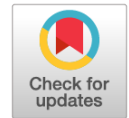


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Determination of Bone Age Based on Hand Radiography: From Classical Methods to Artificial Intelligence (A Review)

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ABSTRACT

Bone age assessment methods are crucial in diagnosing diseases associated with growth and developmental disorders, especially in pediatric practice. These methods have advantages and limitations, and their accuracy may vary depending on population-specific characteristics.

This article outlines the current state and potential of bone age assessment methods, including solutions based on artificial intelligence technologies.

Scientific data on bone age assessment over the past 10 years were explored using PubMed and eLibrary. Earlier publications that serve as reference points in the development of bone age assessment methodology—such as atlases, guidelines, and relevant studies—were included. Publications addressing the prevalence and practical use of various bone age assessment techniques, including radiography, ultrasound, computed tomography, magnetic resonance imaging, and artificial intelligence, were prioritized. The search was performed using the following keywords: bone age, bone age assessment, radiography, artificial intelligence, deep learning, growth development, AI, костный возраст (bone age), рентгенография (radiography), and искусственный интеллект (artificial intelligence).

This review demonstrates the wide range of existing bone age assessment methods and emphasizes the importance of new technologies such as artificial intelligence in improving diagnostic accuracy. Modern automated techniques show potential for optimizing diagnostic workflows in pediatric care and contribute to the early detection of growth and developmental disorders.

Keywords: bone age; artificial intelligence; hand radiography; review.

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Определение костного возраста по данным рентгенографии кисти: от классических методик к искусственному интеллекту (научный обзор)

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АННОТАЦИЯ

Методики оценки костного возраста играют ключевую роль в диагностике заболеваний, связанных с нарушениями роста и развития, особенно в педиатрической практике. Они имеют как преимущества, так и ограничения, а их точность может варьировать в зависимости от популяционных особенностей.

В статье описано текущее состояние и обозначены перспективы развития методик оценки костного возраста, включая решения с использованием технологий искусственного интеллекта.

Поиск релевантной литературы за последние 10 лет по теме оценки костного возраста выполняли с использованием поисковых систем PubMed и eLibrary. Кроме того, включены более ранние работы, представляющие важные ориентиры в развитии методологии оценки костного возраста, включая атласы, руководства и соответствующие исследования. Основное внимание уделяли публикациям, рассматривающим распространённость и практическое применение различных методов оценки костного возраста, включая рентгенографию, ультразвуковое исследование, компьютерную и магнитно-резонансную томографию, а также технологии искусственного интеллекта. Поиск осуществляли с использованием ключевых слов: «bone age», «bone age assessment», «radiography», «artificial intelligence», «deep learning», «growth development», «AI», «костный возраст», «рентгенография», «искусственный интеллект».

Представленный обзор демонстрирует широкий спектр методик оценки костного возраста и подчёркивает значимость новых технологий, таких как искусственный интеллект, для повышения точности диагностики. Современные автоматизированные методы показывают высокий потенциал для совершенствования диагностического процесса в педиатрической практике и могут способствовать раннему выявлению патологий, связанных с нарушениями роста и развития.

Ключевые слова: костный возраст; искусственный интеллект; рентгенография кисти; обзор.

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基于手部X线片的骨龄评估：从经典方法到人工智能 (文献综述)

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摘要

骨龄评估方法在诊断与生长发育障碍相关疾病中发挥关键作用，特别是在儿科实践中尤为重要。尽管这些方法各有优缺点，其准确性可能因人群特征而异。

本文介绍了骨龄评估方法的现状，并探讨其未来发展方向，包括基于人工智能技术的解决方案。

过去10年关于骨龄评估主题的相关文献是通过PubMed和eLibrary检索系统获取的。此外，也纳入了部分较早发表的文献，这些文献在骨龄评估方法的发展中具有重要参考价值，包括骨龄图谱、指南和相关研究。重点关注的是探讨骨龄评估方法的普及程度及其实际应用的相关文献，所涵盖的方法包括X线检查、超声检查、计算机断层扫描、磁共振成像以及人工智能技术。检索关键词包括：“bone age”（骨龄）、“bone age assessment”（骨龄评估）、“radiography”（X线检查）、“artificial intelligence”（人工智能）、“deep learning”（深度学习）、“growth development”（生长发育）、“AI”（人工智能）、“костный возраст”（骨龄）、“рентгенография”（X线检查）、“искусственный интеллект”（人工智能）。

本综述显示，骨龄评估方法种类繁多，人工智能等新兴技术在提高诊断准确性方面具有重要意义。现代自动化方法在儿科诊断流程优化方面展现出巨大潜力，有望促进生长发育障碍相关疾病的早期发现。

关键词：骨龄；人工智能；手部X线片；综述。

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INTRODUCTION

Skeletal age, or bone age, is the most widely used indicator of biological maturity in growing individuals and is determined by analyzing the sequential stages of skeletal development [1]. The order and timing of the appearance of ossification centers and epiphyseal fusion in different

parts of the skeleton objectively reflect a child's growth and developmental processes. Bone age may differ from chronological age by 1–2 years; however, a discrepancy greater than 2 years is considered pathological [2].

Alongside bone age and chronological age, the concept of biological age exists, representing a combination of anthropometric, clinical–laboratory, psychological,

Table 1. Factors influencing bone age

Delayed bone age relative to chronological age	Advanced bone age relative to chronological age	Bone age corresponding to chronological age
<i>Endocrine causes</i>		
<ul style="list-style-type: none"> constitutional growth delay hypothyroidism hypopituitarism panhypopituitarism hypogonadism Cushing syndrome diabetes mellitus, Mauriac syndrome (long-term poor glycemic control) 	<p>Central precocious puberty, GnRH-dependent:</p> <ul style="list-style-type: none"> idiopathic tumors and other central nervous system lesions following late treatment of congenital virilizing adrenal hyperplasia or prolonged exposure to sex steroid hormones functional mutations of KISS1 and KISS1R/GPR54 <p>Peripheral precocious puberty, GnRH-independent:</p> <ul style="list-style-type: none"> premature adrenarche ovarian tumors, Leydig cell tumors, testicular tumors, germ cell tumors, etc. <p>Hyperthyroidism</p>	<ul style="list-style-type: none"> familial short stature
<i>Non-endocrine causes / chronic diseases / skeletal dysplasias</i>		
<ul style="list-style-type: none"> cardiovascular diseases (congenital heart disease) rickets chronic kidney disease juvenile idiopathic arthritis inflammatory bowel disease celiac disease cystic fibrosis severe bronchial asthma (inhaled glucocorticoids) immunodeficiencies, incl. HIV/AIDS active tuberculosis female athlete triad leading to hypogonadism anorexia nervosa 	<ul style="list-style-type: none"> constitutional tall stature 	<ul style="list-style-type: none"> achondroplasia hypochondroplasia pseudoachondroplasia, etc.
<i>Chromosomal abnormalities / genetic syndromes</i>		
<ul style="list-style-type: none"> Klinefelter syndrome Laron syndrome Seckel syndrome Patau syndrome (trisomy 13) Edwards syndrome (trisomy 18) Down syndrome (trisomy 21) Rubinstein–Taybi syndrome 	<ul style="list-style-type: none"> familial testotoxicosis (an autosomal dominant, gonadotropin-independent form of precocious puberty caused by constitutive activation of Leydig and germ cells) McCune–Albright syndrome Marshall–Smith syndrome Sotos syndrome Beckwith–Wiedemann syndrome Marfan syndrome Pyle disease 	<ul style="list-style-type: none"> Noonan syndrome Russell–Silver syndrome Turner syndrome
<i>Medications</i>		
<ul style="list-style-type: none"> glucocorticoids (prednisolone or hydrocortisone, 3–5 or 12–15 mg/m², respectively); amphetamine, dextroamphetamine (moderate effect) GnRH analogs aromatase inhibitors 	<ul style="list-style-type: none"> estrogens oral contraceptives testosterone preparations lavender oil (estrogen-like effect) tea tree oil (estrogen-like effect) 	—
<i>Nutritional disorders</i>		
<ul style="list-style-type: none"> malnutrition weight deficit due to chronic illness poor bone mineralization 	<ul style="list-style-type: none"> exogenous constitutional obesity 	—

Note. GnRH, gonadotropin-releasing hormone; 1, delayed appearance of ossification centers in the hand at an early age, followed by accelerated differentiation at 8–9 years and concordance of bone and chronological age by 10–12 years [57]; 2, bone age lags chronological age during the first three years of life, matches chronological age up to 10 years, and after 10–12 years bone age again falls behind chronological age (by no more than 1–2 years) [2].

and emotional characteristics of a child. Nevertheless, radiographically determined bone age remains the most reliable indicator of biological maturation and the most accurate reflection of somatic growth [3].

Bone age assessment plays an important role across multiple fields of medicine:

- Endocrinology, for diagnosing pathological conditions (Table 1) [4–10] and for therapy monitoring [11]
- Traumatology and orthopedic surgery to guide treatment planning [12, 13]
- Forensic medicine, for patient identification [14]
- Sports medicine, to individualize physical training and reduce injury risk [15–17].
- Chronological age can be determined based on various characteristics identified through diagnostic radiology methods. In adults, the following indicators are commonly used:
 - The degree of aortic calcification [18, 19]
 - Skeletal deformities
 - The condition of bone tissue [20]
 - Other changes characteristic of the aging process [21–23].

Although radiologic methods are valuable for estimating chronological age in adults, they are of greatest diagnostic importance in pediatric practice, where age-related changes are more pronounced and dynamically reflect a child's growth and development [24]. For this reason, we focus on the key techniques for determining bone age in children.

This review analyzes contemporary bone age assessment methods, identifies their advantages and limitations, and evaluates the potential of artificial intelligence technologies to enhance diagnostic accuracy.

DATA SEARCH METHODOLOGY

A search for relevant scientific data on bone age assessment was performed using the PubMed and eLibrary databases. Primary attention was given to key studies published over the past decade. The search was performed using the following keywords: *bone age*, *bone age assessment*, *radiography*, *artificial intelligence*, *deep learning*, *growth development*, *AI*, *костный возраст (bone age)*, *рентгенография (radiography)*, *искусственный интеллект (artificial intelligence)*. Analysis of the retrieved publications identified 156 articles, of which 96 were ultimately included in the review. A total of 60 publications were excluded for the following reasons:

- Irrelevance to the topic, 23
- Duplicate data, 17
- Failure to meet methodological criteria, 3
- Lack of access to a full text, 17.

In addition, to cite foundational sources, 28 earlier works were included, as they provide important reference points for the development of bone age assessment methodology, including atlases, guidelines, and relevant studies.

METHODS FOR BONE AGE ASSESSMENT

Modern approaches to bone age assessment are based on the analysis of data obtained using various radiologic diagnostic modalities, including radiography [25–30], ultrasound imaging [6, 31, 32], computed tomography [33, 34], and magnetic resonance imaging [35–37] (Table 2). It is important to highlight the key advantages and limitations of each of these methods. Radiography is a widely accessible and relatively inexpensive imaging technique that provides high spatial resolution for evaluating small osseous structures. However, its use is associated with ionizing radiation and is limited to two-dimensional imaging, which reduces diagnostic value when assessing complex anatomical regions [26]. Standard hand radiography is the most well-validated method and is regarded as the gold standard in this field [6]. Nevertheless, techniques based on hand radiography have their own characteristics and advantages that influence method selection in clinical practice (Table 3) [38–41].

Among the general limitations of other imaging modalities besides radiography are the small number of studies using these techniques, as well as the lack of well-defined methodology and standardized protocols.

Computed tomography provides three-dimensional visualization of osseous structures with high spatial resolution; however, its use is limited by high cost and restricted availability of equipment [33, 34]. Magnetic resonance imaging does not involve ionizing radiation and offers high-quality visualization of bone marrow and soft tissues. Nonetheless, its application is constrained by high cost, long acquisition times, and insufficient diagnostic value when imaging small bones [35–37]. Ultrasound imaging does not expose patients to ionizing radiation and is widely accessible and relatively inexpensive. However, visualization of bone structures is challenging, particularly when they are located deep, and depends substantially on operator expertise [31, 32]. In addition, no review articles have compared bone age assessment techniques across different imaging modalities.

The developmental characteristics of the pediatric skeleton include the appearance of ossification centers and the closure of growth plates, which must be taken into account when interpreting radiologic findings. There are also reference guides that consider age-related and anatomical variability of different skeletal regions, such as Korolyuk's Radiologic Atlas of the Skeleton (Normal Anatomy, Variants, Interpretation Pitfalls) [42]. Nevertheless, the most convenient and accurate method for determining bone age remains the analysis of hand radiographs in the posteroanterior view.

HAND RADIOGRAPHY-BASED METHODS FOR BONE AGE ASSESSMENT

Bone age determination using hand radiography is an important tool in pediatric practice for evaluating

Table 2. Bone age assessment methods

Method	Assessed structures	Measurement approach / principle	References
<i>Radiography</i>			
Greulich–Pyle method		Comparison with atlas reference	[38]
Tanner–Whitehouse method		Scoring system/assessment method	[49]
Zhukovsky–Bukhman tables		Tabulated ossification timing	[39]
FELS method		Scoring system/assessment method	[25]
Gilsanz–Ratib atlas	Carpal bones, radius and ulna	Comparison with atlas reference	[1, 26]
Korean Child Standard method		Scoring system/assessment method	[28]
China 05 RUS–CHN method		Scoring system/assessment method	[27]
Ebri method		Ebri–carpal, –metacarpophalangeal, and –carpometa­carpophalangeal bone age	[51]
Odontogenesis-based methods	Panoramic dental radiograph	Scoring system/assessment method	[29]
Cervical vertebral maturation method	Cervical spine	Degree of cervical vertebral ossification	[30]
<i>Computed tomography</i>			
Postmortem computed tomography evaluation	Anterior and posterior intraoccipital synchondroses; first cervical vertebra (atlas)	Ossification stages	[34]
Assessment of medial clavicular epiphysis	Medial clavicle	Ossification stages	[33]
<i>Ultrasound Imaging</i>			
Method for assessing anterior femoral head cartilage thickness	Reduced femoral head cartilage integrity	Evaluation method / measurement in mm	[31]
Bone age assessment using the Risser staging system	Iliac apophysis (Risser sign) and distal radial epiphysis	Risser stage assignment (0–V) and assessment of radial growth plates	[6]
Alekseeva–Kinzersky method	Carpal bones, radius and ulna	Degree of ossification of bone ossification centers	[32]
<i>Magnetic Resonance Imaging</i>			
Assessment of images obtained with an open compact MRI scanner		Scoring system/assessment method	[17, 35]
Magnetic Resonance Imaging–based ossification assessment	Carpal bones, radius and ulna	Ossification phases	[36]
Bone age estimation using MRI with the Greulich–Pyle atlas		Scoring system/assessment method	[37]

Note. FELS (Fels Longitudinal Study), a longitudinal study collecting growth, developmental, and physiologic data from early childhood to adulthood; carpal, relating to the wrist; metacarpophalangeal, relating to metacarpal and phalangeal bones; carpometacarpophalangeal, relating to the carpal, metacarpal, and phalangeal bones.

a child's physical development and for timely detection of abnormalities. A discrepancy between bone age and chronological age may indicate [43]:

- growth disorders
- endocrine abnormalities
- genetic syndromes
- and other pathological conditions.

In Russia, radiography of both hands is traditionally performed [39], whereas in many other countries only the left hand is imaged [40]. Russian specialists justify the need for bilateral imaging by the potential asymmetry in the appearance of ossification centers, whereas

Western practitioners generally do not consider this factor diagnostically significant.

For hand radiography, the patient's hand is positioned palmar side down on the horizontal surface of the detector. Before imaging, any jewelry or clothing items on the patient's hands that may cause artifacts must be removed. The radiograph should clearly visualize all fingers, the carpus, and the distal forearm. Radiographic density must allow adequate visualization of trabecular structure and soft tissues of the hand [44]. When evaluating the radiograph, the structure, density, diameter, and curvature of the bones should be assessed to rule out upper-limb skeletal dysplasias [45].

Table 3. Comparison of bone age assessment methods based on hand radiography

Zhukovsky–Bukhman tables	Greulich–Pyle atlas	Tanner–Whitehouse method
<i>Principles of bone age determination</i>		
<ul style="list-style-type: none"> uses tables containing standard age-specific values for various skeletal parameters; radiographs of the child's hands are compared with the reference values in the table 	<ul style="list-style-type: none"> uses an atlas consisting of a series of hand radiographs corresponding to different ages; the child's radiograph is visually compared with the atlas images that most closely match the development 	<ul style="list-style-type: none"> provides quantitative scoring of individual bones in the hand and wrist based on 20 parameters; each parameter is scored; the total score is then converted to bone age using a dedicated scale
<i>Advantages</i>		
<ul style="list-style-type: none"> widely used in Russia; adapted for the Russian population 	<ul style="list-style-type: none"> widely used worldwide; easy to learn; minimal time required 	<ul style="list-style-type: none"> latest version, Tanner–Whitehouse 3, RUS modification, introduced in 2001 higher reproducibility compared with other methods
<i>Limitations</i>		
<ul style="list-style-type: none"> subjectivity of assessment; poor validation against modern standards; introduced in 1980 	<ul style="list-style-type: none"> subjectivity of assessment; accuracy varies depending on the child's ethnicity; introduced in 1959 	<ul style="list-style-type: none"> more time-consuming; requires more complex expert training

In the Russian Federation, the most widely used method for bone age assessment is the approach developed by Zhukovsky and Bukhman in 1987. This method involves the use of a corresponding reference table [39]. The Greulich–Pyle atlas method, which is based on comparing a patient's radiograph with standard reference images from a dedicated atlas, as proposed by American researchers [38], is widely used by pediatricians worldwide (more than 76%) [40]. In pediatric endocrinology, specialists more commonly apply the Tanner–Whitehouse 2 (TW2) method [43].

However, these classical techniques are based on data collected more than 50 years ago, raising concerns regarding their relevance for contemporary populations. Changes in growth patterns and physical development in children, driven by shifts in living conditions, nutrition, and healthcare quality, may lead to discrepancies between a child's bone age and chronological age [46, 47].

Tanner–Whitehouse 3 Method: The RUS Modification

Another technique is the updated version of the Tanner–Whitehouse 3 (TW3) method, in which the radius, ulna, and short bones of the hand are evaluated (TW3–RUS). This version was introduced in 2001 [48]. The original Tanner–Whitehouse method was developed by British researchers Tanner and Whitehouse in 1962 [49]. In the current Tanner–Whitehouse 3 version, additional imaging regions are considered to provide a more detailed assessment of ossification stages across different segments of the hand. The results are expressed as scores rather than through direct comparison with reference radiographs, as in the Greulich–Pyle atlas. This method is widely used in pediatric endocrinology because it allows for more accurate prediction of a child's final height [43].

Gilsanz–Ratib Method

In 2005, Swiss researchers Gilsanz and Ratib introduced a new digital atlas designed for bone age assessment [1]. Unlike earlier atlases based on radiographic images, this atlas contains standardized computer-generated images of the hand, differentiated by the child's age and sex. These images were derived through analysis of the size, shape, morphology, and ossification density from 522 hand radiographs of healthy children from Los Angeles, USA (equal numbers of girls and boys) [1, 17]. A major advantage of the Gilsanz–Ratib atlas is its substantially higher image quality compared with the classical Greulich–Pyle atlas. Its key distinguishing feature is the use of averaged images generated from multiple radiographs corresponding to the same bone age [1].

ETHNICITY AND SECULAR TRENDS IN CHILDREN'S PHYSICAL DEVELOPMENT: IMPACT FOR BONE AGE ASSESSMENT

Modern techniques such as the Gilsanz–Ratib atlas and the Tanner–Whitehouse 3 method in its RUS modification, which rely on detailed quantitative analysis and up-to-date reference data, have the potential to provide more accurate bone age assessment compared with earlier approaches. However, further studies are needed to confirm their diagnostic value across different populations.

In 2018, Dahlberg et al. [50] published a systematic review analyzing numerous studies on the accuracy of the Greulich–Pyle method. The authors found that in several meta-analyses, the mean discrepancy between bone age determined using the Greulich–Pyle atlas and chronological age generally did not exceed one year regardless of age group or sex. However, inter-study heterogeneity, reflecting the variability of results

across different samples of children, was substantial. This indicates that although the Greulich–Pyle method provides acceptable accuracy at the group level, there is variation in concordance between bone age and chronological age between populations. It was concluded that despite good correlation between bone age and chronological age in contemporary populations in general, the classical

Greulich–Pyle method may lead to notable discrepancies in certain groups of children.

Findings from numerous studies show that existing bone age assessment methods, including the Greulich–Pyle technique, demonstrate varying levels of accuracy depending on ethnic background (Table 4): in some cases, bone age advances relative to chronological age [51–56]; in others, it lags [47, 53–59]; and in some cohorts, a high degree of correlation is observed [52–54, 58, 60–65].

Socioeconomic status and nutrition, along with ethnic background, are believed to influence the determined bone age [46, 47]. For example, delayed bone age has been reported in Sudanese women due to low socioeconomic status and inadequate nutrition [58].

Contemporary studies show considerable interest in secular trends¹ in children's physical development, noting a tendency toward earlier skeletal maturation, including epiphyseal fusion and ossification [17, 66]. For instance, Boeyer et al. [66] found that 45% of boys and 66% of girls reach skeletal maturity earlier than previous generations. However, in the United Kingdom, these changes did not result in accelerated skeletal maturation, highlighting regional variation [52].

Secular trends¹ have been examined by both Russian and international researchers [67, 68]. For example, Dorokhov et al. [67] investigated growth and development

patterns in children under varying conditions and found that skeletal development is heterochronous and associated with somatotype and biological maturation pattern. Tanner et al. [68], in turn, note that among the factors contributing to epochal variability, socioeconomic determinants show the strongest empirical support.

According to Safonenkova [69], epochal morphological and functional changes in the child's body represent an adaptive response to changing environmental conditions. Furthermore, the study of secular trends¹ is directed toward predicting future developmental status.

Accounting for secular and regional characteristics is essential when adjusting bone-age assessment atlases for use in regions without mandatory newborn registration. This is important for ensuring comprehensive medical and social care [66].

Likewise, the method of bone age assessment using the Zhukovsky–Bukhman tables does not fully reflect contemporary trends in physical development and requires revision [70].

Thus, physiologically expected bone age depends on ethnic background and socioeconomic factors, which must be taken into account when establishing local normative data, either through the introduction of adjustment coefficients or the development of population-specific reference standards.

The diversity of existing methods and approaches to bone age assessment underscores the need for standardization and unification of this procedure. Accurate and reproducible assessment methods are essential for high-quality, objective monitoring of treatment in conditions accompanied by deviations in bone age. However, the relative labor-intensity of the assessment process, together with the limited

Table 4. Analysis of the alignment of ethnic groups with Greulich–Pyle atlas standards

Bone age advanced relative to chronological age	High concordance between bone age and chronological age	Bone age delayed relative to chronological age
<ul style="list-style-type: none"> United States, children of Asian descent older than 13 years [56]; Saudi Arabia, males older than 13 years [53]; Iran, females [54]; Africa, females [54]; Spain [51]; Turkey, children aged 14–17 years [55]; United States, African American children [54]; 	<ul style="list-style-type: none"> Korea, children younger than 13 years [28]; United Kingdom [52]; Scotland [64]; Saudi Arabia, females [53, 59]; Italy, females [54]; Pakistan, females [54]; Belarus [62, 63, 65]; 	<ul style="list-style-type: none"> Malaysia [57]; Sudan, females older than 13 years [58]; Asian children aged 4–6 years [47]; India, males aged 4–15 years [59]; Turkey, children aged 7–13 years [55]; Taiwan, boys aged 2–12 years [61]; Saudi Arabia, males younger than 13 years [53, 59]; Pakistan, males [54]; Iran, males [54]; Indonesia [54]; United States, Asian American boys younger than 7 years [54]

¹ Secular trends are long-term, sustained changes in biological or social characteristics of an individual or a population that occur over the course of several generations.

number of qualified radiology specialists, hinders its widespread use. In addition, secular trends¹ and population heterogeneity in delayed or advanced bone maturation relative to chronological age complicate the calibration of age-specific normative data. Collectively, these factors highlight the need to develop a universal automated platform for bone age assessment. In this context, the use of artificial intelligence technologies represents a promising direction, capable of standardizing the procedure, improving its accessibility and accuracy, and accommodating patient-specific characteristics [71–74].

AUTOMATED BONE AGE ASSESSMENT FROM HAND RADIOGRAPHS USING ARTIFICIAL INTELLIGENCE TECHNOLOGIES

Various artificial-intelligence- and computer-vision-based solutions have been developed for automated bone age assessment [75–80].

BoneXpert® (Visiana, Denmark)² is an automated system for determining bone age from hand radiographs using advanced computational techniques. It performs high-quality segmentation of anatomical structures through machine learning and artificial intelligence, particularly convolutional neural networks. The system has been calibrated and trained on extensive datasets, ensuring accuracy across diverse ethnic groups. BoneXpert® (Visiana, Denmark)² is integrated with picture archiving and communication systems, providing a user-friendly interface for clinicians. It has undergone clinical validation and demonstrated high accuracy compared with traditional assessment methods. Its performance is largely attributable to a detailed morphometric approach to identifying ossification centers, based on principles similar to those used in the Tanner–Whitehouse method [75, 76].

The BoneAgeAnalyzer software application is built on artificial neural networks. This automated method outperforms both the Greulich–Pyle atlas and the Tanner–Whitehouse system in accuracy of ossification assessment (87% vs. 65%, respectively), analysis speed (less than 2 seconds vs. 15 minutes), reproducibility (100%), and verification capacity [77].

The Med-BoneAge® system (VUNO Inc., Korea)³ was developed using a deep learning algorithm trained on 18,940 radiographs assessed according to the Greulich–Pyle method [78].

In addition, a free web-based tool, Physis® (16Bit AI, Canada)⁴, is available for bone age prediction. The development team achieved first place in the Radiological Society of North America (RSNA) Pediatric Bone Age Challenge, outperforming

other groups in bone age estimation accuracy. For comparison, the BoneXpert® system² ranked fourth in the same competition. The authors emphasize that Physis® (16Bit AI, Canada)⁴ is intended solely for demonstration purposes and must not be used for clinical decision-making [17].

Son et al. [79] proposed a fully automated system that estimates bone age according to the Tanner–Whitehouse 3 method by localizing the growth plates (epiphyseal–metaphyseal regions) of 13 bones.

The MediaI-Ba® system (CRESCOM Co., Korea)⁵ was developed using convolutional neural networks. It analyzes 7 epiphyseal–metaphyseal growth regions in the radius, ulna, first metacarpal bone, and the proximal, middle, and distal phalanges of the third finger [80].

According to several studies, integrating automated software into radiology practice enhances consistency and reduces interobserver variability, whereas combining artificial intelligence with expert clinical evaluation yields superior results compared with either approach alone [81–83].

Before the hackathon held as part of the RSNA 2017 Pediatric Bone Age Challenge, relatively simple fully connected neural networks and convolutional neural networks were used for bone age regression from radiographs. After the release of a large benchmark dataset within the framework of this hackathon, more advanced architectures began to be adopted, including encoder–decoder networks, attention-based convolutional networks, and network ensembles. This led to a substantial improvement in the accuracy of bone age assessment using artificial intelligence technologies [84, 85].

Findings from other studies demonstrated the advantages of neural networks over traditional approaches in terms of accuracy, processing speed, and reduced inter-observer variability [86–89]. Modern automated systems provide rapid and highly accurate results, assist clinicians, and are capable of predicting final bone age [17, 77, 90–94]. In addition, there are some attempts to develop fully automated tools that require no manual annotation [94].

Bone age is a critical criterion in decision-making regarding the initiation and duration of therapy for certain genetically determined musculoskeletal disorders. This is particularly relevant for patients with achondroplasia, for whom disease-modifying growth-promoting therapy has become available. When assessing bone age in such patients, clinicians must take into account the specific features of this condition, including altered timing and progression of ossification centers in the hand skeleton [49].

Because skeletal dysplasias alter hand morphology, existing bone age assessment methods are insufficiently reliable. For example, the widely used BoneXpert®² software

² BoneXpert Online [Internet]. B: BoneXpert; 2009–2024. Available at: <https://bonexpert.com>. Accessed on June 9, 2024.

³ Med-BoneAge [Internet]. B: VUNO; 2018–2024. Available at: <https://www.vuno.co>. Accessed on June 9, 2024.

⁴ Physis® [Internet]. B: 16BIT; 2017–2024. Available at: <https://www.16bit.ai/bone-age>. Accessed on June 9, 2024.

⁵ MediaI-Ba [Internet]. B: CRESCOM; 2020–2024. Available at: <https://mediai.onzaram.com/>. Accessed on June 9, 2024.

has difficulty interpreting radiographs of patients with skeletal dysplasia; moreover, it rejects nearly half of radiographs demonstrating features of achondroplasia [95]. All existing models for predicting final adult height are based on data from children without skeletal conditions; therefore, accurate and valid assessment of bone age in this population requires the development of digital skeletal maturation atlases specifically for children with skeletal dysplasias, such as achondroplasia [96].

Despite the substantial number of available artificial intelligence-based solutions for bone age estimation, the need for locally developed systems remains relevant.

First, existing secular trends¹ and population-specific epidemiologic characteristics cannot always be accommodated when attempting to apply off-the-shelf artificial intelligence software [72, 73]. Second, the accessibility of existing solutions is often limited, and some lack sufficiently mature integration interfaces for image archiving and communication systems, radiology information systems, or geographic information systems [74]. Third, validation of commercial artificial intelligence software is challenging, particularly the evaluation of non-standard studies, such as images showing skeletal malformations or radiographs obtained with atypical positioning (for example, opportunistic screening using hand radiographs acquired for hand injury assessment) [91]. Given the availability of open datasets (RSNA), the experience in preparing own datasets, and the established workflows for developing and validating artificial intelligence-based software, the development of an original automated bone age assessment tool, with accuracy metrics comparable to existing state-of-the-art solutions, appears well justified.

CONCLUSION

Bone age assessment is a key tool for diagnosing and monitoring a wide range of pathological conditions in children and adolescents. In this review, we examined both classical and contemporary bone age assessment techniques based on hand radiography, including the most commonly used approaches such as the Greulich–Pyle atlas, the Tanner–Whitehouse method, and the Zhukovsky–Bukhman tables. Analysis of their advantages and limitations, particularly regarding applicability to modern populations, highlighted several important considerations.

When selecting and interpreting bone age assessment methods, it is essential to account for the population-specific characteristics of the children being evaluated. Classical techniques such as Greulich–Pyle and Tanner–Whitehouse remain widely used; however, in certain ethnic, sex, and socioeconomic groups, substantial discrepancies may arise due to the mismatch between historical reference standards and present-day conditions. These discrepancies are largely attributable to the outdated nature of the original standards, which were based on limited cohorts and do not reflect

the contemporary variability in growth rates and skeletal maturation across heterogeneous populations.

Therefore, large-scale implementation in pediatric practice of new digital atlases featuring high-quality reference images differentiated by sex and age, particularly the Gilsanz–Ratib atlas adapted for specific populations, is warranted. In addition, regular revision of existing maturation standards is necessary to ensure their relevance in light of secular trends¹ observed worldwide, including the acceleration of physical maturation in children driven by changes in living conditions, nutrition, and healthcare.

An independent area of development involves the creation and integration into healthcare systems of artificial intelligence-based tools and models trained on data from specific populations. Such systems would allow for the standardization of interpretations, reduction of variability, and improvement of bone age assessment accuracy. Existing artificial intelligence-based solutions demonstrate high effectiveness, yet they often fail to account for regional characteristics and may face limitations related to availability and integration with local medical infrastructures.

A comprehensive approach that combines modern digital imaging and data-processing technologies with consideration of variability in growth and maturation rates across ethnic, socioeconomic, and sex groups will enable the development of reliable and broadly applicable population-specific standards for bone age assessment. Such standards are crucial for ensuring timely and accurate diagnosis in pediatric practice.

In future work, we plan to evaluate the applicability of the Greulich–Pyle atlas to the Russian population and assess the relevance and accuracy of the Zhukovsky–Bukhman tables under current conditions. Based on these findings, a new approach to bone age assessment will be developed—one that incorporates regional characteristics and contemporary secular trends.¹ In addition, creating original artificial intelligence software trained on local population data will allow automation of bone age determination, increasing both its accuracy and its clinical accessibility.

Thus, integrating traditional methods with modern technologies and accounting for regional characteristics are key factors for improving the diagnosis and management of growth and developmental disorders in children and adolescents. The development of new artificial intelligence-based tools tailored to the characteristics of specific populations will enhance the quality of medical care and provide more accurate and objective bone age assessment in clinical practice.

ADDITIONAL INFORMATION

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