Review

Not peer-reviewed version

The Role of Artificial Intelligence in Predicting and Managing Pediatric Fracture Overgrowth: A Comprehensive Review

Daniela Alessia Marletta , Matteo Nanni , Gabriele Giuca * , Ilaria Sanzarello , Biagio Zampogna , Danilo Leonetti

Posted Date: 18 November 2024

doi: 10.20944/preprints202411.1250.v1

Keywords: Artificial Intelligence; Pediatric Fracture Overgrowth; Machine Learning; Pediatric Orthopedics; Predictive Modeling; Predictive Analytics; Explainable AI; Healthcare Innovation

Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024
doi:10.20944/preprints202411.1250.v1

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Review

The Role of Artificial Intelligence in Predicting and Managing Pediatric Fracture Overgrowth: A Comprehensive Review

Daniela Alessia Marletta [1], Matteo Nanni [1], Gabriele Giuca [1,*], Ilaria Sanzarello [1], Biagio Zampogna [1,2,3] and Danilo Leonetti [1]

[1] Department of Orthopaedics and Traumatology, Department of Biomedical Sciences and Morphological and Functional Images, University of Messina, 98122 Messina, Italy
[2] Department of Orthopaedic and Trauma Surgery, Università Campus Bio-Medico Di Roma, 00128 Rome, Italy
[3] Research Unit of Orthopaedic and Trauma Surgery, Fondazione Policlinico Universitario Campus Bio-Medico, 00128 Rome, Italy.
* Correspondence: gabgiuca@unime.it, Tel.: +39-3315039785

Abstract Pediatric fracture overgrowth is an unpredictable complication of long bone fractures in children, leading to excessive growth of the injured limb and resulting in limb length discrepancies (LLDs) and angular deformities that impact mobility and quality of life. Traditional methods struggle to predict at-risk children, hindering early detection and management. Artificial intelligence (AI), including machine learning and deep learning, offers advanced data analysis capabilities to enhance predictive accuracy and personalize treatment strategies. This comprehensive review explores the current understanding of pediatric fracture overgrowth, examines AI applications in medicine and orthopedics, evaluates potential AI applications specific to fracture overgrowth, and discusses ethical considerations and patient-centric approaches. We highlight how AI can improve diagnostic precision, facilitate early intervention, and optimize clinical outcomes. Though direct studies on AI in fracture overgrowth are limited, evidence from related areas underscores its potential. Embracing AI could revolutionize pediatric fracture management, leading to earlier detection, targeted interventions, and better outcomes for affected children.

Keywords: artificial intelligence; pediatric fracture overgrowth; machine learning; pediatric orthopedics; predictive modeling; predictive analytics; explainable AI; healthcare innovation

---

1. Introduction

Fractures are an unfortunate yet common occurrence in childhood, a time characterized by high levels of physical activity and ongoing skeletal development. Children climb, run, jump, and engage in various sports, all of which increase the risk of injuries, including fractures. Statistics show that up to 42% of boys and 27% of girls sustain at least one fracture before the age of 16 [1]. These injuries pose unique challenges to healthcare providers due to the presence of growth plates, or physes, which are areas of developing cartilage tissue near the ends of long bones. Growth plates are crucial for longitudinal bone growth but also introduce complexities in fracture healing and potential complications. One significant complication that can arise following long bone fractures in children is fracture overgrowth [2]. Unlike adults, where fractures typically heal to restore the bone's original length and structure, children's bones can exhibit accelerated growth during the healing process. This accelerated growth can lead to the injured limb becoming longer than its uninjured counterpart, resulting in limb length discrepancies (LLDs) and angular deformities . These discrepancies can have profound effects on a child's gait, posture, and overall quality of life, potentially leading to functional impairments and psychological distress [3]. The unpredictable nature of fracture overgrowth adds a layer of complexity to pediatric fracture management. Traditional predictors, such as the child's age,

© 2024 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

the type of fracture, and its location, provide only general guidance and often lack the precision needed for individualized risk assessment. This unpredictability makes early detection and effective management challenging, and in many cases, corrective surgeries such as epiphysiodesis or limb lengthening procedures become necessary. These interventions carry inherent risks and can significantly impact the child's life, both physically and emotionally. In the face of these challenges, there is a growing interest in leveraging advanced technologies to improve outcomes in pediatric fracture care. Artificial intelligence (AI), which includes machine learning (ML) and deep learning (DL) techniques, has emerged as a powerful tool in healthcare. AI systems are capable of analyzing vast amounts of complex data, identifying patterns, and making predictions that may not be apparent through traditional analysis. In fields like radiology, pathology, and even adult orthopedics, AI has shown promise in enhancing diagnostic accuracy, predicting disease progression, and personalizing treatment plans. Given the potential of AI to revolutionize various aspects of medicine, its application in predicting and managing pediatric fracture overgrowth is a logical and promising next step. By integrating clinical data, imaging findings, genetic information, and treatment details, AI could provide more accurate risk assessments and facilitate early interventions tailored to individual patients. This could not only improve clinical outcomes but also reduce the burden on healthcare systems and families [4].

This comprehensive review aims to explore the intersection of AI and pediatric fracture overgrowth. We will delve into the current understanding of fracture overgrowth, examining its epidemiology, pathophysiology, and clinical implications. We will discuss the emergence of AI in medicine and orthopedics, highlighting key technologies and applications. Furthermore, we will examine existing evidence and potential applications of AI specific to fracture overgrowth and discuss ethical considerations and patient-centric approaches. By synthesizing existing literature, we hope to shed light on how AI can transform the management of pediatric fractures and stimulate further research and innovation in this critical area.

2. Understanding Pediatric Fracture Overgrowth

Fracture overgrowth in children is a fascinating yet complex phenomenon that defies typical expectations of bone healing. Instead of merely restoring the bone's original length and integrity, the injured bone exhibits accelerated growth, surpassing the length of the uninjured limb. This overgrowth can lead to significant limb length discrepancies (LLDs) and angular deformities, which have lasting impacts on a child's physical function and quality of life. The incidence of fracture overgrowth varies widely in the literature, reflecting the multifactorial nature of this condition. Reports suggest that overgrowth can occur in anywhere from 8% to 41% of pediatric femoral fractures [2,5]. Younger children are at higher risk, particularly those under the age of 10, due to their active growth plates and greater remaining growth potential [6,7]. The femur and tibia are the bones most commonly associated with overgrowth, possibly because of their significant contribution to overall limb length [8,9]. The mechanisms behind fracture overgrowth are not fully understood, but several theories have been proposed. One widely accepted explanation is the hyperemia theory. Following a fracture, increased blood flow (hyperemia) to the injury site facilitates healing. This increased vascularity may extend to the adjacent growth plate (physis), stimulating it to produce more cartilage cells that later ossify, thus accelerating longitudinal bone growth [10]. The hyperemia not only aids in fracture healing but may also inadvertently enhance growth plate activity. Another theory focuses on the mechanical environment of the healing bone. Immobilization of the fractured limb, often necessary for proper healing, reduces mechanical stress on the growth plate. This reduction in stress may alter the normal inhibitory signals that regulate growth plate activity, leading to an increase in growth rate [11,12]. Changes in muscle forces due to immobilization or altered weight-bearing can also impact growth plate stimulation. The fracture healing process involves a complex cascade of biological events, including the release of growth factors and cytokines. Molecules such as insulin-like growth factor-1 (IGF-1), bone morphogenetic proteins (BMPs), and vascular endothelial growth factor (VEGF) play crucial roles in bone repair and regeneration [13]. These factors may have systemic effects, enhancing growth plate activity beyond the immediate vicinity of the fracture. Additionally,

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

injury to nerves and blood vessels during a fracture could disrupt normal growth regulation. Neurovascular mechanisms influence bone growth, and damage to these systems may lead to altered signaling at the growth plate, promoting overgrowth [14]. Emerging research suggests that genetic factors may also play a role. Variations in genes that regulate growth plate activity, bone healing, and response to injury could make some children more susceptible to overgrowth [15]. Understanding these genetic influences could lead to the identification of biomarkers for risk assessment [16]. The consequences of fracture overgrowth extend beyond physical discrepancies. Limb length discrepancies can lead to gait abnormalities, musculoskeletal strain, and functional limitations [17]. Children may develop abnormal gait patterns to compensate for the difference in limb length, such as limping or toe-walking. These compensatory mechanisms place additional stress on muscles, joints, and the spine, potentially leading to pain and discomfort. Activities requiring balance and coordination may be affected, impacting the child's participation in sports and daily activities [18]. When overgrowth occurs asymmetrically across the growth plate, angular deformities like valgus (knock-knees) or varus (bow-legs) can develop. These deformities affect joint alignment and load distribution, increasing the risk of joint degeneration and osteoarthritis in the long term [3]. The psychological impact on children should not be underestimated. Visible limb discrepancies or deformities may lead to self-esteem issues, social withdrawal, and decreased participation in activities [19]. Predicting which children will develop fracture overgrowth remains a significant challenge. Traditional predictors offer only general guidance and lack specificity. Early detection requires careful monitoring over time, but subtle discrepancies may not be clinically apparent until they become more significant [20]. Management options include observation, orthotic devices, and surgical interventions like epiphysiodesis (surgical arrest of the growth plate) or limb lengthening [21]. These interventions carry risks, including surgical complications and psychological effects from multiple procedures [22].

3. Artificial Intelligence in Medicine and Orthopedics

The advent of artificial intelligence has marked a paradigm shift in the landscape of healthcare, moving from a futuristic concept to a tangible reality that is reshaping clinical practice. Artificial intelligence, in its broadest sense, refers to the ability of machines to mimic human cognitive functions such as learning and problem-solving. In medicine, AI's capacity to process and analyze vast amounts of complex data far surpasses that of traditional statistical methods, allowing for the extraction of subtle patterns and insights that can enhance diagnostic accuracy, prognostic assessments, and therapeutic interventions. At the heart of AI are technologies such as machine learning (ML) and deep learning (DL), which have shown remarkable prowess in handling both structured and unstructured data [23]. Machine learning involves the development of algorithms that can learn from and make predictions based on data. It operates by identifying patterns within data sets and using these patterns to make decisions or predictions when presented with new data. This capability is particularly useful in processing structured data, such as numerical values from laboratory results, vital signs, and patient demographics. Deep learning, a subset of machine learning, utilizes artificial neural networks inspired by the human brain's structure and function. These networks consist of multiple layers that can learn representations of data with multiple levels of abstraction. Deep learning excels at processing unstructured data, including images, audio, and text, making it highly effective in fields like medical imaging and natural language processing. Natural language processing (NLP) is another critical component of AI in healthcare. NLP enables computers to interpret, understand, and generate human language in a meaningful way. In the clinical context, NLP can be used to analyze unstructured text from electronic health records (EHRs), extracting valuable information from clinical notes, discharge summaries, and patient narratives. This information can then be used to identify patient cohorts, predict outcomes, or support clinical decision-making [24]. Computer vision, a field that enables machines to interpret and process visual data, has been instrumental in medical imaging analysis [25]. By applying algorithms to interpret images from radiographs, CT scans, MRIs, and ultrasounds, AI can assist in detecting anomalies, quantifying disease progression, and aiding in image-guided interventions. In the realm of

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

diagnostics, AI has made significant strides. For instance, AI algorithms have been developed to detect diabetic retinopathy from retinal images, achieving accuracy levels comparable to experienced ophthalmologists [26]. Similarly, in radiology, AI systems can detect lung nodules, fractures, and other pathologies on imaging studies with high sensitivity and specificity. These tools not only augment the clinician's diagnostic capabilities but also help in reducing the workload and minimizing human error [27]. Predictive analytics is another area where AI has shown great promise. Machine learning models can analyze large datasets to predict disease trajectories, patient responses to treatments, and the likelihood of adverse events. For example, in oncology, AI models can predict tumor growth patterns and patient survival based on genomic data and clinical features, enabling personalized treatment plans [28,29]. Personalized medicine, an approach that tailors medical treatment to the individual characteristics of each patient, benefits immensely from AI's capabilities [30]. By integrating genomic information, environmental factors, and lifestyle data, AI can help identify the most effective therapies for individual patients, minimizing adverse effects and improving outcomes [31].

AI in Orthopedic Practice

In orthopedics, AI applications are expanding rapidly. Imaging analysis is one of the most significant areas where AI has made an impact. Deep learning algorithms can detect and classify fractures on radiographs with remarkable accuracy, sometimes surpassing human experts. These algorithms can highlight areas of concern on images, assisting radiologists and orthopedic surgeons in making prompt and accurate diagnoses [32]. Automated bone age assessment is another application of AI in orthopedics, particularly relevant to pediatrics. Traditional methods of assessing bone age involve manual interpretation of hand radiographs, which can be time-consuming and subject to inter-observer variability. AI-driven tools can automate this process, providing rapid and consistent assessments that are crucial for evaluating growth disorders and planning treatments that may affect growth, such as hormone therapies or orthopedic interventions [33]. AI also plays a role in surgical planning and intraoperative guidance. Preoperative planning software using AI algorithms can assist surgeons in selecting appropriate implants, determining optimal surgical approaches, and simulating surgical outcomes. Intraoperatively, AI can enhance robotic-assisted surgeries by providing real-time feedback and adjustments, improving precision, and reducing the risk of complications. Postoperative care and rehabilitation in orthopedics are also benefiting from AI [34]. Wearable devices and mobile applications equipped with AI can monitor patients' progress, adherence to rehabilitation protocols, and detect signs of complications early. By analyzing data from sensors that track movement, strength, and range of motion, AI can provide personalized feedback and adjust rehabilitation programs to optimize recovery. The potential for AI to predict pediatric fracture overgrowth specifically is significant, though it remains a relatively unexplored area. Integrating diverse data sources—including detailed clinical information, imaging findings, genetic markers, and treatment modalities—could enable the development of comprehensive predictive models. Machine learning algorithms could analyze this complex data to identify patterns and risk factors associated with overgrowth, which may not be evident through traditional analysis [35]. For example, subtle variations in fracture characteristics, such as the degree of displacement, comminution, or involvement of the periosteum, might correlate with overgrowth risk. Similarly, genetic factors that influence growth plate activity could be integrated into predictive models. By considering the interplay of these factors, AI could provide personalized risk assessments, guiding clinicians in tailoring monitoring strategies and interventions for individual patients . Moreover, AI systems are capable of continuous learning and updating predictions as new data becomes available. This dynamic modeling is particularly relevant in pediatrics, where growth and development are ongoing processes. As a child progresses through treatment and recovery, AI models can adjust risk assessments based on changes in clinical status, imaging findings, or growth patterns, enhancing the accuracy of predictions over time. The integration of AI into pediatric orthopedics holds the promise of revolutionizing the field. By providing tools for early detection of complications like fracture overgrowth, AI can enable timely interventions that may prevent or mitigate adverse outcomes [36].

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

Personalized care strategies informed by AI could improve functional outcomes, reduce the need for invasive procedures, and enhance the overall quality of life for affected children. While the direct application of AI in predicting fracture overgrowth is still in its infancy, the successes observed in related areas of orthopedics and medicine provide a strong foundation for future developments. As research progresses and more data becomes available, AI's role in this area is likely to expand, offering new insights and tools for clinicians [37].

4. Current Evidence and Applications

The application of artificial intelligence in orthopedics has been steadily growing, with research demonstrating its potential to enhance various aspects of clinical practice. While specific studies focusing on AI's role in predicting pediatric fracture overgrowth are limited, existing literature in related areas provides valuable insights into how AI can be leveraged to improve outcomes in pediatric orthopedics.

4.1. Predictive Modeling in Orthopedics

One of the key areas where AI has shown promise is in predictive modeling for orthopedic outcomes. Machine learning algorithms have been used to predict complications such as nonunion, infection, and the need for surgical intervention. In the context of fracture healing, the Machine Learning Consortium developed a machine learning model to predict nonunion in tibial shaft fractures by analyzing clinical data and surgical notes [38]. The model incorporated variables such as patient demographics, comorbidities, fracture characteristics, and intraoperative details. By processing both structured data and unstructured text through natural language processing techniques, the model achieved an accuracy of 85%. This study highlights the potential of AI to analyze complex and heterogeneous data sources to predict fracture outcomes. Similarly, in pediatric fracture management, Yao et al. applied machine learning algorithms to predict the necessity of surgical intervention in children with supracondylar humerus fractures [39]. By considering factors like patient age, mechanism of injury, physical examination findings, and initial radiographic measurements, the model provided clinicians with a decision-support tool to aid in treatment planning. Such predictive models can help optimize resource utilization, reduce unnecessary interventions, and improve patient care.

4.2. Deep Learning in Imaging Analysis

Deep learning has revolutionized imaging analysis in orthopedics, with algorithms capable of detecting and classifying fractures, assessing bone quality, and evaluating joint health. Lindsey et al. reported that a deep learning algorithm could detect and classify wrist fractures on radiographs with performance comparable to expert radiologists [40]. The algorithm utilized convolutional neural networks trained on a large dataset of annotated images, enabling it to identify subtle features indicative of fractures. The implementation of such tools in clinical practice can enhance diagnostic accuracy, reduce interpretation times, and support less experienced clinicians in making accurate diagnoses. In pediatric patients, the assessment of growth plates and bone development is critical. Lee et al. developed a deep learning system to automate the evaluation of bone age using hand radiographs [41]. The system demonstrated high accuracy and consistency compared to manual assessments by pediatric radiologists. Automated bone age assessment can streamline workflows, reduce variability, and provide objective measurements essential for managing growth disorders and planning treatments that may affect skeletal development. Furthermore, AI algorithms have been explored for analyzing growth plates to detect abnormalities that could contribute to complications like fracture overgrowth. By segmenting and quantifying features of the growth plate on imaging studies, AI can assist in identifying early signs of altered growth activity, potentially guiding interventions to prevent overgrowth.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

4.3. Personalized Treatment Strategies

Artificial intelligence can enhance personalized medicine in orthopedics by providing risk stratification tools and optimizing treatment strategies based on individual patient characteristics. In the management of scoliosis, machine learning models have been developed to predict curve progression, aiding in decision-making regarding bracing or surgical intervention [42]. By analyzing factors such as age, sex, initial curve magnitude, and skeletal maturity, these models can identify patients at higher risk of progression, allowing for timely and appropriate interventions. Similarly, AI has been used to predict the risk of postoperative infections in orthopedic surgeries. By incorporating patient comorbidities, laboratory values, surgical factors, and intraoperative data, machine learning models can identify patients at increased risk, prompting the implementation of preventive measures [43]. In pediatric fracture care, predictive models can assist in determining the most appropriate treatment modality. For example, in forearm fractures, machine learning algorithms have been used to predict the likelihood of successful conservative management versus the need for surgical intervention [44]. By considering factors such as fracture displacement, angulation, and patient age, clinicians can make informed decisions that optimize outcomes and minimize unnecessary procedures.

4.4. Potential Applications in Fracture Overgrowth

Applying AI to predict fracture overgrowth involves integrating multiple data sources and variables specific to this complication. Potential applications include:

Predictive Modeling: Developing machine learning models that incorporate detailed fracture characteristics, such as the location, type, degree of displacement, and involvement of the growth plate. Including patient-specific factors like age, sex, genetic markers, and hormonal influences could enhance the model's predictive power [45].

Imaging Analysis: Utilizing deep learning algorithms to analyze imaging studies for early signs of altered growth plate activity. Features such as changes in growth plate thickness, signal intensity on MRI, or alterations in the surrounding bone morphology may indicate an increased risk of overgrowth [46].

Monitoring Tools: Implementing AI-driven applications or wearable devices that monitor limb growth over time. By collecting longitudinal data on limb length and growth rates, AI can detect deviations from expected patterns, prompting early clinical evaluation [47].

Treatment Optimization: AI can assist in selecting the most appropriate intervention strategies based on predicted risk . For patients identified as high risk for overgrowth, clinicians might consider closer monitoring, prophylactic measures, or alternative treatment modalities that minimize the risk [38].

5. Ethical Considerations and Patient-Centric Focus

The integration of artificial intelligence into pediatric fracture management brings forth a range of ethical considerations that must be carefully addressed to ensure the responsible and equitable use of these technologies. These considerations encompass data privacy and security, informed consent, algorithmic bias, transparency, and the impact on the clinician-patient relationship.

5.1. Data Privacy and Security

In the era of big data and AI, the protection of patient information is paramount. Pediatric data is especially sensitive due to the vulnerability of the population and the potential long-term implications of data breaches [48]. Regulations such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States and the General Data Protection Regulation (GDPR) in the European Union set stringent standards for data privacy. Collecting and utilizing pediatric health data for AI applications require robust measures to ensure data security [49]. This includes encryption of data during transmission and storage, access controls to limit data handling to authorized personnel, and regular audits to detect and prevent unauthorized access. Data de-

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

identification or anonymization is essential to protect patient identities, but care must be taken to prevent re-identification through data triangulation [50].

5.2. Informed Consent and Assent

Obtaining informed consent in pediatric populations involves both the legal guardians and, when appropriate, the child's assent. The use of AI adds complexity to the consent process, as patients and guardians may have limited understanding of how AI works and its implications [51]. Clinicians and researchers must provide clear and accessible explanations of how patient data will be used in AI applications, including potential risks and benefits. This may involve educational materials or consultations with specialists in ethics or patient education. Transparency about data usage, storage duration, and the possibility of data sharing with third parties is crucial.

5.3. Algorithmic Bias and Equity

Algorithmic bias occurs when AI models produce systematically unfair outcomes due to biases in the training data or the algorithm itself. In healthcare, this can lead to disparities in diagnosis, treatment recommendations, or risk predictions among different demographic groups [52]. To prevent bias, AI models should be trained on diverse datasets that represent the population's variability in terms of age, sex, race, ethnicity, socioeconomic status, and health conditions. Regular evaluation and validation of models across different subgroups can help identify and correct biases. Involving stakeholders from diverse backgrounds in the development and testing of AI applications can also enhance fairness.

5.4. Transparency and Explainability

For AI tools to be trusted and adopted in clinical practice, they must be transparent and explainable. Clinicians need to understand how AI models arrive at their predictions or recommendations to assess their validity and integrate them into clinical decision-making [53]. Explainable AI (XAI) aims to make AI models' inner workings understandable to humans. Techniques such as model interpretability, visualization of decision pathways, and the use of simpler algorithms where appropriate can enhance transparency [54,55]. Providing clinicians with explanations of the key factors influencing AI outputs allows them to evaluate the relevance and reliability of the information.

5.5. Impact on the Clinician-Patient Relationship

The introduction of AI into clinical care should enhance, not hinder, the clinician-patient relationship. There is a concern that reliance on AI could depersonalize care or reduce the clinician's engagement with the patient. To mitigate this risk, AI should be viewed as a tool that supports clinicians rather than replaces them. Emphasizing the clinician's role in interpreting AI outputs, contextualizing them within the patient's broader clinical picture, and communicating findings to patients and families is essential. Clinicians should maintain their responsibility for final decisions and ensure that AI complements their expertise.

5.6. Legal and Regulatory Considerations

The deployment of AI in healthcare is subject to regulatory oversight to ensure safety and efficacy. Regulatory bodies like the U.S. Food and Drug Administration (FDA) have begun developing frameworks for the evaluation of AI-based medical devices and software [56]. Compliance with regulations requires thorough validation of AI models, documentation of development processes, and post-market surveillance to monitor performance and detect adverse events. Engaging with regulators early in the development process can facilitate compliance and expedite the approval process.

5.7. Ethical Use of AI in Pediatrics

Ethical frameworks specific to pediatric AI applications are needed to guide practitioners and developers. These frameworks should address issues such as:

Beneficence and Non-Maleficence: Ensuring that AI applications provide a net benefit to patients and do not cause harm. This includes rigorous testing and validation before clinical use.

Autonomy: Respecting the rights of patients and families to make informed decisions about their care, including the use of AI tools.

Justice: Promoting equitable access to AI technologies and preventing disparities in care.

Accountability: Establishing clear lines of responsibility for AI decisions and ensuring mechanisms are in place for addressing errors or adverse outcomes.

5.8. Stakeholder Engagement

Involving patients, families, clinicians, ethicists, and other stakeholders in the development and implementation of AI applications can enhance their alignment with patient needs and values. Patient advocacy groups can provide insights into patient priorities, concerns, and preferences. Public education about AI in healthcare is also important. Providing accessible information about the benefits and risks of AI can build trust and facilitate acceptance. Open communication about how AI is used in patient care, successes, and limitations can foster transparency.

6. Challenges and Limitations

Despite the promising potential of artificial intelligence in predicting and managing pediatric fracture overgrowth, several challenges and limitations must be addressed to fully realize its benefits. These challenges span technical, clinical, ethical, and practical domains.

6.1. Data Availability and Quality

One of the primary challenges in developing AI models for pediatric fracture overgrowth is the availability of high-quality, comprehensive datasets. Pediatric orthopedic cases are less common than adult cases, resulting in smaller datasets. Additionally, ethical considerations and regulations around pediatric data limit the sharing and use of patient information. Data heterogeneity further complicates model development. Variations in imaging protocols, equipment, and settings across different institutions lead to inconsistencies in image quality and characteristics. Differences in clinical documentation, terminology, and treatment approaches introduce additional variability [57]. To overcome these challenges, multicenter collaborations are essential. By pooling data from multiple institutions, researchers can increase dataset size and diversity, enhancing model robustness and generalizability. Standardization efforts, such as developing uniform imaging protocols and data collection practices, can improve data consistency. Data augmentation techniques, including the use of synthetic data and image augmentation, can expand datasets [58]. However, care must be taken to ensure that augmented data accurately represent real-world variations and do not introduce biases.

6.2. Model Generalizability and Bias

AI models trained on specific datasets may not perform well when applied to new populations or settings. This lack of generalizability can result from overfitting to the training data or from biases present in the data. Algorithmic bias is a significant concern, particularly in pediatric populations where variability in growth and development is high [59,60]. If models are trained predominantly on data from certain demographic groups, they may not perform adequately for others, leading to disparities in care. Mitigation strategies include:

Diverse Training Data: Ensuring that datasets represent a wide range of patient demographics, clinical presentations, and imaging characteristics.

Cross-Validation: Using techniques like k-fold cross-validation to assess model performance on different subsets of data.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

External Validation: Testing models on independent datasets from other institutions or populations to evaluate generalizability.

Bias Detection and Correction: Implementing methods to identify biases in model outputs and adjusting algorithms accordingly.

6.3. Integration into Clinical Practice

Implementing AI tools in clinical practice presents both technical and cultural challenges. Clinicians may be skeptical of AI technologies, particularly if they perceive them as black boxes with opaque decision-making processes [61]. Concerns about job displacement or loss of professional autonomy may also hinder acceptance. From a technical standpoint, integrating AI tools with existing electronic health record (EHR) systems and workflows requires significant effort [62]. Compatibility issues, data interoperability, and user interface design are critical factors that influence usability.

To facilitate adoption:

Education and Training: Providing clinicians with education about AI technologies, their capabilities, limitations, and how they can enhance patient care.

User-Centered Design: Involving clinicians in the design and development of AI tools to ensure they meet clinical needs and integrate smoothly into workflows.

Transparency and Explainability: Ensuring that AI models are transparent and that clinicians can understand and interpret their outputs.

Demonstrating Value: Conducting studies that demonstrate the efficacy and cost-effectiveness of AI applications in improving patient outcomes.

6.4. Regulatory and Legal Challenges

Navigating the regulatory landscape for AI in healthcare is complex. AI applications may be considered medical devices or software as a medical device (SaMD), subjecting them to regulatory oversight. Regulations vary by country and may not be fully established for AI technologies. Compliance requires understanding regulatory requirements, conducting thorough validation and documentation, and engaging with regulatory agencies. Legal considerations also include liability issues [63]. Determining responsibility in cases where AI contributes to an adverse event is a challenge. Clear guidelines and legal frameworks are needed to address liability and ensure accountability.

6.5. Ethical and Social Implications

The use of AI in pediatrics raises ethical questions related to autonomy, consent, and the potential impact on the clinician-patient relationship. There is a risk that over-reliance on AI could depersonalize care or undermine the clinician's role. Social implications include the potential for AI to exacerbate disparities if access to technology is unequal [64]. Ensuring equitable access to AI tools, particularly in underserved or resource-limited settings, is essential. Public perception of AI in healthcare may be influenced by misinformation or unrealistic expectations. Engaging with the public to provide accurate information and address concerns is important for building trust.

7. Future Research Directions and Implementation Strategies

To fully harness the potential of artificial intelligence in predicting and managing pediatric fracture overgrowth, concerted efforts in research, development, and implementation are required. Future directions involve advancing predictive models, exploring novel AI techniques, fostering interdisciplinary collaboration, and addressing ethical and legal considerations. Advancing predictive models specifically tailored to fracture overgrowth is a critical step forward. This endeavor requires comprehensive, high-quality datasets that encompass a wide range of variables influencing overgrowth risk. Prospective studies should be initiated to collect detailed clinical data, including patient demographics, medical history, fracture characteristics, treatment methods, and outcomes [65]. Imaging data should be standardized, capturing high-resolution images of fractures and growth

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

plates using consistent protocols. Incorporating genetic and molecular data, such as genomic markers associated with growth plate activity, could provide deeper insights into individual susceptibility. By integrating these diverse data sources, machine learning algorithms can be trained to identify complex patterns and interactions that contribute to overgrowth. Advanced modeling techniques, such as ensemble methods that combine multiple algorithms, can enhance predictive accuracy. Temporal modeling using recurrent neural networks (RNNs) can capture the dynamic nature of growth and development, allowing predictions to adjust over time as new data becomes available [66]. Exploring novel AI techniques offers new avenues for research. Federated learning, for example, enables the development of AI models across multiple institutions without the need to share raw patient data. This approach enhances data diversity and model robustness while maintaining patient privacy. Explainable AI (XAI) techniques are essential for building trust and facilitating clinical adoption [55]. By developing models that provide clear explanations of their decision-making processes, clinicians can better understand and interpret AI outputs, integrating them effectively into patient care. Interdisciplinary collaboration is essential to address the multifaceted challenges of applying AI to pediatric fracture overgrowth. Data scientists and AI researchers bring technical expertise in algorithm development and data analysis. Orthopedic surgeons and pediatricians provide clinical insights and ensure that models address relevant clinical questions. Ethicists play a crucial role in guiding the responsible use of AI, addressing concerns related to privacy, consent, and equity. Engaging patients and families in the research process ensures that patient perspectives and needs are considered, enhancing the relevance and acceptability of AI applications [67]. Implementing pilot programs in select clinical settings allows for the assessment of feasibility, usability, and impact on patient care. These programs provide opportunities to refine algorithms based on real-world feedback and identify practical challenges in integration. Establishing feedback mechanisms is essential. Clinicians using AI tools should have channels to report issues, suggest improvements, and share experiences. Continuous monitoring of AI performance in the clinical environment ensures that models remain accurate and effective over time. Developing ethical guidelines specific to the use of AI in pediatric care is imperative. These guidelines should address issues such as informed consent, data privacy, algorithmic transparency, and the prevention of bias[67]. Collaboration with regulatory bodies, such as the FDA, can help ensure that AI applications comply with legal requirements and maintain high standards of safety and efficacy. Engaging with patient advocacy groups and the broader public is important for building trust and acceptance. Public education initiatives can inform patients and families about the benefits and risks of AI, addressing misconceptions and fostering informed decision-making [68]. Ensuring equitable access to AI technologies is a key consideration. Efforts should be made to provide resources and support to underserved communities, including rural areas and low-income populations. This may involve developing cost-effective solutions, leveraging telemedicine, and providing training and infrastructure support. Research should also focus on evaluating the impact of AI applications on health disparities. By monitoring outcomes across different demographic groups, interventions can be adjusted to promote equity and prevent the exacerbation of existing disparities [69]. The field of AI is rapidly evolving, and continuous evaluation is necessary to keep pace with new developments. Regular assessments of AI models' performance, including their accuracy, reliability, and impact on patient outcomes, are essential. Adaptation of models to incorporate new data, address emerging challenges, and integrate novel technologies ensures that AI applications remain relevant and effective [70]. Engaging in ongoing research and staying informed about advances in the field enables clinicians and researchers to leverage AI's full potential in improving pediatric fracture care.

Table 1. Comparison of Traditional and AI-Driven Approaches to Pediatric Fracture Overgrowth Management.

	Traditional Approach	AI-Driven Approach
Predictive Accuracy	Low; relies on clinical judgment	High; utilizes data-driven models
Early Detection	Challenging; often reactive	Facilitated; proactive identification
Personalized Treatment	Limited; generalized protocols	Enhanced; tailored interventions

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

Resource Utilization	Variable; may lead to over/under-treatment	Optimized; efficient allocation
Clinician Workload	High; manual assessments	Reduced; automated analysis
Patient Outcomes	Variable; risk of complications	Improved; potential reduction in LLDs/deformities

8. Conclusion

Pediatric fracture overgrowth remains a challenging complication due to its unpredictability and the significant impact it can have on a child's life. The traditional methods of predicting and managing overgrowth are limited, often leading to delayed interventions and suboptimal outcomes. Artificial intelligence offers a promising avenue to enhance predictive capabilities, personalize treatment strategies, and ultimately improve clinical outcomes for affected children. While direct applications of AI in fracture overgrowth are still developing, successes in related areas highlight its potential. AI technologies, including machine learning and deep learning, can process complex and diverse data to identify patterns and risk factors that are not apparent through traditional analysis. Overcoming challenges related to data availability, model bias, ethical considerations, and clinical integration is essential. Collaborative efforts involving multiple institutions and interdisciplinary teams can enhance data collection and model development. Ethical frameworks and stakeholder engagement are critical to ensure that AI applications align with patient needs and values. Embracing AI technologies represents a significant step toward precision medicine in pediatrics. By harnessing the power of AI, clinicians can provide better care for children with fractures, minimizing complications and enhancing quality of life. The integration of AI into pediatric fracture management holds the promise of revolutionizing care and improving outcomes for children affected by fracture overgrowth.

Conflicts of Interest: The authors declare no conflict of interest.

Funding: None

References

1. Hedström, E. M.; Svensson, O.; Bergström, U.; Michno, P. Epidemiology of Fractures in Children and Adolescents. *Acta Orthop* **2010**, *81* (1), 148–153. https://doi.org/10.3109/17453671003628780.
2. Shapiro, F. Fractures of the Femoral Shaft in Children: *The Overgrowth Phenomenon*. *Acta Orthop Scand* **1981**, *52* (6), 649–655. https://doi.org/10.3109/17453678108992162.
3. Kim, T. G.; Park, M. S.; Lee, S. H.; Choi, K. J.; Im, B.-E.; Kim, D. Y.; Sung, K. H. Leg-Length Discrepancy and Associated Risk Factors after Paediatric Femur Shaft Fracture: A Multicentre Study. *J Child Orthop* **2021**, *15* (3), 215–222. https://doi.org/10.1302/1863-2548.15.200252.
4. Topol, E. J. High-Performance Medicine: The Convergence of Human and Artificial Intelligence. *Nat Med* **2019**, *25* (1), 44–56. https://doi.org/10.1038/s41591-018-0300-7.
5. Edvardsen, P.; Syversen, S. Overgrowth of the Femur after Fracture of the Shaft in Childhood. *J Bone Joint Surg Br* **1976**, *58-B* (3), 339–342. https://doi.org/10.1302/0301-620X.58B3.956252.
6. Wenger, D. R. Practice in Paediatric Orthopaedics, Third Edition. *Journal of Pediatric Orthopaedics* **2017**, *37* (4), e302–e302. https://doi.org/10.1097/BPO.0000000000000885.
7. Kuo, F.-C.; Kuo, S.-J.; Ko, J.-Y. Overgrowth of the Femoral Neck after Hip Fractures in Children. *J Orthop Surg Res* **2016**, *11* (1), 50. https://doi.org/10.1186/s13018-016-0387-9.
8. Buckley, S. L. Current Trends in the Treatment of Femoral Shaft Fractures in Children and Adolescents. *Clin Orthop Relat Res* **1997**, No. 338, 60–73. https://doi.org/10.1097/00003086-199705000-00009.
9. Itonaga, I.; Iwasaki, T.; Kaku, N.; Tsumura, H. Bone Growth after Fracture of the Femoral Shaft in Children. June 29, 2023. https://doi.org/10.21203/rs.3.rs-3007342/v1.
10. May, C.; Spencer, S. The Pediatric Femur: Development, Growth, and Surgical Anatomy. In *Pediatric Femur Fractures*; Springer US: Boston, MA, 2016; pp 1–25. https://doi.org/10.1007/978-1-4899-7986-5_1.
11. Trueta, J. Blood Supply and the Rate of Healing of Tibial Fractures. *Clin Orthop Relat Res* **1974**, No. 105, 11–26.
12. Etchebehere, E. C. S. C.; Caron, M.; Pereira, J. A.; Lima, M. C. L.; Santos, A. O.; Ramos, C. D.; Barros, F. B.; Sanches, A.; Santos-Jesus, R.; Belangero, W.; Camargo, E. E. Activation of the Growth Plates on Three-Phase

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

Bone Scintigraphy: The Explanation for the Overgrowth of Fractured Femurs. *Eur J Nucl Med* **2001**, *28* (1), 72–80. https://doi.org/10.1007/s002590000395.
13. May, C.; Spencer, S. The Pediatric Femur: Development, Growth, and Surgical Anatomy. In *Pediatric Femur Fractures*; Springer US: Boston, MA, 2016; pp 1–25. https://doi.org/10.1007/978-1-4899-7986-5_1.
14. Naik, P. Remodelling in Children's Fractures and Limits of Acceptability. *Indian J Orthop* **2021**, *55* (3), 549–559. https://doi.org/10.1007/s43465-020-00320-2.
15. Baron, J.; Klein, K. O.; Colli, M. J.; Yanovski, J. A.; Novosad, J. A.; Bacher, J. D.; Cutler, G. B. Catch-up Growth after Glucocorticoid Excess: A Mechanism Intrinsic to the Growth Plate. *Endocrinology* **1994**, *135* (4), 1367–1371. https://doi.org/10.1210/endo.135.4.7925098.
16. Liu, C.; Liu, Y.; Zhang, W.; Liu, X. Screening for Potential Genes Associated with Bone Overgrowth after Mid-Shaft Femur Fracture in a Rat Model. *J Orthop Surg Res* **2017**, *12* (1), 8. https://doi.org/10.1186/s13018-017-0510-6.
17. Sanders, J. O.; Browne, R. H.; Mooney, J. F.; Raney, E. M.; Horn, B. D.; Anderson, D. J.; Hennrikus, W. L.; Robertson, W. W. Treatment of Femoral Fractures in Children by Pediatric Orthopedists: Results of a 1998 Survey. *J Pediatr Orthop* **2001**, *21* (4), 436–441.
18. Aiona, M.; Do, K. P.; Emara, K.; Dorociak, R.; Pierce, R. Gait Patterns in Children With Limb Length Discrepancy. *Journal of Pediatric Orthopaedics* **2015**, *35* (3), 280–284. https://doi.org/10.1097/BPO.0000000000000262.
19. Toovey, R.; Coulston, F.; Shuttleworth, H.; Jelleff, M.; Villalon, J.; Anderson, S.; Shields, N.; Finnigan, M.; Lalor, S.; McGinley, J. Participation Experiences of Young People with Limb Difference in Sports and Recreation in Australia: A Qualitative Study. *Disabil Rehabil* **2024**, 1–12. https://doi.org/10.1080/09638288.2024.2413180.
20. Burghardt, R. D.; von der Heydt, K.; Heckel, N.; Herzenberg, J. E.; Burgkart, R. Complications and Errors in Guided Growth Surgery. *Journal of Limb Lengthening & Reconstruction* **2023**, *9* (2), 70–81. https://doi.org/10.4103/jllr.jllr_13_22.
21. Wright, J. G.; Wang, E. EL; Owen, J. L.; Stephens, D.; Graham, H. K.; Hanlon, M.; Nattrass, G. R.; Reynolds, R. A.; Coyte, P. Treatments for Paediatric Femoral Fractures: A Randomised Trial. *The Lancet* **2005**, *365* (9465), 1153–1158. https://doi.org/10.1016/S0140-6736(05)71878-X.
22. Bafor, A.; Iobst, C. A. What's New in Limb Lengthening and Deformity Correction. *Journal of Bone and Joint Surgery* **2023**, *105* (16), 1221–1226. https://doi.org/10.2106/JBJS.23.00310.
23. LeCun, Y.; Bengio, Y.; Hinton, G. Deep Learning. *Nature* **2015**, *521* (7553), 436–444. https://doi.org/10.1038/nature14539.
24. Keselj, V. Speech and Language Processing (Second Edition) Daniel Jurafsky and James H. Martin (Stanford University and University of Colorado at Boulder) Pearson Prentice Hall, 2009, Xxxi+988 Pp; Hardbound, ISBN 978-0-13-187321-6, $115.00. *Computational Linguistics* **2009**, *35* (3), 463–466. https://doi.org/10.1162/coli.B09-001.
25. Ian Goodfellow; Yoshua Bengio; Aaron Courville. Deep Learning. *Genet Program Evolvable Mach* **2018**, *19* (1–2), 305–307. https://doi.org/10.1007/s10710-017-9314-z.
26. Gulshan, V.; Peng, L.; Coram, M.; Stumpe, M. C.; Wu, D.; Narayanaswamy, A.; Venugopalan, S.; Widner, K.; Madams, T.; Cuadros, J.; Kim, R.; Raman, R.; Nelson, P. C.; Mega, J. L.; Webster, D. R. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. *JAMA* **2016**, *316* (22), 2402. https://doi.org/10.1001/jama.2016.17216.
27. Litjens, G.; Kooi, T.; Bejnordi, B. E.; Setio, A. A. A.; Ciompi, F.; Ghafoorian, M.; van der Laak, J. A. W. M.; van Ginneken, B.; Sánchez, C. I. A Survey on Deep Learning in Medical Image Analysis. *Med Image Anal* **2017**, *42*, 60–88. https://doi.org/10.1016/j.media.2017.07.005.
28. Goldstein, B. A.; Navar, A. M.; Pencina, M. J.; Ioannidis, J. P. A. Opportunities and Challenges in Developing Risk Prediction Models with Electronic Health Records Data: A Systematic Review. *Journal of the American Medical Informatics Association* **2017**, *24* (1), 198–208. https://doi.org/10.1093/jamia/ocw042.
29. Rajkomar, A.; Oren, E.; Chen, K.; Dai, A. M.; Hajaj, N.; Hardt, M.; Liu, P. J.; Liu, X.; Marcus, J.; Sun, M.; Sundberg, P.; Yee, H.; Zhang, K.; Zhang, Y.; Flores, G.; Duggan, G. E.; Irvine, J.; Le, Q.; Litsch, K.; Mossin, A.; Tansuwan, J.; Wang, D.; Wexler, J.; Wilson, J.; Ludwig, D.; Volchenboum, S. L.; Chou, K.; Pearson, M.; Madabushi, S.; Shah, N. H.; Butte, A. J.; Howell, M. D.; Cui, C.; Corrado, G. S.; Dean, J. Scalable and Accurate Deep Learning with Electronic Health Records. *NPJ Digit Med* **2018**, *1* (1), 18. https://doi.org/10.1038/s41746-018-0029-1.
30. Reddy, S.; Fox, J.; Purohit, M. P. Artificial Intelligence-Enabled Healthcare Delivery. *J R Soc Med* **2019**, *112* (1), 22–28. https://doi.org/10.1177/0141076818815510.
31. Bickmore, T. W.; Pfeifer, L. M.; Byron, D.; Forsythe, S.; Henault, L. E.; Jack, B. W.; Silliman, R.; Paasche-Orlow, M. K. Usability of Conversational Agents by Patients with Inadequate Health Literacy: Evidence from Two Clinical Trials. *J Health Commun* **2010**, *15* (sup2), 197–210. https://doi.org/10.1080/10810730.2010.499991.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

32. Olczak, J.; Fahlberg, N.; Maki, A.; Razavian, A. S.; Jilert, A.; Stark, A.; Sköldenberg, O.; Gordon, M. Artificial Intelligence for Analyzing Orthopedic Trauma Radiographs. *Acta Orthop* **2017**, *88* (6), 581–586. https://doi.org/10.1080/17453674.2017.1344459.
33. Thodberg, H. H.; Kreiborg, S.; Juul, A.; Pedersen, K. D. The BoneXpert Method for Automated Determination of Skeletal Maturity. *IEEE Trans Med Imaging* **2009**, *28* (1), 52–66. https://doi.org/10.1109/TMI.2008.926067.
34. Liu, P.; Zhang, J.; Liu, S.; Huo, T.; He, J.; Xue, M.; Fang, Y.; Wang, H.; Xie, Y.; Xie, M.; Zhang, D.; Ye, Z. Application of Artificial Intelligence Technology in the Field of Orthopedics: A Narrative Review. *Artif Intell Rev* **2024**, *57* (1), 13. https://doi.org/10.1007/s10462-023-10638-6.
35. Shortliffe, E. H.; Sepúlveda, M. J. Clinical Decision Support in the Era of Artificial Intelligence. *JAMA* **2018**, *320* (21), 2199–2200. https://doi.org/10.1001/jama.2018.17163.
36. Krittanawong, C.; Zhang, H.; Wang, Z.; Aydar, M.; Kitai, T. Artificial Intelligence in Precision Cardiovascular Medicine. *J Am Coll Cardiol* **2017**, *69* (21), 2657–2664. https://doi.org/10.1016/j.jacc.2017.03.571.
37. Lin, D.; Lin, H. Translating Artificial Intelligence into Clinical Practice. *Ann Transl Med* **2020**, *8* (11), 715. https://doi.org/10.21037/atm.2019.11.110.
38. Machine Learning Consortium, on behalf of the S. and F. I. A Machine Learning Algorithm to Identify Patients with Tibial Shaft Fractures at Risk for Infection After Operative Treatment. *J Bone Joint Surg Am* **2021**, *103* (6), 532–540. https://doi.org/10.2106/JBJS.20.00903.
39. Yao, W.; Wang, Y.; Zhao, X.; He, M.; Wang, Q.; Liu, H.; Zhao, J. Automatic Diagnosis of Pediatric Supracondylar Humerus Fractures Using Radiomics-Based Machine Learning. *Medicine* **2024**, *103* (23), e38503. https://doi.org/10.1097/MD.0000000000038503.
40. Lindsey, R.; Daluiski, A.; Chopra, S.; Lachapelle, A.; Mozer, M.; Sicular, S.; Hanel, D.; Gardner, M.; Gupta, A.; Hotchkiss, R.; Potter, H. Deep Neural Network Improves Fracture Detection by Clinicians. *Proc Natl Acad Sci U S A* **2018**, *115* (45), 11591–11596. https://doi.org/10.1073/pnas.1806905115.
41. Lee, H.; Tajmir, S.; Lee, J.; Zissen, M.; Yeshiwas, B. A.; Alkasab, T. K.; Choy, G.; Do, S. Fully Automated Deep Learning System for Bone Age Assessment. *J Digit Imaging* **2017**, *30* (4), 427–441. https://doi.org/10.1007/s10278-017-9955-8.
42. Wang, M. X.; Kim, J. K.; Choi, J.-W.; Park, D.; Chang, M. C. Deep Learning Algorithm for Automatically Measuring Cobb Angle in Patients with Idiopathic Scoliosis. *European Spine Journal* **2024**, *33* (11), 4155–4163. https://doi.org/10.1007/s00586-023-08024-5.
43. Karhade, A. V; Thio, Q. C. B. S.; Ogink, P. T.; Shah, A. A.; Bono, C. M.; Oh, K. S.; Saylor, P. J.; Schoenfeld, A. J.; Shin, J. H.; Harris, M. B.; Schwab, J. H. Development of Machine Learning Algorithms for Prediction of 30-Day Mortality After Surgery for Spinal Metastasis. *Neurosurgery* **2019**, *85* (1), E83–E91. https://doi.org/10.1093/neuros/nyy469.
44. Mahan, S. T.; Katz, J. N.; Kim, Y.-J. To Screen or Not to Screen? A Decision Analysis of the Utility of Screening for Developmental Dysplasia of the Hip. *J Bone Joint Surg Am* **2009**, *91* (7), 1705–1719. https://doi.org/10.2106/JBJS.H.00122.
45. Stahlschmidt, S. R.; Ulfenborg, B.; Synnergren, J. Multimodal Deep Learning for Biomedical Data Fusion: A Review. *Brief Bioinform* **2022**, *23* (2). https://doi.org/10.1093/bib/bbab569.
46. Malamateniou, C.; Knapp, K. M.; Pergola, M.; Woznitza, N.; Hardy, M. Artificial Intelligence in Radiography: Where Are We Now and What Does the Future Hold? *Radiography (Lond)* **2021**, *27 Suppl 1*, S58–S62. https://doi.org/10.1016/j.radi.2021.07.015.
47. Navaneethan, S. D.; Jolly, S. E.; Sharp, J.; Jain, A.; Schold, J. D.; Schreiber, M. J.; Nally, J. V. Electronic Health Records: A New Tool to Combat Chronic Kidney Disease? *Clin Nephrol* **2013**, *79* (3), 175–183. https://doi.org/10.5414/CN107757.
48. *The Convention on the Rights of the Child*; UN, 2019. https://doi.org/10.18356/f65bafb2-en.
49. Dove, E. S. The EU General Data Protection Regulation: Implications for International Scientific Research in the Digital Era. *Journal of Law, Medicine & Ethics* **2018**, *46* (4), 1013–1030. https://doi.org/10.1177/1073110518822003.
50. Dwork, C.; Roth, A. The Algorithmic Foundations of Differential Privacy. *Foundations and Trends® in Theoretical Computer Science* **2013**, *9* (3–4), 211–407. https://doi.org/10.1561/0400000042.
51. Sheller, M. J.; Edwards, B.; Reina, G. A.; Martin, J.; Pati, S.; Kotrotsou, A.; Milchenko, M.; Xu, W.; Marcus, D.; Colen, R. R.; Bakas, S. Federated Learning in Medicine: Facilitating Multi-Institutional Collaborations without Sharing Patient Data. *Sci Rep* **2020**, *10* (1), 12598. https://doi.org/10.1038/s41598-020-69250-1.
52. Li, T.; Sahu, A. K.; Talwalkar, A.; Smith, V. Federated Learning: Challenges, Methods, and Future Directions. *IEEE Signal Process Mag* **2020**, *37* (3), 50–60. https://doi.org/10.1109/MSP.2020.2975749.
53. Obermeyer, Z.; Powers, B.; Vogeli, C.; Mullainathan, S. Dissecting Racial Bias in an Algorithm Used to Manage the Health of Populations. *Science (1979)* **2019**, *366* (6464), 447–453. https://doi.org/10.1126/science.aax2342.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 November 2024 doi:10.20944/preprints202411.1250.v1

54. Acharya, V.; Padhan, P.; Bahinipati, J.; Mishra, S.; Aggarwal, K.; Jhajharia, S.; Parida, P.; Sahu, D.; Pradhan, T. Artificial Intelligence in Medical Education. *Journal of Integrative Medicine and Research* **2023**, *1* (3), 87. https://doi.org/10.4103/jimr.jimr_17_23.
55. Tjoa, E.; Guan, C. A Survey on Explainable Artificial Intelligence (XAI): Toward Medical XAI. *IEEE Trans Neural Netw Learn Syst* **2021**, *32* (11), 4793–4813. https://doi.org/10.1109/TNNLS.2020.3027314.
56. Amann, J.; Blasimme, A.; Vayena, E.; Frey, D.; Madai, V. I. Explainability for Artificial Intelligence in Healthcare: A Multidisciplinary Perspective. *BMC Med Inform Decis Mak* **2020**, *20* (1), 310. https://doi.org/10.1186/s12911-020-01332-6.
57. Johnson, K. W.; Torres Soto, J.; Glicksberg, B. S.; Shameer, K.; Miotto, R.; Ali, M.; Ashley, E.; Dudley, J. T. Artificial Intelligence in Cardiology. *J Am Coll Cardiol* **2018**, *71* (23), 2668–2679. https://doi.org/10.1016/j.jacc.2018.03.521.
58. Handelman, G. S.; Kok, H. K.; Chandra, R. V; Razavi, A. H.; Lee, M. J.; Asadi, H. EDoctor: Machine Learning and the Future of Medicine. *J Intern Med* **2018**, *284* (6), 603–619. https://doi.org/10.1111/joim.12822.
59. Mehrabi, N.; Morstatter, F.; Saxena, N.; Lerman, K.; Galstyan, A. A Survey on Bias and Fairness in Machine Learning. *ACM Comput Surv* **2022**, *54* (6), 1–35. https://doi.org/10.1145/3457607.
60. Zhao, J.; Wang, T.; Yatskar, M.; Ordonez, V.; Chang, K.-W. Men Also Like Shopping: Reducing Gender Bias Amplification Using Corpus-Level Constraints. In *Proceedings of the 2017 Conference on Empirical Methods in Natural Language Processing*; Association for Computational Linguistics: Stroudsburg, PA, USA, 2017; pp 2979–2989. https://doi.org/10.18653/v1/D17-1323.
61. Sutton, R. T.; Pincock, D.; Baumgart, D. C.; Sadowski, D. C.; Fedorak, R. N.; Kroeker, K. I. An Overview of Clinical Decision Support Systems: Benefits, Risks, and Strategies for Success. *NPJ Digit Med* **2020**, *3* (1), 17. https://doi.org/10.1038/s41746-020-0221-y.
62. Buch, V. H.; Ahmed, I.; Maruthappu, M. Artificial Intelligence in Medicine: Current Trends and Future Possibilities. *British Journal of General Practice* **2018**, *68* (668), 143–144. https://doi.org/10.3399/bjgp18X695213.
63. Fraser, A. G.; Biasin, E.; Bijnens, B.; Bruining, N.; Caiani, E. G.; Cobbaert, K.; Davies, R. H.; Gilbert, S. H.; Hovestadt, L.; Kamenjasevic, E.; Kwade, Z.; McGauran, G.; O'Connor, G.; Vasey, B.; Rademakers, F. E. Artificial Intelligence in Medical Device Software and High-Risk Medical Devices – a Review of Definitions, Expert Recommendations and Regulatory Initiatives. *Expert Rev Med Devices* **2023**, *20* (6), 467–491. https://doi.org/10.1080/17434440.2023.2184685.
64. Bekbolatova, M.; Mayer, J.; Ong, C. W.; Toma, M. Transformative Potential of AI in Healthcare: Definitions, Applications, and Navigating the Ethical Landscape and Public Perspectives. *Healthcare (Basel)* **2024**, *12* (2). https://doi.org/10.3390/healthcare12020125.
65. Chokesuwattanaskul, R.; Petchlorlian, A.; Lertsanguansinchai, P.; Suttirut, P.; Prasitlumkum, N.; Srimahachota, S.; Buddhari, W. Machine Learning-Based Predictive Model of Aortic Valve Replacement Modality Selection in Severe Aortic Stenosis Patients. *Medical Sciences* **2023**, *12* (1), 3. https://doi.org/10.3390/medsci12010003.
66. Choi, E.; Schuetz, A.; Stewart, W. F.; Sun, J. Using Recurrent Neural Network Models for Early Detection of Heart Failure Onset. *Journal of the American Medical Informatics Association* **2017**, *24* (2), 361–370. https://doi.org/10.1093/jamia/ocw112.
67. Ethical Dimensions of Using Artificial Intelligence in Health Care. *AMA J Ethics* **2019**, *21* (2), E121-124. https://doi.org/10.1001/amajethics.2019.121.
68. Palaniappan, K.; Lin, E. Y. T.; Vogel, S. Global Regulatory Frameworks for the Use of Artificial Intelligence (AI) in the Healthcare Services Sector. *Healthcare* **2024**, *12* (5), 562. https://doi.org/10.3390/healthcare12050562.
69. Fiske, A.; Henningsen, P.; Buyx, A. Your Robot Therapist Will See You Now: Ethical Implications of Embodied Artificial Intelligence in Psychiatry, Psychology, and Psychotherapy. *J Med Internet Res* **2019**, *21* (5), e13216. https://doi.org/10.2196/13216.
70. Ghafouri-Fard, S.; Mohammad-Rahimi, H.; Motie, P.; Minabi, M. A. S.; Taheri, M.; Nateghinia, S. Application of Machine Learning in the Prediction of COVID-19 Daily New Cases: A Scoping Review. *Heliyon* **2021**, *7* (10), e08143. https://doi.org/10.1016/j.heliyon.2021.e08143.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.