



Techniques used for determination of Biological Age

Nikita Sharma*
Biomedical Engineering Department
Amity University
Gurugram, Haryana

Sakshi Sethi
Biomedical Engineering Department
Amity University
Gurugram, Haryana

Abstract: The human body has two different ages: a chronological age and a biological age. Chronological age refers to the time a human has been alive, while biological age refers to how old the body seems in terms of functionality. The need to determine biological age viz a viz chronological age is important as it indicates an individual's present as well as future health status. In fact, it plays a very important role in determining people who might be at risk for age related physical and physiological disorders and can also predict disability in later life. There are numerous techniques presently used to determine the biological age and they all are valid in their own way. The purpose of this review is to recapitulate the different techniques used to determine the biological age.

Keywords: Biological Age, Chronological Age, Physical Disorders, Health Status, Age-Related Disorders.

I. INTRODUCTION

The average life span of overall people denotes the life expectancy of the people. Life expectancy has improved in recent years; however, there has been no effect on the main aging process [1]. Aging successfully basically refers to being disease free and avoid any kind of disability, then consistently maintain physical and mental health, engaging socially through lifetime, and latterly they underwent quantitative genetic analysis [2,3].

A. Biological age: definition and estimation

It is a simple question asking for someone's age. In the end, all we want to know is the time that has passed since their birth, i.e. the chronological age. However, it is way more intricate to answer such a simple question. Aging of tissue and varies immensely and depends on the individual, just as the diseases do and all this leads to the difference in which people age from one another [4]. The time period a person has lived i.e. the chronological age, is an inaccurate indicator of prominence of process of aging [5]. Whereas, the biological age is an individual's status of functionality in reference to their chronological peers on the basis of how well the individuals function in regard to the individuals of same chronological age [6]. This basically signifies that for any given age group biological age can be found irrespective of any bias [4]. Henceforth, the differences between the chronological age and biological age is a consequence of the disparity in the rate of process of aging among people [7], consequently, at any given chronological age the value of biological age can vary broadly [8]. One of the great importance of biological age is that it directly relates to the one's active life expectancy, their rest of the healthy life span and their overall health status [6]. Biological age can thus, be of great help in envisaging disability in near future, contributing towards the measurement of relative fitness, aids in recognizing people which are prone to age-related disorders and predicting mortality irrespective of the chronological age [8,9]. Actually, individuals whose physiological functioning is poor are referred to as "biologically older" in comparison to their chronological peers; on the contrary, individuals whose physiological functioning is healthy are considered as "biologically

younger" [4]. Developing a catalog which is a derivative of various number of biological variables known as "Biomarkers of Aging" can signify the theory of biological age and these hold a close relation to the maintenance of life a moreover it is associated to some extent with the chronological age. [11]. As we know, that the aging of tissues and organs happen at a variable rate [5], henceforth, to specify the overall aging of an organism it is important to acquire biomarkers from greater part of systems and compile them broadly [4].

II. LITERATURE REVIEW

A. Use of X-Ray in Age Determination

Evaluation of biological maturity corresponds accurately to the method of skeletal age [12]. Moreover, clinical conditions in children can be evaluated significantly with the help of skeletal maturity. A few of those conditions comprise of inequality between two paired limbs i.e. anisomelia (could be hereditary or acquired), disorder of spine such as scoliosis, and any hormonal condition that might influence maturity [13-18].

As a matter of fact, the ends of each bone are called epiphysis where articulation takes place it includes an ossification center with a supportive growth plate known as physis, which is at ninety degrees to the long axis of the bone [19]. Factors contributing to the growth of diaphysis are: the multiplication of cartilage cells of physis and its transformation due to mineralization leads to the formation of a new bone [19]. The fusion of epiphysis with the rest of bone takes place when skeletal maturity is attained and then the physis or the growth plate disappears [19]. The timing of the fusion of bones and the timing of epiphysial ossification is not concurrent across the body. Actually, some bone's ossification takes place straight away after birth and in some it starts between 14 and 17 years of age [19]. Moreover, variation in the timing of epiphysial fusion and closure of physis is in between 10 to 25 years of age, and female's skeletal maturation is approximately two years prior to boys [20-21].

For determination of skeletal maturity there are three most imperative and commonly used techniques: the Greulich-Pyle, [22] the Tanner-Whitehouse [23,24,25] and

the Fels method;[26] all of which have a common basis of working i.e. the radiographs of the left hand and the wrist.

The Tanner, Whitehouse and Healy (TW1), [23] is a more authentic and accurate radiographic method, which was published in 1962 and subsequently was revised in 1975 and 1983 as TW2 [24] and in 2001 it was once again modified as TW3 [25]. In this method, the relative maturity scores are given to the radius, ulna, carpal bones and phalanges and the resultant combined score is used to determine the skeletal age [19].

B. 3D-Facial Imaging

For intricate diseases, aging is a major risk factor [27]. The importance of accurately estimating the biological age are: evaluating the level of aging process and its reversal quantitatively [28,29], evaluating the possibility of developing age-related diseases and design a type of treatment which can be individualized [30]. Despite of the meticulous research that has been done till this date, there are no consistent or unambiguous aging marker to specifically assess an individual’s biological age [30]. On the other hand, the latest development of the 3D (three-dimensional) imaging technology, for example the extensively used camera system i.e. the stereo photogrammetric camera system or the 3dMDface System,

and the technique used to reform the 3D images using a single-pixel detectors [31]. Moreover, the 3D facial data is being used in various fields these days, like in the diagnosis of diseases (such as age-related disorders) and comparison between the ethnic population of facial morphology [32-34].

III. METHODOLOGY

A. Tanner and Whitehouse (TW2) Method:

The TW method is not an age based method, instead it depends on the maturation level of 20 selected Regions of Interest (ROI) in particular bones of hand and wrist in each age population [35]. Each ROI’s development level is classified into definite stages which are labeled as (A, B, C...I). Each stage of development for each bone is assigned a numerical score separately and the total maturity score can be calculated by adding all the scores from the ROI’s. Then correlating this score with the bone age discretely for males and females [35]. Although the Tanner and Whitehouse method is somewhat complex and needs more time; when compared to the GP method the TW method seems more reliable and reproducible [36].

Bone	Scores L			Scores M		
	Stage			Stage		
	A	B	C	A	B	C
R	0	10	20	0	8	16
U	0	10	25	5	12	26
M	0	12	17	0	9	14

Bone	Scores		
	Observed Stage	System L	System M
	R	B	10
U	A	0	5
M	C	17	14
Mean :		9	9
Sum of squares of deviations :		146	42

(R = Radius; U = Ulna; M = Metacarpal)

Data: The Assessment of Skeletal Maturity and Prediction of Adult Height, 2nd Ed. 1984
J.M. Tanner, R.H. Whitehouse, N. Cameron, W.A. Marshall, M.J.R. Healy and H. Goldstein Academic Press, London

Figure 1. Two different systems for scoring bone maturity [41].

B. 3-D Facial Imaging

Less than 300 subjects of broad age group ranging from 17 to 77 years old was taken, and then their 3D human facial images and blood profiles were collected to reveal the

features of face which directly corresponds to the chronological and age and overall health, further they generated the first comprehensive map of aging human facial phenome by enumerating detailed aging-related facial phenotypes from the data of images [37]. For different

individuals, the comparison of 2D facial images was done by, Turaga et al. [38], which basically gave a description of face shapes and their relative differences with the help of geometric and landmark relationships. Since the 3D facial data acquired basically are in the form of spatial coordinates, with the help of formerly developed 3D facial image registration tool all the facial images can be aligned together [39,40]. Afterwards, each vertex is taken as a scaled milestone for the comparison of facial morphological or geometric changes throughout the process of aging, where any kind of alteration between different images is already relative to position changes [37]. Moreover, the enumeration of ten intuitive facial features was done on the basis of 17 salient landmarks to present a subset of the most apparent facial indexes among less than thirty thousand vertices that were observed [37]. Now, to extract the facial changes that became prevalent due to aging all vertices' values are aligned and transformed and then the information for all 3D geometric vertices is used [37].

IV. OBSERVATION

A. Tanner and Whitehouse Test:

The relationship between the genetic and environmental influences directly corresponds to the rate of skeletal maturation. Henceforth, it is probable that in the population there will be differences between both in the mean of skeletal maturity at a specified age and in the pattern of growth from one age to next. For that reason, it is enviable to develop definite standards for each pertinent population. There is no problem when it comes to the TW II scoring system, in which, the maturity score of a source sample can be allied to the age of the same [41]. On the other hand, when it comes to bone age technique, the maturity score is measured against the original source, which is a setback [41]. The radiographs from normal children can be acquired and utilized to represent the bone maturity scores. The bone scoring technique (i.e. TW II) is independent to that of the existing maturity standards. This is one of the foremost advantages of TW II technique [41].

B. 3-D facial imaging:

This study's results revealed a consistent and suitable aging marker. On the whole, the state of aging can be evaluated correctly by making use of a non – invasive procedure on the face which is much more accurate than the routine physical examinations. We know that individuals of same chronological age have different physiological ages and at regular level it can differ by ± 6 years [37]. One great importance of the 3D facial image base predictor of the physiological age is that it will evaluate the degree of aging process and its reversal quantitatively, and in order to design treatments for individual's assessment of risks of age related diseases is important [37].

V. DISCUSSION

Presently, there are various methods being used to determine an individual's biological age. The traditional method of Physical Examination has been replaced with more refined and accurate techniques to determine the biological age.

Nominal time requirement and establishment of adequate reproducibility are the prominent attributes of the

methods based on radiographs of hand and wrist in the assessment of the biological age [19]. The necessity to use the ionizing radiation is one of the disadvantages. Although, the dose of ionizing radiation with a left-hand radiograph is approximately negligible, numerous ethical committees of different countries do not approve the usage of x-ray for the sole purpose of age determination in hale and hearty adolescents and children [19]. For assessment of biological maturity, the skeletal age is taken as a reliable method, even though it is incapable in resolving an accurate chronological age and has limitations in the evaluation of skeletal age by x-ray scanning. It has been examined that there is disparity of several years in bone age of adolescents with same chronological age [19].

Numerous features of face, like the slope of the eye and the distance between the nose and the mouth, associate radically with aging [37]. Lastly, even though, the features of facial morphology correlate extensively with health indicators found in the blood, the blood profiles are found to be less reliable aging biomarkers than the facial features and, therefore reveals an enhanced overall health status than the chronological age.

VI. REFERENCES

- [1]. Shephard R. Constitution or Environment? In: Shephard R, ed. *Gender, Physical Activity, and Aging* Boca Raton (FL): CRC Press; 2002:151–174.
- [2]. Scott W, Gaskell P, Jackson C, Haines JL, Pericak-Vance MA. Combinatorial mismatch scan for successful aging loci in the Amish. *Am J Hum Genet* 2003; 73:124.
- [3]. Reed T, Dick DM, Uniacke SK, Foroud T, Nichols WC. Genome-wide scan for a healthy aging phenotype provides support for a locus near D4S1564 promoting healthy aging. *J Gerontol A BiolSci Med Sci* 2004;59: B227–B232.
- [4]. David Karasik, SerkalemDemissie, L. Adrienne Cupples, and Douglas P. Kiel, "Disentangling the Genetic Determinants of Human Aging: Biological Age as an Alternative to the Use of Survival Measures", *J Gerontol A BiolSci Med Sci.* 60(5): 574–587, 2005 .
- [5]. Finkel D, Whitfield K, McGue M. Genetic and environmental influences on functional age: a twin study. *J Gerontol B PsycholSciSocSci* 1995;50: P104–P113. [PubMed: 7757832]
- [6]. Borkan GA, Norris AH, "Assessment of biological age using a profile of physical parameters", *JGerontol* 1980;35:177–184. [PubMed: 6967883]
- [7]. Anstey K, Lord S, Smith G, "Measuring human functional age: A review of empirical findings", *Exp Aging Res*, 1996;22:245–266. [PubMed: 8872080]
- [8]. Mitnitski AB, Graham JE, Mogilner AJ, Rockwood K., "Frailty, fitness and late-life mortality in relation to chronological and biological age. *BMC Geriatr* 2002; 2:1. [PubMed: 11897015]
- [9]. Uttley M, Crawford M, "Efficacy of a composite biological age score to predict ten-year survival among Kansas and Nebraska Mennonites", *Hum Biol*,1994;66:121–144. [PubMed: 8157261]
- [10]. Seeman E, Hopper J., "Genetic and environmental components of the population variance in bone density", *OsteoporosInt*, 1997;7(Suppl 3):S10–S16. [PubMed: 9536296]
- [11]. Dean W, Morgan RF, "In defense of the concept of biological aging measurement—current status", *Arch GerontolGeriatr*, 1988;7:191–210. [PubMed: 3052338]

- [12]. Malina RM, Chamorro M, Serratos L, et al., "TW3 and Fels skeletal ages in elite youth soccer players", *Ann Hum Biol* 2007;34:265–72.
- [13]. Wang WW, Xia CW, Zhu F, et al. Correlation of Risser sign, radiographs of hand and wrist with the histological grade of iliac crest apophysis in girls with adolescent idiopathic scoliosis. *Spine* 2009; 34:1849–54.
- [14]. Inan M, Chan G, Littleton AG, et al. Efficacy and safety of percutaneous epiphysiodesis. *J Pediatr Orthop* 2008; 28:648–51.
- [15]. Friend L, Widmann RF. Advances in management of limb length discrepancy and lower limb deformity. *Curr Opin Pediatr* 2008; 20:46–51.
- [16]. Sanders JO, Browne RH, Cooney TE, et al. Correlates of the peak height velocity in girls with idiopathic scoliosis. *Spine* 2006; 31:2289–95.
- [17]. Steen H, Terjesen T, Bjerkreim I. Anisomelia. Clinical consequences and treatment. *Tidsskr Nor Laegeforen* 1997; 117:1595–600.
- [18]. Skogland LB, Miller JAA. Growth related hormones in idiopathic scoliosis: an endocrine basis for accelerated growth. *Acta Orthopaedica* 1980; 51:779–80.
- [19]. Lars Engebretsen, Kathrin Steffen, Roald Bahr, Carolyn Broderick, Jiri Dvorak, Per-Mats Janarv, Amanda Johnson, Michel Leglise, Tallal Charles Mamisch, Damien McKay, Lyle Micheli, Patrick Schamasch, Gurcharan Dato Singh, Diane E J Stafford, Harald Steen, "The International Olympic Committee Consensus Statement on age determination in high-level young athletes", *Br J Sports Med*, 44:476–484, 2010
- [20]. Malina RM, Eisenmann JC, Cumming SP, et al. Maturity-associated variation in the growth and functional capacities of youth football (soccer) players 13–15 years. *Eur J Appl Physiol* 2004; 91:555–62.
- [21]. Diméglio A. Growth in pediatric orthopaedics. *J Pediatr Orthop* 2001; 21:549–55.
- [22]. Greulich WW, Pyle SI. Radiograph atlas of skeletal development of the hand and wrist, 2nd edn. Stanford, California, USA: Stanford University Press, 1959.
- [23]. Tanner JM, Whitehouse RH. Growth at adolescence. 2nd edn. Springfield, Illinois, USA: Blackwell Scientific Publications, 1962.
- [24]. Tanner JM, Whitehouse RH, Cameron N, et al. Assessment of skeletal maturity and prediction of adult height (TW2 method), 2nd edn. London: Academic Press, 1983.
- [25]. Tanner JM, Whitehouse RH, Cameron N, et al. Assessment of skeletal maturity and prediction of adult height (TW3 method), 3rd edn. London: Saunders, 2001.
- [26]. Roche AF, Chumlea WC, Thissen D, et al. Assessing the skeletal maturity of the hand–wrist: Fels method. Springfield, Illinois, USA: Charles T Thomas, 1988.
- [27]. Lopez-Otin C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. *Cell* 2013; 153:1194-1217.
- [28]. Han JD. An aging program at the systems level? *Birth Defects Res C Embryo Today* 2012; 96:206-211.
- [29]. Rando TA, Chang HY. Aging, rejuvenation, and epigenetic reprogramming: resetting the aging clock. *Cell* 2012; 148:4657.
- [30]. Pallis AG, Hatse S, Brouwers B, et al. Evaluating the physiological reserves of older patients with cancer: the value of potential biomarkers of aging? *J Geriatr Oncol* 2014; 5:204-218.
- [31]. Sun B, Edgar MP, Bowman R, et al. 3D computational imaging with single-pixel detectors. *Science* 2013; 340:844-847.
- [32]. Wirthlin J, Kau CH, English JD, Pan F, Zhou H. Comparison of facial morphologies between adult Chinese and Houstonian Caucasian populations using three-dimensional imaging. *Int J Oral Maxillofac Surg* 2013; 42:1100-1107.
- [33]. Kasperaviciute D, Catarino CB, Chinthapalli K, et al. Uncovering genomic causes of co-morbidity in epilepsy: gene-driven phenotypic characterization of rare microdeletions. *PLoS One* 2011; 6: e23182.
- [34]. Cox-Brinkman J, Vedder A, Hollak C, et al. Three-dimensional face shape in Fabry disease. *Eur J Hum Genet* 2007; 15:535-542.
- [35]. Mughal AM, Hassan N, Ahmed A. Bone age assessment methods: A critical review. *Pak J Med Sci* 2014;30(1):211-215.
- [36]. Khan K, Elayappen AS. Bone Growth Estimation Using Radiology (Greulich–Pyle and Tanner–Whitehouse Methods). In: Preedy VR, editor. *Handbook of Growth and Growth Monitoring in Health and Disease* [Internet]. Springer New York; 2012 [cited 2013 Jul 13]. p. 2937–53. Available from: http://link.springer.com/chapter/10.1007/978-1-4419-1795-9_176
- [37]. Weiyang Chen, Wei Qian, Gang Wu, Weizhong Chen, Bo Xian, Xingwei Chen, Yaqiang Cao, Christopher D Green, Fanghong Zhao, Kun Tang, Jing-Dong J Han, "Three-dimensional human facial morphologies as robust aging markers", *Cell Research* (2015) 25:574-587.
- [38]. Turaga P, Biswas S, Chellappa R. The role of geometry in age estimation. *IEEE International Conference on Acoustics Speech and Signal Processing (ICASSP)* 2010:946-949.
- [39]. Guo J, Mei X, Tang K. Automatic landmark annotation and dense correspondence registration for 3D human facial images. *BMC Bioinformatics* 2013; 14:232.
- [40]. Peng S, Tan J, Hu S, et al. Detecting genetic association of common human facial morphological variation using high density 3D image registration. *PLoS Comput Biol* 2013;9: e1003375.
- [41]. Noel Cameron, "The Tanner-Whitehouse II Skeletal Maturity Method: Rationale and Applicability", *Clin Pediatr Endocrinol*, 2(Suppl 1):9-18, 1993.