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Artificial intelligence in orthodontics: Part 3 – Potential limitations and pitfalls



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Artificial intelligence is now involved in many aspects of our everyday life. In digital orthodontic practice in particular, practitioners are constantly and mostly unknowingly confronted with different levels of implementations of artificial intelligence. The present article, the third in a three-part series, will seek to shed light on some of these algorithms using common examples from a standard orthodontic digital workflow.

Introduction

Artificial intelligence (AI) appears to be becoming the next industrial revolution and is set to influence every part of our

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everyday life^{1,2}. After a long process of development, this technology may now be ready for clinical use, particularly in highly specialised fields like orthodontics^{3,4}. AI has been adopted in various domains in medicine and with a respectable degree of success in some of these, both in more manageable fields like nephropathology⁵, thyroid cancer diagnosis⁶ and histopathology⁷, and more complex ones like health care⁸. One example is the online application Ada (Ada Health, Berlin, Germany) for medical diagnosis⁹.

Following a long period of development¹⁰, successful applications of AI have been demonstrated in dentistry for caries detection, risk assessment of oral cancer, differentiation of periodontitis forms and orthognathic surgery¹¹⁻¹³. Some authors have even predicted that AI will prove to be a disruptive innovation in dentistry¹⁴.

In orthodontics, the use of AI of any kind has been described in scientific reports for aspects of diagnosis, automated cephalometric tracing, growth estimation, recognition of facial proportions, extraction decision, appliance selection and estimation of treatment results^{15,16}. A broad spectrum of AI algorithms have been used (including pattern matching, deep learning networks, fuzzy clustering and convolutional and artificial neural networks); thus, there does not seem to have been a 'one size fits all' AI algorithm until now¹⁷.

Orthodontic treatment is not only about the correct use of appliances; it also involves a sophisticated interactive process to identify the treatment goal and how to success-

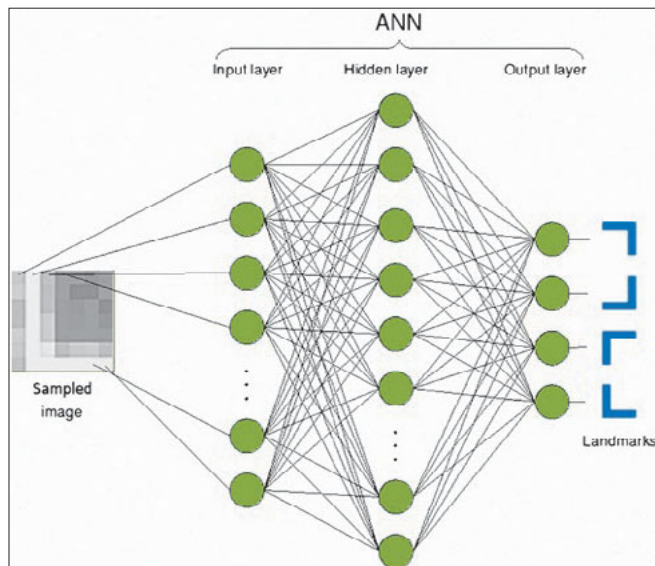


Fig 1 Simplified example of a neural network with a hidden layer (https://commons.wikimedia.org/wiki/File:Artificial_neural_network_image_recognition.png) by Cyberbotics, 29 January 2009. ANN, artificial neural network.

fully reach and maintain this goal with the patient. The question is, what are the possible aims for AI in orthodontics? The steps involved in orthodontic treatment are valid for all such treatment approaches independent of the appliance used, whether aligners or fixed appliances, and are as follows:

- patient history;
- clinical examination and conversation;
- paraclinical findings, such as cast analysis, cephalometrics and radiographic analysis;
- problem list (medical, dentistry-related, psychosocial, functional, skeletal, dentoalveolar, dental);
- definition of treatment goals through shared decision making in agreement with the patient;
- treatment plan, selection of biomechanics and appliances;
- delivery of treatment and continuous diagnostics (complications, quality assurance);
- retention of the treatment result and observation;
- patient-related outcome: was the treatment successful?

Individual aspects like tooth segmentation in virtual models and CBCT reconstruction may be supported by AI, as can the entire process or combinations of single tasks like diagnostics¹⁸⁻²⁰. In the future, fully AI-guided orthodontic treat-

ment may be a possibility. The previous parts in this series examined the basic principles and current applications of AI in aligner orthodontics²¹.

Aim

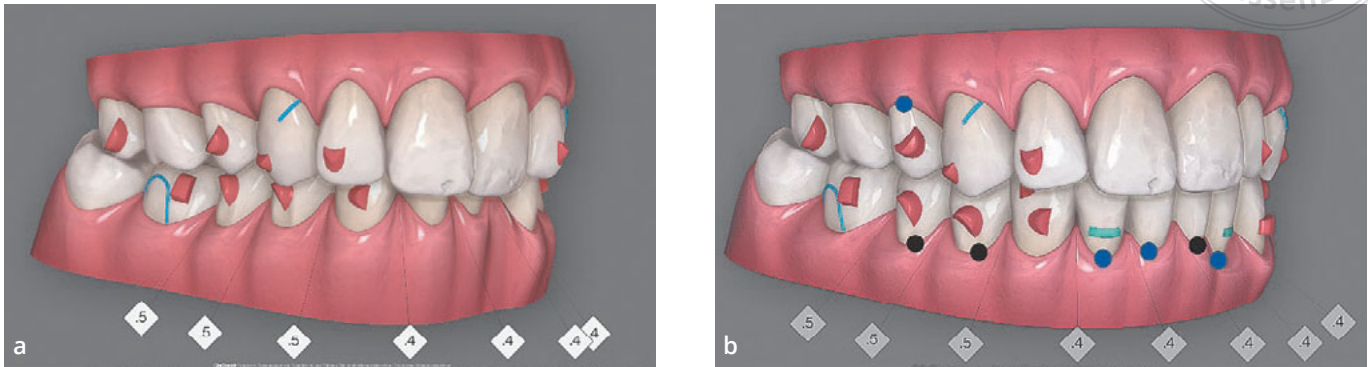
In an extensive literature search using PubMed, Web of Science and Google Scholar, state of the art information on the topics addressed below was identified to examine the potential pitfalls and limitations in the application of AI in orthodontics.

Data for AI training as a source of bias

All available AI systems need quantitative data for training. These data may come from image files like radiographs or 3D stereolithography (STL) files from scans, or other sources of information like results from the cephalometric analysis. According to these input data, neural networks learn, for example, to distinguish extraction from non-extraction cases (outcome variable); in this example, however, the network learns the philosophy held by the orthodontist who treated the training cases towards extraction or non-extraction. The information relating to which factors are important for the network's decision making is invisible, in the hidden layers (Fig 1). Extraction in orthodontics has been a topic of discussion for over 100 years, and we see surprisingly high differences in the extraction rates in different countries and orthodontic 'schools'²²⁻²⁵. All decisions are based on comparable diagnostic sources of information and result in completely different decisions and outcomes.

Another example is racial bias exhibited by commercial software for predicting complex health needs²⁶. The examined algorithm used in the US health care system exhibited significant racial bias when predicting health care costs, caused by the fact that access to care is unequal²⁶.

Most higher-level AI processes require a significant database containing massive amounts of high-quality data to develop more robust, varied and reliable approaches. This is akin to clinical experience in the real world. Unfortunately, few clinics or universities have such rich databases. Although millions of patients undergo orthodontic treatment each year, it is unlikely that a large amount of this data



Figs 2a-b ClinCheck (Align Technology, San Jose, CA, USA) of the treatment plan for a 58-year-old patient, leaving a reverse articulation uncorrected.

will be shared and made available for the development of AI approaches in the near future due to laws governing privacy and data use. This issue could be resolved by requesting patients' permission to use their data in this manner from this point on. Similarly, patients may consent to use of collective data in which their dataset is just one component. Even with adequate data, AI approaches will be challenged by the diversity of biology. Atypical and unforeseen dysmorphologies and variations in growth and development will continue to limit algorithms based on prior data.

Treatment goal: optimal occlusion according to the six keys is not always worthwhile

To the present authors' understanding, an ideal occlusion, often defined according to the six keys to normal occlusion outlined by Andrews²⁷ that were originally created for straight-wire appliances, correlates with a balanced dynamic occlusion, harmonic muscular function and optimal aesthetics; however, this may be only partially true. For instance, closure of a hereditary medial diastema may be desirable to the practitioner, but from the patient's perspective, it may be an individual characteristic that has to be preserved. Thus, even if AI is capable of arranging the teeth like beads on a necklace, this tooth position may not necessarily be functional or ideal, and it may not reflect the patient's primary concern²⁸.

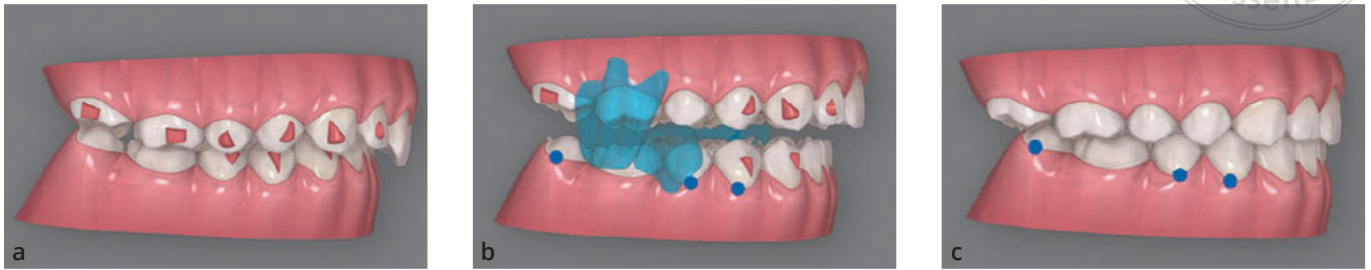
It is important to consider that virtual treatment planning using AI often includes micromovement in the posterior region, which from an occlusal point of view does not improve but rather worsens the occlusal bite situation. In this case too, it is important to avoid unnecessary movements and, if required, to fix the teeth virtually. In some cases involving adult patients, the optimal treatment goal may be to leave a bilateral reverse articulation untouched (Fig 2).

Furthermore, the treatment goal is different in disabled patients or those affected by cleft lip and palate or syndromes. For example, as Bergland et al²⁹ wrote, "... despite great efforts, ideal results cannot always be achieved in the orthodontic treatment of cleft patients".

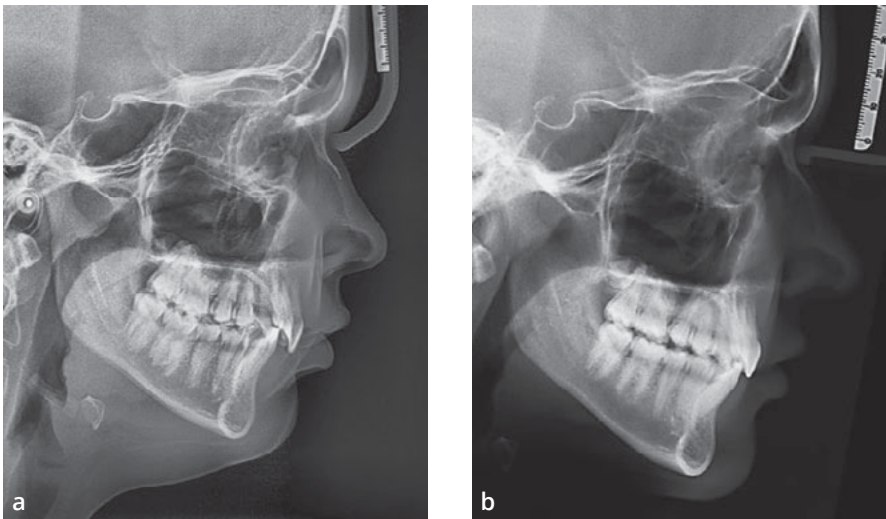
Definition of the visual treatment objective (VTO) is a crucial step towards achieving success in aligner orthodontics. The biological-anatomical borders must be respected (for instance, the anterior limit according to Segner and Hasund³⁰) and the patients' functional and aesthetic demands must be met. It is questionable whether AI can anticipate this.

Growth, growth pattern and reaction to bite jumping in growing patients

In contrast to the situation observed in the earlier years of aligner orthodontics, an increasing number of children and teenagers are now treated with aligners^{31,32}. This coincides with a period of growth and development that is both phys-



Figs 3a-c ClinCheck images illustrating use of a bite jumping appliance (precision wings, Align Technology).



Figs 4a-b Corresponding cephalometric images showing the reduction of horizontal overlap and successful functional influence of precision wings from the case presented in Fig 3.

ical and mental. For several years, attempts were made to generate predictive values for growth and reaction to treatment like functional appliance therapy. A recent study by Kök et al³³ successfully demonstrated AI-supported classification of cervical vertebra ratios on cephalometric radiographs.

The present authors believe that the individual reaction to fixed or removable bite jumping appliances (Figs 3 and 4), and also to aligner orthodontics, will always be a source of uncertainty. Generalised effectiveness can be expected, but high individual variability must be taken into account³⁴. Based on this information, growth may be predictable, but the individual reaction to the bite jumping appliance may be uncertain.

Individual rate of tooth movement

For decades, orthodontists have known that patients exhibit individual differences in the speed of their tooth movement. From in vivo observations, a higher rate of tooth movement can be seen in the maxilla and a decrease with age has been noted, although the statistical power is limited. Patients can be considered as “fast movers” or “slow movers”³⁵. Until now, there has been no accurate indication of how to predict the rate of tooth movement on an individual level. In addition, diet and consumption of medication may influence tooth movement due to their side effects on tissue systems³⁶. In aligner orthodontics, the time between aligner changes may be highly dependent on the individual. In fixed appliance treatment, these effects on the metabolism on a cellular level can be observed in different reactions to levelling arches or when closing spaces.



Figs 5a-c An example of unsuccessful aligner treatment. There were problems with attachment loss and poor oral hygiene, and serious compliance issues. The photographs were taken after 1 year of treatment with 11 aligners and following discontinuation of treatment.

Patient-related factors (pharmaceutical, previous trauma, etc.)

It is well known that medication exerts a significant influence on the rate of tooth movement³⁷. Several substances are suspected to decrease the rate of orthodontic tooth movement, such as thromboxane, leukotrienes and non-steroidal anti-inflammatory drugs (NSAIDs) (acetylsalicylic acid, indomethacin, ibuprofen).

There is evidence, though not always statistically significant, that prostacyclin, prostaglandins and corticosteroids may increase the rate of tooth movement. The results are derived mainly from experimental studies in animals, however, and transmissibility to humans is uncertain; for this reason, the effects are not reliably predictable.

In addition, vitamin D is suspected to enhance tooth movement and stability of tooth position³⁸. Consequently, it may be assumed that medication can influence the biological reaction and affect the amount of tooth movement that occurs at each aligner stage.

A history of dental trauma can interfere with orthodontic treatment. Pulp vitality, replacement resorption and surface resorption may be affected, but the scientific evidence is inconclusive³⁹. Successful prediction of such events with the help of AI appears unlikely.

Compliance

The most detailed diagnosis and sophisticated treatment concepts can only be realised with optimal patient compliance. Adult aligner patients tend to wear their aligners exemplarily, with few exceptions; in children or teenagers, however, this is not always the case (Fig 5). Compliance in-

dicators may help, but there may be hidden factors that influence cooperation. Compliance is a general phenomenon in orthodontics that also applies to maintaining oral hygiene or wearing elastics when using multibracket appliances.

Social indices are weak predictors of patient cooperation. Different psychological scales in combination may be able to predict future compliance, but only for around 17% of cases⁴⁰. Nevertheless, it is likely that the motivation of the patient and, where appropriate, their parents through the orthodontist and careful support during the treatment process with close personal contact would be difficult to replace with AI.

Periodontal status and biomechanical considerations

For any orthodontic treatment, an inflammation-free periodontium is *conditio sine qua non*. As the number of older patients increases, so too does the number of cases of attachment loss that are observed (Fig 6). It is well known that attachment loss changes the force–moment ratios for tooth movement dramatically, and the centre of resistance also changes⁴¹. In conventional fixed orthodontics, carefully adjusted segmented arch mechanics are necessary in the majority of such cases. The biomechanical principles of forces and anchorage remain the same when using aligners. Companies like 3D Predict (New York, NY, USA) make great promises, but high-quality studies are required to prove their claims of outstanding results. As the underlying biological process for periodontitis is complex and not only about measuring attachment loss, it remains questionable whether these problems can be solved by AI in the short term.

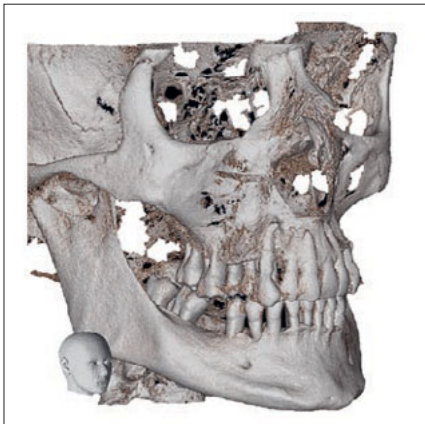


Fig 6 3D reconstruction from CBCT in a patient with advanced attachment loss. The situation of each tooth can be individual; thus, anchorage quality and the force level required vary.

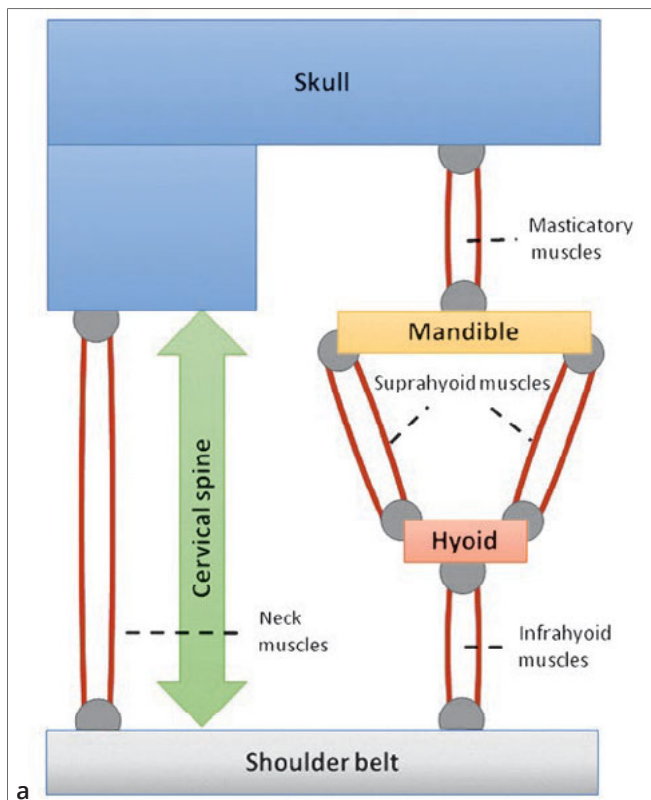
Muscular function, temporomandibular joint, tongue function, speech and habits

Muscular function and all its related concepts are composed of various aspects that are barely amenable to objectification. For instance, the composition of muscles with regard to fast- and slow-twitch fibres is difficult to measure

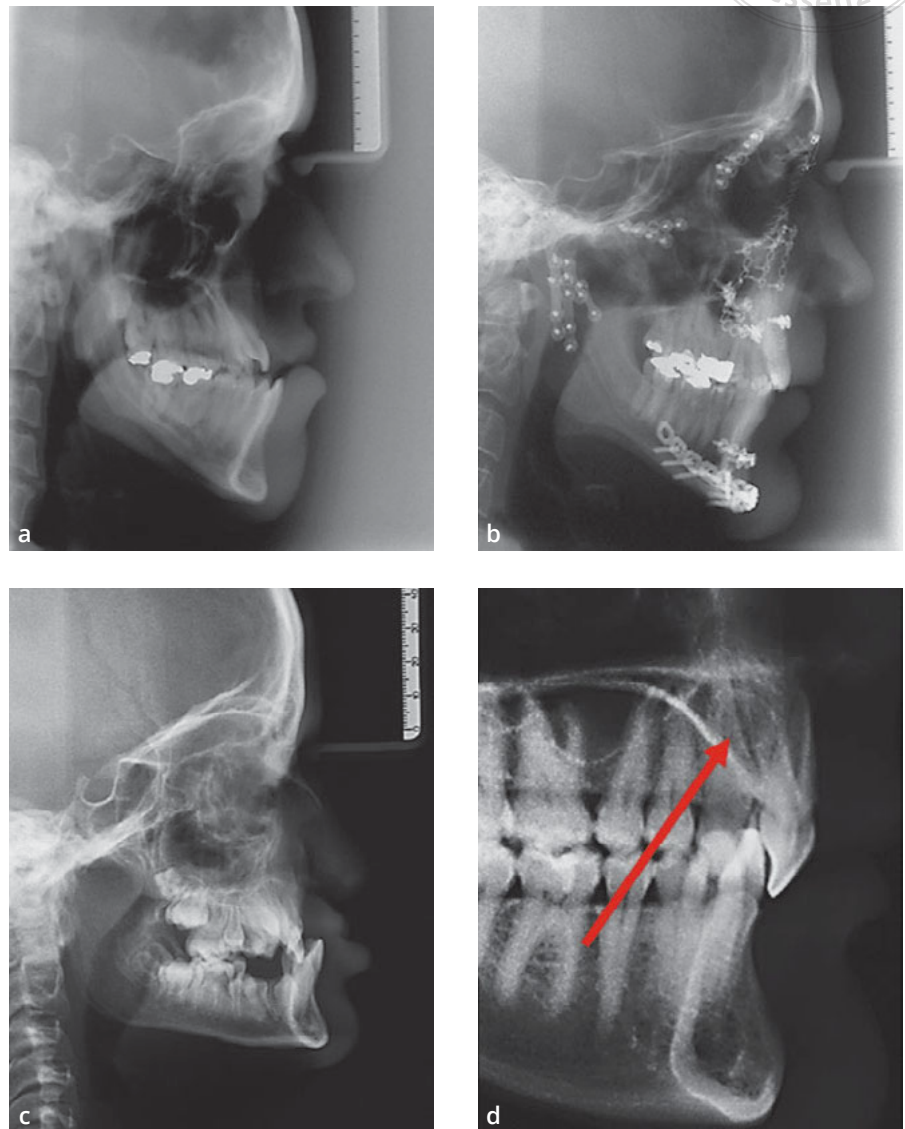
in vivo. Even after decades of research, the interrelations of the human body's muscular chains, fascia, joints and neuromuscular control loops are not well understood. If the interaction of breathing, speaking and chewing as basic functions of the orofacial system is added, the situation becomes even more complicated.

The musculoskeletal system, including the temporomandibular joint, connects the orofacial, suprahyoid and infrahyoid muscles to the whole body via the cervical spine (Fig 7). The scientific evidence for this is still low, but should not be denied⁴²⁻⁴⁴.

Since the advent of orthodontics, practitioners have known that tongue function is not only a relevant factor in children regarding long-term stability and reaction to treatment efforts, for example in open bite cases^{45,46}. The relation between the perioral muscles and the tongue creates a functional space for the development of occlusion. Dysfunctions or habits can lead to types of malocclusion like open bite and reverse articulation. Balanced function is also a prerequisite for a stable treatment result. As functional aspects are difficult to quantify, it is challenging to integrate them into an AI system.



Figs 7a-b Schematic display of the connection between cranial and cervical anatomical structures and example of tongue dysfunction and the effect on the alveolar process and tooth position (adapted from Koeck⁴⁷).



Figs 8a-d Examples of cephalometric radiographs with deviations from the 'norm'. **(a)** A patient with Crouzon syndrome and altered midfacial morphology. **(b)** Post-traumatic image captured prior to orthodontic therapy to reconstruct the occlusion and improve facial balance. **(c)** A cleft lip and palate patient with a severe midface growth deficiency and a horizontal growth pattern. **(d)** Random finding of a nasopalatal cyst.

Cephalometric analysis with AI: a gift to orthodontics?

The idea of automated AI-supported tracing of cephalometric radiographs is appealing as it offers the promise of saving time. Several systems have been shown to detect landmarks in a stable, precise and reproducible manner⁴⁸. As such, the AI-generated results can be trusted according to current knowledge; however, the present authors have some concerns. Radiographic diagnostics does not only set landmarks for orthodontics but also involves careful observation of anatomical structures. Even if cases are rare, it is necessary to identify pathological conditions in the full field of view. In

addition, structural and morphological analysis of growth patterns are independent of landmarks^{30,49}. On the other hand, with the advanced software that is now available, it only takes a few minutes to click the points on the monitor, partially under magnification, but in this period of time, the practitioner is thinking about the case in question. The present authors believe that every additional minute the orthodontist spends carefully collecting information and developing an individual treatment plan benefits the patient.

In addition, there is a whole group of patients that are not reflected in any of the applications available today, namely those who need special care due to cleft lip and palate, syndromes, trauma or cancer (Fig 8).



Psychological aspects affecting the patient

It is well known that the orthodontist–patient relationship may have a significant impact on treatment outcomes⁵⁰. The patient's reaction to the new situation that alters the oral equilibrium through orthodontic treatment is highly individual. The experience of pain is not correlated with the force applied. The amount of attention the patient receives from the practitioner is also a factor that determines the patient-related success of treatment. Disturbances to this relationship lead to failure to attend appointments and follow instructions, and ultimately to poor results.

Oral habits are also related to patients' psychology. Numerous publications have studied oral habits and their treatment. For instance, thumb-sucking is seen as a response to an emotional or interpersonal disturbance⁴⁵. It is highly unlikely that the broad spectrum of psychological relations and social interactions could be replaced by AI.

Ethical implications: who is responsible?

According to a recent review of 178 publications regarding AI in dentistry, 12% of all the investigated studies mentioned potential ethical issues⁵¹. The Montreal Declaration⁵² may provide a useful guideline, with ten items concerning ethical aspects when using AI (prudence, equity, privacy and intimacy, responsibility, democratic participation, solidarity, diversity inclusion, well-being, respect for autonomy and sustainable development). The current literature suggests that AI systems perform well, but most studies were only validated internally. Future studies should focus on the question of how trustworthy and reproducible AI is.

In clinical situations, the orthodontist should take a critical look at AI-based setups or treatment suggestions. The final responsibility lies with the dental practitioner. Researchers and developers of AI systems should identify and communicate about ethical issues. Furthermore, the environmental impact has been more or less unknown until now.

Discussion

AI is currently in a transition stage from use in experimental research to clinical routine⁵³. The first complex systems for diagnostics are emerging^{54,55}. In the previous sections, the present authors highlighted some areas that might cause uncertainty or error when using any system based on AI. A potential danger is automated estimation of treatment need using AI; Shan et al⁵⁶ state that patients' perception and expectations cannot be replaced.

Some authors believe that AI may need to be regulated through authorities in the future⁵⁷. Data also need to be controlled strictly to prevent bias as, according to Zou and Schiebinger⁵⁸, "biases in the data often reflect deep and hidden imbalances in institutional infrastructures and social power relations". Amidst the euphoria surrounding AI, it is vital to remember the concerns related to data security and the handover of complex decisions to AI software⁵⁹.

At present, AI can facilitate cephalometrics and analysis of cervical vertebral maturation and save time. Most ideas for use of AI still do not relate to daily practice. Whether the promise of AI-supported orthodontics will ever be realised is uncertain and depends on future prospective studies⁶⁰. The overall goal of AI in orthodontics can be a synergy or convergence of the orthodontist's professional competence and AI's ability to achieve better patient care^{61,62}. Although AI can automate certain steps and assist dental practitioners in performing diagnoses and treatment planning, in no case will it replace practitioners' knowledge and competence⁶³. For example, the present authors believe it would be dangerous to delegate decisions like extractions to AI, and this would also have ethical and legal consequences^{64,65}.

In aligner orthodontics, simulation of the treatment objective, forces and biomechanics for efficient staging is complex and involves far more than defining an optimal occlusion⁶⁶. Against the background of the factors discussed, the value of automated setups seems questionable⁶⁷. This also applies to setup-based planning in lingual orthodontics and labial customised multibracket appliances.

Orthodontists should be aware that for a significant group of patients who require special care and attention, such as disabled patients or those with cleft lip and palate or syndromes, potential AI systems may offer misleading recommendations.



For those wishing to examine the subject in more detail, the publications by Mohammad-Rahimi et al⁶⁸, Monill-González et al⁶⁹ and Schwendicke et al⁵⁹ are recommended.

Amidst all the enthusiasm and our desire for perfection, we should bear in mind that the treatment goal is a functional optimum as described by Hotz⁷⁰ that is and will remain valid in the future: “the result of treatment to be aimed for in the individual case, which can be achieved without risk of recurrence, without damage to the dentition, in a time and by means that are tolerable for the patient”.

We end this article series on the status, trends in and limitations of AI in (aligner) orthodontics with a quote from Oscar Wilde: “Progress is the realisation of utopias”⁷¹.

Conclusion

We can expect exciting future developments in orthodontics with a combination of digital technology and AI, but ultimately we also need to develop our natural intelligence and imagination. AI can help to avoid planning errors, monitor treatment and support the orthodontist, and we recommend that all orthodontists follow the future development of its applications closely. Taking into account all the risks and weak points of AI can assist us in the same way a helpful colleague might in identifying potential problems or suggesting treatment alternatives. The aim of AI-supported orthodontics is to continuously improve therapy for patients' benefit.

Declaration

The authors declare that they have no competing interests. The present study is in accordance with the ethical standards of the institutional and national ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

- Kampakaki E, Papahristou E. Digital intelligence as prerequisite of artificial intelligence's integration in the clothing industry 4.0. In: Giannakopoulos G, Galiotou E, Vasillas N (eds). Workshops of the 11th EETN Conference on Artificial Intelligence 2020 Co-located with the 11th EETN Conference on Artificial Intelligence (SETN 2020), 2–4 Sep 2020, Athens, Greece. Aachen: CEUR Workshop Proceedings, 2021;36–41.
- Kinkel S, Baumgartner M, Cherubini E. Prerequisites for the adoption of AI technologies in manufacturing – Evidence from a worldwide sample of manufacturing companies. *Technovation* (in press).
- McCulloch WS, Pitts W. A logical calculus of the ideas immanent in nervous activity. *Bull Math Biophys* 1943;5:115–133.
- Hammond RM, Freer TJ. Application of a case-based expert system to orthodontic diagnosis and treatment planning: A review of the literature. *Aust Orthod J* 1996;14:150–153.
- Becker JU, Mayerich D, Padmanabhan M, et al. Artificial intelligence and machine learning in nephropathology. *Kidney Int* 2020;98:65–75.
- Verburg F, Reiners C. Sonographic diagnosis of thyroid cancer with support of AI. *Nat Rev Endocrinol* 2019;15:319–321.
- Tizhoosh HR, Pantanowitz L. Artificial intelligence and digital pathology: Challenges and opportunities. *J Pathol Inform* 2018;9:1–6.
- He J, Baxter SL, Xu J, Xu J, Zhou X, Zhang K. The practical implementation of artificial intelligence technologies in medicine. *Nat Med* 2019;25:30–36.
- Ada Health website. www.ada.com. Accessed 3 April 2022.
- Park WJ, Park JB. History and application of artificial neural networks in dentistry. *Eur J Dent* 2018;12:594–601.
- Chen YW, Stanley K, Att W. Artificial intelligence in dentistry: Current applications and future perspectives. *Quintessence Int* 2020;51:248–257.
- Chhetri P, Devi N, Lepcha K. View of artificial intelligence in dentistry. *J Clin Res Comm Health* 2021;1:3–8.
- Choi HI, Jung SK, Baek SH, et al. Artificial intelligent model with neural network machine learning for the diagnosis of orthognathic surgery. *J Craniofac Surg* 2019;30:1986–1989.
- Joda T, Yeung AWK, Hung K, Zitzmann NU, Bornstein MM. Disruptive innovation in dentistry: What it is and what it could be next. *J Dent Res* 2021;100:448–453.
- Akdeniz BS, Tosun ME. A review of the use of artificial intelligence in orthodontics. *J Exp Clin Med* 2021;38:157–162.
- Tanikawa C, Yamashiro T. Development of novel artificial intelligence systems to predict facial morphology after orthognathic surgery and orthodontic treatment in Japanese patients. *Sci Rep* 2021;11:1–11.
- Bichu YM, Hansa I, Bichu AY, Premjani P, Flores-Mir C, Vaid NR. Application of artificial intelligence and machine learning in orthodontics: A scoping review. *Prog Orthod* 2021;22:1–11.
- Huang K, Yeung AWK, Tanaka R, Bornstein MM. Current applications, opportunities, and limitations of AI for 3D imaging in dental research and practice. *Int J Environ Res Public Health* 2020;17:1–18.
- Huang HC, Wang YC, Wang YC. Applications of artificial intelligence in orthodontics. *Taiwanese J Orthod* 2020;32:85–92.
- Borohovitz CL, Abraham Z, Redmond WR. The diagnostic advantage of a CBCT-derived segmented STL rendition of the teeth and jaws using an AI algorithm. *J Clin Orthod* 2021;55:361–369.
- Schupp W, Abu-Tarif-A, Haubrich J, Elkholy F, Mah J, Krey KF. Artificial intelligence in orthodontics: Part 1. *J Aligner Orthod* 2021;5:251–258.
- Xie X, Wang L, Wang A. Artificial neural network modeling for deciding if extractions are necessary prior to orthodontic treatment. *Angle Orthod* 2010;80:262–266.
- Rinchuse DJ, Busch LS, DiBagno D, Cozzani M. Extraction treatment, part 1: The extraction vs. nonextraction debate. *J Clin Orthod* 2014;48:753–760.
- Jung SK, Kim TW. New approach for the diagnosis of extractions with neural network machine learning. *Am J Orthod Dentofac Orthop* 2016;149:127–133.
- Del Real A, Del Real O, Sardina S, Oyonarte R. Use of automated artificial intelligence to predict the orthodontic need of extractions. *Korean J Orthod* 2022;52:102–111.



26. Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. *Science* 2019;366:447–453.
27. Andrews LF. The six keys of normal occlusion. *Am J Orthod* 1972;62:296–309.
28. Van der Linden FPGM. Sheldon Friel memorial lecture 2007: Myths and legends in orthodontics. *Eur J Orthod* 2008;30:449–468.
29. Bergland O, Semb G, Abyholm FE. Elimination of the residual alveolar cleft by secondary bone grafting and subsequent orthodontic treatment. *Cleft Palate J* 1986;23:175–205.
30. Segner D, Hasund A. Individualisierte Kephalmetrie, ed 4. Hamburg: Dietmar Segner Verlag und Vertrieb, 2003.
31. Meuli S, Cozza P, Lombardo E. Management of a mesiodens in mixed dentition with Invisalign First. *J Aligner Orthod* 2021;5:131–137.
32. Haubrich J, Schupp W. Invisalign treatment in early years to avoid potential extraction treatments – Case reports. *J Aligner Orthod* 2018;2:39–52.
33. Kök H, Izgi MS, Acilar AM. Evaluation of the artificial neural network and naive Bayes models trained with vertebra ratios for growth and development determination. *Turk J Orthod* 2020;34:2–9.
34. Burhan AS, Nawaya FR. Dentoskeletal effects of the bite-jumping appliance and the twin-block appliance in the treatment of skeletal Class II malocclusion: a randomized controlled trial. *Eur J Orthod* 2015;37:330–337.
35. Giannopoulou C, Dudic A, Pandis N, Kiliaridis S. Slow and fast orthodontic tooth movement: An experimental study on humans. *Eur J Orthod* 2016;38:404–408.
36. Krishnan V, Davidovitch Z. The effect of drugs on orthodontic tooth movement. *Orthod Craniofac Res* 2006;9:163–171.
37. Bartzela T, Türp JC, Motschall E, Maltha JC. Medication effects on the rate of orthodontic tooth movement: A systematic literature review. *Am J Orthod Dentofacial Orthop* 2009;135:16–26.
38. Almoammar K. Vitamin D and orthodontics: An insight review. *Clin Cosmet Investig Dent* 2018;10:165–170.
39. Kindelan SA, Day PF, Kindelan JD, Spencer JR, Duggal MS. Dental trauma: An overview of its influence on the management of orthodontic treatment. Part 1. *J Orthod* 2008;35:68–78.
40. Serogl HG, Klages U, Pempera J. On the prediction of dentist-evaluated patient compliance in orthodontics. *Eur J Orthod* 1992;14:463–468.
41. Cortez MAF, Bourauel C, Reichert C, Jäger A, Reimann S. Numerical and biomechanical analysis of orthodontic treatment of recovered periodontally compromised patients [epub ahead of print 16 July 2021]. *J Orofac Orthop* doi: 10.1007/s00056-021-00324-z.
42. Doepel M, Le Bell Y, Liljestrom MR, Vahlberg T, Nilner M. Oral appliance treatment reduces headache in myofascial TMD patients with localized and widespread pain. *J Craniomandib Func* 2021;13:277–293.
43. Kuzmanovic P, Dodic S, Lazik V, Trajkovic G, Milic N, Milic B. Occlusal stabilization splint for patients with temporomandibular disorders: Meta-analysis of short and long term effects. *PLoS One* 2017;12:e0171296.
44. Meyer G. Short clinical screening procedure for initial diagnosis of temporomandibular disorders. *J Aligner Orthod* 2018;2:91–98.
45. Chakraborty P, Dhingra R, Chandra P, Tandon R, Azam A, Chauhan A. Tongue: Anatomy, functions and orthodontic implications. *Indian J Orthod Dentofacial Res* 2020;6:1–4.
46. Swinehart DR. The importance of the tongue in the development of normal occlusion. *Am J Orthod* 1950;36:813–830.
47. Koeck B (ed). *Implantologie: Praxis der Zahnheilkunde, Band 8. Funktionsstörungen des Kauorgans, ed 3.* Munich: Urban & Schwarzenberg, 1989.
48. Kunz F, Stellzig-Eisenhauer A, Zeman F, Boldt J. Artificial intelligence in orthodontics: Evaluation of a fully automated cephalometric analysis using a customized convolutional neural network. *J Orofac Orthop* 2020;81:52–68.
49. Björk A. Prediction of mandibular growth rotation. *Am J Orthod* 1969;55:585–599.
50. Ukra A, Bennani F, Farella M. Psychological aspects of orthodontics in clinical practice. Part one: Treatment-specific variables. *Prog Orthod* 2011;12:143–148.
51. Mörch CM, Atsu S, Cai W, et al. Artificial intelligence and ethics in dentistry: A scoping review. *J Dent Res* 2021;100:1452–1460.
52. Université de Montréal. The Montreal Declaration for a Responsible Development of Artificial Intelligence. <https://www.montrealdeclaration-responsibleai.com/>. Accessed 12 April 2021.
53. Kelly CJ, Karthikesalingam A, Suleyman M, Corrado G, King D. Key challenges for delivering clinical impact with artificial intelligence. *BMC Med* 2019;17:1–9.
54. Li P, Kong D, Tang T, et al. Orthodontic treatment planning based on artificial neural networks. *Sci Rep* 2019;9:1–9.
55. Liu J, Chen Y, Li S, Zhao Z, Wu Z. Machine learning in orthodontics: Challenges and perspectives. *Adv Clin Exp Med* 2021;30:1065–1074.
56. Shan T, Tay FR, Gu L. Application of artificial intelligence in dentistry. *J Dent Res* 2021;100:232–244.
57. Wu E, Wu K, Daneshjou R, Ouyang D, Ho DE, Zou J. How medical AI devices are evaluated: Limitations and recommendations from an analysis of FDA approvals. *Nat Med* 2021;27:582–584.
58. Zou J, Schiebinger L. Design AI so that it's fair. *Nature* 2018;559:324–326.
59. Schwendicke F, Samek W, Krois J. Artificial intelligence in dentistry: Chances and challenges. *J Dent Res* 2020;99:769–774.
60. Pethani F. Promises and perils of artificial intelligence in dentistry. *Aust Dent J* 2021;66:124–135.
61. Topol EJ. High-performance medicine: The convergence of human and artificial intelligence. *Nat Med* 2019;25:44–56.
62. Thurzo A, Kurilová V, Varga I. Artificial intelligence in orthodontic smart application for treatment coaching and its impact on clinical performance of patients monitored with AI-TeleHealth system. *Healthcare (Basel)* 2021;9:1–23.
63. Tandon D, Rajawat J. Present and future of artificial intelligence in dentistry. *J Oral Biol Craniofac Res* 2020;10:391–396.
64. Etemad L, Wu TH, Heiner P, et al. Machine learning from clinical data sets of a contemporary decision for orthodontic tooth extraction. *Orthod Craniofac Res* 2021;24:193–200.
65. Khanagar SB, Al-Ehaideb A, Vishwanathai S, et al. Scope and performance of artificial intelligence technology in orthodontic diagnosis, treatment planning, and clinical decision-making – A systematic review. *J Dent Sci* 2021;16:482–492.
66. Machado RM. Space closure using aligners. *Dental Press J Orthod* 2020;25:85–100.
67. Retrouvey JM. The role of AI and machine learning in contemporary orthodontics. *APOS Trends Orthod* 2021;11:74–80.
68. Mohammad-Rahimi H, Nadimi M, Rohban MH, Shamsoddin E, Lee VY, Motamedian SR. Machine learning and orthodontics, current trends and the future opportunities: A scoping review. *Am J Orthod Dentofacial Orthop* 2021;160:170–192.
69. Monill-González A, Rovira-Calatayud L, d'Oliveira NG, Ustrell-Torrent JM. Artificial intelligence in orthodontics: Where are we now? A scoping review. *Orthod Craniofac Res* 2021;24(suppl 2):6–15.
70. Hotz R. *Orthodontie in der täglichen Praxis, ed 3.* Bern: Huber, 1961.
71. Vaid NR. Artificial intelligence (AI) driven orthodontic care: A quest toward utopia. *Semin Orthod* 2021;27:57–61.