical periapical radiographs were taken of the premolar-molar region and, for comparison, the subjects’ BMD was evaluated at the spine, left and right femur as well as total body by dual-energy x-ray absorptiometry (DXA). Mandibular BMD by either high or low single-energy RA measurements was positively correlated with skeletal BMD, as assessed by DXA, at the arms, legs, trunk, ribs, pelvis, total body and femoral neck. ROC analysis of the single-energy techniques for identification of osteopenic and osteoporotic female subjects, as defined by DXA at the left femoral neck, yielded an area under the curve of 0.73. This is comparable to commercial devices currently used for screening and indicates that the RA method may be valuable for early diagnosis of low bone mass.
# TABLE OF CONTENTS

Overview ........................................................................................................................................ 1

Appendices

A. List of abbreviations .................................................................................................................. 4

B. Deblurring of x-ray spectra acquired with a NaI-photomultiplier detector
by constrained least-squares deconvolution ................................................................................. 5
   Abstract ..................................................................................................................................... 6
   I. Introduction .......................................................................................................................... 6
   II. Background ......................................................................................................................... 6
   III. Experimental Setup ........................................................................................................... 8
   IV. Experimentally Measured Spectra ..................................................................................... 8
   V. Methods for Spectral Correction ......................................................................................... 10
   VI. Results ............................................................................................................................... 12
   VII. Discussion ......................................................................................................................... 12
   VIII. Conclusion ....................................................................................................................... 14

References ...................................................................................................................................... 14
TABLE OF CONTENTS (continued)

C. Feasibility of radiographic absorptiometry of the mandible as an osteoporosis screening method

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>17</td>
</tr>
<tr>
<td>1. Introduction</td>
<td>18</td>
</tr>
<tr>
<td>2. Background</td>
<td>19</td>
</tr>
<tr>
<td>3. Mandibular Measurement Device</td>
<td>27</td>
</tr>
<tr>
<td>4. Pilot Study</td>
<td>34</td>
</tr>
<tr>
<td>5. Results</td>
<td>37</td>
</tr>
<tr>
<td>6. Discussion</td>
<td>39</td>
</tr>
<tr>
<td>7. Conclusion</td>
<td>48</td>
</tr>
<tr>
<td>References</td>
<td>49</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

B1. 40-90 kVp spectra collected with NaI-photomultiplier detector ............ 9
B2. 40-90 kVp reference spectra generated from the TASMIP code ........ 9
B3. 40-90 kVp x-ray spectra collected with the Ge system ...................... 9
B4. Contribution of characteristic tungsten peaks to second peak ........... 10
B5. Results of convolving reference spectra with blurring operator ........ 10
B6. High counts at low energies are likely due to thermionic emission ...... 12
B7. Results of constrained least-squares spectral deconvolution ........... 13
B8. Difference histograms after application of the technique ................ 13
C1. Diagram of the film holder .......................................................... 55
C2. K-edge filtration technique ......................................................... 56
C3. Ratio of average energies of the filtered spectra ............................. 57
C4. Effect of filter thicknesses on measurement uncertainty ................. 58
C5. Theoretical and experimental filtered x-ray tube spectra .................. 59
C6. Sample film acquired using the special holder ............................... 60
C7. Sample high- and low-energy calibration curves ............................ 61
C8. Sample patient film with high- and low-energy ROIs shown .............. 62
C9. Plot used to determine the homogeneous sub-ROIs ....................... 63
C10. Correlation between mandibular BMD by RA and arm BMD by DXA .. 64
C11. Simulated high-energy copper-equivalent thickness values ............. 65
C12. Bone/soft-tissue combinations producing a fixed copper thickness .... 66
## LIST OF TABLES

B1. FWHM of Gaussian curve fit to the difference histograms....................... 13

C1. Skeletal BMD status as assessed by DXA............................................. 52

C2. Correlation between mandibular BMD and skeletal BMD....................... 53

C3. ROC analysis of mandibular BMD by single-energy RA......................... 54
OVERVIEW

This dissertation is presented in two parts. The first section describes the development of a deconvolution technique to correct diagnostic x-ray tube energy spectra for inherent blurring by scintillation detectors. This procedure was necessary to accurately characterize spectra to be used in a radiographic osteoporosis screening method. An analytical post-processing technique was developed and implemented for NaI-acquired spectra. This constrained least-squares method seeks to find an estimate of a true function from its degraded form. A priori knowledge of the degradation phenomenon as well as the statistical nature of the noise is required. In our case, the detector response as a function of energy was the degradation operator and a Poisson probability distribution for the noise estimate was assumed. A criterion function was defined that combined an assessment of goodness of fit with a weighted measure of the smoothness of the solution. Application of the correction resulted in a 20-60% improvement in matching of the acquired spectra to reference spectra. This work is described in the published article Deblurring of x-ray spectra acquired with a NaI-photomultiplier detector by constrained least-squares deconvolution

Although the analytical correction works well to retrieve the general spectral shape, it is less successful for spectra that are not smooth. The x-ray
tube spectra for the screening device were to be filtered using K-edge techniques and this introduces discontinuities in the spectra. We, thus, acquired a high-resolution semiconductor detector system to accurately measure the x-ray tube output.

The second section of this dissertation describes the theory, method and results of our novel approach to osteoporosis screening. The manuscript *Feasibility of radiographic absorptiometry of the mandible as an osteoporosis screening* (Appendix C) has been submitted for publication. Forty-six subjects participated in a pilot study, in which high- and low-energy images were acquired simultaneously on a calibrated dental radiograph.

The results of the pilot study indicate that single-energy radiographic absorptiometry (RA) shows promise for osteoporosis screening. Using receiver-operator characteristics (ROC) analysis, with positive cases defined as females whose T-score from dual-energy x-ray absorptiometry (DXA) at the left femoral neck was below -1.0, the areas under the curve (AUC) for the high- and low-energy mandibular RA techniques were 0.73 and 0.70, respectively. A T-score threshold of -1.0 is ideal for screening purposes because this cutoff identifies persons at risk for developing osteoporosis, yet their bone loss is not so great that it is too late for treatment to be effective.

In addition to osteoporosis screening, the low implementation and procedure costs of our method make it ideally suited for evaluating patients for possible bone loss in areas of the world with limited access to healthcare resources. The single-energy method could also be easily incorporated in any
dental setting for assessment of bone integrity for dental implant planning.

To overcome the design constraints associated with an intraoral device and the uncertainties introduced by inhomogeneity of the general mandibular ROI, measurement of phalangeal BMD with a similar technique is planned. While a finger measurement might be unanticipated at a dentist’s office, the same benefits exist for the patient and practitioner: inexpensive and highly available screening for low bone mass.

References


### APPENDIX A

**LIST OF ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC</td>
<td>analog-to-digital converter</td>
</tr>
<tr>
<td>AUC</td>
<td>area under the curve</td>
</tr>
<tr>
<td>BMD</td>
<td>bone mineral density</td>
</tr>
<tr>
<td>BUA</td>
<td>broadband ultrasound attenuation</td>
</tr>
<tr>
<td>DAC</td>
<td>digital-to-analog converter</td>
</tr>
<tr>
<td>DPA</td>
<td>dual photon absorptiometry</td>
</tr>
<tr>
<td>DSA</td>
<td>digital spectrum analyzer</td>
</tr>
<tr>
<td>DXA</td>
<td>dual-energy x-ray absorptiometry</td>
</tr>
<tr>
<td>FWHM</td>
<td>full width at half maximum</td>
</tr>
<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
</tr>
<tr>
<td>kVp</td>
<td>kilovoltage peak</td>
</tr>
<tr>
<td>L1-L4</td>
<td>1st-4th lumbar vertebrae</td>
</tr>
<tr>
<td>MCA</td>
<td>multichannel analyzer</td>
</tr>
<tr>
<td>OD</td>
<td>optical density</td>
</tr>
<tr>
<td>PA</td>
<td>posterior-anterior</td>
</tr>
<tr>
<td>QCT</td>
<td>quantitative computed tomography</td>
</tr>
<tr>
<td>RA</td>
<td>radiographic absorptiometry</td>
</tr>
<tr>
<td>RC</td>
<td>resistor-capacitor</td>
</tr>
<tr>
<td>ROI</td>
<td>region of interest</td>
</tr>
<tr>
<td>ROC</td>
<td>receiver-operator characteristics</td>
</tr>
<tr>
<td>SERM</td>
<td>selective estrogen receptor modulator</td>
</tr>
<tr>
<td>SOS</td>
<td>speed of sound</td>
</tr>
<tr>
<td>SPA</td>
<td>single photon absorptiometry</td>
</tr>
<tr>
<td>SXA</td>
<td>single-energy x-ray absorptiometry</td>
</tr>
<tr>
<td>US</td>
<td>ultrasound</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Deblurring of x-ray spectra acquired with a NaI-photomultiplier detector by constrained least-squares deconvolution

Julie A. Skipper and Thomas N. Hangartner
BioMedical Imaging Laboratory, Wright State University and Miami Valley Hospital, 504 East Building, One Wyoming Street, Dayton, Ohio 45409

(Received 9 October 2001; accepted for publication 11 February 2002; published 16 April 2002)

A constrained least-squares technique to correct diagnostic x-ray tube energy spectra for inherent blurring by scintillation detectors was developed. The measured detector response function to monoenergetic sources was used to construct a matrix that modeled the energy broadening in the crystal. This blurring operator, along with an estimate of statistical noise in the count data, comprised the a priori system knowledge required for application of the method. Tungsten anode spectra up to 90 kVp were acquired with a NaI-photomultiplier detector system at a source-to-detector distance of 30 cm. X-ray tube output was collimated at the detector by a 0.5 mm diameter pinhole collimator. Measured NaI spectra were compared to both published reference data and to spectra acquired in our laboratory with a Ge detector system. Application of the constrained least-squares technique involved first defining a criterion function that combined an assessment of the goodness of fit with a weighted measure of the smoothness of the solution. Minimization of this function resulted in the corrected spectrum. While it is not possible to recover the characteristic tungsten peaks, the success of our method in deconvolving the measured spectra was demonstrated by a significant improvement in agreement with reference data. To provide a measure of this agreement, a histogram of the differences between the two curves was generated. The full width at half maximum (FWHM) of the Gaussian distribution fit to the histogram was used to quantify the similarity between the spectra and the reference data, both before and after correction. As spectral agreement improves, the FWHM becomes smaller. We show that application of the constrained least-squares technique improved spectral matching by 20%–60%. © 2002 American Association of Physicists in Medicine. [DOI: 10.1118/1.1469628]

Key words: x-ray spectrum, NaI detector, energy resolution, deconvolution

I. INTRODUCTION

Accurate measurement of x-ray tube energy spectra is precluded by inherent distortion of the signal at the detector. Misrepresentation of count and energy information occurs, to some degree, in all types of radiation detectors. This is particularly true for the most commonly available detector type, the scintillation detector. Popular for their low cost and fast counting capability, the scintillators are not well suited for measuring continuous spectra because of their poor energy resolution. To arrive at the underlying spectrum, the measured spectrum must be corrected for many spurious effects.1-5 The degree to which each factor influences the spectrum is dependent on the detector type and geometry, x-ray tube potential, high-voltage generator stability, photon count rate, and measurement setup. Several published techniques for correcting spectra acquired with scintillation detectors are available; in general, they are valid for a broad energy range that includes both diagnostic and therapeutic energies. Individual or multiple corrections for intrinsic broadening of the spectrum by the detector, k escape, Compton scatter and detector efficiency are accomplished with matrix techniques,6 iterative calculations,7,8 or point-by-point adjustments.9,10 Monte Carlo simulation may be necessary to determine the appropriate input parameters, such as the Compton continuum, for each particular setup.11 Certain methods require trial and error to determine the influence of tungsten characteristic radiation.12,13 Thus these corrections can be cumbersome.

We investigated many factors that influence spectral measurement using a NaI-photomultiplier detector in the diagnostic energy range and developed a technique for recovering the true energy spectrum from the measured data. Previously published methods for spectral correction require a thorough understanding and modeling of each process that influences the measured spectrum. In contrast, our proposed technique requires only a background spectrum measurement and quantification of the detector response function, which is easily accomplished. While unable to recover the characteristic tungsten peaks, deconvolution allows rapid deblurring of a collected spectrum to obtain the fundamental spectral shape. Since all of the matrices needed in the computations may be precalculated, actual computing time to find an optimum corrected spectrum is less than 5 s.

II. BACKGROUND

A. Factors influencing spectral data

Statistical fluctuations occurring at each stage of the detector system determine its response function. The number of light photons produced in the crystal per unit photon energy
input, the number of electrons produced at the photocathode per light photon input, and the amplification of electrons in the dynode chain of the photomultiplier tube follow a Poisson distribution. The result is a predictable broadening of the detector response to a monoenergetic event.

Several factors distort the number of counts recorded. Background radiation introduces additional counts. Preamplifier and discriminator hysteresis, along with oscillatory ringing of the preamplifier output signal, can retrigger the discriminator and generate multiple pulses from a single event. Primary and secondary scatter result in artificially elevated counts over defined energy ranges.

Other factors lead to misrepresentation in the recorded energy of a measured photon; many are count-rate dependent. With high count rates, the preamplifier voltage may not return to baseline between events, leading to a voltage offset. Another consequence of high count rates is pulse pileup, which may result in the summation of photon energies. When pileup occurs, the recorded energy will be the sum of a fraction of the energy of the first photon plus the energy of the second photon. Thus the measured photon can appear in the energy range from partially summed to fully coincident events. Inadequate crystal thickness may lead to incomplete absorption of higher-energy events and thus produce a reduced energy reading.

The geometry of the crystal and coupling of the crystal to the photomultiplier tube influence the efficiency of counting. Crystal and end cap materials, along with the air path at large source-to-detector distances, introduce attenuation and k-edge effects. Measurement electronics also influence how a spectrum is recorded. Linearity of the analog-to-digital converter (ADC) in a multichannel analyzer (MCA) system, or of the digital-to-analog converter (DAC) in a lower-level discriminator, determines the resolution of the energy bins. Timing pulse circuitry influences the counting interval at each threshold.

B. Methods to calculate energy spectra

Because accurate measurement of x-ray tube energy spectra is difficult, researchers and clinicians frequently rely on published sources of spectral data. These spectra have been acquired under carefully controlled laboratory conditions. Since catalog data are limited to a finite set of target materials, tube potentials, and filtration, several researchers have developed and refined methods for calculating spectra using semiempirical methods. Kramers' early theory describing the bremsstrahlung spectrum generated by an x-ray tube neglected target attenuation and assumed a constant value for the differential cross-section coefficient used to calculate the intensity of emitted photons at the point of production. One of the earliest models for spectrum calculation was based on data from Kramers' theory adjusted for absorption within the target. Calculated data were compared to attenuation measurements to determine the differential energy intensity of bremsstrahlung production. The attenuation parameters used in this model were later modified by Birch and Marshall to generate spectra that more closely match measured data over a range of tube potentials, filtration, and target angles. A subsequent model, developed by Tucker et al., incorporated bremsstrahlung and characteristic x-ray production at varying depths within the target and used a nonlinear least-squares technique to fit the calculated data to measured spectra. Several researchers have compared the various models and codes for calculating spectra.

To concisely describe x-ray spectra, a parametric approach has been suggested. Three parameters, including anode angle, equivalent kilovoltage, and equivalent aluminum filtration, can be used to describe a particular x-ray spectrum. Using the Birch and Marshall model, the algorithm generates an idealized spectrum that is of equivalent quality, in terms of attenuation characteristics, as the actual spectrum. While the input anode angle is the actual anode angle, the equivalent kilovoltage and equivalent aluminum filtration parameters are adjustable so that the calculated spectrum matches the true spectrum.

Monte Carlo simulations have more recently been employed to calculate spectra in the diagnostic range. While the results for 30 kVp spectra and 30–150 kVp spectra compare well to measured data, this is not a straightforward means for determining spectra. Beam and target geometries and exact target composition must be appropriately modeled, and modifications to standard Monte Carlo radiation transport code are necessary for diagnostic medical physics applications.

Alternative methods have been proposed that require measurements from the particular system of interest. Silberstein recognized the relationship between the attenuation curve, measured with absorbers of various thicknesses, and the energy spectrum. Others subsequently applied different methods of numerical analysis of the attenuation data, including Laplace transform techniques, iterative methods, and matrix manipulation.

Application of catalog or theoretical spectral data is valid only if the x-ray system is well characterized. Rarely is the inherent filtration or applied high-voltage known with certainty, and these quantities are difficult to measure directly. Additionally, these theoretical approaches do not confirm proper operation of the x-ray system. Calculation of an energy spectrum from attenuation data is also problematic. There are errors associated with ion chamber measurements (the type of detector usually employed for the attenuation measurements) and it has been shown that very differently shaped spectra can yield identical attenuation data. Furthermore, since detector efficiency intrinsically affects photon attenuation, sets of transmission measurements must be acquired for each piece of equipment.

Our proposed method for determining the energy spectrum requires only a characterized NaI-photomultiplier system. Correction of the acquired spectral data to ascertain the true spectrum is possible in a few seconds. Since no further measurements or simulations are necessary, routine spectral measurement is possible.
III. EXPERIMENTAL SETUP

A. Spectrum acquisition with NaI-photomultiplier detector

X-ray tube energy spectra were acquired from a fixed-anode tube with a 0.5 mm focal spot size and a 15° anode angle (Comet, Bern, Switzerland) powered by a high-voltage supply with a ripple of less than $10^{-4}$ Vpp (Fug, Rosenheim, Germany). The tube output is collimated at the exit window by a Cerrabend (lead alloy) collimator that fits over the tube housing and has a 1 cm×1 cm opening. Further collimation is accomplished with a 0.5 mm $\varnothing$ pinhole collimator placed at the detector. This 1/8-in-thick lead collimator is mounted on an adjustable frame for precise alignment in two directions within the plane of the collimator. The detector is a 10 mm $\varnothing$×8 mm NaI crystal (Harshaw, Solon, OH) coupled to a 13 mm $\varnothing$ photomultiplier tube (model R647-14, Hamamatsu Corporation, Bridgewater, NJ) and high-voltage power supply (model HV4032A, LeCroy Research Systems, Chestnut Ridge, NY). Factory testing of the detector showed a nominal energy resolution [full width at half maximum (FWHM)] of 25% at 22 keV. The crystal is sealed in a 0.4 mm Al casing and housed in a 0.4 mm polyethylene insert. To maximize the path length available for absorption, a side-entry configuration is used. The end cap of the crystal is covered with lead; a 5 mm×6.5 mm window in the side of the detector housing allows photons to enter the crystal. With an absorption path length of 10 mm, over 99% of 90 keV photons will be captured.

Photon counting was accomplished with CAMAC modules, including a discriminator (model 3412E, LeCroy Research Systems) and scaler (model 4434, LeCroy Research Systems), that are controlled by a crate controller (model 3922, KineticSystems Corporation, Lockport, IL) interfaced to an AlphaStation 400 workstation (Compaq Computer Corporation, Houston, TX).

The discriminator is a 200 MHz lower-level discriminator. If the detector output pulse height is greater than the set voltage threshold, the discriminator generates a logic pulse that is read by the scaler. A 12 bit digital-to-analog converter (DAC) generates the voltage threshold based on digital input from the workstation. One bit corresponds to a voltage step size of 1/4096 V, or approximately 0.25 mV. Our typical combination of high-voltage, preamplifier gain and digital step input resulted in a voltage threshold step size that corresponds to about 0.9 keV. By sweeping through the energy range and counting photons at each threshold level, a cumulative spectrum is obtained. At each threshold, at least 100 count measurements were averaged to improve precision. Subtraction of adjacent data points yielded the number of photons per 0.9 keV energy bin.

Spectra were acquired with tube potentials from 30 to 90 kVp and tube currents of 0.05–0.20 mA. For a typical source-to-detector distance of 30 cm, the count rate at the detector is less than 10,000 cps at a discriminator threshold level just above noise. A custom-built preamplifier shapes the detector signal and provides an output pulse with a width that is typically less than 500 ns. The duration of the leading edge of the pulse is about 100 ns, regardless of pulse height. The time constant of the trailing edge is generally about 220 ns, but can range from 150 to 250 ns, depending on pulse height and shape. Calculation of dead time for the detector-discriminator system requires a measurement of the time between threshold crossings on either side of the wave form peak. Therefore, dead time is dependent on the threshold setting. For a given wave form, when the threshold is high (near the peak) the signal recrosses the threshold setting much earlier than when the threshold is low (near the baseline). As an example, for a typical 40 keV pulse, the dead time with a threshold setting of 80% of the peak value is 52 ns, while with a threshold setting of 20% of the peak value, the dead time is 242 ns. However, even with low thresholds, the dead time is usually less than 285 ns. Using the formula for a nonparalyzable counting system, for input count rates of up to $10^6$ cps, the dead time correction is less than 0.4%.

B. Spectrum acquisition with Ge detector

An 8 mm $\varnothing$×5 mm Ge detector with an active area of 50 mm² (model GL0055R/S, Canberra Industries, Meriden, CT) was used to collect the same spectral dataset as with the NaI-photomultiplier system. The manufacturer-quoted resolution (FWHM) of this L₂O₂-cooled detector system is 210 eV at 5.9 keV and 500 eV at 122 keV. The crystal is mounted in a cryostat with a 0.6 mm carbon composite window. A RC preamplifier (model 2002CP, Canberra Industries) is configured for performance at count rates exceeding 100,000 cps. Data collection is achieved with a 32 bit digital spectrum analyzer (DSA-2000, Canberra Industries) and spectroscopy software (GENIE 2000, version 1.3, Canberra Industries). With 16k channels available, resolution is limited by the detector rather than the MCA.

C. Preprocessing

An n-point averaging filter was applied to the NaI-acquired spectra to smooth the data. The value of n ranged from 3 to 15, and was typically 7. Collected spectra were compared to computer-generated reference spectra to confirm general agreement of spectral shape. The simulated spectra were obtained using the published code for Boone and Seibert’s tungsten anode spectral model using interpolating polynomials (TASMIP), which is based on spectra measured by Fewell. Input parameters of tube voltage, Al-equivalent filtration, and generator ripple allow simulation of a particular x-ray unit operating at tube potentials from 30 to 140 kVp.

IV. EXPERIMENTALLY MEASURED SPECTRA

A. Results

Spectra obtained with the NaI detector are shown in Fig. 1. Data have been adjusted to simulate constant tube current. Comparison of these experimental spectra to the reference spectra in Fig. 2 shows several differences in spectral shape. The presence of a concave high-energy tail is evident in each of the measured curves. Second, with 60 kVp and higher
tube voltages, a shoulder on the high-energy side of the peak is seen to increase in magnitude with increasing tube voltage. At 80 and 90 kVp, this shoulder is prominent enough to be considered a second peak. Another difference between reference and measured curves is the lack of a peak shift in the experimentally measured curves which is evident in the reference data. In contrast, as illustrated in Fig. 3, spectra acquired with the Ge detector agree with the reference data. From this we can conclude that the high-voltage generator and x-ray tube are working properly.

B. Investigation of potential causes for observed NaI-photomultiplier-acquired spectra

Measurement of background radiation was performed both with and without the x-ray tube high-voltage supply operating. Background counts did not exceed 5 cps in energy bins greater than 10 keV, and no predictable background pattern was observed. The background spectrum also allowed quantification of system noise. From 10 to 0 keV, the recorded counts rose exponentially, exceeding 5000 cps at about 7 keV. These counts may be attributed to thermionic emission; therefore very low energy data are not considered reliable.

Increasing count rate can influence the detector baseline voltage. With a count rate of $10^6$ cps, a positive shift in baseline voltage was observed. This shift was linear with count rate and reached 100 mV at $10^6$ cps. As this artifact is linear and predictable, data can easily be corrected for detector base-line shift.

A single ripple in the decay portion of the detector's output signal was evident in most of the measured pulses. Generally this ripple occurred about 350 ns after the peak, which is greater than the double pulse resolution (typically, 5 ns) of the discriminator. Data were usually acquired with the discriminator operating in updating mode with burst guard enabled. In updating mode the discriminator's output pulse is extended if a second pulse arrives before the output from the first pulse returns to zero. The result is that the second pulse is not counted. Enabling burst guard prevents prolonged paralysis due to high count rates. The maximum discriminator output-width that may be set is about 135 ns. Therefore a ripple event occurring at 350 ns would, in theory, produce an artificial count. This is, however, a threshold-dependent process. To prevent multiple triggering by noisy signals, the discriminator also has a built-in hysteresis provision. Only if the ripple exceeds the threshold by 5 mV is a second pulse recorded.

An external circuit was designed to test whether the discriminator was able to avoid retriggering on the observed ripple. By elongating the discriminator's output logic pulse to 600 ns, the discriminator becomes unresponsive to further inputs generated during the 500 ns duration of the input signal from the detector. Comparison of the number of counts measured with and without elongation of the discriminator output pulse showed that retriggering was not occurring.

Unwanted pileup, coincidence and scatter effects were
minimized by narrow collimation of the primary beam. In designing the pinhole collimator, the aperture size and the thickness of the lead were chosen to eliminate primary scatter from the shielding around the tube housing, detector, and collimator itself. With tube potentials less than 90 kVp, Compton scatter effects are minimal. Calculations simulating our detector geometry revealed an expected scatter fraction of only about 3%. Furthermore the simulated scattered spectra were shifted only slightly in energy from the primary beam spectra.

The position and magnitude of the second peak suggested that the four prominent characteristic tungsten peaks (in the range of 57–69 keV) might be responsible for the additional higher-energy counts. However, as seen in Fig. 4, by modeling the detector response function as a Gaussian function with an energy-dependent FWHM and convolving this function with reference spectra, we were able to show that characteristic tungsten peaks alone cannot explain the second peak.

Detector efficiency was also considered. Monte Carlo simulations of NaI scintillators predict high efficiency over the diagnostic energy range. The maximum deviation in photpeak efficiency, due to the iodine k edge, is about 30% and occurs at 33.2 keV. Efficiency correction had little effect on the general spectral shape.

Even with careful setup to control those factors known to influence the spectrum of photons reaching the detector, considerable distortion in the measured energy spectra remains. It is evident that, to recover the true spectra, other tools are necessary.

V. METHODS FOR SPECTRAL CORRECTION

A. Analytical blurring correction

Since the predominant spectral distortion is due to blurring introduced by the detector, deconvolution of the measured spectrum by the detector response function will yield the true energy spectrum. A matrix describing the blurring response of the detector was created from Gaussian curves with a FWHM equal to the resolution specification of the detector at 22 keV and extrapolated for other energies according to the following relationship:

$$\frac{\text{FWHM}}{E} \propto \frac{1}{\sqrt{E}}$$

(1)

where $E$ is the photon energy. Resolution at several energies was experimentally confirmed with radionuclide sources, including $^{125}$I, $^{131}$Ba, $^{57}$Co, and $^{99}$Tc (39.6, 81.0, 122.1 and 140.5 keV, respectively). As depicted in Fig. 5, convolution of this matrix with theoretical spectra yielded blurred spectra that exhibit the same convex high-energy tail. However, this matrix is not suited for direct analytical correction of the measured data. Using an inverse matrix operation, the near-zero terms of the Gaussian distributions in the denominator cause computational problems. As a set of equations, the system is ill-conditioned. Alternatively, an iterative approach to finding the unblurred spectrum was developed. When this method was applied to theoretical data that had been convolved with the blurring operator, convergence to a near-perfect fit was rapid. Unfortunately this iterative method was prone to errors when measured spectra, having statistical and electronic noise components, were input. Oscillatory solutions or unrealistic deconvolved spectra were frequently produced. Fourier transform techniques were considered, but as the energy resolution of the detector is a function of energy, such systems do not meet the criterion of shift invariance.

B. Constrained least-squares technique

1. Theory

Originally derived for two-dimensional image restoration, the constrained least-squares technique seeks to find
an estimate \( f'(x) \) of a true function \( f(x) \) from its degraded form \( g(x) \). A priori knowledge of the degradation phenomenon as well as the statistical nature of the noise is required when using this technique. The degradation operator \( H \) operates on \( f'(x) \) to yield a function that, when combined with the additive noise \( n(x) \), produces \( g(x) \). In matrix notation, this may be summarized by

\[
g - b - H f' = n. \tag{2}
\]

where \( b \), background counts, has been distinguished from statistical noise. As our background counts are less than 1% of total counts, we neglect this term.

In unconstrained algebraic restoration, a criterion function that provides a measure of performance is first defined. For example, it might be desired to minimize, in a least-squares sense, the noise term. In this case, we wish to find the solution \( f' \) such that

\[
\|n\|^2 = \|g - H f'\|^2. \tag{3}
\]

is minimized (\( \|n\| \) is the norm of the noise and is equal to \( n^t n \)). A criterion function is defined as

\[
J(f') = \|g - H f'\|^2, \tag{4}
\]

which is minimized in the traditional way of differentiating \( J \) with respect to \( f' \), setting the result equal to zero and solving for \( f' \).

Constrained restoration introduces conditionality on the solution. In this case, the function to be minimized is \( \|Q f'\|^2 \), where \( Q \) is a linear operator on \( f \). The transformation matrix \( Q \) is chosen to achieve the desired results, for \( Q \) governs the form of the solution. However, the solution is still subject to the constraint \( \|g - H f'\|^2 = \|n\|^2 \). Minimization of a function with an equality constraint is accomplished using the method of Lagrange multipliers. The constraint term is multiplied by a constant \( \alpha \) (the Lagrange multiplier) and is appended to the function \( \|Q f'\|^2 \). Thus the criterion function for the constrained least-squares restoration technique becomes

\[
J(f') = \|Q f'\|^2 + \alpha(\|g - H f'\|^2 - \|n\|^2). \tag{5}
\]

In our application of constrained least-squares restoration, the goal is to minimize the oscillations that can occur with ill-conditioned data sets. One possibility is to choose a \( Q \) that gauges the smoothness of the solution. In this case a function of the second derivative is suitable. The central difference approximation for the second derivative,

\[
\frac{\partial^2 f(x)}{\partial x^2} \approx f(x+1) - 2f(x) + f(x-1), \tag{6}
\]

may be expressed in matrix operator form as

\[
\begin{bmatrix}
1 \\
-2 & 1 \\
1 & -2 & 1 \\
& & & \ddots \\
& & & & 1 & -2 & 1 \\
& & & & & & 1
\end{bmatrix}
\]

Substituting \( C \) for \( Q \) in Eq. (5), the criterion function to be minimized now becomes

\[
J(f') = \|C f'\|^2 + \alpha(\|g - H f'\|^2 - \|n\|^2). \tag{8}
\]

Using the general matrix property \((\partial/\partial x)Ax = A^T \) (Ref. 50) in the differentiation of Eq. (8), minimization of \( J(f') \) yields

\[
f' = (H^T H + \gamma C^T C)^{-1} H^T g, \tag{9}
\]

where \( \gamma = 1/\alpha \). To find the parameter \( \gamma \) that satisfies the constraint, an iterative procedure, such as the Newton–Raphson algorithm, may be used. A residual vector \( r \) is defined as follows:

\[
r = g - H f'. \tag{10}
\]

The function

\[
\phi(\gamma) = r^T r = \|r\|^2 \tag{11}
\]

is a positive monotonically increasing function of \( \gamma \). This means that there is a unique value of \( \gamma \) that satisfies

\[
\|r\|^2 = \|n\|^2. \tag{12}
\]

Alternatively, the value of \( \gamma \) can be adjusted so that

\[
\|r\|^2 = \|n\|^2 \pm a, \tag{13}
\]

where \( a \) is an accuracy tolerance. Practically, the \( \gamma \) parameter provides a means of balancing the goodness of fit and smoothness of solution.

2. Implementation

An estimation of the expected noise term is a prerequisite of the constrained least-squares technique. We assume a Poisson probability distribution in the counting experiments; therefore values of the noise array \( n(E) \) are calculated as the square root of the raw (cumulative) mean counts.

Electronic noise results in artificially elevated counts in the low energy range. Data below the first reliable data point, chosen as the minimum of the valley that occurs in the range of 5–10 keV, were replaced. New points were calculated using a spline fit to the segment of the spectrum between the valley minimum and the peak. An example is given in Fig. 6. Truncation of the blurring matrix operator for values below 0 keV was also necessary.

Since each change in the detector high-voltage requires recalibration of the energy scale, an alternative to calibration with radionuclide sources was sought. After smoothing the acquired spectra, a single point on the voltage (energy) axis was selected to correspond to 70 keV. Next, a compression/
expansion factor was specified and the data were rebinned using nearest-neighbor interpolation. These two parameters—the 70 keV point (a shift factor) and the compression/expansion value (a scale factor)—determine the energy axis to which the energy-dependent blurring operator is then aligned. For the 90 kVp spectrum under multiple shift/scale combinations, the deconvolution was carried out and the residual vector (and associated gamma) was found. This process was repeated for the 70 and 50 kVp spectra. The residuals for 90, 70, and 50 kVp spectra under each shift/scale combination were summed and the combination that produced the minimum summed residual was chosen as the energy calibration pair. Subsequent confirmation of the validity of this calibration was performed using $^{57}$Co and $^{99m}$Tc sources.

Once the energy scale was fixed, the optimal gamma for each spectrum was found using an iterative approach. Beginning with an initial value for gamma $\gamma_1$, the residual vector $r$ and $\phi(\gamma_1)$ was calculated. The value of $\phi(\gamma_1)$ determined the second estimate of the optimal gamma $\gamma_2$: if $\phi(\gamma_1) < \|n\|^2$ then $\gamma_1$ was incremented; if $\phi(\gamma_1) > \|n\|^2$ then $\gamma_1$ was decremented. This process was continued until the interval $[\gamma_a, \gamma_b]$ that resulted in residuals $\phi(\gamma_a)$ and $\phi(\gamma_b)$ where $\phi(\gamma_a) < \|n\|^2 < \phi(\gamma_b)$ was found. The gamma that solves the equation

$$\phi(\gamma) = \|n\|^2$$

must be contained in the interval $[\gamma_a, \gamma_b]$ and was found using a successive bisection algorithm. The gamma at the midpoint of the interval $\gamma_m$ was used to calculate $\phi(\gamma_m)$. Using the above-mentioned criterion, the appropriate subinterval (either $[\gamma_a, \gamma_m]$ or $[\gamma_m, \gamma_b]$) that contained the solution was chosen as the new interval for testing. The midpoint in the new interval was tested to determine which subinterval contained the optimal gamma, one half of the interval was chosen as the new testing interval and the process was continued. When the residual matched the noise within a satisfactory accuracy tolerance, the $r'$ that had been calculated with that gamma was deemed to be the solution.

The quantitatively optimum solution was found with regard to the full energy range of a spectrum. This overall best fit might not be the most meaningful criterion for finding the true spectrum. In terms of x-ray quality, the position of the peak and the slope of the line from peak energy to maximum energy of the spectrum are the most relevant shape features. The low-energy portion of the spectrum plays a less important role in determining the characteristics of a particular spectrum. With that in mind, a qualitative approach to finding the best fit was investigated. The value of $\gamma$ was adjusted interactively, and the visually best-fitting spectra were noted. Spectra that more closely matched the reference curve in the peak and upper-energy regions were favored, and discrepancies in the low-energy portion of the curve were tolerated.

With $\gamma$ as a free parameter and visual criteria determining the best fit, a number of solutions are possible. To compare the solutions, a measure of the agreement between the deconvolved and reference curves is required. Several means for describing the degree of coincidence of two curves are feasible. Our method of choice was to generate a histogram of the differences between the two area-normalized curves and to report the FWHM of the Gaussian curve fit to this histogram. A narrower FWHM, representing most differences being distributed in a narrow range around zero, indicates better spectral agreement.

VI. RESULTS

Results of deconvolution for 90, 70, and 50 kVp spectra are plotted in Fig. 7. For comparison, the spectra before deconvolution are also shown. Scaling to minimize the sum of the squared differences between the deconvolved and reference curves has been applied in all cases. Clearly the deconvolution technique yields spectra that are more consistent with the reference spectra. For all energies, the primary peak is seen to align nicely with the theoretical curve and for 90 kVp, the second peak disappears. Excellent agreement of the slope in the upper energy portions of the spectra is also evident. Qualitatively the x-ray beams would be considered very similar.

Difference histograms between the 90 kVp curve and the reference data, both before and after deconvolution, are presented in Fig. 8. As seen in Table I, after application of the constrained least-squares technique, there is a significant reduction in the FWHM measurement of the difference histogram for each spectrum.

VII. DISCUSSION

The results of spectral deconvolution using the constrained least-squares restoration technique demonstrate that this technique is valuable for reducing spectral distortion introduced by a NaI-photomultiplier detector. A marked improvement in spectral agreement to reference data is seen after deconvolution; this is evident both visually and quantitatively.
TABLE I. FWHM of the Gaussian curve fit to the difference histograms between the measured spectra and the reference spectra both before and after application of the constrained least-squares technique. The FWHM values are used to calculate the percent improvement in spectral agreement given in the last column.

<table>
<thead>
<tr>
<th>Tube potential (kVp)</th>
<th>FWHM before</th>
<th>FWHM after</th>
<th>Improvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>14.68</td>
<td>11.54</td>
<td>21</td>
</tr>
<tr>
<td>70</td>
<td>43.54</td>
<td>20.28</td>
<td>53</td>
</tr>
<tr>
<td>90</td>
<td>63.83</td>
<td>25.62</td>
<td>60</td>
</tr>
</tbody>
</table>

The ability to change the \( \gamma \) parameter to achieve a solution that is both realistic and reasonably accurate is a key feature of the technique. Our extension of this concept to allow interactive selection of \( \gamma \) and generate solutions that maintain important spectral features, such as the position of the peak and the slope of the curve from the peak to the maximum energy, makes this an attractive alternative to methods requiring more sophisticated modeling.

Intelligent adjustment of \( \gamma \) is necessary to prevent the norm of the blurring operator from dominating the denominator in Eq. (9). When \( \gamma \) is small, oscillatory solutions are likely. This constraint is actually useful for choosing an initial value of \( \gamma \) when using either the successive bisection algorithm or the interactive method for finding a solution.

The obvious advantage of this method is ease of implementation. Estimating statistical noise and measuring the detector response function are straightforward tasks. With a calibrated energy axis, acquired data can be corrected almost immediately.

The drawback is that the result is less accurate than those obtained with the more complex methods for backcorrecting spectra collected with NaI-photomultiplier systems. Since the blurring operator represents only intrinsic broadening by the detector, other spurious effects are ignored. Some of these effects become increasingly important at higher energies. Above 90 kVp, it is not prudent to ignore Compton scatter. Likewise, with higher energies, \( k \) escape must be considered. Fortunately these effects can be included in the blurring operator by modification of the individual response function profiles at each energy. As an example, refining the operator to include detector efficiency would be a simple matter of multiplying the Gaussian response function with a corresponding efficiency profile. The expectation is that an operator that more accurately models photon interactions will lead to a solution that better fits reference data over the full energy range of the spectrum. Specifically, a good fit in the portion of the curve below the peak and a more accurate peak intensity would be anticipated.

Due to our high-voltage generator peak operating voltage, experiments were limited to spectra at or below about 90 kVp. We did not attempt to recover the characteristic tungsten peaks since they contribute relatively little to the average energy of spectra below 90 kVp. Using known relative

![Figure 8](image_url)
intensities, each peak could be added to our deconvolved spectrum. Of course, with higher tube potentials the tungsten peaks become increasingly important and must be considered. The success with which this technique could be used at higher energies to resolve the tungsten peaks remains to be investigated.

In addition to providing a means for measurement of x-ray tube spectra in a clinical setting where the use of semiconductor detectors is not practical, this method might be considered as part of a quality-assurance program in detector monitoring. Scintillation-detector failure is often due to compromises in the crystalline structure, which result from moisture accumulation or small cracks within the crystal. The consequence is a gradual loss of efficiency which may be more pronounced at a particular energy. Measurements using radionuclides away from that specific energy may not reveal a problem until efficiency is significantly reduced. If, however, the entire spectrum were monitored, energy-specific defects might be exposed earlier. Changes in the shape of deconvolved spectra measured with a certain detector could indicate early detector failure.

VIII. CONCLUSION

We have demonstrated the usefulness of a constrained least-squares technique for spectral deconvolution. Spectra acquired with a NaI-photomultiplier detector in the diagnostic energy range can be corrected for intrinsic broadening by the detector. Significant improvement in the peak position and spectral shape is possible with our easily implemented method.
APPENDIX C
FEASIBILITY OF RADIOGRAPHIC ABSORPTIOMETRY OF THE MANDIBLE AS AN OSTEOPOROSIS SCREENING METHOD

ABSTRACT

The purpose of this work was to develop and evaluate single- and dual-energy radiographic absorptiometry (RA) for the measurement of mandibular bone mineral density (BMD), using standard dental equipment, that would allow for inexpensive and widespread osteoporosis screening. High- and low-energy images were acquired simultaneously on a single dental radiograph by appropriate filtering of the dental x-ray tube output. Computer simulations were performed to optimize the filters with respect to error in bone measurement. A custom-designed film holder houses the beam filters and calibration wedges. Forty-six male and female subjects, ages 27 to 87 years, participated in a pilot study to assess the RA techniques. Left and right periapical radiographs were taken of the premolar-molar region and, for comparison, BMD was evaluated at the spine, left and right femur as well as total body by dual-energy x-ray absorptiometry. Mandibular BMD by high or low single-energy RA measurements was positively correlated with skeletal BMD, as assessed by DXA, at the arms, legs, trunk, ribs, pelvis, total body and femoral neck. ROC analysis of the single-energy techniques for identification of osteopenic and osteoporotic female subjects (area under the curve = 0.73) indicates that this method may have potential as a screening tool.
1. INTRODUCTION

Whereas instruments for diagnosis of osteoporosis provide a reasonably accurate quantitative measure of bone mineral density (BMD), the purpose of a screening technique is to classify a patient’s bone density as either “normal” or “below normal.” Patients in the latter category would be referred for a follow-up measurement with traditional densitometry equipment. There are several requirements of a successful screening program. Widespread accessibility and high acceptability in terms of cost, convenience and comfort are necessary to ensure patient participation. A screening method must be sufficiently sensitive so that the presence of the disease is detected in time for treatment to be effective and must have satisfactory specificity to limit the number of false-positive results.

An opportunistic approach to osteoporosis screening exists in the dental health-care setting. Routine dental check-ups and hygiene visits are typically scheduled semi-annually. Patients can be screened at these visits using standard x-ray equipment that is available at the dentist’s office. This not only allows high availability, but also minimizes provider and patient costs.

The proposed measurement site is the alveolar bone at the body of the mandible. This site meets several criteria that define a good site for diagnostic evaluation of bone status for osteoporosis assessment. The bone is easily accessible for radiologic measurement, contains a large proportion of trabecular bone and is regularly subjected to mechanical stresses, particularly during chewing. The use of a dual- rather than single-energy technique is expected to minimize the effects of individual variation in soft-tissue thickness and
composition at the measurement site and should result in improved measurement accuracy. To limit problems associated with registration of multiple radiographs from a single patient, the two images made at different energies are recorded simultaneously on one film by aligning filter materials in a side-by-side configuration over the region of interest (ROI). Quantitative evaluation of the amount of bone is possible if the imaged bone and soft-tissue layers are sufficiently homogeneous over most of the high- and low-energy images.

2. BACKGROUND

2.1 Osteoporosis

Osteoporosis is a significant public health problem. 30% of Caucasian women over age 50 have osteoporosis (World Health Organization (WHO) 1994). In 2001, the direct medical costs for osteoporotic patients in the United States were $47 million per day. Due to an increase in the number of older people worldwide, the WHO describes an “impending epidemic” of osteoporotic fractures: the number of hip fractures is expected to triple over the next 50 years (Melton et al. 1987).

Osteoporosis is a disease in which the structural properties of bone are compromised due to thinning of the trabeculae. Osteoporosis is characterized by fractures from mild trauma, such as a fall from standing height, or, in severe cases, fractures that occur independent of any associated trauma. In postmenopausal women, the most common fracture sites are the lumbar spine, hip and distal radius. Vertebral compression fractures are painful and lead to
kyphosis or “dowager’s hump”. Hip fractures often require long-term institutionalization of the patient, and mortality rates from hip fracture in individuals above age 50 years range from 1.4% to over 23% for females and 2% to 33% in males, depending upon the age at fracture (Kanis et al. 2003). The majority of those patients die within one year from secondary causes, such as pneumonia or blood clots in the lung, related to either the fracture itself or the ensuing hip surgery.

Eighty percent of patients diagnosed with, or at risk for, osteoporosis are women. The reason for this is two-fold. First, women obtain a lower peak bone mass than men. Second, when women reach menopausal age, there is a reduction in estrogen level. Since estrogen has a positive effect on bone production during the remodeling process, there is a concurrent rapid reduction in bone mineral density with menopause. In men, the reduction in testosterone level begins at a later age and is more gradual. Therefore, bone loss is delayed and occurs at a much slower rate. With increased life expectancy, gradually more men are showing evidence of osteoporosis. Additional risk factors include Caucasian or Asian ethnicity, small stature, a family history of osteoporosis, use of certain medications such as corticosteroids and anticonvulsants, cigarette smoking and excessive alcohol use.

Fortunately, osteoporosis is highly preventable. Because peak bone mass is achieved between the ages of 28-35 years, adequate calcium intake during adolescence and young adulthood is critical. Sufficient vitamin D intake and a healthy lifestyle that includes weight-bearing exercise are also important.
Regularly scheduled bone density measurements can facilitate early diagnosis of osteoporosis. The gold standard for bone densitometry is dual-energy x-ray absorptiometry (DXA). DXA instruments measure areal bone mineral density, which is the amount of bone mineral in a projection measurement. To assess fracture risk, the patient's measured values are compared to young, adult normal values that have been matched for gender, race and stature. The difference between the patient's value and the reference value is expressed in units of reference population standard deviation and is termed the T-score. A patient is classified as normal if the T-score is greater than -1.0, osteopenic if the T-score is between -1.0 and -2.5 and osteoporotic if the T-score is less than -2.5.

With early detection, dietary and lifestyle changes can be implemented to improve bone health. If warranted, drug therapy may be prescribed. In addition to hormone replacement therapy (HRT), recent pharmaceutical advancements have led to many new osteoporosis-combating drugs including bisphosphonates (Liberman et al. 1995, Harris et al. 1999) and selective estrogen receptor modulators (SERMs) (Ettinger et al. 1999). Early intervention can help reduce the number of fractures that occur and consequently reduce the debilitation and mortality associated with osteoporosis.

2.2 Oral bone research

As summarized in reviews by Hildebolt 1997 and von Wowern 2001, the relationship between osteoporosis and oral bone status has been investigated by numerous researchers. The studies fall generally into three categories.

Several investigators have examined the relationship between skeletal bone
mineral status and geometric measurements made on panoramic dental radiographs. Measurement of mandibular cortical width and indices derived from this primary measurement, such as the panoramic mandibular index, have been the focus of many such studies. (Kribbs 1990a, Kribbs et al. 1990b, Klemetti et al. 1993a, Klemetti et al. 1994, Taguchi 1996a and Devlin and Horner 2002). The reproducibility of these indices has been questioned (Horner and Devlin 1998, Jowitt et al. 1999).

Other studies focused on mandibular morphology. Cortex morphology, evaluated on an ordinal scale, was investigated for its usefulness in predicting mandibular BMD (Klemetti et al. 1994) and skeletal osteoporosis (Taguchi et al. 1996a, Klemetti and Kolmakow 1997). Trabecular morphology using fractal dimensions (Law et al. 1996) or principal components analysis (White and Rudolph 1999) has also been studied.

Direct measurement of mandibular BMD has been used to assess its relationship to skeletal status. Single- or dual-energy quantitative computed tomography (QCT) was used to establish the correlation between mandibular and skeletal BMD (Kribbs et al. 1990b, Klemetti et al. 1993b, Klemetti et al. 1993c, Taguchi et al. 1996b, Lindh et al. 1996). Others utilized DXA (Horner et al. 1996) or microdensitometry of periapical (Kribbs et al. 1983, Kribbs et al. 1989) or vertical bitewing (Payne et al. 1999) radiographs for measurement of areal mandibular BMD.

These studies have not identified a reliable technique that clearly identifies patients at risk for developing osteoporosis.
2.3 Principles of single-energy measurement

Quantitative measurement is based on the physical principle of x-ray attenuation, which is described by the following equation:

\[ I(E) = I_0(E)e^{-\mu(E)d}, \]

where \( I(E) \) is the transmitted x-ray intensity at energy \( E \), \( I_0(E) \) the incident x-ray intensity, \( \mu \) the linear attenuation coefficient \([\text{cm}^{-1}]\) of the attenuating material and \( d \) the material thickness \([\text{cm}]\).

The energy-dependent attenuation coefficient describes the likelihood of photon interaction within the material. Coefficient values have been tabulated for all elements at discrete energies. For composite materials, attenuation coefficients may be calculated from the chemical formula based on a percent by weight composition. The incident and transmitted x-ray intensities are measured quantities. Thus, Eq. [1] may be used to solve for material thickness, \( d \).

When more than one material is in the beam path, the equation becomes

\[ I(E) = I_0(E)e^{-\mu_1(E)d_1 - \mu_2(E)d_2}, \]

where the subscripts 1 and 2 refer to different materials. In this case, there are two unknowns, \( d_1 \) and \( d_2 \), and only one equation. In the anatomical situation of interest, the two materials are soft-tissue and bone. By adding a soft-tissue equivalent material above and below the body part, the soft-tissue path length can be fixed. If the total thickness of the body part plus compensating medium is constant across the body part, then the changes in measured signal (whether it be photon flux or film optical density) must be due solely to changes in bone thickness.
In single-photon absorptiometry (SPA), where the photon source is a radionuclide, or single x-ray absorptiometry (SXA), where the photon source is an x-ray tube, the soft-tissue equivalent material most often used is water. The body part to be measured is placed in a water bath or surrounded by water-filled bags. One drawback of these techniques is that the need for a water bath limits the areas of the body that can easily be measured. Another limitation is that additional materials in the beam path will introduce errors. For example, in a spine measurement, the beam may pass through air in the lungs or digestive tract. The problem then becomes one of three unknowns, and SPA or SXA is not a suitable measurement technique.

2.4 Principles of dual-energy measurement

Dual-energy techniques allow mathematical subtraction of the amount of soft-tissue that exists in the marrow space and overlies the bone in a projection measurement. Since the thickness and composition (fat-to-lean ratio) of the soft-tissue layer varies between patients, subtraction of those effects results in a more accurate measurement of bone density. No additional compensating medium is necessary. However, when compared to a single-energy measurement, there is a reduction in precision due to error-propagation effects within the dual-energy measurement.

Dual-energy methods exploit the energy-dependence of the attenuation coefficients. For the two-component problem, two independent equations may be written:
\[ I_L = I_{0L} e^{-(\mu_L d_L + \mu_L d_H)} \]
\[ I_H = I_{0H} e^{-(\mu_H d_L + \mu_H d_H)} \]

where the subscripts \( L \) and \( H \) refer to low and high energies, respectively.

Again, if materials 1 and 2 are bone and soft-tissue, respectively, then the set of equations [3] may be solved for the bone and soft-tissue thicknesses. The bone thickness, \( d_B \) is given by

\[ d_B = \frac{R \ln \left( \frac{I_{0H}}{I_H} \right) - \ln \left( \frac{I_{0L}}{I_L} \right)}{R \mu_B - \mu_B} \]

where

\[ R = \frac{\mu_S}{\mu_S} \]

and the subscripts \( B \) and \( S \) refer to bone and soft-tissue, respectively. \( R \) is determined, on a patient-by-patient basis, from an independent measurement through a region that contains only soft-tissue. The composition of this region is assumed identical to that of the soft-tissue overlying the bone. \( R \) is, thus, a patient-specific parameter that quantifies the lean-to-fat ratio of the soft-tissue.

Error analysis of Eq. [4] results in the following expression for bone measurement variance:

\[ \sigma_B^2 = \frac{R^2 \left( \frac{1}{I_{OH}} + \frac{1}{I_H} \right) + \left( \frac{1}{I_{OL}} + \frac{1}{I_L} \right)}{(R \mu_B - \mu_B)^2} \]
2.5 Radiographic absorptiometry

Radiographic absorptiometry (RA) is grey-level analysis of radiographs acquired with a reference object in place. The use of a reference object in each radiograph provides a normalization factor for differences in x-ray intensity, exposure time and chemical development conditions. This concept was first demonstrated over 100 years ago when a copper step wedge was included in dental radiographs to assess the relative densities and thicknesses of tooth structures and oral bone (Price 1901). In RA techniques, the optical density of the film at the measurement site is compared to that of the reference object. Film optical density (OD) is the term used to describe the lightness or darkness of the radiograph after development. It is determined by passing a finely collimated beam of light through the film and measuring the intensity of the transmitted light.

RA as a bone densitometry method was first introduced about 30 years ago in the analysis of hand radiographs. With a small aluminum wedge placed near the phalanges, an exposure is made of the hand in standard posterior-anterior (PA) position. The resulting radiograph is digitized and analyzed. Phalangeal density is expressed in units of “aluminum-equivalent thickness”. The accuracy of this technique in its original form was about 6%, with an in-vivo, inter-radiograph precision error of about 2% (Colbert and Bachtell 1981). The application of dual-energy principles, special film and automatic or semi-automatic computer analysis improved the accuracy of the technique to 4.1% (Gulam et al. 2000). No comparative data for current in-vivo, inter-radiograph precision were found.

Knowledge of the film behavior is required for success in RA methods. The
response of a particular x-ray film type to radiation is described by its characteristic (“H-D”) curve. By plotting film OD versus the logarithm of exposure, the linear range of the film can be determined. In quantitative measurements, radiographs produced by exposures outside the film’s linear range must be analyzed carefully, for in these regions the degree of film blackening is not proportional to exposure.

To determine the range of exposures over which the film exhibits linearity, one could consult characteristic curve data provided by the film manufacturer. However, measuring x-ray exposure directly is not straightforward, and the optical density value obtained with a particular exposure is dependent upon processing factors, such as the age and temperature of the chemicals used in film development. Therefore, characteristic curves for the types of dental film commonly used in dental practices are best determined experimentally.

3. MANDIBULAR MEASUREMENT DEVICE

The mandibular measurement device was designed to provide both single- and dual-energy data from a single patient measurement. Whereas a filtered beam is not necessary for single-energy measurement, our approach was to include both high- and low-energy filters in the prototype. In this way, three data sets were obtained from each film: the high single-energy data, the low single-energy data and the dual-energy data. Not only did this increase data collection efficiency in the pilot study, but it also reduced patient dose.
3.1 Film holder

A film holder was designed to accommodate the calibration step wedge, beam holders and film (Figure 1). The custom-made polycarbonate holder consists of an imaging portion and an attached biting block. The rectangular imaging portion is similar in size to a #2 film. It consists of two polycarbonate sheets, each 1.6 mm thick, that sandwich the step wedge, step wedge filters and mandible filters. The step wedge and wedge filters are oriented horizontally across the top of the holder, and the mandible filters, each 25 mm x 3 mm, are oriented horizontally and adjacent to one another across the bottom of the holder. Since cerium metal oxidizes upon contact with oxygen, assembly was performed in an inert atmosphere, and the seal was tested periodically. The biting block, a hollow rectangular bar with 3.2 mm thick sides, was aligned over the upper third of the imaging portion so that its sides framed the step wedge and prevented the wedge from being obscured by the patient’s teeth. The film is loaded flush with the imaging portion, and the entire holder is inserted into the patient’s mouth with the imaging portion parallel to the premolar-molar teeth and between the teeth and tongue. The patient is then instructed to bite down gently on the biting portion (to stabilize the holder) and to close the lips so that the entire image is covered with soft-tissue.

3.2 Reference wedge

Cadaver mandible samples were measured on a Lunar DPX-L bone densitometer (GE Lunar Corporation, Madison, WI) to determine the approximate range of expected mandibular bone density. A copper step wedge was designed
to cover the range of optical density values observed in the imaged mandibles. A thin layer of copper is sufficient to attenuate the x-ray beam by a similar amount as the imaged portion of the mandible, and several steps can be formed without the wedge becoming too thick for intraoral use. Also, thin copper foil is available commercially, is relatively inexpensive and requires no special handling procedures.

The step wedge consists of a 25 mm x 12.5 mm x 0.05 mm copper base piece and six additional steps in 0.04 mm increments, each with an area of 3 mm x 12.5 mm, to provide seven copper steps ranging in thickness from 50 to 290 microns. Each half of the wedge is overlaid with one of the beam filters so that both the high- and low-energy images may be appropriately calibrated.

3.3 Optimization of x-ray spectra for dual-energy measurement

Most dental x-ray systems operate at constant potential. To obtain high- and low-energy measurements, k-edge filtration was chosen to selectively filter a portion of the energy spectrum and generate two x-ray beams with different energy profiles. K-edge techniques involve passing the x-ray tube output through a filter material that has a k-shell absorption edge within the energy range of the tube’s output spectrum. As illustrated in Figure 2, the resulting spectrum is effectively split into high- and low-energy components. Filter choice determines the relative weighting of high- and low-energy portions.

Computer simulations were used to determine the optimal high- and low-energy filters and the thickness of each filter to minimize bone measurement uncertainty. In these simulations the incident x-ray beam was generated by first
creating an input spectrum described by:

\[ I_o(E) = K(E_{\text{max}} - E) \]  

where \( I_o \) is the photon intensity at a given energy \( E \), \( K \) is a constant that describes the tube output fluence and \( E_{\text{max}} \) is the maximum energy of the electrons bombarding the target (which corresponds to the x-ray tube voltage in kVp). The output fluence at \( E = 0 \) keV was taken to be \( 10^6 \) s\(^{-1}\). K and L emission lines of the target material were neglected. The spectrum of photons exiting the x-ray tube window was calculated from 5 keV to \( E_{\text{max}} \) in 1 keV steps according to the equation

\[
N(E) = \left[ \frac{I_o(E)}{E} \right] e^{-\mu_{Al}(E) x_{Al}}
\]

where \( \mu_{Al}(E) \) is the linear attenuation coefficient of aluminum at energy \( E \) and \( x_{Al} \) is the equivalent aluminum thickness of the inherent filtration of the x-ray tube. For the simulation, the tube voltage was 70 kVp, and the inherent Al-equivalent thickness was 0.9 mm.

A standard patient jaw was defined as 0.3 cm of bone, modeled as calcium hydroxyapatite (39.9% Ca, 18.5% P, 41.4% O, 0.2% H by weight) (Sorenson et al. 1989) and 3.0 cm of soft-tissue which was assumed to be water equivalent (\( \rho = 0.998 \text{ g/cm}^3 \)).

Minimal spectral overlap of the high- and low-kVp beams ensures maximum separation of effective beam energies and, therefore, independence of the defining equations [3]. As evidenced by Eq. [6], a larger separation of the high and low attenuation coefficients reduces measurement variance. To determine
the filter combination that would yield high- and low-energy spectra with maximum energy separation, the ratio of average beam energies of the filtered spectra were plotted for high filters with atomic numbers ranging from \( Z = 40 \) to 53 and low filters from \( Z = 52 \) to 61 (Figure 3). For this purpose, the average beam energy was calculated as the first moment of the spectrum. As a comparison, the effective beam energy \( E_{\text{eff}} \) was also calculated for all spectra. The effective energy is defined as the single energy at which the linear attenuation coefficient \( \mu_x \) for a given material produces the same attenuation as the polyenergetic spectrum, i.e.

\[
\mu_x(E_{\text{eff}}) = \frac{\ln \left( \frac{I_o}{I} \right)}{t_x}
\]

where \( I_o \) and \( I \) are the summed incident and transmitted spectral intensities and \( t_x \) is the thickness of the attenuating material \( x \).

As seen in Figure 3, the ratio of average beam energies is more strongly dependent on the choice of low filter material than on high filter material. To achieve a ratio greater than 1.5, the choice of low-filter material was limited to elements with atomic numbers ranging from \( Z = 56 \) to 60 (corresponding to k-edge energies \( E_K = 37.4 \) to 43.6, respectively). A greater range of high-filter elements, \( Z = 40 \) to 50, \( E_K = 18.0 \) to 29.2, were suitable candidates. For maximal beam energy separation, the combination of \( Z = 58 \) (cerium (Ce), \( E_K = 40.4 \) keV) as a low filter and \( Z = 42 \) (molybdenum (Mo), \( E_K = 20.0 \) keV) as a high filter yielded a ratio of 1.57.

Examination of Eq. [6] reveals that the choice of filter thickness is an
optimization problem. On one hand, photon flux is inversely proportional to the measurement variance which would suggest the use of very thin filters. However, for maximum beam energy separation, the filters must be sufficiently thick. With too little filtration, the shape of the filtered beam becomes more like that of the unfiltered beam, and the beam energy separation is reduced. Also, filter thicknesses must be paired such that the high- and low-beam intensities are nearly equal, a criterion necessary for uniform exposure of both halves of the film.

The effect of filter thickness on measurement uncertainty of the standard jaw is shown in Figure 4, where contour lines delimit precision levels. It should be noted that small changes in filter thickness have pronounced effects on the transmitted beam intensity and, therefore, precision. For example, a 100 µm increase in Ce filter thickness reduces the beam intensity by a factor of ten.

From our simulations, we concluded that the combination of an 80 µm Mo high filter and a 110 µm Ce low filter is optimal for minimizing the error in bone measurement. To meet the requirement of nearly equal high- and low-intensity beams, the filter thicknesses were adjusted slightly to 76 µm of Mo and 100 µm of Ce.

Filtered spectra were acquired with our laboratory x-ray system. The system consists of a fixed-anode tube with a 0.5 mm focal spot size and a 15° anode angle (Comet, Bern, Switzerland) powered by a high-voltage supply with a ripple of less than $10^{-4}$ Vpp (Fug, Rosenheim, Germany). The tube output is collimated at the exit window by a ¼"-thick lead collimator with a 1 mm horizontal slit.
opening. The filters were affixed to the front of this collimator so that they covered the slit. A Cerrabend (lead alloy) collimator with a 1 cm x 1 cm opening was then fitted onto the front of the tube housing. An additional 2” Ø x 6” cylindrical lead collimator was placed at the detector to reduce scatter acceptance. The detector was an 8 mm Ø x 5 mm Ge planar detector with an active area of 50 mm² (model GL0055R/S, Canberra Industries, Meriden, CT). The manufacturer-quoted resolution (full width at half maximum, FWHM) of this LN₂-cooled detector system is 210 eV at 5.9 keV and 500 eV at 122 keV. An RC preamplifier (model 202CP, Canberra Industries) is configured for performance at count rates exceeding 100,000 cps. Data were collected with a 32 bit digital spectrum analyzer (DSA-2000, Canberra Industries) and spectroscopy software (Genie 2000, version 1.3, Canberra Industries). Source-to-detector distance was 30 cm. Ce-filtered and Mo-filtered spectra were collected at tube potentials of 65 and 70 kVp.

Experimentally collected filtered spectra are compared to those predicted by the simulations in Figure 5. Although the intensity of the Mo-filtered (high-energy) spectrum is greater than that predicted by our spectral model, the average beam energies between simulated and collected spectra are in agreement. For the low-energy beam, the model predicts an average beam energy of 37.5 keV, and our measured average spectral energy was 34.9 keV. For the high-energy spectra the predicted value is 41.8 keV, whereas the measured value was 40.5 keV.

**3.4 Dental film characterization**

Test exposures were made with a Philips Oralix Dens-O-Mat x-ray system
(Koninklijke Philips Electronics N.V., Eindhoven, the Netherlands) operating at 65 kVp, 7.5 mA, and #2-sized Kodak Ultra-Speed DF-58 intraoral dental film (Eastman Kodak Company, Rochester NY). Coarse adjustment of exposure was possible with the electronically-controlled timer of the x-ray system and resulted in 7 discrete exposure times ranging from 0.2 to 0.85 s. However, additional data points were necessary to more accurately represent the characteristic film curve. Finer control of exposure was accomplished by inserting Plexiglas absorbers of various thicknesses in the beam path. By combining the different time settings and absorber thicknesses, additional data points were generated over the full exposure range.

4. PILOT STUDY

4.1. Subjects and measurement procedures

Forty-six subjects participated in a study to assess the dual-energy RA technique. The study was conducted in accordance with Wright State University and Miami Valley Hospital IRB-approved protocols. Male and female subjects, aged 27 to 87 years, were recruited from local dental practices. Exclusion criteria included more than one missing tooth in the region to be imaged and current or recent inflammation or infection in the region. Data regarding race, menopausal status, medical and medication history, alcohol use, smoking and caffeine use were obtained by questionnaire, and the subjects’ height and weight were measured. Left and right posterior vertical periapical radiographs were acquired of the mandible in the area of the second premolar and first molar using the dual-
energy film holder (Figure 6). All patient radiographs were taken with the same Philips x-ray unit and Ultra-Speed film described previously, with the axis of the x-ray tube head aligned perpendicularly to the plane of the film. All exposures were made with a technique setting of 4.5 mAs and developed in a single automatic film processor (A/T 2000, Air Techniques Inc., Hicksville, NY). Each patient also underwent DXA evaluation of the lumbar spine (L1-L4), left and right femoral necks as well as total body with a GE Lunar Prodigy bone densitometer and enCORE 2002 software (GE Lunar Corporation, Madison, WI).

4.2 Film analysis

The films were digitized using a 12-bit film digitizer (Howtek MultiRAD 460, Howtek, Inc., Hudson, NH) with a resolution setting of 292 dots per inch. One film from each patient was selected for analysis. Generally, the film with the larger areas in the high- and low-energy regions was chosen.

4.2.1 WEDGE ANALYSIS

Wedge analysis was completed manually using commercial image processing software (Image-Pro Plus, Media Cybernetics, Silver Spring, MD). Rectangular ROIs with an area of 132 pixels were selected on each step of each part of the wedge, and the mean intensity values and standard deviations of the step ROIs were recorded. A second order polynomial was fitted to each set of mean step values to create a unique pair of high- and low-energy calibration curves for each film (Figure 7).

4.2.2 MANDIBLE ANALYSIS

4.2.2.1 Single-energy analysis
The digitized images were imported into Adobe Photoshop (version 6.0.1, Adobe Systems, Inc., San Jose, CA) for analysis of the mandibular bone. Two freehand ROIs were manually drawn on each image in the trabecular portion of the mandible (Figure 8). Both ROIs extended anteriorly and posteriorly as far as possible between the second premolar and the first molar but excluded lamina dura and the superior alveolar crest. The low-energy ROI included alveolar bone from the superior border of the mandible to the inferior border of the low filter, whereas the high-energy ROI extended from the superior border of the high filter to approximately one-half the length of the molar root. The ROI selection was saved as a binary mask, which was then ANDed with the image file. This allowed the ROI intensity values to be stored in a rectangular matrix with all values outside the ROI set equal to zero. Statistical parameters of each ROI, including the mean, standard deviation, maximum and minimum, were calculated. The high- and low-ROI mean intensity values were converted to units of copper-equivalency using the appropriate calibration curve (Figure 7).

As illustrated in Figure 9, homogeneity of the premolar-molar region was investigated by calculating and plotting horizontal line averages of each ROI. Adjacent high- and low-energy subregions were selected with two goals in mind: the subregions were kept as large as possible to improve statistical measures but were limited to selection of adjacent lines that exhibited acceptable homogeneity. Frequently, the optical density values at the borders of the filters were distorted by edge effects and were not representative of the general ROI. In these cases, one to three lines at the filter edge were excluded. The mean values of the high-
and low-energy homogenous ROIs were then expressed in copper-equivalent units.

4.2.2.2 Dual-energy analysis

The soft-tissue-corrected bone thickness measurement was calculated from the high- and low-copper-equivalent mandible measurements. At the point on the fitted high-energy calibration curve where the optical density is identical to that of the high-energy mandible ROI, the following equation applies:

\[ e^{-\mu_{WH}(E)d_{WH}} = e^{-\mu_{SH}(E)d_{SH} + \mu_{BH}(E)d_{BH}}. \]  

[10]

A second similar equation can be created with the corresponding low-energy data:

\[ e^{-\mu_{WL}(E)d_{WL}} = e^{-\mu_{SL}(E)d_{SL} + \mu_{BL}(E)d_{BL}}. \]  

[11]

where the subscript \( W \) refers to the wedge material. Bone thickness is then computed from [10] and [11]:

\[ d_B = \frac{\mu_{SH}\mu_{WL}}{a} d_{WL} - \frac{\mu_{SL}\mu_{WH}}{a} d_{WH}, \]  

[12]

where \( a = \mu_{SH}\mu_{BL} - \mu_{SL}\mu_{BH} \).

5. RESULTS

5.1. DXA evaluation

Using the standard WHO criteria for defining osteoporosis and osteopenia, approximately 7% of the subjects were classified as osteoporotic at one or more measurement sites, whereas 35% were classified as osteopenic at one or more
sites. Table 1 summarizes these results by gender and site.

### 5.2 Single-energy RA method

Even though the high- and low-energy mandibular BMD measurements were highly correlated \( r=0.88, \ p<0.0001 \), the plots for analysis of homogeneity revealed a general superior-to-inferior systematic increase in trabecular BMD within the area between the teeth (Figure 9). Although selection of a smaller subregion within the ROI reduced the amount of variation, most homogeneous sub-ROIs still exhibited this same trend in density.

Mandibular BMD of the female subjects, as assessed by single-energy RA, was significantly negatively correlated with age (high-energy RA: \( r=0.40, \ p<0.05 \); low-energy RA: \( r=0.37, \ p<0.05 \)). In the male subjects, the correlation with age was much weaker. This may be due to this particular group of men, for in this small set of male subjects, the correlation of standard DXA measurements (spine and both femurs) and age showed a positive relationship.

The RA–DXA correlation values are given in Table 2. Mandibular BMD was significantly positively correlated with the arms, legs, ribs, trunk, pelvis, both femurs and total body \( r=0.31–0.44, \ p\)-values less than 0.05). The highest correlation was with the arms \( r=0.44, \ p=0.003 \) (Figure 10).

Within the homogeneous ROIs, the variance of the intensity values increased with decreasing average intensity (high-energy: \( r=0.51, \ p<0.001 \); low-energy: \( r=0.37, \ p<0.05 \)). Although this was not a primary measurement variable in the study, it may provide an additional piece of information for further classifying patients.
The results of fully paired receiver-operator characteristics (ROC) analysis of the single-energy RA measurements are presented in Table 3. DXA results at three skeletal measurement sites were used to categorize subjects as osteoporotic (T-score less than -2.5), osteopenic (T-score less than -1.0) or below average (T-score less than 0.0), and these thresholds defined the true positive/true negative groups in each test. The analyses were performed both for the entire cohort and for the females only. In ROC analysis, an area under the curve (AUC) of 0.5 indicates that the test is unable to distinguish between the positive and negative cases (it is a random classifier). A test with perfect sensitivity and specificity has an AUC of 1.0. As indicated by larger areas under the ROC curves, the method was most successful in identifying females with BMD less than -1.0 at the left femur (areas for the high- and low-energy methods = 0.73 and 0.70, respectively). Although the areas under the ROC curves for the entire group and the female-only group at a -2.5 femur threshold are quite large (0.95–0.96), this is likely an artifact due to the small number of true cases (2 individuals in each instance).

5.3 Dual-energy RA method

Using the high- and low-energy copper-equivalent thickness as $d_{WH}$ and $d_{WL}$ to explicitly solve for bone thickness (Eq. [12]) produced invalid bone and soft tissue thicknesses. For most subjects, the results ranged from about 1 to 2 cm of bone and a negative 2 to 7 cm thickness of soft tissue.

6. DISCUSSION
Both the development of a method for osteoporosis screening and a pilot study to assess its usefulness have been described. Single- and dual-energy RA measurement of mandibular BMD was accomplished with a standard dental x-ray tube and dental film using our custom film holder. Results of the mandibular RA measurements were compared to those from traditional DXA evaluations for a small group of subjects.

Multiple factors influence the predictive power of our RA screening method. These factors relate to the patients, to the method and to data acquisition. For the technique to be useful, it must be shown that 1) mandibular bone density is correlated with skeletal bone density at sites of interest in osteoporosis assessment and 2) mandibular bone density can be accurately measured.

Much of the research undertaken to determine the relationship of mandibular and skeletal bone status has focused on the use of panoramic radiographs. In acquiring these radiographs, anatomical structures, such as the hyoid bone, spine and soft-tissue structures of the mouth, may be superimposed in the mandible image. The degree to which these appear is largely dependent upon patient positioning, and multiple positioning errors are possible in one acquisition. Quantitative assessment of bone density and geometric measurements from panoramic films are, therefore, problematic.

Correlations between BMD at skeletal sites have been examined by Horner et al. (1996), who used DXA to determine BMD at the mandible, lumbar spine, femoral neck and radius of edentulous females. ROC analysis, with true cases defined as those patients with T-scores less than -1.0 at all three skeletal sites,
indicated mandibular DXA measurements could predict low skeletal mass with high sensitivity (0.8) and specificity (0.97). However, the measurement precision was poor due to difficulties in positioning patients comfortably and keeping the lateral portions of the mandible superimposed in the acquisition. Repeatability of ROI selection was also problematic in the smaller regions of the mandible.

Results of QCT measurements of cortical and trabecular mandibular bone have shown high variability within and between patient mandibles (Lindh et al. 1996). This may be why results from other QCT-based studies are difficult to interpret. Klemetti et al. found that trabecular BMD of the mandible was not correlated with BMD of the lumbar spine or femoral neck in postmenopausal women (1993c). In another analysis, the same researchers showed that BMD of the buccal cortex of the mandible was highly correlated with BMD of the skeleton but that trabecular and cortical BMD of the mandible were not correlated. Further, the lingual mandibular cortex correlated moderately with the post-cranial sites and with the trabecular bone of the mandible (1993b). Taguchi et al. (1996b) showed significant correlations between BMD in the mandibular cortex and the L3 vertebra in females less than five years from menopause and between total mandibular BMD and trabecular BMD of the L3 vertebra in long-term (greater than five years) postmenopausal females.

In studies with a single-energy absorptiometry technique that is similar to ours, Kribbs et al. reported significant correlations between measurement of mandibular bone mass and vertebral BMD, as measured with dual-photon absorptiometry. They reported a correlation coefficient of 0.37 in normal patients
ages 50–85 years (1990b) and 0.33 in an osteoporotic population (1989). Although the correlation coefficient between the results from our method and DXA of the lumbar spine were only 0.15–0.16, we did see similar correlation values with other regions of the skeleton.

Our results suggest that mandibular BMD is more highly correlated with the regions of the skeleton that are least likely to exhibit osteoporotic fractures. Highest correlations between mandibular BMD and skeletal BMD were in the arms (which includes the humerus, radius and ulna), legs, pelvis and ribs. Moderate correlations were observed with BMD of the femoral necks, whereas BMD of the lumbar spine was poorly correlated with mandibular BMD.

With our small sample size, patient variability cannot be neglected. We did not professionally assess, or correct for differences in, periodontal health status. Periodontal disease will undoubtedly affect local mandibular bone remodeling processes, but as most of our subjects were under the routine care of a dentist, few were expected to suffer from severe periodontitis. Still, even moderate periodontal disease might explain why some patients with above-normal skeletal bone mass exhibited low mandibular bone mass. Similarly, we did not control for smoking, which might be expected to influence mandibular bone density sooner than skeletal bone density.

Response of the mandible to systemic factors, such as hormones that influence bone remodeling rates, might also act differently at the mandible than at other skeletal sites. The mandible, as well as the rest of the cranial skeleton, has different embryonic origins and develops differently than the post-cranial
skeleton. Mandibular bone is formed intramembranously via condensation of the mesenchyme, whereas the majority of the skeleton is formed via mineralization of a cartilaginous precursor. In a histomorphological study by Kingsmill and Boyde (1999), which compared cranial and post-cranial bone in elderly individuals, no correlation was observed between the apparent density (mass per unit volume of bone space) and mineralization density at the micrometer level. As illustrated in their results, there is considerable interpatient variability in the cross-sectional size and shape of mandibular bone, in the thickness of its cortex and in the quality of its trabecular bone. Also, within a patient, the cortical thickness and trabecular quality may differ at cranial and post-cranial sites.

Homogeneity of the mandibular ROI was an important criterion in our study. The BMD of the selected ROI should reflect that of the general bone. In the present study, care must be taken to exclude anatomical features such as the internal oblique ridge (a horizontal band of increased mandibular thickness, where the mylohyoid muscle attaches to the lingual aspect of the mandible) or mental foramen (the opening of the canal that houses the mental vessels and nerves) from the ROI. As these features would appear in the inferior-most portion of the image, they would influence the high- but not low-energy ROI.

The homogeneity issue is even more critical in the dual-energy study, where we have assumed constant bone and soft-tissue thickness across the high- and low-energy ROIs (Eq. [4]). Based on our erroneous dual-energy results, it would appear that the homogeneity assumption has been violated. Even the selection
of visually and numerically more homogeneous sub-ROIs did not improve the results in the dual-energy study.

An alternative method of solving for bone thickness from the dual-energy data was tested. Rather than explicitly solving for bone thickness from the set of equations [12], a graphical approach for finding $d_B$ was investigated. Assuming a 65-kVp incident tube spectrum, the high copper-equivalent thickness values of anatomically reasonable combinations of bone and soft-tissue thicknesses (0-10 mm each) were calculated. Equivalency was defined as equal beam intensities (area under the spectrum) after attenuation in the two parts of the image: the mandible region (where the beam is attenuated by the cheek, gum and bone) and the wedge region (where the beam is attenuated by the cheek and the copper wedge). In this simulation, the cheek and gum were assumed to be 85% and 100% lean soft-tissue, respectively. The resulting set of ordered data triplets (bone thickness, soft-tissue thickness, high-energy copper-equivalent thickness) formed a plane (Figure 11). The process was repeated for the low-energy case. Two-dimensional polynomials (second order in $x$ and second order in $y$) were fitted to each of these planes.

The analytical expressions for the high- and low-energy planes were then used to solve for bone thickness for all study subjects. Each subject’s high- (low-) energy ROI value defines a curve in the high- (low-) energy plane that describes possible combinations of bone and soft-tissue, yielding the equivalent copper thickness. The intersection of the high- and low-energy curves then gives the unique solution of that subject’s bone thickness and soft-tissue thickness for the
Applying this method to the set of data collected (single-energy high- and low-ROI copper equivalent thickness values) we obtained pairs of curves that were oriented at a small angle to one another (Figure 12). Intersection points for most patients were at unreasonably large positive values of bone thickness and large negative values for soft-tissue thickness. Even if some broadening of each curve was permitted to allow for measurement error, no reasonable intersection point was found. The non-equivalent tissue amounts of the upper and lower regions of the ROI are sufficient to account for the erroneous solutions. Examination of the curve pairs, like those in Figure 12, for all patients revealed a consistent pattern. Assuming a fixed soft-tissue thickness, the estimate of bone thickness from the low-energy measurement always exceeded the high-energy value. This is consistent with what we observed in the homogeneity plots (Figure 9). The low filter covered the superior portion of the ROI, where increased optical density values were noted.

In addition to inhomogeneities within the mandible, other sources of error may be responsible for the poor performance of the dual-energy method. The sensitivity to statistical noise was investigated using the high- and low-energy fitted planes described previously. The simulated pair of high- and low-copper equivalent thickness values that corresponds to 4 mm of bone and 3 mm of soft tissue are 124.7 µm and 108.2 µm, respectively. By holding the low-energy copper-equivalent value constant and varying the high-energy copper-equivalent value, it was noted that a variation of only 11 µm in high-energy copper-
equivalent thickness was sufficient to produce bone thickness results that spanned a range of 0-10 mm. Similar results were obtained from fixing the high-energy copper value and varying the low-energy copper value. For comparison, standard deviations of wedge step intensity values were converted to copper thicknesses via the calculated calibration curve for several films. Typically, one standard deviation was equivalent to about 3.5 µm. This implies that the statistical variation of the wedge step intensity values could be responsible for significant errors in the bone thickness measurement.

Other sources of error in both the single- and dual-energy measurements include possible distortion due to non-orthogonal projection of the x-ray beam onto the film. Images taken at oblique angles would record more bone than those taken orthogonally to the beam. Additionally, the heel effect of the x-ray beam might result in uneven exposure of the wedge along its length. However, the well-collimated x-ray tube output minimizes this effect.

The ROC analysis results indicate some usefulness of this method for osteoporosis screening. The observed area under the ROC curve of > 0.70 for the single-energy method’s ability to identify patients with osteopenia or osteoporosis at the femoral neck is comparable to that of other current osteoporosis screening methods such as ultrasound measurements of the calcaneus (area = 0.68) and DXA of the femur (area = 0.70) (Hans et al. 1996). Whereas the sensitivity and specificity of our RA method increased when the -2.5 threshold was used to define true cases, this result is of little value in the context of this application. A screening method must identify at-risk patients early enough
for intervention to be successful, and a patient with a T-score of -2.5 has already irreversibly lost a considerable amount of bone. In most cases, the ROC analyses improved with exclusion of male subjects. This may be due to the small number of males in the study, or it may indicate a true difference in the mandibular–skeletal BMD relationship between males and females. Another study with a larger cohort and more males is necessary to explain this result.

In addition to osteoporosis screening, the single-energy method has potential for assessment of bone integrity for dental implant planning. Whereas QCT has been suggested for this purpose (Lindh et al. 1996), the limited availability and high procedure costs of QCT may make this modality impractical for routine use. On the other hand, our method could be easily incorporated in a dental setting.

Further modifications are necessary to successfully implement the dual-energy RA method. Several alternatives exist to overcome the problems introduced by inhomogeneity in the mandibular ROI. One possibility is to select a different region in the mandible that is inherently more homogeneous. For example, the area between the roots of the molars might provide better results. Another option is to adjust the orientation of the filters from a horizontal arrangement to a vertical arrangement so that the effects of the superior-to-inferior inhomogeneity are reduced. A third scheme would involve interlacing the high- and low-energy filters so that multiple, adjacent high- and low-energy ROIs could be analyzed from a single exposure. Or lastly, if multiple exposures can be properly registered so that the ROIs are equivalent, two successive exposures under different filtering conditions would eliminate the errors due to
inhomogeneity.

7. CONCLUSION

For osteoporosis screening using RA of the mandible, the single-energy method is superior to the dual-energy method, which is heavily influenced by ROI inhomogeneity. Based on ROC results, our single-energy method is comparable to current screening techniques and can be easily implemented for widespread testing.
REFERENCES

Colbert C and Bachtell RS 1981 Radiographic absorptiometry (photodensitometry) Non-Invasive Measurements of Bone Mass and Their Clinical Applications ed S H Cohn (Boca Raton, FL: CRC Press)

Devlin H and Horner K 2002 Mandibular radiomorphometric indices in the diagnosis of reduced skeletal bone mineral density Osteoporos. Int. 13 373-8


Harris ST, Watts NB, Genant HK, McKeever CD, Hangartner TN, Keller M, Chestnut III CH, Brown J, Eriksen EF, Hoseyni MS, Axelrod DW and Miller PD 1999 Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis – a randomized controlled trial JAMA. 282 1344-52

Hildebolt CF 1997 Osteoporosis and oral bone loss Dentomaxillofac. Radiol. 26 3-15


Jowitt N, MacFarlane T, Devlin H, Klemetti E and Horner K 1999 The reproducibility of the mandibular cortical index Dentomaxillofac. Radiol. 28 141-4

Kingsmill VJ and Boyde A 1999 Mineralization density and apparent density of bone in cranial and postcranial sites in the aging human *Osteoporos. Int.* **9** 260-8


Kribbs PJ 1990a Comparison of mandibular bone in normal and osteoporotic women *J. Prosthet. Dent.* **63** 218-22


Liberman UA, Weiss SR, Broll J, Minne HW, Quan H, Bell NH, Rodriguez-Portales J, Downs RW Jr, Dequeker J and Favus M 1995 Effect of oral alendronate on bone mineral density and the incidence of fractures in


Melton LJ, O’Fallon WM and Riggs BL 1987 Secular trends in the incidence of hip fractures *Calcif. Tissue Int.* **41** 57-64


Price WA 1901 The science of dental radiography *Dent. Cosm.* **43** 483-503


Table 1. Skeletal BMD status as assessed by DXA. Subjects are classified as osteopenic if their T-score is more than 1.0 SD below the young adult mean and as osteoporotic if their T-score is more than 2.5 SD below the young adult mean. The number of subjects and fraction of the same-gender group that meet the criteria are given.

<table>
<thead>
<tr>
<th></th>
<th>Lumbar Spine</th>
<th>Left Femur</th>
<th>Right Femur</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEMALES (n=35)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>22 (0.63)</td>
<td>24 (0.68)</td>
<td>24 (0.68)</td>
</tr>
<tr>
<td>Osteopenic</td>
<td>12 (0.34)</td>
<td>9 (0.26)</td>
<td>9 (0.26)</td>
</tr>
<tr>
<td>Osteoporotic</td>
<td>1 (0.03)</td>
<td>2 (0.06)</td>
<td>2 (0.06)</td>
</tr>
<tr>
<td><strong>MALES (n=11)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>8 (0.73)</td>
<td>7 (0.64)</td>
<td>7 (0.64)</td>
</tr>
<tr>
<td>Osteopenic</td>
<td>2 (0.18)</td>
<td>4 (0.36)</td>
<td>4 (0.36)</td>
</tr>
<tr>
<td>Osteoporotic</td>
<td>1 (0.09)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
</tbody>
</table>
Table 2. Correlation between mandibular BMD, as assessed by high and low single-energy RA of the homogeneous sub-ROI, and skeletal BMD, as assessed by DXA.

<table>
<thead>
<tr>
<th>SKELETAL SITE</th>
<th>HIGH-ENERGY</th>
<th>LOW-ENERGY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>0.15</td>
<td>0.333</td>
</tr>
<tr>
<td>Femoral neck, left</td>
<td>0.28</td>
<td>0.064</td>
</tr>
<tr>
<td>Femoral neck, right</td>
<td>0.30</td>
<td>0.052</td>
</tr>
<tr>
<td>Total body</td>
<td>0.36</td>
<td>0.018*</td>
</tr>
<tr>
<td>Trunk</td>
<td>0.37</td>
<td>0.015*</td>
</tr>
<tr>
<td>Ribs</td>
<td>0.35</td>
<td>0.018*</td>
</tr>
<tr>
<td>Arms</td>
<td>0.44</td>
<td>0.003**</td>
</tr>
<tr>
<td>Pelvis</td>
<td>0.35</td>
<td>0.018*</td>
</tr>
<tr>
<td>Legs</td>
<td>0.39</td>
<td>0.008**</td>
</tr>
</tbody>
</table>

*   \( p < 0.05 \)

**  \( p < 0.01 \)
Table 3. ROC analysis of mandibular BMD as assessed by single-energy RA of homogeneous sub-ROIs. Positivity is defined from DXA results at the spine, left femur and right femur for three thresholds: osteoporotic (-2.5), osteopenic (-1.0) and average (0.0). Gender codes: Females (F), combined females and males (C). Areas under the ROC curve for the high/low-energy measurement are given.

<table>
<thead>
<tr>
<th>THRESHOLD</th>
<th>GENDER</th>
<th>SPINE</th>
<th>LEFT FEMUR</th>
<th>RIGHT FEMUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>F</td>
<td>0.66 / 0.55</td>
<td>0.61 / 0.63</td>
<td>0.55 / 0.54</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>0.62 / 0.54</td>
<td>0.57 / 0.61</td>
<td>0.56 / 0.57</td>
</tr>
<tr>
<td>-1.0</td>
<td>F</td>
<td>0.61 / 0.52</td>
<td>0.73 / 0.70</td>
<td>0.65 / 0.61</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>0.56 / 0.53</td>
<td>0.63 / 0.66</td>
<td>0.57 / 0.60</td>
</tr>
<tr>
<td>-2.5</td>
<td>F</td>
<td>*</td>
<td>0.95 / 0.95</td>
<td>0.95 / 0.95</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>0.60 / 0.61</td>
<td>0.96 / 0.96</td>
<td>0.96 / 0.96</td>
</tr>
</tbody>
</table>

* insufficient number of true cases for analysis
Figure 1. Diagram of the film holder for simultaneous collection of two sets of single-energy data (high and low), which can also be combined for dual-energy measurement.
Figure 2. K-edge filtration technique. (a) Simulated 70 kVp x-ray tube output spectrum. (b) Linear attenuation coefficient vs. energy for cerium (Z=58). (c) Spectrum after attenuation by 0.4-mm thick cerium filter. Intensity of the filtered x-ray spectrum is relative to that of the unfiltered spectrum.
Figure 3. Ratio of average energies of the filtered spectra as a function of high and low filter materials. The tube voltage was 70 kVp, and the filter thickness was determined for each element such that the number of transmitted photons was constant for all elements.
Figure 4. The effect of filter thicknesses on dual-energy measurement uncertainty of the standard patient mandible. Contour lines define high and low filter combinations that yield coefficients of variation of less than 5%, 4%, 3%, 2% and 1%. Overall, measurement uncertainty is reduced with decreasing filter thicknesses because transmitted photon counts are increased. However, when the filters become very thin, the measurement error begins to increase. With thinner filters, the k-edge effect is diminished, and the spectra become more similar in shape. Hence, the average beam energies approach one another, and the dual-energy equations cease to be linearly independent.
Figure 5. (a) Theoretical and (b) experimental filtered x-ray tube spectra. The purchased filters were 120 µm of cerium for the low-energy beam and 60 µm of molybdenum for the high-energy beam. The presence of low-energy escape peaks and characteristic radiation seen in the collected spectra are induced by the measurement system and can be neglected in the calculation of the average beam energies, which are well-matched between simulated and collected spectra.
Figure 6. Films were acquired using the special holder that houses the calibration wedge and beam filters. One set of filters overlies the wedge, and another set covers the bone. Here, the superior portion of the mandibular ROI is filtered by cerium (low-energy beam), and the inferior portion is filtered by molybdenum (high-energy beam).
Figure 7. Sample high- and low-energy calibration curves for a film from one study participant. A second-order polynomial is fitted to the set of step wedge data (●). This curve is then used to determine the copper-equivalent thicknesses of the patient’s high- and low-energy ROIs (●).
Figure 8. Sample patient film with high-energy (more inferior) and low-energy (more superior) ROIs shown. The average intensity (grayscale) values of each region are translated to copper-equivalent thickness values via the appropriate calibration curves (Figure 7).
Figure 9. Example of a plot used to determine the homogeneous sub-ROIs for each patient. The average grayscale intensity value of each horizontal line of pixels in the ROI is shown. The values are plotted with the same orientation that exists anatomically, i.e. the 0 position is the most superior line of the ROI. Higher grayscale intensity values indicate increased BMD. A discontinuity in line average values occurs when the filtration is changed (seen here at positions 39-40) due to the shift in average beam energy. The boxed points represent the lines that were chosen as the homogeneous sub-ROIs. Except for a few data points at the borders of the filters, where edge effects appear to influence the density values (indicated by the arrows), the sub-ROIs were always chosen adjacent to one another.
Figure 10. Correlation between mandibular BMD, as measured by single-energy (high) RA, and BMD of the arms, as measured by DXA ($r = 0.44$, $p = 0.003$).
Figure 11. Simulated high-energy copper-equivalent thickness values for combinations of bone and soft tissue thickness. A two-dimensional second-order polynomial fit to this plane yields an analytical expression that allows us to define bone and soft-tissue pairs corresponding to the patient’s high-ROI value. An analogous low-energy expression is derived. These equations are then used to generate a unique set of high- and low-energy curves for each patient (Fig. 12).
Figure 12. Bone and soft-tissue combinations that produce the same film optical density as a fixed copper thickness. For each patient, the pair of high- and low-energy curves that corresponds to their measured ROI values was plotted. The intersection of these curves should provide a unique solution for the patient’s bone thickness and soft-tissue thickness. As seen in this example, the intersection point was outside the reasonable range of bone and soft-tissue values (2.60 cm and -7.41 cm, respectively). The vertical separation of these curves is indicative of non-equivalent high- and low-energy ROIs, most likely due to the observed systematic superior to inferior increase in mandibular BMD within the general ROI.