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Multiple Inputs Deep Neural Networks for Bone Age Estimation Using Whole-Body Bone Scintigraphy

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ABSTRACT

The cosmetic and behavioral aspects of aging have become increasingly evident over the years. Physical aging in people can easily be observed on their face, posture, voice, and gait. In contrast, bone aging only becomes apparent once significant bone degeneration manifests through degenerative bone diseases. Therefore, a more accurate and timely assessment of bone aging is needed so that the determinants and its mechanisms can be more effectively identified and ultimately optimized. This study proposed a deep learning approach to assess the bone age of an adult using whole-body bone scintigraphy. The proposed approach uses multiple inputs deep neural network architectures using a loss function, called mean-variance loss. The data set was collected from Chonnam National University Hwasun Hospital. The experiment results show the effectiveness of the proposed method with a mean absolute error of 3.40 years.

Key words: Bone Age Estimation, Bone Scintigraphy, Mean-Variance Loss, Multiple Inputs Deep Neural Networks.

1. INTRODUCTION

Humans have two types of age: chronological and biological. Chronological age is the number of years a person is alive, while biological age is a measure of how aging progress has affected your body. The study by Belsky et al. [1] indicates that; some young adults are aging three times faster than others; the aging processes can be assessed in young adults and be used to prevent age-related illness, opening a new direction for anti-aging therapies. The increased aging rate increased the incidence of age-related illnesses. Demand for anti-aging intervention to reduce the burden of illness and protect the productive population is high. Young adults are the best subject for therapies to prolong health due to it can still prevent illness in young adults.

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The age estimation is an important aspect in the line of work of health informatics, forensic science and anthropology. The approach to quantify the biological age of the brain of an adult using neuroimaging has attracted a lot of attention in recent years [2-4]. This interest in brain age prediction is promoted by the importance of biological age estimation in health informatics, which is extremely significant before neurodegeneration manifests through cognitive impairment and dementia.

In addition, recent studies indicate the relationship between the aging process bones and bone degradation diseases [5 - 7] as well as the age-related bone uptake of Tc-99m-HDP measured by whole-body bone scintigraphy [8-11]. To quantify the biological age of bone of an adult before the appearance of significant bone degeneration, bone age estimation (BAE) method using whole-body bone scintigraphy based on multiple inputs deep neural networks was proposed. Bone scintigraphy [12] is a diagnostic imaging technique of nuclear medicine has high sensitivity. This technique uses radioactivity to assess the distribution of active bone formation in the skeleton related to malignant, and benign diseases, as well as physiological processes. It is a sensitive technique that can detect early significant metabolic changes before they become apparent in conventional X-ray images. Moreover, it also provides an overview of the entire skeleton. This study's experiment results demonstrate the effectiveness of the proposed method.

The structure of this paper is as follows: the related works are introduced in Section II, the proposed method is described in Section III, the experimental results are detailed in Section IV and the conclusions are given in Section V.

2. RELATED WORKS

The development of bones of left hand from fingertips to wrist [13], the presence of ossification centres, and the fusion of the epiphyses [14, 15] can be used in children. The development of the third molar [16], the development of bones of left hand from fingertips to wrist [13, 17], the spheno-occipital fusion [18, 19] and the fusion of sternum [20, 21] are appropriate indicators for adolescents and young adults.

Adserias-Garriga et al. [22] showed that in the above cases, the skeleton's age indicators are based on an individual's growth; but when the growth is over, the skeleton's age indicators are based on degenerative changes and the age estimation accuracy decreases as individual's age increases. Indicators of bone age in adults include the pubic symphysis [23, 24], the sacropelvic surface of the ilium [25], and the acetabulum [26].

Lottering et al. [27] conducted the prediction of adult age using multislice CT scans of the pubic symphysis. The mean error of this method was 7.24 years for individuals less than 55 years old and 5.89 for individuals above 55 years old.

Lovejoy et al. [25] proposed a method for estimating adult bone age based on the sacropelvic surface of the ilium. The mean error of this method is 7.8 years.

San-Millán et al. [28] suggested a new approach to predict the age of adults based on the morphological characteristics of the acetabulum. The method has an average absolute error of 7.28 years and 7.09 years for males and females, respectively, based on the specific gender reference patterns.

Besides, other methods have been developed to estimate the age of an adult individual such as telomere shortening analyzes and recently epigenetic modifications [29]. Various studies showed that during the aging process, telomeres are shortened [30, 31]. Thus, some researchers studied them to predict age [32, 33, 34]. Ren et al. [32] achieved a mean prediction error of 9.213 years with this technique.

Recently, age estimation from the correlation between methylation levels and age has grown

rapidly. Bekaert et al. [29] achieved a mean error of 3.75 years for blood samples and a mean error of 4.86 years for dentine samples. There were no differences in results for samples obtained from dead and alive individuals or between two genders.

3. PROPOSED METHOD

This section presents the details of the multiple-input models that are trained by the mean-variance loss to automatically BAE using whole-body bone scintigraphy. The architecture and parameters of the proposed VGG model are designed to optimize its performance on age estimation based on whole-body bone scintigraphy and is shown in Fig. 1.

A multiple inputs VGG16 model for BAE were proposed. The proposed base models are two VGG16 models pre-trained on the ImageNet data set. Two inputs to the proposed VGG16 models are 224 × 224 × 3 RGB images. VGG16 model includes five 2D convolutional blocks (CBs). The two early CBs have two convolutional layers (CLs). The three last convolutional blocks have three CLs. The numbers of feature maps in each convolution block are 64, 128, 256, 512, 512. Each 2D convolutional layer has a kernel size of 3 × 3 and each convolutional block ends with one max pooling layer.

A global spatial average pooling layer was added to each VGG16 model. Each VGG16 model also includes two fully connected layers of 320, 160 neurons each. The outputs of these two branches are combined by concatenation layer. Then fully connected layers of 160 neurons are applied. The non-linear mapping functions are set up as rectified linear unit for all CLs and these fully connected layers. In addition, a drop out of 0.2 is used after each fully connected layer. The output layer of the proposed model contains a softmax layer.

The proposed model is trained by joint loss, which includes softmax loss and mean-variance loss [35] as follows:

$$L = L_s + L_m + L_v \tag{1}$$

where and are two hyperparameters to balance the influence of sub-losses in the joint loss.

The softmax loss is computed as:

$$L_s = \frac{1}{N}\sum_{i=1}^{N} -\log p_{i,\ y_i} \tag{2}$$

The mean loss is computed by the formula:

$$L_m = \frac{1}{2N}\sum_{i=1}^{N}\left(\sum_{j=1}^{K} j^* p_{i,j} - y_i\right)^2 \tag{3}$$

and the variance loss is computed as follows:

$$L_v = \frac{1}{N}\sum_{i=1}^{N}\sum_{j=1}^{K} p_{i,j}^* \left(j - \sum_{k=1}^{K} k^* p_{i,k}\right)^2 \tag{4}$$

where N is the batch size, i is the i-th of sample,

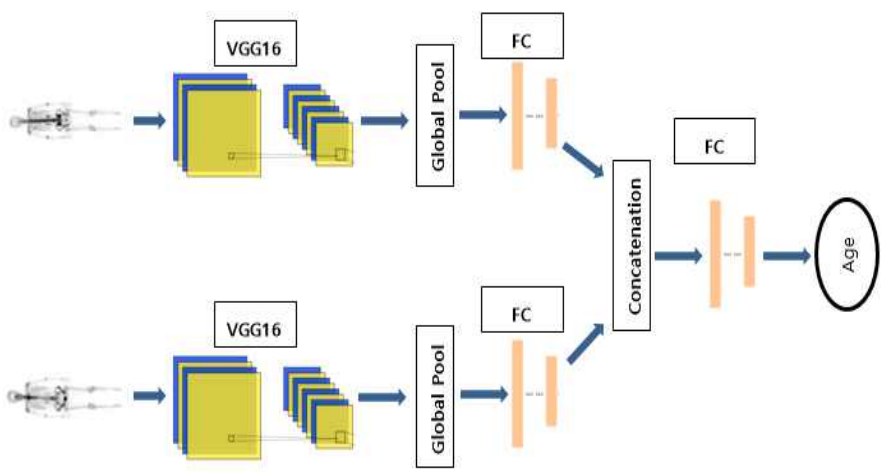


Fig. 1. The proposed model.

$j \in \{1, 2, \ldots, K\}$ expresses label of classes; p_i expresses the distribution of sample i over all classes and $p_{i,j}$ expresses the probability that sample i belongs to class j. In the test phase, estimated bone age is calculated as follows:

$$y_t = \sum_{j=1}^{K} j^* \ p_j \tag{5}$$

4. EXPERIMENT

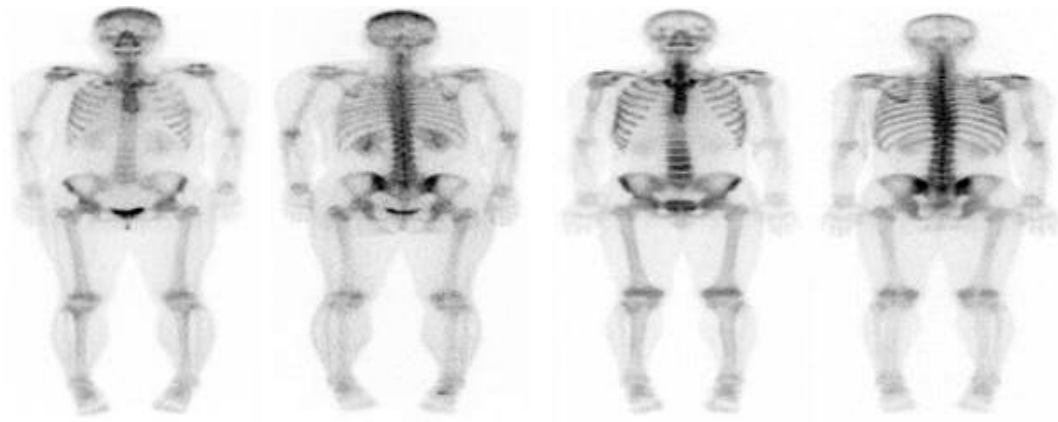
4.1 Data set

The data set was collected from Chonnam National University Hwasun Hospital. IRB number is CNUHH-2019-177. Each person has anterior and posterior images, along with age and gender as shown in Fig. 2.

The data set contains 8948 images of 4474 subjects, ranging from 40 to 80 years old. The ratio of females to males is approximately 1,69: 1. The distribution of ages for females and males are shown in Fig. 3. Five-fold cross-validation was used to evaluate model performance.

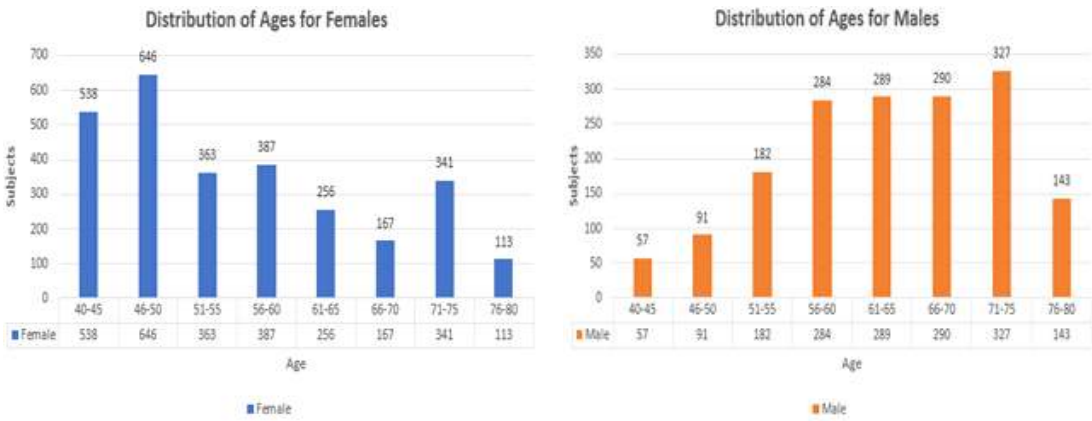
4.2 Results

The input of the proposed model is anterior and



(a) Age: 43, Gender: Female (b) Age: 42, Gender: Male

Fig. 2. The anterior and posterior of whole-body bone scintigraphy.



(a) Females (b) Males

Fig. 3. The distribution of ages for females and males.

Table 1. The performance for proposed algorithm and conventional algorithms

Model	Method	MAE (years)	r
InceptionV3	Mean squared loss	3.73 (3.05)	0.90
	Softmax loss	7.69 (6.02)	0.54
	Softmax + Mean-Variance loss	4.59 (3.78)	0.84
ResNet50	Mean squared loss	3.75 (3.04)	0.90
	Softmax loss	7.27 (6.30)	0.59
	Softmax + Mean-Variance loss	4.56 (3.77)	0.84
VGG16	Mean squared loss	3.92 (3.15)	0.89
	Softmax loss	4.42 (3.94)	0.85
	Softmax + Mean-Variance loss	3.59 (3.04)	0.90
Multiple inputs VGG16 (proposed)	Mean squared loss	3.75 (3.04)	0.90
	Softmax loss	4.24 (3.74)	0.86
	Softmax + Mean-Variance loss	3.40 (2.87)	0.91

posterior of whole-body bone scintigraphy. The proposed model is trained with the joint loss (JL) which includes softmax loss and mean-variance loss function using the Adam optimizer with a 1e-4 learning rate and a batch size of 64 samples. During the training phase, the learning rate will decrease by 10 times after 15 iterations without improving validation loss.

To compare with the proposed method, experiments with mean square error (MSE) loss, softmax loss and the JL function on VGG16 [36], ResNet50 [37, 38], Inception v3 [39] models, which are pretrained on the ImageNet data set [40]. Their input is anterior of whole-body bone scintigraphy. The MSE is calculated as follows:

$$\mathrm{MSE} = \frac{1}{N}\sum_{i=1}^{N}(y_i^{\wedge} - y_i)^2 \tag{6}$$

The models were evaluated by mean absolute error (MAE) and Pearson correlation (r) between predicted age and actual age:

$$\mathrm{MAE} = \frac{1}{N}\sum_{i=1}^{N}\left|y_i^{\wedge} - y_i\right| \tag{7}$$

$$\mathrm{r} = \frac{\sum_{i=1}^{N}(y_i^{\wedge} - \overline{y^{\wedge}}))(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{N}(y_i^{\wedge} - \overline{y^{\wedge}})^2 \sum_{i=1}^{N}(y_i - \bar{y})^2}} \tag{8}$$

where $\overline{y^{\wedge}}$ and $\bar{y}$ are the means of the predicted age and actual age.

The performance comparison table between the proposed model and other models are listed in Table 1. When the models are trained with mean-variance loss, they achieve superior performance. The proposed method outperforms the other models with mean absolute error (standard deviation) of 3.40 (2.87) years and Pearson's r is 0.91 (p-value < 0.0001). Fig. 4 shows the predictions of the proposed method.

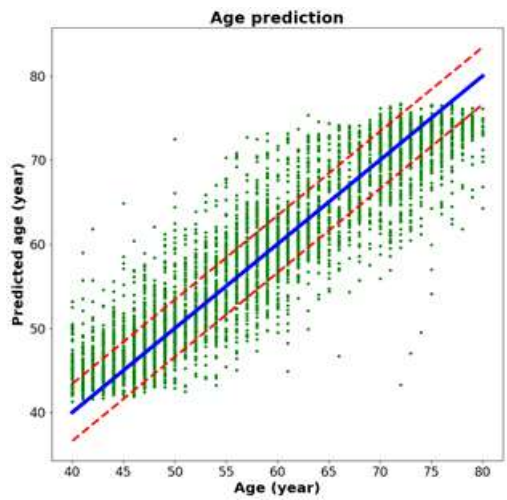


Fig. 4. The prediction of the proposed method. The dots, line and dash line are the predicted age, perfect prediction and mean absolute error, respectively.

5. CONCLUSION

This study proposed multiple inputs VGG 16 model. The proposed model is trained with the joint loss which includes softmax loss and mean-variance loss function to assess bone age using whole-body bone scintigraphy. Experiment results show the effectiveness of the proposed method with a mean absolute error of 3.40 years. We are going to improve the result by using gender in future works.

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