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# Artificial Neural Networks Analysis for Estimating Bone Mineral Density in an Egyptian Population: Towards Standardization of DXA Measurements

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**Abstract:** An extensive amount of information is currently available to clinical specialists, ranging from detailed demographic characteristics to physical examination and various types of biochemical data. The most important concern in the medical field is to consider the interpretation of data and perform accurate diagnosis. Artificial intelligence method and especially artificial neural network (ANN) algorithms can handle diverse types of medical data and integrate them into categorized outputs. A common bone disease 'osteoporosis' does not depend only on bone mineral density (BMD) but also on some other factors e.g., age, weight, height, life-style etc., which play considerable role in the diagnosis of osteoporosis. In this study, we propose a decision making system using demographic variables in an Egyptian population to provide a convenient, accurate and inexpensive solution to predict segmental and total BMD and expect future fracture risk for healthy persons and those with pathologic condition known to be related to BMD. We believe the ANN is a promising tool for estimating and predicting segmental and total BMD values using simple demographic characteristics.

**Keywords:** Bone Mineral Density (BMD), Dual-energy X-ray Absorptiometry (DXA), Osteoporosis, Artificial Neural Network (ANN)

## 1. Introduction

Bone is a living tissue that undergoes a continuous cycle of formation and resorption, both of which are affected by the impact of mechanical loading on the skeleton, circulating hormones, and local humoral factors [1, 2]. A complex interplay of factors such as sex, race, age, weight, height, cigarette smoking, and certain pathologies are known to affect bone health, with osteoporosis being a possible end point [3, 4]. Osteoporosis is a metabolic bone disease characterized by low bone mass and micro architectural deterioration of bony tissue, with consequent enhanced bone fragility and increased risk of fracture [2-5]. Moreover, osteoporosis not only causes fractures, but also causes people to become bedridden with secondary complications that may be life threatening in the elderly.

Currently, the best predictor of future osteoporotic fracture is the level of bone mineral density (BMD) measured by Dual-energy X-ray Absorptiometry (DXA) scanning, as recommended by the World Health Organization (WHO) [6, 7]. However, due to the lack of technology and the existing debates regarding the cost-effectiveness of BMD large-scale screening there are no studies in developing countries, especially in Egypt. Thus, there is need for a fast and accurate method for frequently monitoring bone health, identifying patients at risk of fracture so that preventive strategies or treatment can be targeted towards those at greatest fracture risk. Mathematical modeling lends itself as the method of choice for such studies [8, 9].

The objective of this study was to use an advanced Artificial Neural Networks (ANN) to estimate segmental (i.e., arms, legs, spine and pelvis) and total BMD using demographic measurements such as sex, age, height, weight, and body mass index (BMI) in an Egyptian population in health and disease.

# 2. Subjects and Methods

### *2.1. Study Population*

The study population comprised 2,000 male and female Egyptian participants with an age rage 20-79 years, who were referred to the Internal Medicine Department, Medical Research Institute, Alexandria University for diagnosis and/or treatment and for a total body DXA scan at the Medical Biophysics Department, in the period from June 2006 till December 2009. All participants were asked to freely volunteer and a written informed consent from participants were signed before their inclusion in the study. The study protocol was approved by the Ethics Committee of the Medical Research Institute, Alexandria University, Alexandria, Egypt.

Complete medical examinations, demographic variables and body composition investigations were carried out for all participants. Based on the health status, they were categorized into nine groups. Participants who did not suffer from any particular condition or disease were categorized into Healthy group (n = 400). Participants with pathologic conditions that may distress the BMD were categorized into the Obesity group (n = 400), the Overweight group (n = 290), the Renal Dialysis group (n = 400), the Renal Transplantation group (n = 150), the Chronic Kidney Disease group (n = 190), the Hepatocellular Carcinoma group (n = 60), the Hypertension group (n = 70); and finally, the Diabetes Type II group (n = 40), as shown in Table 1.

### *2.2. Methods*

A. Bone Mineral Density Measurements:

We measured demographic and body-composition characteristics for all participants. Specifically, body weight (kg) (participants clothed in underwear, bare feet) was measured using a sensitive digital scale (to the nearest 0.01 kg) (Body Master, Rowenta, Germany). Height (m) was measured using a stadiometer. BMI was expressed as Weight/Height$^2$ (kg/m$^2$). Segmental (i.e. arms, legs, lumbar spine ($L_1$–$L_4$), pelvis) and total BMD were measured using a DXA total-body scanner (Lunar DPX Pro, GE Healthcare, USA) for all participants, as we described earlier [9, 10].

B. Artificial Neural Network Analysis:

The quantitative estimation of the segmental and total BMD was carried out using an ANN software package for Windows (NeuroSolutions 7.0 NeuroDimension Inc., Gainesville, FL, USA). It combines a modular, icon-based network design interface with an implementation of advanced artificial intelligence and learning algorithms using intuitive wizards together with an Excel™ interface. This provides a user-friendly intuitive interface to easily setup a simulation that automatically builds, trains and tests multiple neural network topologies and generates a report of the results including the best performing model.

There are three basic phases in ANN analysis: training the network using known data, testing the network for accuracy and making predictions/classifying from new data. The variables: sex, age, weight, height, and BMI in addition to reference segmental (i.e., $BMD_{arms}$, $BMD_{legs}$, $BMD_{spine}$ and $BMD_{pelvis}$) and $BMD_{total}$ for all participants were prepared in an Excel database as the input parameters. The Excel database was loaded within the NeuroSolutions and used for classification according to reference segmental and total BMD experimental measurements by DXA.

The procedure of operation was according to the following scheme: At first, we obtained the necessary input variables from patients as defined earlier and developed a history for each patient. Secondly, we preprocessed patients' variables/attributes by inserting a column for labels, cleaned missing data by replacing blank cells and error codes, and created some additional parameters to indicate population and sample. This process builds the database for training purpose. Thirdly, we randomized rows of data and wrote the results to a new sheet. Fourthly, we tagged rows of data (according to user-defined percentages) within the active worksheet as: Training (60% of data and is fixed) ,Cross Validation (15%), and Testing (25%). That is, of the 2000 records examined by the ANN for segmental and total BMD, there were 1400 records for training, 200 for cross validation, and 400 for testing. Fifthly, we selected an appropriate ANN type and architecture, training algorithm and verification method. The training took place as part of a looped training and validation process. In this process, a core set of parameters was used for the initial training, and then the testing data set was used to evaluate its performance. Errors were then mapped back to absent inputs, and the set re-trained with the additional input. This process was to be repeated until a minimum error is obtained, where the importance and weighting of each input parameter is assessed. The confusion matrix of the results as well as the general statistics describing the performance of the ANN [e.g., root mean squared error (RMSE), normalized root mean squared error (NMSE), mean absolute error (MAE), minimum absolute error, maximum absolute error, and correlation coefficient (R)] for segmental and total BMD output was given. Finally, the system was tested for an unknown set of patients carefully and if diagnosis was correct, their data were included in database.

C. Statistical Analysis:

The data was analyzed using the StatView® statistical package (Version 5.0, SAS Institute Inc., Cary, NC, USA). One-way analysis of variance (ANOVA) and Scheffe's post-hoc test of significance was applied to compare the groups in terms of different variables. The significance level was defined as $p < 0.05$. Errors in segmental and total BMD estimations using ANN were calculated as the mean square error (MSE).

# 3. Results and Discussion

DXA, which is the most commonly used method for the diagnosis and followup of human bone health, is known to produce accurate estimates of BMD for healthy persons and those with conditions known to be associated with BMD. The

mean values of the demographic and segmental and total BMD characteristics, grouped by pathologic condition, are presented in Table 1. Generally, the mean values of the age, weight and BMI variables were significantly higher than Healthy group for all pathologic groups, except for the Renal Transplantation group, which was not different for age, and for Chronic Kidney Disease group, which was not different for age, weight and BMI. In addition, height was not different among all groups. These observations are in line with a previous study on an Italian population by Mohamed *et al.* [9], who showed that Diabetes Type II patients had a significantly higher BMI, while the Hepatocellular Carcinoma patients had a significantly lower BMI as compared to Healthy controls.

***Table 1.*** *Demographic and reference segmental and total bone density, as measured by Dual-energy X-ray Absorptiometry (DXA), characteristics of the whole study population (n = 2000) as divided by health condition.*

| | Healthy Controls | Pathologic Condition | | | |
|---|---|---|---|---|---|
| | | Obesity | Overweight | Hypertension | Diabetes Type II |
| Number | *400* | *400* | *290* | *70* | *40* |
| Sex, M/F | 290/110 | 40/360 | 30/260 | 20/50 | 15/25 |
| Age, years | 38.8 ± 11.1 | 64.6 ± 14.1* | 42.1 ± 13.03 | 58.5 ± 2.8* | 57.1 ± 4.7* |
| Weight, kg | 65.5 ± 12.9 | 92.5 ± 16.1* | 75.4 ± 10.1* | 77.1 ± 8.3* | 90.4 ± 20.6* |
| Height, m | 1.65 ± 0.09 | 1.60 ± 0.10 | 1.62 ± 0.08 | 1.61 ± 0.08 | 1.58 ± 0.04 |
| BMI, kg/m$^2$ | 24 ± 4.01 | 36.2 ± 5.6* | 28.5 ± 3.5* | 29.5 ± 6* | 36.1 ± 7.7* |
| $BMD_{arms}$, g/cm$^2$ | 0.83 ± 0.08 | 0.94 ± 0.05* | 0.93 ± 0.06* | 0.85 ± 0.07 | 0.94 ± 0.14* |
| $BMD_{legs}$, g/cm$^2$ | 1.16 ± 0.13 | 1.22 ± 0.01* | 1.21 ± 0.06* | 1.19 ± 0.12 | 1.26 ± 0.09* |
| $BMD_{spine}$, g/cm$^2$ | 1.13 ± 0.15 | 1.17 ± 0.07* | 1.16 ± 0.08* | 1.17 ± 0.15* | 1.40 ± 0.64* |
| $BMD_{pelvis}$, g/m$^2$ | 1.16 ± 0.15 | 1.19 ± 0.08 | 1.19 ± 0.08* | 1.18 ± 0.12 | 1.21 ± 0.11* |
| $BMD_{total}$, g/m$^2$ | 1.15 ± 0.09 | 1.22 ± 0.05 | 1.21 ± 0.06* | 1.16 ± 0.11 | 1.28±0.23* |

***Table 1.*** *Continued.*

| | Pathologic Condition | | | |
|---|---|---|---|---|
| | Renal Dialysis | Renal Transplantation | Chronic Kidney Disease | Hepatocellular Carcinoma |
| Number | *400* | *150* | *190* | *60* |
| Sex, M/F | 200/200 | 70/80 | 120/70 | 40/20 |
| Age, years | 57.7 ± 14.3* | 37.1 ± 6.8 | 41.6 ± 12.9 | 63.7 ± 12.8* |
| Weight, kg | 67.9 ± 17.1 | 73.4 ± 17.6* | 62.6 ± 13.7 | 74.3 ± 8.9* |
| Height, m | 1.58 ± 0.10 | 1.66 ± 0.10 | 1.66 ± 0.10 | 1.63 ± 0.08 |
| BMI, kg/m$^2$ | 28.1 ± 6.10* | 26.6 ± 5.9* | 22.1 ± 5.4 | 27.9 ± 2.13* |
| $BMD_{arms}$, g/cm$^2$ | 0.76 ± 0.11* | 0.83 ± 0.09 | 0.84 ± 0.11 | 0.83 ± 0.05 |
| $BMD_{legs}$, g/cm$^2$ | 1.06 ± 0.17* | 1.10 ± 0.12 | 1.11 ± 0.21* | 1.21 ± 0.12* |
| $BMD_{spine}$, g/cm$^2$ | 1.09 ± 0.27* | 1.02 ± 0.07* | 1.05 ± 0.12* | 1.06 ± 0.08* |
| $BMD_{pelvis}$, g/m$^2$ | 1.05 ± 0.20* | 1.07 ± 0.07* | 1.05 ± 0.13* | 1.09 ± 0.09* |
| $BMD_{total}$, g/m$^2$ | 1.08 ± 0.13* | 1.09 ± 0.07* | 1.11 ± 0.13* | 1.13 ± 0.08* |

All values are expressed as mean ± SD.

*BMI* body mass index, $BMD_{arms}$ Arms bone mineral density, $BMD_{legs}$ legs bone mineral density, $BMD_{spine}$ lumbar spine bone mineral density; $BMD_{pelvis}$ pelvis bone mineral density; and $BMD_{total}$ total Bone Mineral density.

** $P<0.01$ as compared to Healthy Controls.

The mean values of segmental and total BMD for Obesity, Overweight, Hypertension and Diabetes Type II groups were significantly higher than Healthy Controls group, except for the Hypertension group which showed no difference for $BMD_{legs}$ and $BMD_{total}$. However, mean values of segmental and $BMD_{total}$ for Renal Dialysis, Renal Transplantation, Chronic Kidney Disease and Hepatocellular Carcinoma groups were significantly lower than those for Healthy Controls group. Furthermore, the Renal Transplantation, the Chronic Kidney Disease and the Hepatocellular Carcinoma groups showed no significant difference for the $BMD_{arms}$ as compared to Healthy Controls group. These observations are in line, only for the Hepatocellular Carcinoma group, with the study by Mohamed *et al.* [9], who showed that Italian Hepatocellular Carcinoma and Diabetes Type II patients had significantly lower $BMD_{spine}$, $BMD_{pelvis}$ and $BMD_{total}$ as compared to Healthy Controls.

The multilayer perceptron network is most often used in medical diagnosis systems. In the present work, we used a multilayer perceptron method for accurately estimating segmental and total BMD for predicting the future fracture risk. The demographic variables (i.e., sex, age, weight, height, and BMI) were fed to a multilayered ANN (input layer), which learns associations among these variables and reference values for the BMD compartment, using an adaptive propagation algorithm for automatic training. In the hidden layers, the ANN constructs a predictor function in which the demographic variables are used to determine the corresponding value for the compartment of interest for a given individual. Quantitative estimates of $BMD_{arms}$, $BMD_{legs}$, $BMD_{spine}$, $BMD_{pelvis}$, and $BMD_{total}$ are given in the output layer. Typically, multilayer perceptron uses learning algorithm that minimizes the error between output (i.e., actual BMD) and desired (i.e., reference BMD) values by using recursively delta rule. Backpropogation calculates error, computes delta, propagates error backwards and then

updates the weights. After updating, these weights feed in training patterns [11].

The actual output in training, testing and cross validation showed a very high correlation coefficient (R > 0.99) with reference segmental and total BMD, as shown in Figures 1 and Table 2. Performance results of the "Testing" phase of the ANN of actual and reference values for $BMD_{arms}$, $BMD_{legs}$, $BMD_{spine}$, $BMD_{pelvis}$ and $BMD_{total}$ after cross validation were nearly identical with RMSE of ±0.07, ±0.07, ±0.07, ±0.008 and ±0.0009; and accuracy exceeding 99% for all predictions; respectively, as shown in Table 2. These findings are better than those achieved by Jensen *et al.* [12], who used DXA values as input in an ANN and predicted fracture risk with an accuracy of 86.6%. Moreover, our results based only on the demographic characteristics: sex, age, weight, height and BMI; are better than the system developed by Sarah *et al.* [13], who trained a multiversion ANN using 20 risk factors of 274 women for predicting their T-Scores and diagnosing osteoporosis.

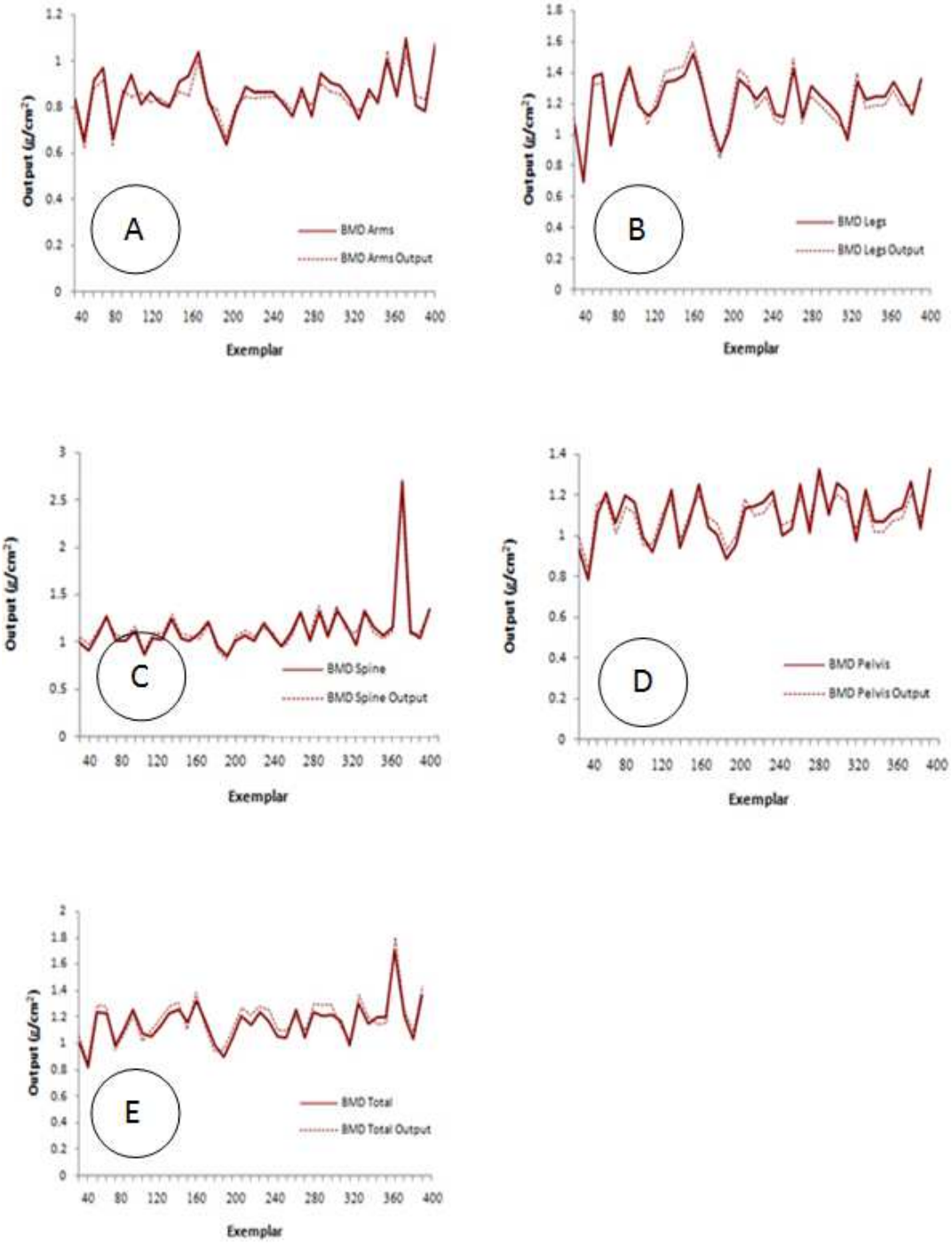


***Figure 1.*** *Results of the "Testing" phase (n = 400) of the artificial neural network of actual and reference values of arms ($BMD_{arms}$, A), legs ($BMD_{legs}$, B), spine ($BMD_{spine}$, C), pelvis ($BMD_{pelvis}$, D), and total ($BMD_{total}$, E) bone mineral density.*

***Table 2.*** *Performance results of the "Testing" phase (n = 400) of the artificial neural network of actual and reference segmental and total actual and reference values for bone mineral density (in g/cm$^2$) of the arms ($BMD_{arms}$), legs ($BMD_{legs}$), spine ($BMD_{spine}$), pelvis ($BMD_{pelvis}$) and total ($BMD_{total}$).*

| | $BMD_{arms}$ | $BMD_{legs}$ | $BMD_{spine}$ | $BMD_{pelvis}$ | $BMD_{total}$ |
|---|---|---|---|---|---|
| Root mean Squared Error (RMSE) | 0.07254 | 0.07094 | 0.07474 | 0.00767 | 0.00093 |
| Normalized Root Mean Squared Error (NMSE) | 0.07254 | 0.07094 | 0.07474 | 0.00767 | 0.00093 |
| Mean Absolute Error (MAE) | 0.03811 | 0.01070 | 0.03948 | 0.00118 | 0.00017 |
| Minimum Absolute Error | 0.00058 | 2.40110E-09 | 0.00286 | 9.14050E-08 | 2.00599E-10 |
| Maximum Absolute Error | 0.41360 | 0.47058 | 0.42728 | 0.05144 | 0.00501 |
| Correlation Coefficient (R) | 0.99078 | 0.99004 | 0.99019 | 0.99989 | 0.99999 |

# 4. Conclusions

A low BMD is considered as an accurate estimator of fracture risk, which increases exponentially with the decrease of the BMD. DXA bone density testing is the most accurate method available for the diagnosis of osteoporosis and osteopenia. However, problems with availability, high cost analysis, and difficult application for morbidly obese persons may prevent DXA wide use for mass screening. We proposed a method for accurately estimating segmental and total BMD using a commercially available ANN software package. The demographic variables: sex, age, weight, height, and BMI in addition to reference segmental and total BMD values were fed to a multilayered ANN (input layer) and quantitative estimates of $BMD_{arms}$, $BMD_{legs}$, $BMD_{spine}$, $BMD_{pelvis}$ and $BMD_{total}$ are produced in the output layer. We believe the proposed ANN system is a promising approach for estimating segmental and total BMD values, using simple demographic measurements, to facilitate clinical diagnosis of osteoporosis.

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