Current and emerging artificial intelligence applications for pediatric musculoskeletal radiology

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Received: 16 March 2021 / Revised: 28 April 2021 / Accepted: 10 June 2021 / Published online: 16 July 2021
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Abstract
Artificial intelligence (AI) is playing an ever-increasing role in radiology (more so in the adult world than in pediatrics), to the extent that there are unfounded fears it will completely take over the role of the radiologist. In relation to musculoskeletal applications of AI in pediatric radiology, we are far from the time when AI will replace radiologists; even for the commonest application (bone age assessment), AI is more often employed in an AI-assist mode rather than an AI-replace or AI-extend mode. AI for bone age assessment has been in clinical use for more than a decade and is the area in which most research has been conducted. Most other potential indications in children (such as appendicular and vertebral fracture detection) remain largely in the research domain. This article reviews the areas in which AI is most prominent in relation to the pediatric musculoskeletal system, briefly summarizing the current literature and highlighting areas for future research. Pediatric radiologists are encouraged to participate as members of the research teams conducting pediatric radiology artificial intelligence research.

Keywords Artificial intelligence · Bone · Children · Musculoskeletal · Pediatric radiology

Introduction
Simply put, artificial intelligence (AI) can be defined as software that automates (or semi-automates) a cognitive task. AI applications in the musculoskeletal system can be fully automated (e.g., bone age assessment) or semi-automated (e.g., vertebral fracture assessment). Although AI tools in general can be categorized as AI-assist (helping the radiologist), AI-replace (replacing the radiologist) or AI-extend (exceeding the capability of the radiologist) [1], as far as the author is aware, no clinical tool functions in the AI-extend mode in pediatric musculoskeletal radiology practice.

Existing AI tools can help to improve image quality; aid in the measurement of lengths, angles and volumes; or aid in the detection of pathological processes, the last through recognition and classification of morphological or textural abnormalities.

Of the 144 AI products that are CE (Conformité Européenne) marked and commercially available, 74 also have United States Food and Drug Administration (FDA) approval and 18 are related to the musculoskeletal system [2]. Of these 18, one is for image enhancement and post-processing rather than being a diagnostic aid, per se. Considering the remaining 17 AI musculoskeletal products, the majority (14) have been designed for aiding diagnosis from radiographs, while use in pediatric radiology is only explicitly stated in the information available for 3 of the 17 tools. Table 1 summarizes these 17 available musculoskeletal AI tools; all 3 tools intended for use in pediatric radiology are for bone age assessment [2].

Although commercially available tools are currently only for bone age assessment, ongoing and published research pertains to tasks such as fracture diagnosis (appendicular and vertebral), scoliosis and leg-length discrepancy measurements. Other areas where pediatric research is being performed include determining bone health using the bone health index and diagnosing metopic craniosynostosis and developmental dysplasia of the hip. These emerging applications could achieve commercial release within the next decade.
This review also identifies and briefly discusses areas in which very little AI research has been conducted but in which there is potential for AI to play a significant role; these areas include inflicted injury (child abuse) and skeletal dysplasias.

The main focus of this article is on diagnosis/detection of pathology. For AI applications related to image-quality improvement, image post-processing, quality control, etc., the reader is directed to other articles in this special issue and to the 2019 review by Koska [3].

### Current applications: bone age assessment

Although three bone age assessment AI tools are on the market, the oldest and probably best known is BoneXpert (Visiana, Hørsholm, Denmark). Indeed, BoneXpert is the oldest musculoskeletal AI-replace software tool on the market (Table 1), and more than 150 departments are using BoneXpert in day-to-day clinical practice across Europe, each performing more than 100 analyses per year (personal communication with H.H. Thodberg and P. Bak, November 2020).

BoneXpert automatically calculates bone age according to the Greulich and Pyle and the Tanner and Whitehouse standards in a process that takes less than 15 s per hand and wrist radiograph. The method is based on traditional machine-learning methodology and involves prediction of bone age based on shape, intensity and texture scores as derived from principal component analysis. It is worth noting that there are no General Data Protection Regulation (GDPR)-related issues, because BoneXpert is configured as a Digital Imaging and Communications in Medicine (DICOM) node for local

| Date on market | Company | Product name | Disease targeted | Modality | Pediatrics | CE class | FDA |
|----------------|---------|--------------|------------------|----------|------------|----------|-----|
| Mar 2009       | Visiana (Hørsholm, Denmark) | BoneXpert | Bone age | Radiography | Y | I | N |
| 2012           | Medimaps (Geneva, Switzerland) | TBS iNsight (Osteo) | Osteoporosis | Radiography | N | Ila | II |
| Nov 2017       | Aidoc (Tel Aviv, Israel) | C-Spine | C-spine fracture | CT | N | I | II |
| May 2018       | VUNO (Seoul, Korea) | VUNO Med-BoneAge | Bone age | Radiography | Y | I | N |
| Jan 2019       | QUIBIM (Valencia, Spain) | 2D Bone Microarchitecture QTS Score | Osteoporosis Oncology Osteopenia Osteoarthritis | Radiography | N | Ila | N |
| Jan 2019       | QUIBIM | 2D Bone Microarchitecture QTS Score | Osteoporosis Oncology Osteopenia Osteoarthritis | CT, MRI | N | Ila | N |
| Jan 2019       | QUIBIM | Cartilage T2 Mapping | Osteoarthritis Degeneration Sports diseases | MRI | N | Ila | N |
| Jan 2019       | QUIBIM | Texture Analysis | Tumors Osteoporosis Osteopenia Osteoarthritis | Radiography, CT, MRI, PET, US, SPECT | N | Ila | N |
| Jun 2019       | AZMed (Paris, France) | Rayvolve | Fracture | Radiography | N | I | N |
| Aug 2019       | ImageBiopsy Lab (Vienna, Austria) | IB Lab KOALA | Osteoarthritis (knee) | Radiography | N | I | II |
| Nov 2019       | Radiobiotics (Copenhagen, Denmark) | RBknee | Osteoarthritis (knee) | Radiography | N | I | N |
| Feb 2020       | Arterys (San Francisco, CA) | Chest/MSK AI | Fracture Dislocation | Radiography | N | Ila | N |
| Mar 2020       | Gleamer (Paris, France) | BoneView | Fracture | Radiography | N | Ila | N |
| Oct 2020       | ImageBiopsy Lab | IB Lab HIPPO | Hip measurements | Radiography | N | I | N |
| Oct 2020       | ImageBiopsy Lab | IB Lab LAMA | Leg geometry | Radiography | N | I | N |
| Nov 2020       | ImageBiopsy Lab | IB Lab PANDA | Bone age | Radiography | Y | I | N |
| U              | Zebra (Kibbutz Shefayim, Israel) | Bone Health | Vertebral compression fractures | CT | N | U | II |

*CE* Conformité Européene, *FDA* United States Food and Drug Administration approval, *MSK* musculoskeletal, *N* no, *PET* positron emission tomography, *SPECT* single-photon emission computed tomography, *U* unknown, *Y* yes

*a* Derived from [2]

*b* Only includes those tools for which pediatric use is explicitly stated
picture archiving and communication systems (PACS) and is
an image-analysis application only. In other words,
BoneXpert does not store data, share data or transfer data
outside the local PACS. The pathway and output are illustrated
in Figs. 1 and 2, respectively, and the terminology used in
the output is explained in Table 2.

Although launched in 2009 as an AI-replace tool, approx-
imately 70% of departments that have the software installed
use BoneXpert as an AI-assist tool (A. Offiah, unpublished
work). The reason for this is simple: while BoneXpert rejects
radiographs with significant abnormality (e.g., poor position-
ing, abnormal bone morphology, poor image quality), it does
not reject radiographs with subtle abnormality of morphology
(e.g., early rickets) or abnormality of texture (e.g.,
metaphyseal striations). If a radiologist does not review the
radiographs, then these subtle changes will be missed. The
detection of such abnormalities is outside the scope of the
software as developed, and radiologists are advised to bear
this in mind.

The percentage of radiographs rejected by BoneXpert be-
cause of abnormal anatomy depends on the types of patients
seen, ranging from approximately 0.4% in general hospitals to
up to 3% in hospitals specializing in skeletal dysplasias. The
percentage of radiographs rejected by BoneXpert because of
poor image quality is generally very low (reflecting radiogra-
pher competence). However, departments in which significant
data-enhancement is applied as part of the post-processing of
images might see rejection rates of up to 10%, accompanied
by the error message, “Too sharp” (personal communication
with H.H. Thodberg and P. Bak, April 2021). The software
has been tested in multiple populations and ethnicities, includ-
ing Caucasian, African American, Hispanic, Asian Chinese
and Saudi Arabian populations [4–9]; while generally appli-
cable to all ethnicities, some caution is advised, but this is
related to the applicability of the standards (Greulich and
Pyle, Tanner and Whitehouse 3) and not to the BoneXpert
software itself. The latter claim can be made based on diag-
nostic accuracy studies that have compared manual to
Table 2  BoneXpert outputs

| Term                  | Interpretation                                                                 |
|-----------------------|--------------------------------------------------------------------------------|
| BA (GP)               | Greulich and Pyle bone age (gender)                                           |
| BA SDS                | Bone age standard deviation score (ethnicity)                                 |
| BA (TW3)              | Tanner and Whitehouse three-bone age                                          |
| Age                   | Chronological age                                                              |
| BHI                   | Bone health index (digital X-ray radiogram)                                    |
| BHI SDS               | Bone health index standard deviation score (ethnicity)                         |

automated bone age assessments [10–17], with reported root mean square errors being as low as 0.63 [18].

In 2017, the Radiological Society of North America launched a Machine Learning Challenge, making freely available a set of more than 14,000 hand and wrist radiographs [19]. The best-performing entry achieved a concordance correlation coefficient of 0.99 and differed from ground truth by only 4.3 months, compared to 7.3 months for radiologists [20]. It is possible for readers to test the application for themselves but note that it is for demonstration purposes only (i.e., it is not for clinical use) [21].

Other bone age tools have also been tested and found to be reliable and accurate and to reduce reporting times [22–26] and it is worth pointing out the encouraging results obtained for bone age estimation of the index finger alone (as opposed to the entire left hand and wrist radiograph) when using a neural-network-based AI application, which paves the way for hand-held bone age estimation machines [26].

While some authors have focused their work on AI determination of bone age from other sites, such as the pelvis [27] or knee [28], and other modalities, such as MRI [29–32], a relatively recent systematic review highlighted the lack of such studies, in addition to the need for more research assessing potential socioeconomic and ethnic variations on the performance of such AI tools [33].

Emerging/future applications

Bone health index

There is no reliable method of predicting fracture risk in children. While dual-energy X-ray absorptiometry is the gold standard for bone mineral density assessment in children, it has limitations [34–36]. As such, other quantitative bone imaging techniques have been developed including AI applications (predominantly related to adults; Table 1). Of relevance to pediatrics is radiogrammetry. Originally performed manually [37], this technique lends itself to automation because it measures cortical thickness of the phalanges in relation to their lengths, thereby producing an index of bone strength.

In addition to determining bone age, the BoneXpert software discussed in the previous section also performs “digital X-ray radiogrammetry,” providing an indication of bone health called the “bone health index” or “BHI” (Fig. 2 and Table 2). Bone health index is derived from a measurement of the cortical thickness, width and length of the three middle metacarpals. A standard deviation score is also provided, allowing comparison with the bone health index of healthy Caucasian children of the same age and gender.

While a few studies have been performed with favorable results [38–41], the clinical role of the bone health index in monitoring and assessing bone strength in children (of any ethnicity) has not been elucidated. In a recent systematic review, peripheral quantitative computed tomography (pQCT), bone health index and quantitative ultrasound (QUS) were compared with dual-energy X-ray absorptiometry. Meta-analysis showed BHI to have the strongest correlation with dual-energy X-ray absorptiometry, with a pooled estimate of correlation of 0.71 compared to 0.57 for both pQCT and QUS [42]. These results encourage further research into the potential clinical application of BHI.

Fracture assessment

Appendicular fractures

The few studies that have assessed the utility of AI for appendicular fracture detection in children have predominantly concentrated on the elbow joint, possibly because of the complexity of the elbow joint and multiple unossified epiphyseal centers that are found in children. England et al. [43] used a relatively small set of lateral radiographs to train (657 images), validate (115 images) and test (129 images) a convolutional neural network for the identification of elbow joint effusions. Compared to the reference standard of radiologists’ reports, the network had sensitivity, specificity and accuracy of 0.91.

In a significantly larger study consisting of 21,456 anteroposterior and lateral elbow radiographs, Rayan et al. [44] determined the feasibility of deep learning to correctly classify elbow radiographs as normal or abnormal. The true positive rate (i.e., those radiographs correctly classified as abnormal) was highest for supracondylar fractures (0.996) and lowest for osteochondral lesions (0.000), although it should be noted that there were only two cases of osteochondral lesions in the entire dataset. Most recently, Choi et al. [45] assessed the ability of a convolutional neural network to correctly identify supracondylar fractures from 1,266 anteroposterior and lateral elbow radiographs.

The results of these three studies (summarized in Table 3; [43–45]) are encouraging. However, particularly given their
Axial fractures

A decision tree might be seen as a flowchart-like structure, with each branch representing a potential outcome. Optimal trees are predictive AI algorithms that limit the number of outcomes while encompassing as much of the available data as possible [48]. Bertsimas et al. [49] used an optimal trees artificial intelligence approach to predict cervical spine trauma in children. However, this model was based on history and clinical parameters (including Glasgow Coma Scale) and used imaging interpretation by radiologists as an outcome measure for presence or absence of fracture, rather than using the algorithm to classify radiographs. Given the difficulty associated with obtaining adequate views (particularly in younger children) and complexity of the cervical spine [50], this would be a worthy field for the development of an AI diagnostic tool.

Other studies assessing AI tools for detecting vertebral fractures in children relate to osteoporotic compression fractures rather than post-traumatic fractures and are briefly reviewed next.

The diagnosis of vertebral crush fractures from dual-energy X-ray absorptiometry scans is termed vertebral fracture assessment, and the Lunar iDXA machine (GE Healthcare Lunar, Buckinghamshire, UK) has been shown to be as reliable as radiographs for vertebral crush fracture diagnosis in children at a lower radiation dose penalty [51, 52]. The use of software tools to diagnose vertebral fractures from dual-energy X-ray morphometry scans is termed morphometric vertebral analysis [52]. Such software tools are widely available for clinical use in adults; however, they have not been licensed for use in children. Given both the wide variability in diagnosis of vertebral fractures in children [53] and that the recognition of vertebral shape (morphometry) lends itself to AI applications, researchers have assessed the accuracy and reliability of existing adult software, specifically SpineAnalyzer (Optasia Medical, Cheadle, UK) and AVERT (Optasia Medical) in the diagnosis of vertebral fractures in children [54–56]. The AI tools SpineAnalyzer and AVERT are semi-automated; they require an individual to identify and label the centers of vertebral bodies T4 to L4 (any non- or poorly visible vertebrae can be omitted). The tools then automatically outline the vertebral bodies using 6 (SpineAnalyzer) or 33 (AVERT) points and provide an output indicating normal or fractured vertebrae and severity of fracture based on height loss ratios (Fig. 3; [56]). The reader can manually reposition any points that were erroneously identified by the software. The conclusion of these studies is that the diagnostic accuracy of existing adult (semi-automated) software tools for vertebral fracture assessment in children is insufficiently adequate for clinical use (Table 4). Reasons for this include unossified ring apophyses, variation in vertebral shape with age and normal variants in children, all issues that are less problematic (if at all) in adults. The adult tools were trained using the radiographs of post-menopausal women and (despite the misleading final column in Fig. 3, which suggests otherwise) are based on the Genant et al. [56] classification for vertebral fractures. If morphometric vertebral analysis is to be accurate in children, then any tool developed must be trained using the spine radiographs of a cohort of healthy children [57].

Inflicted fractures (child abuse)

Inflicted metaphyseal and rib fractures in infants and young children are often difficult to detect and yet are highly predictive of abuse [58, 59]. United Kingdom national guidelines (adopted by the European Society of Paediatric Radiology) advise that images be double-reported by at least one pediatric radiologist [60, 61]; therefore in centers where this is not possible because of staffing issues, it would be helpful to have an AI-assist tool, if only to highlight suspicious areas for closer review by the radiologist on either skeletal surveys performed for suspected abuse or (perhaps more important) on radiographs performed for other indications, e.g., a chest radiograph for cough. Work has been

| Author [reference] | Sensitivity | Specificity | Accuracy | Positive predictive value | Negative predictive value |
|--------------------|-------------|-------------|----------|--------------------------|--------------------------|
| England et al. 2018 [43] | 0.91 | 0.91 | 0.91 | – | – |
| Rayan et al. 2019 [44] | 0.91 | 0.84 | 0.88 | 0.87 | 0.89 |
| Choi et al. 2020 [45] (temporal test set) | 0.93 | 0.92 | – | 0.80 | 0.98 |
| Choi et al. 2020 [45] (geographic test set) | 0.10 | 0.86 | – | 0.70 | 0.10 |
done on the AI-assisted detection of rib fractures in adults, with encouraging results [62–65], including the development of fully automated convolutional neural networks to perform this task [66, 67]. However, to the author’s knowledge, no such studies have been carried out for suspected abusive fractures in infants and young children. Research in this area should be encouraged.

To assist radiologists and others in the field, a web-based tool to unify the investigative protocol in suspected abuse and to support training and multicenter national and international research, a knowledge base to be populated with clinical information, radiographs and radiographic information has been described [68] and continues to be developed (ongoing work of author).

**Other emerging/future pediatric musculoskeletal applications**

**Developmental hip dysplasia**

Two studies have assessed the ability of neural networks to diagnose developmental hip dysplasia in children [69, 70]. Li et al. [69] used a training set of 11,473 anteroposterior pelvic radiographs.

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**Table 4** Diagnostic accuracy of artificial intelligence (AI) applications for morphometric vertebral fracture assessment in children

| Author [reference] | Sensitivity | Specificity | False-positive rate | False-negative rate | Kappa       |
|--------------------|-------------|-------------|---------------------|---------------------|-------------|
| Crabtree et al. 2017 [52] (6-point technique) | 0.79 | 0.71 | 0.13 | 0.27 | 0.24–0.60 |
| Alqahtani 2019 [54] (SpineAnalyzer) | 0.31 | 0.96 | 0.04 | 0.69 | 0.16–0.44 |
| Alqahtani 2019 [54] (AVERT) | 0.41 | 0.91 | 0.09 | 0.59 | 0.26–0.46 |
| Alqahtani 2020 [55] (AVERT) | 0.4 | 0.92 | 0.08 | 0.58 | 0.26–0.46 |
| Single radiographer | 0.8 | 0.9 | 0.1 | 0.2 | - |
| Additional observers | 0.89 | 0.79 | 0.21 | 0.11 | 0.29–0.69 |

*From dual-energy X-ray absorptiometry scans
*The precise software tool used was not specified

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**Fig. 3** Lateral spine dual-energy X-ray absorptiometry scan in a 12-year-old boy, left, with deformity results right. Morphometric vertebral fracture assessment using SpineAnalyzer identifies four mild (T4, T10, T11, L1) and three moderate (T9, T12, L3) fractures. **Bicon.** biconcave, SQ semi-quantitative score (of Genant et al. [56])

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**Image**

*Not for diagnostic use.*

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**Table 4**

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a From dual-energy X-ray absorptiometry scans
b The precise software tool used was not specified
radiographs and a test set of 101 images for the diagnosis of developmental dysplasia of the hip based on the Sharp angle (acetabular index). They found that accuracy was similar when compared to orthopedic surgeons and required less time, and they concluded that their AI tool could potentially replace orthopedic surgeons [69]. Zhang et al. [70] used 9,081 anteroposterior pelvic radiographs as their training set and a further 1,138 anteroposterior pelvic radiographs as their test set for the diagnosis of developmental hip dysplasia based on the acetabular index. They concluded that their deep-learning system improved consistency, convenience and effectiveness compared to clinician-led diagnosis and suggested that it might simplify current screening pathways [70].

As far as can be ascertained, neither of these tools was compared to a reference standard of pediatric radiologists. In the author’s opinion, this would be an important next step before widespread use of such AI tools by pediatric radiology departments.

**Spinal alignment**

Several studies have been conducted to determine the degree of scoliosis and other measurements of the spine using conventional radiographic images [71], biplanar radiographic images [72] or moiré images [73]. All such studies have shown promising results and indeed automated spine and lower limb measurements are performed by the biplanar imaging system installed at the author’s institution.

Other authors have assessed the ability of AI to predict scoliosis progression [74], assess the Risser stage [75], detect evidence of scoliosis treatment from radiographs [76] and to automate three-dimensional (3-D) spine reconstructions from biplanar images [77].

**Miscellaneous**

A few other studies conducted in children (or children and adults) and assessing AI applications in the musculoskeletal system are worthy of mention and include determining leg-length discrepancy from radiographs [78], quantifying the degree of metopic craniosynostosis from skull CT scans [79], predicting the presence of discoid lateral menisci from radiographs [80], determining muscle mass from dual-energy X-ray absorptiometry scans in cerebral palsy [81] and discerning sexual dimorphism from hand and wrist radiographs [82]. Further applications of some of these tools are obvious, e.g., diagnosis of premature fusion of sutures other than the metopic suture and determination of muscle mass in other conditions such as myopathies and juvenile dermatomyositis. The clinical utility of a tool that identifies gender from hand and wrist radiographs is limited to forensic imaging, perhaps helping with the identification of bodies destroyed by mass disasters, but it is significant because (to the author’s knowledge) it is the only example of a potential AI-extend tool in pediatric musculoskeletal imaging (i.e. a tool that performs a task over and above the capability of radiologists).

Computer-assisted diagnosis of skeletal dysplasias might be based both on AI-assisted morphological analysis and on the creation of “ontologies” in the skeletal dysplasia domain. An ontology organizes large datasets into sets of categories/concepts and forms relationships between them [83]. Ontologies related to skeletal dysplasias include the Human Phenotype Ontology [84], the Bone Dysplasia Ontology [85] and the dynamic Radiological Electronic Atlas of Malformation Syndromes (dREAMS) [86].

Pertaining to AI-assisted diagnosis of skeletal dysplasias based on skeletal morphometry, preliminary work using radiographs of infants from the dREAMS database has shown an accuracy of 78.0% to 87.5% for lateral spine, 68.0% to 75.0% for anteroposterior spine and 87.5% to 88.0% for anteroposterior chest radiographs in dichotomizing images to “achondroplasia” or “not achondroplasia” categories [87]. Accuracy and confidence intervals would be expected to improve using a dataset larger than that used by the authors (40 lateral spine, 16 anteroposterior spine and 26 anteroposterior chest radiographs in a ratio of 70% to 30% for training and testing, respectively). Nevertheless, the results provide proof of concept and suggest that the task is worth pursuing.

**Conclusion**

Bone age assessment tools are the only pediatric musculoskeletal AI tools available on the market. In recent years, increasing research has been conducted in areas such as elbow fractures, developmental hip dysplasia and scoliosis assessment. However, there is significant scope for more work, particularly in areas such as the diagnosis of vertebral fractures, inflicted injury, skeletal dysplasias and musculoskeletal oncology. Pediatric radiologists are encouraged to be members of the research teams conducting such studies, so that the reference standard used is the diagnostic accuracy of pediatric radiologists, rather than the diagnostic accuracy of clinicians from other specialties, which is the case in some publications. AI tools will not replace the pediatric musculoskeletal radiologist in the near future, if ever.

**Declarations**

**Conflicts of interest**  Professor Offiah has conducted research with Visiana in relation to BoneXpert software and has received funding for the development of dREAMS.

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