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Ultra-weak photon emission of hands in aging prediction

Xin Zhao [a,b], Eduard van Wijk [c,d], Yu Yan [c], Roeland van Wijk [c,d], Huanming Yang [b,e], Yan Zhang [b,*], Jian Wang [a,b,e,*]

[a] BGI Education Center, University of Chinese Academy of Sciences, Shenzhen 518083, China
[b] BGI-Shenzhen, Shenzhen 518083, China
[c] Meluna Research, Geldermalsen, The Netherlands
[d] Sino-Dutch Centre for Preventive and Personalized Medicine/Centre for Photonics of Living Systems, Leiden University, Leiden, The Netherlands
[e] James D. Watson Institute of Genome Sciences, Hangzhou 310058, China

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ABSTRACT

Aging has been one of the several topics intensely investigated during recent decades. More scientists have been scrutinizing mechanisms behind the human aging process. Ultra-weak photon emission is known as one type of spontaneous photon emission that can be detected with a highly sensitive single photon counting photomultiplier tube (PMT) from the surface of human bodies. It may reflect the body's oxidative damage. Our aim was to examine whether ultra-weak photon emission from a human hand is able to predict one's chronological age. Sixty subjects were recruited and grouped by age. We examined four areas of each hand: palm side of fingers, palm side of hand, dorsum side of fingers, and dorsum side of hand. Left and right hand were measured synchronously with two independent PMTs. Mean strength and Fano factor values of photon counts were utilized to compare the UPE patterns of males and females of different age groups. Subsequently, we utilized UPE data from the most sensitive PMT to develop an age prediction model. We randomly picked 49 subjects to construct the model, whereas the remaining 11 subjects were utilized for validation. The results demonstrated that the model was a good regression compared to the observed values (Pearson's $r = 0.6$, adjusted R square $= 0.4$, $p = 9.4E-7$, accuracy $= 49/60$). Further analysis revealed that the average difference between the chronological age and predicted age was only 7.6 ± 0.8 years. It was concluded that this fast and non-invasive photon technology is sufficiently promising to be developed for the estimation of biological aging.

1. Introduction

Aging is known as a progressive loss of physiological functions and an increase in risk for many diseases, such as cancer, cardiovascular diseases, neurodegenerative diseases, and endocrine diseases [1,2]. Additional research has focused on the genetic loci of longevity. Genes like APOE, FOXO1 and, TOMM40 have been found in the population of longevity when compared to a control group [3,4]. Although, molecular mechanisms about longevity have been extensively studied, the progress of how aging occurs still needs to be elucidated.

Aging is a complex process which is directly associated with the generation of reactive oxygen species during metabolic processes and accumulation of cellular damages induced by oxidative stress [5,6]. Many researchers are interested in predicting aging by objective ways. The difference between chronological age and predicted age could reflect the aging speed to a certain extent.

One approach to aging prediction is to focus on telomere length, and by the comparison of the quantity of a telomere and the housekeeping genes (i.e., a telomere/standard gene (T/S) ratio) [7]. Another approach to predict aging is vis-à-vis lots of human biochemical biomarkers [8,9]. Recently, Chen et al. utilized three-dimensional human facial morphologies to evaluate the aging, and proved that it was more reliable than normal blood tests [10].

Ultra-weak photon emission (UPE) is the phenomenon of spontaneous and incessant emission of photons by living organisms. This phenomenon was first observed by Gurwitsch in 1920s [11] and almost a hundred years later, researchers have documented that all biological systems (including human beings) emit UPE [12]. The emitted photons are mainly in the visible range and their spectrum has suggested that UPE is related to the excited species formed through oxidative reactions with biomolecules [13]. In most cases of this chemical excitation process, reactive oxygen species (ROS) are known to be involved. Most ROS are produced in mitochondria and ROS triggered lipid peroxidation, triplet excited carbonyls, and other compounds excited through energy

* Correspondence to: Y. Zhang. BGI-Shenzhen, Shenzhen 518083, China and J. Wang. BGI Education Center, University of Chinese Academy of Sciences, Shenzhen 518083, China.

E-mail addresses: yanzhang@genomics.cn (Y. Zhang), Jianwang@genomics.cn (J. Wang).

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transfer from the carbonyl groups are recognized as producers of photons in the visible range [14].

It is hypothesized that UPE of human beings is a fast and non-invasive approach to evaluate their aging. Research on human ultra-weak photon emission began in the 1990's and more recently focused on whole body measurements [15–18]. Some research has illustrated the use of pervasive, spontaneous photon emission of hands to evaluate states of health and disease [13,19–25]. With respect to age, only one pilot study suggested that increased age parallels the rise of spontaneous UPE of skin [26] but that care must be taken since it could be influenced by antioxidants (like vitamin c and oligomeric proanthocyanidins) [27,28].

In this paper, we report the measurements of ultra-weak photon emission from hands of different aged people. From the photon count distribution of the signal, we calculated the intensity and Fano factor [13,22,29]. The data were used to construct and validate a model to predict aging vis-à-vis UPE properties.

2. Methods and Materials

2.1. Ethics Statement

According to Medical Research Involving Human Subjects Act, this study did not require a medical ethics review. All subjects adequately understood the study procedure and gave their oral informed consent.

2.2. Experimental Setup

In the study, the researchers utilized a two-hand photon counting system (PMS07) which is a desktop model designed for measurements of ultra-weak photon emission from both hands. The equipment was provided by Meluna Research B.V. (Geldermalsen, the Netherland). The system (PMS07) has low background noise (10 counts per second) and included two measurement units including a photomultiplier and housing located on top of each dark chamber, two control boxes for measurement control and data acquisition plus one computer with data acquisition and analyzing software. The photomultiplier tubes (PMT) (type 9235QA; ET Enterprises) were sensitive in the spectral range of 160–630 nanometers (nm) and had a 51 millimeter (2 in.) diameter window. Measurements were controlled automatically vis-à-vis computer software.

2.3. Subjects

Sixty healthy volunteers (27 males and 33 females, chronological age 21 to 69) participated voluntarily in the experiment. No physical or emotional disorders of the 60 subjects were found by interview. Randomly, 49 subjects were chosen to build the prediction model while the remaining 11 subjects validated the model.

2.4. Measurement Procedures

Before each measurement, a subject was asked to wash their hands with clean tap water and dry their hands. Subsequently, subjects were asked to wear light tight black gloves for at least 20 min to avoid the effect of delayed luminescence caused by previous external light exposure. Before the measurements of a subject's hand began, a background noise was recorded for 5 min with intervals of 50 milliseconds (ms) resulting in 6000 measurement points.

A subject was then asked to sit in front of the measurement device and insert both hands into the measurement chambers. The hands were placed under the windows of both sensors. Four locations of each hand were measured in the following order: palm side of fingers (PF), palm side of hand (pH), dorsum side of fingers (DF), and dorsum side of hand (DH) (Fig. 1). Each location was recorded for 5 min at intervals of 50 ms. Once the measurement of one location was completed, the subject positioned the hands to the next measurement location and a new measurement started immediately.

2.5. Data Analysis

Signal strength (mean photon intensity of hand measurement subtracted by background noise) and Fano factor (variance divided by mean corrected for the background) were calculated for each measurement [29]. Statistical comparisons of the results were made utilizing Fisher exact test and analysis of variance (one-way ANOVA). A value of $p < 0.05$ was considered to be statistically significant. Pearson's correlation was calculated to analyze the relationship between age and both the UPE strength and Fano factor from 4 hand locations. In order to decrease the effect of multi-collinearity in the following prediction model, the parameters were selected according to the rule that the correlations between the selected parameters were in the range of -0.8 to $+0.8$. A multi-variate regression model was built by using these parameters to predict the age. Statistical analysis was performed by using SPSS 19.0 software (SPSS, USA). Data calculation and graphing were performed with Origin 8.5 (Origin Lab Corporation, Northampton, USA).

3. Results

3.1. Identification of Two Age Groups by PCA Analysis of UPE

Sixty subjects (27 male; 33 female) were involved in the research. UPE strength is one important factor for our analysis. In addition to mean (M) values of photon strength we also focused on the Fano factor (F) values of the 50 ms window size. The Fano factor describes the shape of the photon statistical distribution. The combination of 8 strengths and 8 Fano factors of all volunteers were utilized in a principal component analysis (PCA) to transform this set of observations of possible correlated variables into a set of values of linearly uncorrelated values called principal components. The transformation resulted in three principal component scores of all subjects, which accounts for 46.8%, 16.0% and 12.9% of whole data variation, respectively.

From this PCA analysis, it was obvious that the entire population could be separated into two parts, the subjects with <40 years were grouped in the left side while the older subjects were grouped in the right part of the diagram (Fig. 2). The younger group had an average age of 29.0 ± 1.2, while the older group had an average age of 56.2 ± 0.7.

3.2. UPE Strength Distribution in Males and Females

The further analysis focused on the comparison of these two groups and different genders. Because the two PMT to measure the two hands had different sensitivities the data of the right and left hand are presented (for visual inspection) as a dual figure (Fig. 3). When we compared the ultra-weak photon emission strength between the younger group and the older group, the differences were significant for each location (average increase is 57.7%). Palm fingers, palm, dorsum fingers and dorsum of the right hand showed an increase by 60.7% ($p = 2.0E-4$), 66.7% ($p = 8.5E-4$), 62.1% ($p = 4.4E-4$) and 45.3% ($p = 1.5E-3$) in the older group. Left hand showed the same trend, with an increase of 64.5% ($p = 2.3E-3$), 60.1% ($p = 1.6E-3$), 66.4% ($p = 1.9E-3$) and 35.6% ($p = 2.9E-2$) in older group. It is clear that the older group had higher UPE strength than the younger group for each location.

If we check the UPE of the different parts of the hand in every subject, we found that in both hands the sum of the finger parts (PFR, DFR, PFL, DFL) is higher than the sum of the palm and dorsum hand sides (PHR, DHR, PHL, DHL). Regarding the UPE of dorsum and palm sides of the hands, the palm sides are higher than the dorsum sides with the exception of the finger locations of the left hand, where they are almost similar.

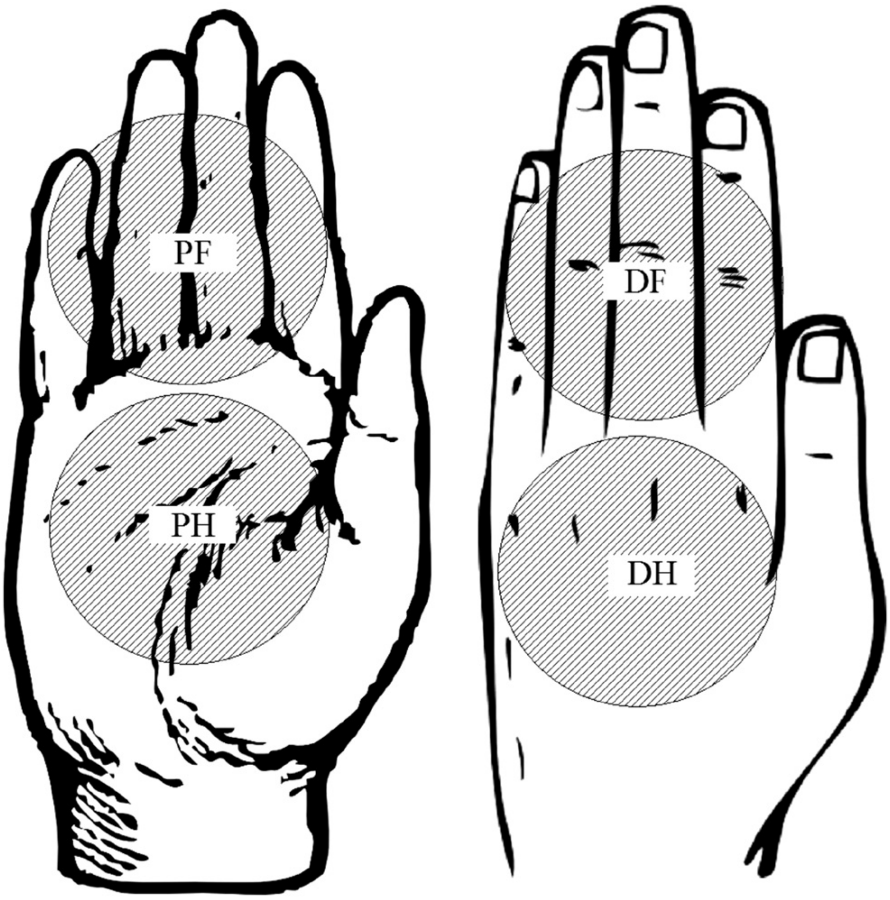

Fig. 1. Illustration of the measurement positions of one hand: Palm side fingers right (PFR); palm hand right (PHR); dorsal side fingers right (DFR); dorsal hand right (DHR); palm side fingers left (PFL); palm hand left (PHL); dorsal side fingers left (DFL); dorsal hand left (DHL).

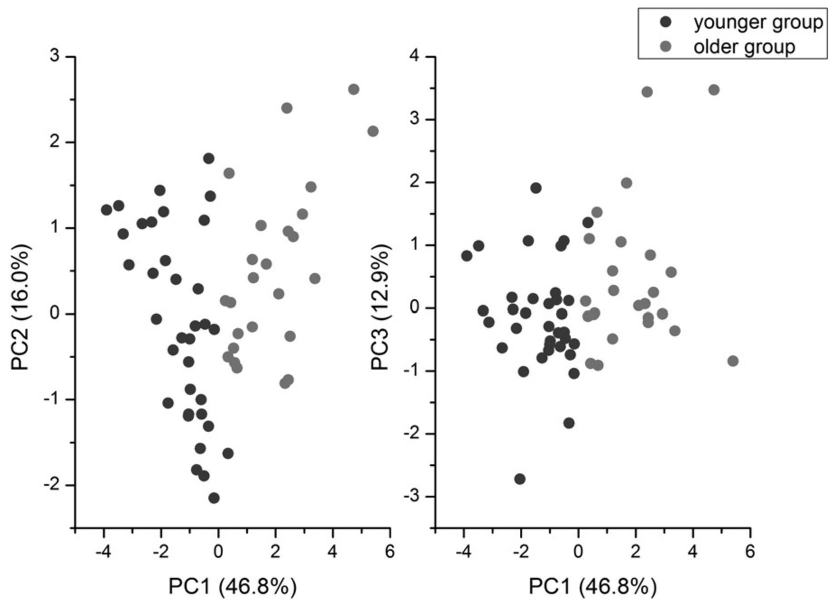

Fig. 2. 60 subjects were clustered utilizing the parameters strength and FF of 4 locations of both hands. Principal component analysis (PCA) was used to separate the subjects. The different color circles indicate the older group (grey) and younger group (dark grey). PCA1, PCA2, and PCA3 represented the top three principle component scores of all subjects which accounted for 46.8%, 16.0%, and 12.9% of whole data variation, respectively.

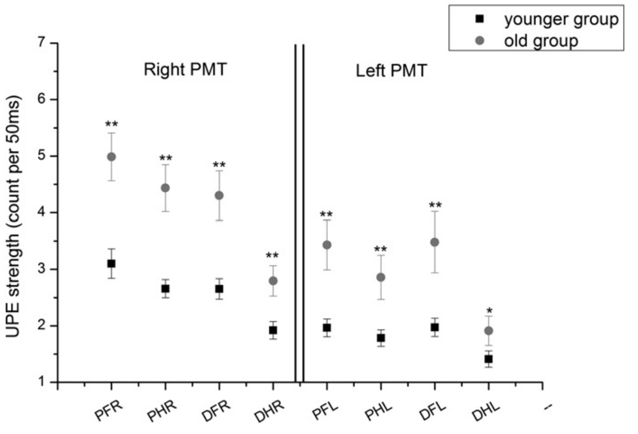

Fig. 3. Difference in ultra-weak photon emission strength between older group (circle) and younger group (square) as measured with the right PMT and left PMT. X-axis indicated different locations with the order: PFR, PHR, DFR, DHR and PFL, PHL, DFL, DHL. For coding, see Fig. 1. UPE strength of 50 ms was shown by Y-axis, *p < 0.05 and **p < 0.01.

When we compared the UPE strength between males and females in each age group, there were no differences (data not shown). However, when we separate the females and males to younger and older subgroups, we observed that the UPE difference between the younger and older groups in case of males is much larger than in the case of the females (Fig. 4). The older female group demonstrated a significant ($p < 0.05$) increase of UPE strength of 54.5% ($p = 1E-2$), 39.1% ($p = 4.9E-2$), 51.6% ($p = 2.2E-2$) respectively of the PFR, DFR and DHR, locations compared to the younger female group. The older male group demonstrated a significant increase of UPE strength of 113.1% ($p = 6.0E-3$), 76.7% ($p = 1.0E-3$), 81.5% ($p = 3.0E-3$), 114.0% ($p = 6.0E-3$), 82.1% ($p = 1.7E-2$), 88.8% ($p = 3.5E-2$), respectively of the PFR, PHR, DFR, PFL, PHL, and DFL locations compared to the younger male group. It seemed that aging causes a larger UPE increase in males than in females.

The distribution of UPE over the individual hands is not fully identical for all subjects. It resulted in the question whether the (left-right) distribution is more identical for symmetric locations as compared to non-symmetric locations. Any symmetry can be calculated because each location of both hands was measured synchronously. The left-right correlations were calculated for the younger and older group separately using the UPE strength values. The outcome of the correlation analysis is presented in Table 1. It is concluded that symmetry at PF is significantly higher in older subjects than in younger ones, whereas for the other locations there is hardly of any difference between the two age groups.

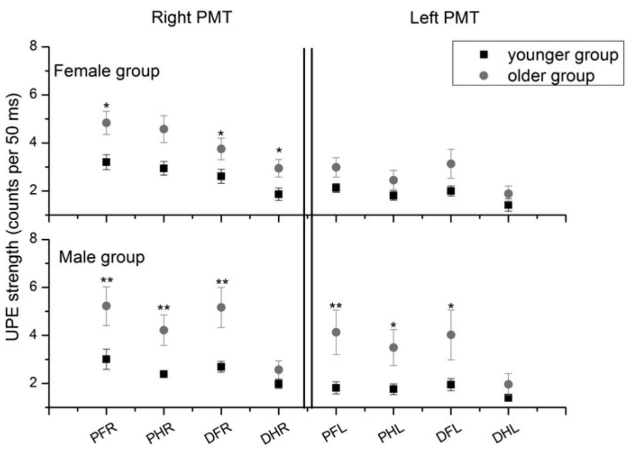

Fig. 4. The different distribution of male and female when compared between younger group (square) and older group (circle). X-axis indicates different hand locations with the order of PFR, PHR, DFR, DHR as well as PFL, PHL, DFL, and DHL. For coding, see Fig. 1. UPE strength of 50 ms was shown in the Y-axis, *p < 0.05 and **p < 0.01.

3.3. Model Construction

We randomly chose 49 subjects in order to construct a model to predict age. Because of the higher signal to noise ratio in the right hand measurements, and the high left-right symmetry in UPE strength, we used the UPE parameters from the right hand to build the prediction model. The data of the remaining 11 subjects were subsequently used for validation of the model.

A Pearson correlation analysis was performed for each UPE parameters of the right hand and chronological age. The correlations to chronological age were shown in Table 2.

A multiple linear regression was done with the eight parameters of the right hand measurements in relationship to chronological age, and used for the construction of the model. Fig. 5 illustrates this model. The UPE parameters of the four measurement locations could clearly differentiate between the younger group (<40 years) and the older group (>40 years). With the Pearson's correlation $r = 0.6$ and the adjusted $R^2 = 0.4$, there were three persons who had an older prediction and four older persons who had a younger prediction ($p = 9.4E-7$), and one person was just on the threshold of 40.

3.4. Model Validation

As a next step, we included the eleven remaining subjects to validate the model. The result demonstrated that only three persons became outliers, two were predicted to be younger and the other one was predicted to be older.

According to this regression model, ten people had the wrong prediction and one person was on the threshold of 40. It was interesting that the average difference between chronological age and the predicted age (based on the model) for all subjects fitting in the correct (lower-left and upper-right squares) was 7.6 ± 0.8 years. The outliers (i.e., subjects in the upper-left and lower-right squares) revealed an average difference of 18.8 ± 1.3 years.

The sexual composition of outliers was also interesting wherein 8 female had the wrong prediction. Only 3 male had the wrong prediction. This difference may be explained by the smaller differences between older and younger female subjects as compared to the difference between older and younger male subjects (Fig. 4).

4. Discussion

China has the largest population in the world. As early as 2001, the people older than 60 years had risen to approximately 5.3% of the total population of China. Ten years later, the percentage increased to 13.3% [30,31]. It becomes important to find a technology to objectively predict aging speed to gain information about a subject biological aging. In this particular research, our purpose was to predict the chronological age by measuring the ultra-weak photon emission from different hand locations. The selection for the hands as measurement locations is based on a measurement protocol development that established the

Table 1
Correlation coefficient for left-right UPE of different hand locations (PF, PH, DF, DH) for all subjects, and for the young and old group separately (all Pearson's r values are significant).

	All subjects	Younger group	Older group
PF	0.7	0.3	0.7
PH	0.7	0.6	0.7
DF	0.8	0.7	0.7
DH	0.8	0.8	0.8

Table 2
The parameters used in model construction and their correlations to chronological age.

Parameters	Correlation to chronological age
Strength of PFR	0.4
Strength of PHR	0.6
Strength of DFR	0.5
Strength of DHR	0.5
FF of PFR	−0.4
FF of PHR	−0.3
FF of DFR	−0.2
FF of DHR	−0.3

conclusion that hands are representative for overall human intensity [12,13,17,18,22]. The complex process of aging includes oxidative stress as one of its characters. Mutations in the mitochondria could lead to defects in energy production and to increased production of ROS by faulty electron transport [32]. A series of findings in various organisms suggested that reduction of oxidative stress is associated with prolongation of life expectancy [33–36]. It is well known that ultra-weak photon emission is correlated with oxidative stress [37,38]. That may be one link between UPE and aging prediction and other mechanisms may still need to be explored.

The results demonstrated a significant relationship between chronological age and ultra-weak photon emission of hands. The correlation analysis (Table 2) illustrates a positive correlation between photon emission strength with chronological age whereas the Fano factor (FF) had a negative correlation with chronological age. Ultra-weak photon emission's strength is the intensity of the photon reflecting the strength of oxidative stress. The FF is the ratio of variance to the mean of the ultra-weak photon emission signals of a subject. The negative correlation between a subject's FF and chronological age indicates a decreasing variance/ mean ratio by increasing chronological age. By using the multiple linear regression model, most subjects could be categorized correctly in the younger or older group suggesting that the ultra-weak photons emitted from human beings can be useful in examining their chronological ages.

The actual differences between the predicted age and the chronological age is of interest for the calculation of biological aging, and thus for objectively predicting the aging speed of individual subjects. Such differences may then be explained by positive or negative life experiences

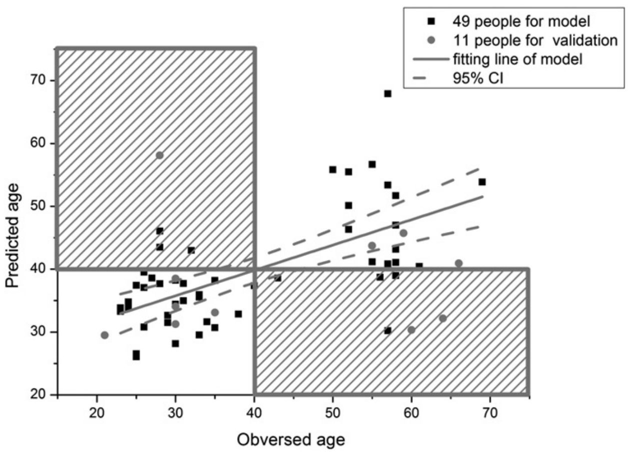

Fig. 5. Illustrates the model which was constructed with 4 different locations of right hand (palm finger, palm, dorsum finger and dorsum), the subjects used for the model construction were marked with square. The subjects used for validation of the model were marked with a circle. The solid line was the fitting line of model. X-axis indicated observed chronological age; predicted age was shown in Y-axis. The graph was divided to 4 areas through the threshold lines of 40 years at X- and Y-axis, where the shadowed areas marked the wrong prediction.

(such as diseases and lifestyle). Already some studies have shown that FF and strength are associated with life style characteristics, such as relaxation [19,21,22]. However, such claim needs further analysis. A further improvement of the method may be expected from our gender data. When we separated the two genders and made comparison of UPE strength between young and old groups of each gender, we found that the difference in UPE was higher in case of males than females. Somehow, the old female group looks "younger" than the old male group according to their UPE strength. This may be related to the gender difference in life duration expectancy. Such plea for exploring the technology vis-à-vis gender specific calibration also needs further study.

To establish whether the difference between predicted and chronological ages points to biological aging and how precisely the non-invasive UPE technology is compared to other tools such as the (invasive) telomere length test and (non-invasive) facial morphology analysis requires a comparative study between these methods in an identical population. In any case the UPE technology is sufficiently promising to be developed for the estimation of biological aging.

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