



UNESP - Universidade Estadual Paulista
“Júlio de Mesquita Filho”
Faculdade de Odontologia de Araraquara



Pedro Henrique José de Oliveira

**Aplicação da inteligência artificial na predição de cirurgia ortognática ou
ortodontia convencional**

Araraquara

2023



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ortodontia convencional**

Dissertação apresentada à Universidade Estadual Paulista (Unesp), Faculdade de Odontologia, Araraquara para obtenção do título de Mestre em Ciências Odontológicas, na Área de Ortodontia

Orientador: Prof. Dr. Jonas Bianchi

Araraquara

2023

O48a

Oliveira, Pedro Henrique José de

Aplicação da inteligência artificial na predição de cirurgia ortognática ou ortodontia convencional / Pedro Henrique José de Oliveira. -- Araraquara, 2023

83 p.

Dissertação (mestrado) - Universidade Estadual Paulista (Unesp), Faculdade de Odontologia, Araraquara

Orientador: Jonas Bianchi

1. Ortodontia. 2. Inteligência artificial. 3. Cirurgia ortognática.
I. Título.

Sistema de geração automática de fichas catalográficas da Unesp. Biblioteca da Faculdade de Odontologia, Araraquara. Dados fornecidos pelo autor(a).

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Aplicação da inteligência artificial na predição de cirurgia ortognática ou ortodontia convencional.

Comissão Julgadora

Qualificação para obtenção do grau de Mestre em Ciências Odontológicas

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Dedico este trabalho a meu pai, Melchiades Alves de Oliveira Junior, que desde pequeno despertou em mim o amor pela ortodontia e pela docência. Meu grande professor desde o dia que nasci e que levarei todos os ensinamentos até meus últimos dias. A minha mãe, Patricia Beraldo José de Oliveira, que sempre me incentivou a ser um sonhador, acreditar em mim e colocar amor em tudo que faço. Dedico também a minha família, amigos e todos aqueles que, de alguma forma, contribuem, torcem e acreditam nas minhas conquistas! Tem um pouco de cada um de vocês aqui!

AGRADECIMENTOS

Agradeço primeiramente a **Deus**, por permitir que eu concluísse esta etapa, sempre me guiando durante bons e maus momentos.

Ao meu orientador e amigo, **Prof. Dr. Jonas Bianchi**, minha eterna gratidão. Obrigado por acreditar no meu potencial, me conduzir, guiar, ensinar e apoiar durante todas as etapas desta pesquisa. Agradeço a orientação amigável, serena e segura. Tenho uma admiração enorme pelo profissional e pessoa que és. Um exemplo de dedicação, conhecimento e amor pela profissão!

Aos meus pais, **Melchiades Alves de Oliveira Junior e Patricia Beraldo José de Oliveira**, agradeço por todo apoio, amor, presença e compreensão. Vocês sonham junto comigo e me dão condições de realizar meus sonhos. Obrigado por tanto! Faltam palavras para descrever o quanto sou grato por tudo que fazem por mim! Essa conquista é de nossa família!

A minha família, especialmente meus avós **Sebastião Antonio José Filho, Olga Beraldo José e Wanda Gabriel (in memoriam)**, por sempre cuidarem tanto de mim, me mostrarem os melhores caminhos, me criarem junto a meus pais e por criarem um apeço pela educação em nossa família.

A minha namorada, **Juliana Fernanda da Silva**, por tanto amor, carinho e cuidado. Obrigado por entender o quão importante esta jornada é para mim, apoiar meus passos, ajudar nas minhas inseguranças e tornar tudo mais leve. Agradeço imensamente seu apoio incondicional e por sempre me motivar e mostrar que sou capaz!

Ao **Prof. Dr. Luiz Gonzaga Gandini Junior** por sempre compartilhar tanto sua experiência, abrir portas, acreditar em mim e me fazerem crescer tanto como ortodontista e ser humano. Me espelho muito no senhor! Um agradecimento especial também à **Profª. Drª. Marcia E. R. Gandini** pelo carinho conosco, por compartilhar tantos momentos bons e conhecimentos.

Ao **Prof. Dr. João Roberto Gonçalves** por orientação durante todas as fases deste trabalho! Obrigado por sempre me fazer enxergar as coisas por uma outra perspectiva e trazer reflexões importantes, tanto para esta dissertação como para meus atendimentos.

A todos os professores do Departamento de Ortodontia, **Prof. Dr. Ary dos Santos Pinto, Prof. Dr. Dirceu Barnabé Raveli e Prof. Dr. Helder Baldi Jacob**. Obrigado por todo conhecimento compartilhado e por sempre mostrarem as melhores diretrizes. Vocês são grandes exemplos para todos nós.

A todos que colaboraram diretamente com a construção dos artigos desta dissertação, **Prof^a. Dr^a. Lucia Cevidanes, Prof^a. Dr^a. Karine Evangelista, Prof. Dr. Antonio Augusto Campanha, Prof^a. Dr^a. Claudia Toyama, Tengfei Li, Haoyue Li e Dr. Guilherme Paladini Feltrin**, por toda a prontidão, dedicação e carinho com este trabalho.

A todos os **funcionários do Departamento de Clínica Infantil**, assim como os da **Faculdade de Odontologia de Araraquara – UNESP**, por sempre proporcionarem um ótimo ambiente de trabalho e organizarem esta faculdade de forma maravilhosa.

A todos os **meus amigos de Pós-Graduação e Graduação da FOAr**. Esta jornada ficou bem melhor e mais simples tendo amigos como vocês ao meu lado.

A **meus professores, e hoje colegas de ensino, do Instituto Clínico de Especialidades Odontológicas – ICEO**, por me ensinarem tanto sobre ortodontia e confiarem em mim em todos os momentos. Levarei sempre os ensinamentos de cada um junto comigo.

A todos os **meus amigos de Campinas**. Obrigado por sempre se manterem próximos e presentes, mesmo com a distância e compromissos.

As colaboradoras da nossa clínica e instituto, **Bianca, Camila, Luciana, Maria Eduarda e Rafaela** por toda a ajuda no cotidiano e me ajudarem a conciliar meus estudos com meus atendimentos

A **Prof^a. Dr^a. Larissa Gonçalves Cunha Rios** por gentilmente aceitar fazer parte da banca desta dissertação.

Ao **programa de Pós-graduação em Ciências Odontológicas da Faculdade de Odontologia de Araraquara – UNESP**, representado pela coordenadora Prof^a. Dr^a. Andreia Bufalino e pelo vice coordenador Prof. Dr. Milton Carlos Kuga.

Por fim, agradeço a **Faculdade de Odontologia de Araraquara, da Universidade Estadual Paulista “Júlio de Mesquita Filho” – UNESP**, nas pessoas do diretor Prof. Dr. Edson Alves de Campos e vice-diretora Prof^a. Dr^a. Patrícia P. Nordi Sasso Garcia. Foi uma honra ter sido acolhido novamente nesta casa onde me formei. Tenho muito orgulho e amor por esta faculdade.

“A menos que modifiquemos nossa maneira de pensar, não seremos capazes de resolver os problemas causados pela forma como nos acostumamos a ver o mundo.”
Albert Einstein*

* Einstein A. Como vejo o mundo. Rio de Janeiro: Nova Fronteira; 1981.

Oliveira PHJ. Aplicação da inteligência artificial na predição de cirurgia ortognática ou ortodontia convencional [dissertação de mestrado]. Araraquara: Faculdade de Odontologia da UNESP; 2023.

RESUMO

Quando as alterações esqueléticas, oclusais e estéticas apresentadas são tão severas que não podem ser tratadas com ortodontia compensatória, deve ser realizado tratamento ortodôntico-cirúrgico para que possa restabelecer a harmonia facial e função para o paciente. No entanto, para alguns casos limítrofes, o conhecimento empírico de profissionais experientes pode ser um fator decisivo na tomada de decisão. Hoje, com aumento de dados e melhorias tecnológicas é possível utilizar modelos de inteligência artificial (*machine learning*) como suporte para tomadas de decisão. O objetivo principal desse estudo foi de avaliar se modelos de inteligência artificial podem ser utilizados como auxílio na tomada de decisão em ortodontia, por meio de dois artigos. No primeiro artigo, o objetivo foi de revisar sistematicamente como a inteligência artificial pode ser aplicada ao diagnóstico e planejamento ortodôntico utilizando exames radiológicos e testar se diferentes modelos de inteligência virtual eram capazes de prever o tratamento. O segundo artigo, avaliou se um paciente necessita ou não de cirurgia ortognática a partir dos valores obtidos em telerradiografias laterais, previamente ao tratamento avaliando tanto tecido duro e mole em pacientes classe II ou classe III esquelética, por meio de diferentes algoritmos de inteligência artificial. Como resultados, o primeiro artigo resultou em 12 estudos divididos em 5 categorias diferentes de diagnóstico: osteoartrite de articulação temporomandibular, maturação óssea, classificação esquelética, síndrome da apnéia obstrutiva do sono e necessidade de cirurgia ortognática. Em geral, a IA aumentou a acurácia do diagnóstico. Os resultados para o segundo artigo mostraram que o modelo combinado de algoritmos de *machine learning* apresentou alta performance para todos os grupos (amostra total, classe II e classe III), sendo que os pacientes classe III mostraram valores superiores para acurácia (0.873), *F1-score* (0.8) e curva AUC (0.923). Concluindo assim que a inteligência artificial pode ser utilizada como auxílio na tomada de decisão para tratamento ortodôntico e cirúrgicos.

Palavras - chave: Ortodontia. Inteligência artificial. Cirurgia ortognática.

Oliveira PHJ. Application of artificial intelligence in the prediction of orthognathic surgery or conventional orthodontics [dissertação de mestrado]. Araraquara: Faculdade de Odontologia da UNESP; 2023.

ABSTRACT

When skeletal, occlusal, and aesthetical discrepancies are too severe that cannot be treated with compensatory orthodontics, orthodontic preparation to orthognathic surgery must be done to restore the patient's facial harmony and function. However, some borderline patients can be a challenge. For these cases, the experience and clinician's empirical knowledge plays an important role in the decision-making process for planning. The increasing amount of data and technological advancements can make it possible for artificial intelligence (AI) models (machine learning) to support the decision-making process. Thus, this study aimed to evaluate if artificial intelligence models can be used as an auxiliary tool to predict if a patient needs orthognathic surgery, by presenting two papers. The first paper's objective was to systematically review how artificial intelligence can be applied to orthodontic diagnosis and planning using X-ray-based images and test if different AI models were capable to predict the treatment. The second paper's objectives were to evaluate the machine learning models' capacity to predict if class II and class III patients need orthognathic surgery using soft and hard tissue values obtained from lateral radiographs. As results, the first article resulted in 12 studies that were divided in 5 different categories: TMJ osteoarthritis, skeletal maturation/development, skeletal pattern, obstructive sleep apnea, and orthognathic surgery. The results for the second article showed that the combined machine learning prediction model showed top ranked performance in the testing-set for all groups (entire sample, class II and class III) and the best results were observed for class III validation-set (accuracy 0.873, F1-score 0.8, and AUC 0.923). In conclusion, artificial intelligence can be used as an aid for orthognathic surgery decision.

Keywords: Orthodontics. Artificial intelligence. Orthognathic surgery.

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1 INTRODUÇÃO

Na Ortodontia, a má-oclusão é objeto de estudo há muitos anos. Existem diversas formas de classificá-la com o intuito de padronizar diagnóstico e facilitar a comunicação entre profissionais. A classificação de Angle de 1899, amplamente utilizada, é baseada na relação antero-posterior dos primeiros molares permanentes, em: Classe I, Classe II e Classe III, com suas divisões e subdivisões¹. Lischer, em 1911, citado por Moyers² complementou esta classificação, ao considerar as posições individuais de cada dente dentro da arcada.

Andrews³, em 1974, publicou uma classificação para determinar a relação oclusal de forma mais ampla denominada seis chaves de oclusão normal, onde na primeira chave está englobada a classificação de Angle. Em seu livro de lançamento da técnica Straigh-wire: o conceito e o aparelho, as más-oclusões foram divididas em normais e anormais, sendo que a má-oclusão normal é aquela que pode ser tratada pela ortodontia. Já a anormal é toda má-oclusão que a ortodontia é incapaz de solucionar sem auxílio de outras especialidades, como por exemplo a cirurgia ortognática.

Reis⁴, em 2001, pesquisou sobre a análise facial por meio da Pirâmide da Agradabilidade Estética e classificou os indivíduos em esteticamente agradáveis, aceitáveis ou desagradáveis com o intuito de facilitar a comunicação com pacientes e leigos. De acordo com o artigo, o papel do ortodontista é manter os pacientes dentro do limite entre agradável e aceitável e, para isso, pacientes considerados desagradáveis devem se submeter a procedimentos ortodôntico-cirúrgicos. Capellozza⁵ em 2004, utilizou o padrão de crescimento craniofacial como principal fator etiológico e concluiu que, quando a evolução genética tem tendência negativa e impacta tanto oclusão como a face do paciente, a cirurgia ortognática deverá ser associada ao tratamento ortodôntico.

Apesar de diversas formas de classificar a má-oclusão é consenso dizer que indivíduos com grandes discrepâncias esqueléticas que impossibilitam o tratamento ortodôntico compensatório, devem ser submetidos a tratamentos ortodônticos cirúrgicos para a correção da oclusão, estética e função.

No entanto, análises quantitativas são necessárias para classificar a verdadeira necessidade de tratamento seja ortodôntico ou cirúrgico. A literatura

apresenta tanto métodos quantitativos quanto qualitativos para avaliar as discrepâncias, seja por meio de radiografias, modelos, análise de tecidos moles, tomografias computadorizadas e análises faciais subjetivas^{4,6-11}. Tais métodos auxiliam o ortodontista a compreender melhor a localização, etiologia e gravidade do problema do paciente. Estes elementos somados a idade e a agradabilidade facial do paciente, são determinantes para que o ortodontista trace o prognóstico e plano de tratamento⁵.

O tratamento do paciente poderá ser ortodôntico corretivo para pacientes com bases ósseas e face equilibradas; ortodôntico compensatório para pacientes com aceitáveis discrepâncias esqueléticas e faciais; ortodôntico descompensatório cirúrgico para pacientes com grandes discrepâncias esqueléticas e desagradabilidade facial que impossibilitam que o tratamento ortodôntico sozinho restabeleça estética, oclusão e função^{4,5,12-15}.

Um grande desafio no tratamento compensatório são os pacientes borderline. Para estes pacientes existem duas possibilidades de tratamento: a compensação dentária, que consiste na inclinação axial dos dentes no sentido contrário ao erro esquelético do paciente, ou o tratamento com descompensação ortodôntica e cirurgia ortognática. Nestes casos, a tomada de decisão dependerá da experiência clínica, análises científicas quantitativas e qualitativas do ortodontista e também da percepção do problema pelo paciente, relacionada a sua auto-estima e problemas sociais¹⁶.

Steiner¹⁷, em 1959, demonstrou como deveriam se posicionar os incisivos de um paciente tratado ortodonticamente dentro da normalidade, para que seja possível alcançar aquilo que os autores denominam como uma “face agradável”, a partir do ângulo ANB, inclinação dos incisivos superiores e inferiores, e a suas distâncias da linha NA e NB. Esclarecem também que a depender da má oclusão, os valores de normalidade são alterados para se obter resultado satisfatórios ao final. Além disso, os autores demonstram estimativas que consideram ser ideais para compensações ortodônticas de pacientes com alterações esqueléticas, na tentativa de estabelecer limites de movimentações dentárias. Apesar de concordar que padrões de normalidade e limites de compensações a partir de valores pré-fixados podem não ser a melhor forma de ditar um tratamento, os autores ressaltam que, para profissionais menos experientes, os gráficos podem servir de guias na tomada de decisão¹⁷.

Outros estudos já foram feitos na tentativa de quantificar a necessidade de cirurgia ortognática. Um estudo clássico nesta tomada de decisão é o envelope de diagnóstico de Proffit¹⁸. No entanto, medidas isoladas, geralmente, não são capazes de definir um diagnóstico final correto, por isso alguns autores descreveram correlações cefalométricas com o objetivo de auxiliar no planejamento e tomada de decisão de um caso^{19,20}. Hoje, com o advento de novas tecnologias, como as ancoragens esqueléticas e tomografias, ampliaram-se os limites da ortodontia, possibilitando maiores compensações^{18,21,22}.

Novas tecnologias não se limitam a técnicas ou exames. Temos, hoje, um alto volume de dados dentro da área da odontologia graças a digitalização e a demanda maior por diagnósticos precisos, possibilitando assim que novas técnicas sejam agregadas ao diagnóstico^{23,24}. Porém, esse alto volume de exames e dados, são subutilizados, quando avaliados individualmente. Nesse contexto, a inteligência artificial (IA), mais especificamente a área de *Machine Learning* (ML), é uma das novas ferramentas que vem sendo introduzida na pesquisa odontológica. Com esta metodologia, é possível fazer com que programas sejam capazes de auxiliar profissionais em suas tomadas de decisão, por meio de fórmulas, equações e integração dos dados (variáveis)²⁵⁻³¹.

Diferentemente das abordagens tradicionais, a inteligência artificial não se baseia em estudos de hipóteses ou depende de parâmetros restritos. Ela utiliza padrões de dados e é capaz de avaliar simultaneamente múltiplas variáveis e fazer interações entre elas. Isto possibilita que computadores formem regras pela repetição dos valores, assemelhando-se, assim, ao processo de aprendizado humano^{24,32,33}.

Yu *et al.*³⁴, buscaram utilizar redes neurais convolucionais (RNC) para realizar classificação esquelética de pacientes a partir de telerradiografias laterais. Foram utilizadas imagens de 5890 pacientes para classificar os pacientes de acordo com suas alterações sagitais e verticais. Para análises sagitais, os principais pontos avaliados pelo modelo estavam na região de incisivos e do ponto nasio, apontando para possível relação com o ângulo ANB e a medida AB-Oclusal. Já para as alterações verticais, a base do crânio e o ângulo da mandíbula foram os principais fatores levados em consideração. Para todas as métricas avaliadas, houve resultados maiores que 90% quando

avaliado sagital e vertical de forma única. Quando separados, a acurácia para a alteração vertical foi maior.

Choi *et al.*³², demonstraram uma técnica de machine learning com o objetivo de desenvolver um novo modelo de inteligência artificial capaz de tomar a decisão da necessidade de cirurgia e de extrações, e avaliar a performance deste método. No entanto, ressaltaram que em estudos futuros seria necessário subdividir as queixas dos pacientes em valores de entrada, uma vez que a tomada de decisão da cirurgia por pacientes muitas vezes provém de motivação estética.

Lee *et al.*³³, avaliaram diferentes algoritmos de RNC que tinham como objetivo auxiliar no diagnóstico diferencial para indicação de cirurgia ortognática pelo uso de telerradiografias laterais de 333 pacientes, sendo que 174 foram submetidos a cirurgia ortognática. Os traçados cefalométricos utilizaram 50 marcos e as imagens foram alinhadas pelo plano de Frankfurt. O modelo com maiores acurácias foram o Alexnet modificado, ResNet50 e MobileNet (96,4%, 95,6% e 95,4%, respectivamente). Os principais fatores que resultaram nestes diagnósticos foram: inclinações dentárias, a mandíbula e sínfise da mandíbula.

Kim *et al.*³⁵, avaliaram em radiografias laterais o diagnóstico para cirurgia ortognática pela utilização de redes neurais. Foram utilizados 960 pacientes nesta pesquisa sendo que 320 eram cirúrgicos. Para o grupo de teste foram utilizados 150 pacientes, os demais foram divididos em 5 grupos para realizar o *5-fold cross-validation*. Foram utilizados 4 diferentes modelos de redes neurais convolucionais sendo eles ResNet-18, 34, 50 e 101, sendo que a ResNet-18 foi a que apresentou as melhores métricas para AUC (0.979), acurácia (0.938), sensibilidade (0.882) e especificidade (0.966).

Tanikawa e Yamashiro³⁶, tiveram como objetivo desenvolver um novo modelo de inteligência artificial para prever a morfologia facial que 137 pacientes teriam após serem submetidos a tratamento ortodôntico-cirúrgico ou tratamento com extração de pré-molares. Utilizaram radiografias laterais e imagens faciais 3D para avaliar por métodos de geometria morfométrica baseado em pontos cefalométricos associados a *deep learning*. Como resultados finais, obtiveram que para casos cirúrgicos o erro do modelo era de 0.94mm enquanto casos de extrações 0.69. Já a taxa de sucesso foi de 100% quando o sistema foi calibrado para taxas de erro menores que 2mm.

Na odontologia, o uso de imagens e radiografias vêm crescendo exponencialmente. Com isso, pode-se afirmar que as ferramentas de IA terão grande influência na melhoria da precisão do diagnóstico, planejamento, abordagem e mecânica de nossos tratamentos, pelo fato de que tais sistemas necessitam de um grande número de dados “*big data*”^{37,38}. Outra grande vantagem da IA é a possibilidade de conectar profissionais do mundo todo^{24,39,40}. No entanto, devemos levar em conta alguns desafios desta nova modalidade: a necessidade de grande número de dados para que seja possível o correto aprendizado da máquina, é preciso padronizar as informações, ter pessoas treinadas para manipular os programas e garantir a segurança dos dados dos pacientes (dados desidentificados)^{24,37}. Outro desafio que pode ser levantado está relacionado a necessidade de evitar que vieses sejam levados aos sistemas de decisão baseados em IA. Se faz necessário avaliar as fontes pelas quais o modelo foi treinado para que seja possível integrar teorias, experimentos e conhecimentos empíricos, diminuindo, assim, a possibilidade de que vieses humanos ou de experimentos possam diminuir a credibilidade de modelos baseados em IA^{41,42}.

Mesmo com a crescente quantidade de estudos envolvendo IA e a grande quantidade de dados na odontologia, a Ortodontia ainda não foi muito explorada. Ainda é necessária uma integração dos dados, por meio de avaliação de exames padronizados. Nesse contexto as radiografias laterais são exames existentes na maioria dos centros odontológicos, contendo informações e variáveis facilmente extraídas por pessoas treinadas^{26,27}.

Deste modo a hipótese do nosso estudo é de que o uso de algoritmos de IA e dados clínicos podem prever com acurácia a necessidade de cirurgia em pacientes ortodônticos.

2 PROPOSIÇÃO

O objetivo principal foi avaliar se modelos de inteligência artificial podem ser utilizados como auxílio na tomada de decisão em ortodontia e em especial para pacientes que necessitam de cirurgia ortognática.

2.1 Proposições Específicas

- Avaliar por meio de uma revisão sistemática como a inteligência artificial pode ser aplicada ao diagnóstico e planejamento ortodôntico utilizando exames radiológicos.
- Testar se diferentes modelos de inteligência virtual são capazes de prever se um paciente necessita ou não de cirurgia ortognática a partir dos valores obtidos em telerradiografias laterais, previamente ao tratamento avaliando tanto tecido duro e mole, e avaliar se estes modelos são precisos em suas tomadas decisões.
- Avaliar se a acurácia dos resultados é alterada quando os algoritmos de IA são alimentados com dados de pacientes com padrão esquelético classe II ou classe III.
- Avaliar quais são os fatores cefalométricos mais importantes nesta tomada de decisão.
- Avaliar e comparar os resultados da IA com o consenso de ortodontistas e cirurgiões bucomaxilofaciais ou de acordo com o tratamento realizado.

3 PUBLICAÇÕES

Essa dissertação é apresentada no formato de publicações sendo elas:

- Clinical decisions in orthodontics using X-ray-based images and artificial intelligence approaches: a Systematic Review.
- Artificial intelligence as a prediction tool for orthognathic surgery assessment.

3.1 Publicação 1*

Clinical decisions in orthodontics using X-ray-based images and artificial intelligence approaches: a Systematic Review

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ABSTRACT

Artificial intelligence (AI) in health has increased its applications over the last years. The large amount of data available due to the improvement of data storage and digital exams provided better knowledge in treatment planning and opened new possibilities of applications of AI in orthodontics' diagnosis and treatment planning. This study aimed to systematically review the approaches using AI models to a better clinical decision-making process in orthodontic diagnosis and planning using X-ray-based images. Individual electronic search strategies were developed and conducted on PubMed/Medline, Scopus, Web of Science, Embase, Lilacs, and Cochrane Library (only English language articles published from January 2000 to October 20, 2021), aiming for relevant studies that met the

* Artigo escrito conforme as normas bibliográficas da revista *Orthodontics & Craniofacial Research* para a qual foi submetido.

eligibility criteria. As results, 12 studies were included with 5 different categories: Orthognathic surgery, TMJ osteoarthritis, skeletal pattern, obstructive sleep apnea, and skeletal maturation/development. Most of the AI models used were DL based and the X-ray image that was most used was lateral radiographs. In conclusion, AI can be used to improve the performance to assess diagnostic and treatment planning using X-ray-based images. The best applications were over temporomandibular joint osteoarthritis, skeletal maturation, and classification, OSA and the need for orthognathic surgery.

Keywords: Artificial intelligence, Orthodontics, X-Rays.

INTRODUCTION

Artificial intelligence (AI) is a term used to describe the ability that computational models can learn and improve their accuracy based on experience or labeled data, imitating the way that humans can learn. Its application is over streaming services, cellphones, websites, social medial etc^{1,2}.

The inclusion of AI systems in the health area is an emerging topic, that has increased over the last years mainly because clinicians and researchers have more access to different exams generating a large volume of data¹. However, this data may be underused due to the lack of proper decision-making support systems, lack of standardization, and there is still a need for more collaborative data pooling to fuel databases.³ Ideally any data must follow the "4vs" (volume, velocity, variety, and veracity), which could lead to more robust data analysis ¹.

Several studies with AI have been made in different fields of dentistry³⁻⁵, with different purposes, from detecting teeth and caries⁶⁻⁹, periapical pathosis¹⁰⁻¹², and tonsils hypertrophy^{13,14}, to predict treatments, such as the need for extractions¹⁵⁻¹⁸ or orthognathic surgery¹⁹⁻²⁵.

One subset of AI that is commonly used in the health area is convolutional (artificial) neural networks (CNN or ANN) that can be used to identify and classify images. They are called neural networks because their structure reminds the human brain networks. It can be used for raw to high-definition specific images, detection of cephalometric landmarks on lateral cephalograms, or cone-beam computed tomography (CBCTs)²⁶⁻³⁰. AI can also be used to assist and improve the decision-making process. It may happen because these models take large

amounts of data and usually are based on expert experience or gold standard patterns^{5,18,20,31–34}.

Dentistry usually provides unstructured data such as clinical data, models, photographs, and X-ray images. This type of data is difficult to analyze than structured because it's usually composed by qualitative data. However, it is possible to conduct researches using only unstructured data, like X-ray-based images, by using non-relational databases or by transferring unstructured data (qualitative) to structured data (quantitative)^{1,35,36}.

Radiographic image exams, such as CBCTs and lateral radiographs, are widely used because of the standardization and capability to provide quantitative data and images that can be extracted, segmented, and enhanced so imaging deep learning (DL) models can recognize them. In addition, the X-ray images play an essential role in diagnosis and planning^{26,27}.

Still, there is a large amount of information on this field, and this systematic review aimed to systematically review how AI models can provide a better clinical decision-making process in orthodontic diagnosis and planning using X-ray-based images.

METHODS

Protocol and registration

The protocol of this systematic review was registered with the PROSPERO under the number: CRD42021259994 at the NHS (National Institute for Health Research) database at <https://www.crd.york.ac.uk/prospero/>. The present review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines³⁷ (Supplementary Table 1).

Eligibility criteria

The PICOS plus inclusion criteria was used as inclusion criteria (Table I). All included manuscripts were focused on AI applied to radiographic imaging exams and its application to orthodontics diagnosis and treatment planning. Also, they should provide performance metrics or predictive outcomes that could be quantified, such as accuracy, sensibility, ROC curves, and there should be a clear mention regarding the data sets used for assessing the model. The exclusion

criteria were articles that were not AI related, used more than just X-ray-based images, were not applied to diagnosis or treatment planning, were written in languages different than English, case reports, expert opinions, and letters to editors.

Information sources and search strategy

Individual electronic search strategies were developed and conducted on PubMed/Medline, Scopus, Web of Science, Embase, Lilacs, and Cochrane Library published from January 2000 to October 20, 2021, and only English publish articles (Figure I).

Selection Process

The selection was completed in phases. First, titles, keywords and abstracts were reviewed by two investigators (PHJO and JOLP) separately using the inclusion and exclusion criteria to screen the articles. Duplicated articles were accessed using Mendeley (<https://www.mendeley.com>)³⁸ and double checked using Microsoft Excel®. Secondly, full texts of the possible eligible studies were assessed and classified as no, maybe, or yes according to the inclusion and exclusion criteria by the two investigators. The ones marked with no for both investigators were excluded, while the ones marked as maybe were resolved through consensus to decide if they would be included or not based on the PICOS and inclusion criteria.

Database	Keywords	No Results
Pubmed	((((("Orthodon*[Title/Abstract] OR ("Orthognathic Surgery"[Title/Abstract])) AND (((((Artificial Intelligence[Title/Abstract] OR (neural network[Title/Abstract]) OR (deep learning[Title/Abstract]) OR (machine learning[Title/Abstract])) AND (((((((lateral radiographic[Title/Abstract] OR (lateral radiographics[Title/Abstract]) OR (lateral X-ray[Title/Abstract]) OR (CBCT[Title/Abstract]) OR (Cone Beam Computed Tomography[Title/Abstract]) OR (Cone-Beam Computed Tomography[Title/Abstract]) OR (Cephalo*[Title/Abstract])) AND (((((((accuracy[Title/Abstract] OR (sensitivity[Title/Abstract]) OR (specificity[Title/Abstract]) OR (Intraclass Correlation Coefficient[Title/Abstract]) OR (Predictive Values[Title/Abstract]) OR (Success Rate[Title/Abstract]) OR (ROC Curve[Title/Abstract])) AND (((((((Decision Making[Title/Abstract] OR ("Decision-Making"[Title/Abstract]) OR ("Treatment plan*[Title/Abstract]) OR ("Diagn*[Title/Abstract] OR ("Prediction"[Title/Abstract])) AND english [Language] Filters: from 2000/1/1 - 2021/10/20 Sort by: Publication Date	24
Scopus	TITLE-ABS-KEY (((("orthodon*" OR "Orthognathic Surgery") AND "artificial intelligence" OR "neural network" OR "deep learning" OR "machine learning") AND "lateral radiographic" OR "lateral radiographics" OR "lateral X-ray" OR "cbct" OR "cone beam computed tomography" OR "cone-beam computed tomography" OR "cephalo*") AND "accuracy" OR "sensitivity" OR "specificity" OR "intraclass correlation coefficient" OR "predictive values" OR "Success Rate" OR "ROC Curve") AND "Decision Making" OR "Decision-Making" OR "Treatment Plan*" OR "Diagn*" OR "Prediction") AND (PUBYEAR > 2000) AND (LIMIT-TO (LANGUAGE , "English"))	43
Web of Science	(((ALL=(Orthodon* OR "Orthognathic Surgery")) AND ALL=(("artificial intelligence" OR "neural network" OR "deep learning" OR "machine learning") AND ALL=(("lateral radiographic" OR "lateral radiographics" OR "lateral X-ray" OR cbct OR "cone beam computed tomography" OR "cone-beam computed tomography" OR cephalo*)) AND ALL=(accuracy OR sensitivity OR specificity OR "intraclass correlation coefficient" OR "predictive values" OR "Success Rate" OR "ROC Curve") AND ALL=(("Decision Making" OR "Decision-Making" OR "Treatment Plan*" OR "Diagn*" OR "Prediction") AND English (Idioms)	48
Embase	(orthodon*:ti,ab,kw OR 'orthognathic surgery':ti,ab,kw) AND (('artificial intelligence':ti,ab,kw OR 'neural network':ti,ab,kw OR 'deep learning':ti,ab,kw OR 'machine learning':ti,ab,kw) AND (('lateral radiographic':ti,ab,kw OR 'lateral radiographics':ti,ab,kw OR 'lateral x-ray':ti,ab,kw OR 'cbct':ti,ab,kw OR 'cone beam computed tomography':ti,ab,kw OR 'cone-beam computed tomography':ti,ab,kw OR 'cephalo':ti,ab,kw) AND (accuracy:ti,ab,kw OR sensitivity:ti,ab,kw OR specificity:ti,ab,kw OR 'intraclass correlation coefficient':ti,ab,kw OR 'predictive value':ti,ab,kw OR 'success rate':ti,ab,kw OR 'roc curve':ti,ab,kw) AND ('decision making':ti,ab,kw OR 'treatment plan':ti,ab,kw OR 'diagn':ti,ab,kw OR 'prediction':ti,ab,kw) AND [1-1-2000]/sd AND [english]/lim	25
The Cochrane Library	((Orthodon*:ti,ab,kw OR ("Orthognathic surgery":ti,ab,kw) AND (("artificial intelligence"):ti,ab,kw OR ("neural network"):ti,ab,kw OR ("deep learning"):ti,ab,kw OR ("machine learning"):ti,ab,kw) AND ((("lateral radiographic"):ti,ab,kw OR ("lateral X-ray"):ti,ab,kw OR ("CBCT"):ti,ab,kw OR ("cephalo"):ti,ab,kw OR ("cone beam computed tomography"):ti,ab,kw) AND (accuracy:ti,ab,kw OR sensitivity:ti,ab,kw OR specificity:ti,ab,kw OR ("intraclass correlation coefficient"):ti,ab,kw OR ("predictive values"):ti,ab,kw OR ("Success Rate"):ti,ab,kw OR ("ROC Curve"):ti,ab,kw) AND ((("Decision Making"):ti,ab,kw OR ("Decision-Making"):ti,ab,kw OR ("treatment plan"):ti,ab,kw OR ("diagn"):ti,ab,kw OR ("prediction"):ti,ab,kw)	0
LILACS/MEDLINE	((((((((orthodon* OR "Orthognathic Surgery") AND ("artificial intelligence" OR "neural network" OR "deep learning" OR "machine learning") AND ("lateral radiographic" OR "lateral radiographics" OR "lateral X-ray" OR "cone beam computed tomography" OR "cone-beam computed tomography" OR cbct OR cephalo*) AND (accuracy OR sensitivity OR specificity OR "Intraclass Correlation Coefficient" OR "predictive values" OR "success rate" OR "ROC curve") AND ("Decision making" OR "Decision-making" OR "treatment planning" OR "diagn" OR "prediction")))))) AND (la:(en") AND (year_cluster:[2000 TO 2021])	30

Figure I – Search strategy

Data charting process and Data Items

Data charting was conducted by an independent investigator (PHJO) and checked by a second (JOLP). The following data were collected from each article: author, year of publication, country, study design, sample, mean/range of age, which X-ray based exam was used, aim, algorithm architecture, performance metrics, author suggestion, recommendations, and limitation, results, and conclusions.

Study risk of bias assessment and critical appraisal of individual studies

We have not assessed the risk of bias, because the aim of the included manuscripts was to assess statistical machine-learning approaches based on pre-selected imaging exams, rather than the clinical aspects of the sample recruitment, or methodologies during the study's conduction. In AI systems, the BIAS usually is resulted from the algorithm training itself, which there is no specific standard tool to measure this in systematic reviews. Meta-analysis was not conducted since the risk of bias was not assessed. Also, intervention, metrics or outcomes, and study settings were different in the selected studies³⁹.

Synthesis of results

For didactic purposes, we have separated the included studies were in 5 different categories, according to what was evaluated: (1) Orthognathic surgery, (2) TMJ osteoarthritis, (3) Skeletal pattern, (4) Obstructive Sleep Apnea, and (5) Skeletal maturation/development.

RESULTS

Study Selection

A total of 170 studies were retrieved in our search following the previously defined strategy. Duplicate removal and screening were performed, and 30 studies were selected for full-text assessment. After eligibility criteria was carefully applied to the full texts, 18 studies were excluded because they weren't based only on x-ray images, didn't provide quantitative results, couldn't be applied directly to diagnosis or treatment planning, or aimed to detect cephalometric landmarks. Finally, 12 studies met the eligibility criteria and were

included. The PRISMA flowchart showing the process of selection is presented in Figure 3.

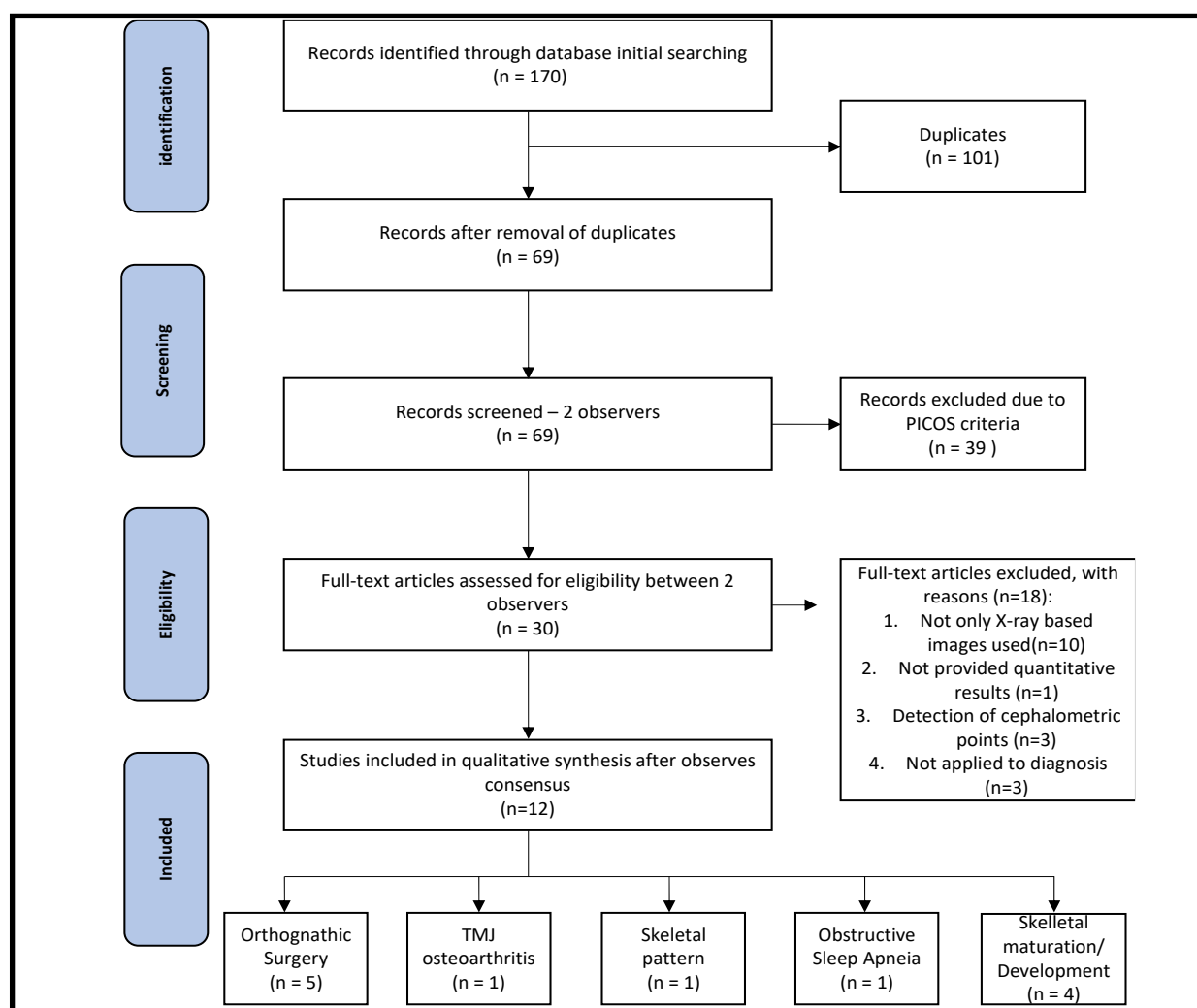


Figure 2 - Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the study selection process

Study Characteristics

The studies were divided into groups according to the AI application and what was evaluated. These divisions can be seen in Figures 3 and 4.

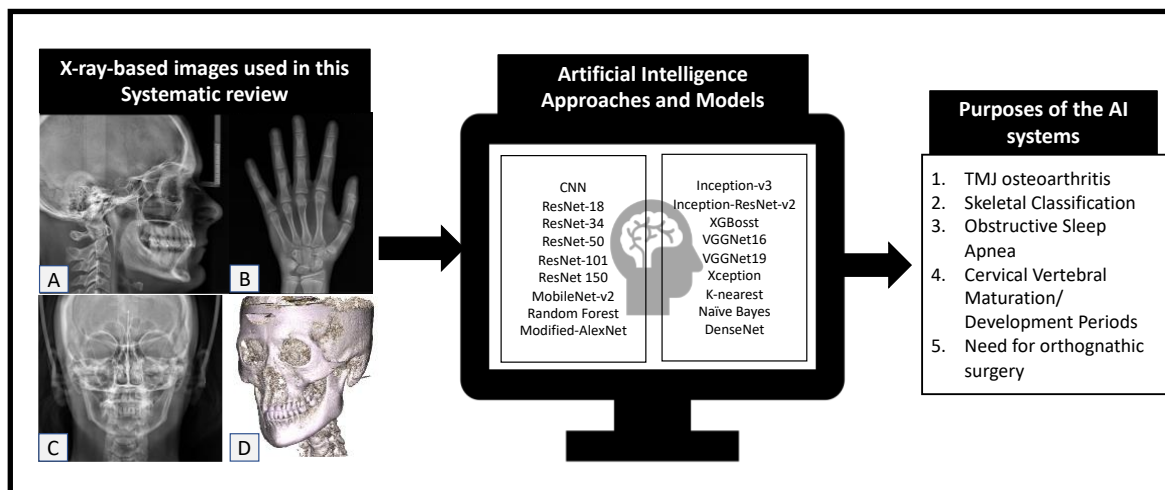


Fig.3 – The different X-ray-based images that were used in this systematic review such as lateral radiographs (A), hand-wrist radiographs (B), Posterior radiographs (C), and CBCTs (D). Followed by different machine/deep learning methods that are present in the selected studies and the purposes of the use of AI systems in orthodontics that are shown in this systematic review.

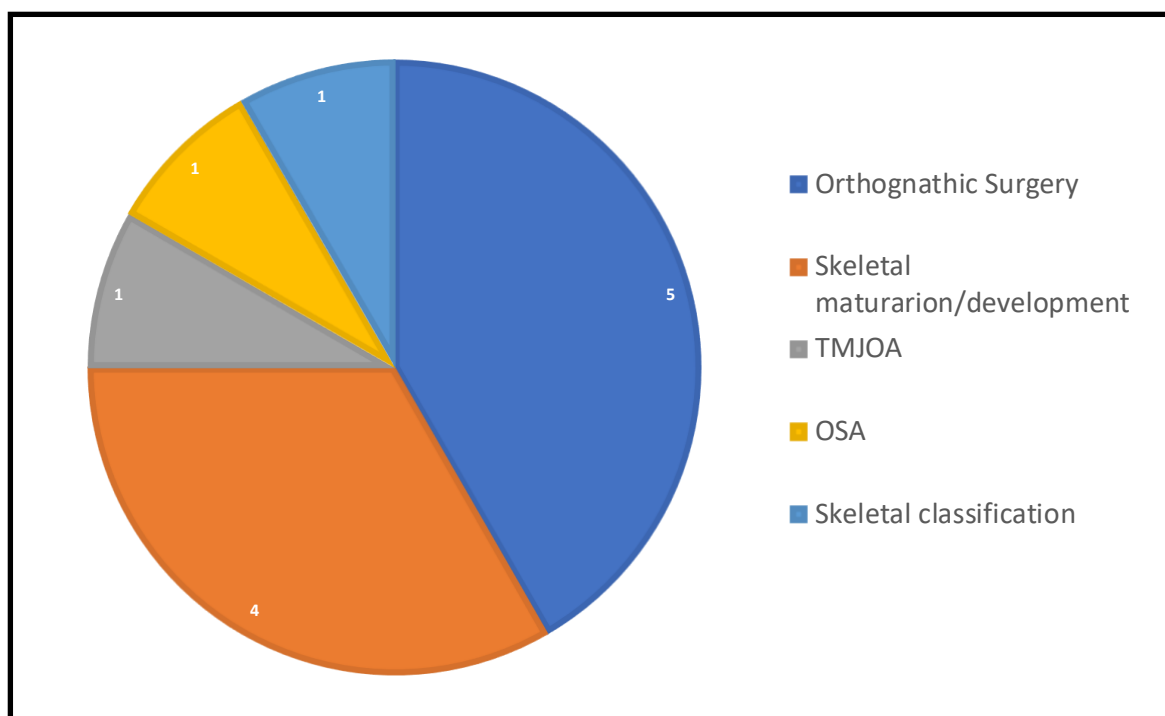


Figure 4 – Number of included studies in each group.

Chart II. Summary of descriptive characteristics of individual articles

Name	Author, Year, Country	Study Design	Sample (n)	Mean/Range of Age(yr)	Imaging Analysis	Aim	Algorithm Architecture	Performance metrics	Author suggestions/recommendations	Limitations	What was evaluated	Results	Conclusions
AUTOMATED DETECTION OF TMJ OSTEOARTHRITIS BASED ON ARTIFICIAL INTELLIGENCE	Lee et al.,2020, Korea	Retro spect ive	314 (3,514 images)	mean ± SD age, 39.5 ± 18.2 y	CBCT	To develop a diagnostic tool to detect condylar resorption from CBCT images with AI	A single-shot detector (SSD)—a deep learning framework designed for object detection	Accuracy, precision, recall, and F1 score	additional imaging modalities, such as contrast enhanced MRI and bone scintigraphy, could provide more information with higher accuracy over TMJ's inflammation.	Only 1 observer classified the TMJ images in the training data set.	TMJ osteoarthritis on CBCT on adult patients	The average accuracy, precision, recall, and F1 score over were 0.86, 0.85, 0.84, and 0.84, respectively.	TMJOA from sagittal CBCT images is possible by using a deep neural networks model.
AUTOMATED SKELETAL CLASSIFICATION WITH LATERAL CEPHALOMETRY BASED ON ARTIFICIAL INTELLIGENCE	Yu et al., 2020, Korea	Retro spect ive	5890 patients	mean 25.4 y	Lateral radiographs	Propose a novel deep learning system that provides the fully automated, 1-step, end- to-end diagnosis for skeletal classification solely from the lateral cephalogram.	A multimodal convolutional neural network architecture with a modified DenseNet with pretrained weights for the ImageNet data set	Sensitivity, Specificity, AUC and Accuracy	To optimize diagnosis, skeletal components and severity of the discrepancy should be evaluated in future studies. Also, further research comparing this system and the original approach with landmark detection and additional studies on enhancing model performance are needed.	Data was collected from a single organization which may cause a selection bias	Three different models to evaluate sagittal and vertical skeletal pattern of patients	Sensitivity, Specificity, AUC and Accuracy for sagittal discrepancies were 93.55%, 96.77%, 0.965 to 0.991 and 95.70%, respectively. Sensitivity, Specificity, AUC and Accuracy for vertical discrepancies were 94.59%, 97.29%, 0.967 to 0.995 and 96.40%	Skeletal classification can be made with an AI-aided tool for sagittal and vertical discrepancies

MACHINE LEARNING FOR IMAGE-BASED DETECTION OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: AN EXPLORATORY STUDY	Tsuiki et al., 2020, Japan	Retro spect ive	1389 patients (OSA = 867; control = 522)	OSA = 49.7 ± 8.9 Control = 41.2 ± 13.0	Lateral radiographs	test the hypothesis that a machine learning model could be used to differentiate severe OSA and non-OSA by 2-dimensional images	DCNN model called Visual Geometry Group (VGG-19)	Sensitivity, Specificity, Positive and negative likelihood ratio, Positive and negative predictive values and AUC area were evaluated for the three different groups	By the combination of demographic characteristics, anthropometric features and lateral cephalometric images may provide different AI models that could contribute to detect OSA	Data includes only Asian males from a single center	If this DCNN model could be used to detect patients with OSA based on 2-D images using three different areas of interest: Original image, main region and head only	Sensitivity, Specificity, Positive and negative likelihood ratio, Positive and negative predictive values and AUC area were evaluated for the three different groups: - Full image: 0.90, 0.77, 3.88, 0.14, 0.87, 0.82 and 0.89, respectively. - Main Region: 0.84, 0.81, 4.35, 0.20, 0.88, 0.75 and 0.92, respectively. - Head only: 0.71, 0.63, 1.91, 0.46, 0.85, 0.42 and 0.70, respectively	The DCNN accurately identified individuals with severe OSA using lateral cephalometric radiographs
COMPARISON OF DEEP LEARNING MODELS FOR CERVICAL VERTEBRAL MATURATION STAGE CLASSIFICATION ON LATERAL CEPHALOMETRIC RADIOGRAPHS	Seo et al, 2021, Korea	Obse rvatio nal	600	6-19 years	Lateral radiographs	evaluate and compare the performance of six state-of-the-art CNN-based deep learning models for	Different CNN models (ResNet-18, MobileNet-v2, ResNet-50, ResNet-101, Inception-v3	accuracy (1), recall (2), precision (3), F1-score (4), and area under the curve (AUC) values from	Higher quality data and development of better CNN architectures may improve the model's performance. It would be easier to evaluate if cervical vertebrae were segmented from surrounding structures	Small data	If different CNN models can distinguish the CVM classification on lateral	Accuracy was higher than 90% for all models.	Inception-ResNet-v2 showed the best results for all metrics

						CVM on lateral cephalometric radiographs, and implement visualization of CVM classification for each model using Grad-CAM technology	and Inception-ResNet-v2)	the ROC curve			cephalometric radiographs		
DEEP CONVOLUTIONAL NEURAL NETWORKS BASED ANALYSIS OF CEPHALOMETRIC RADIOGRAPHS FOR DIFFERENTIAL DIAGNOSIS OF ORTHOGNATHIC SURGERY INDICATIONS	Lee et al., 2020, Korea	Retro spect ive	333 individuals	23.1 ± 5.1	Lateral radiographs	Create a model for the differential diagnosis of orthognathic surgery and orthodontic treatment with a DL algorithm using cephalometric radiographs.	Three DL models were tested: Modified-Alexnet, MobileNet and Resnet50	Sensitivity, Specificity, AUC and Accuracy	Future studies can be obtained when assessed with more data. Also, should analyze the impact of better model construction and their comparison with other models	Comparison of the performance was limited due to the lack of data	Differential diagnosis for orthognathic surgery based on cephalometric radiographs using three different DL models	Modified-Alexnet: 0.852 (Sensitivity), 0.973 (Specificity), 0.969 (AUC) and 0.919 (Accuracy). MobileNet: 0.761 (Sensitivity), 0.931 (Specificity), 0.908 (AUC) and 0.838 (Accuracy). Resnet50: 0.750 (Sensitivity), 0.944 (Specificity), 0.923 (AUC) and 0.838 (Accuracy).	DCNN can be applied to predict orthognathic surgery. Also it was possible to predict the most important diagnosis structures
DEEP LEARNING BASED PREDICTION OF NECESSITY FOR ORTHOGNATHIC SURGERY OF SKELETAL MALOCCLUSION USING	Shin et al, 2021, Korea	Obse rvatio nal	840 (Class II:244, Class III: 477, Assimetry:	23.2y	Posterior and lateral radiographs	Develop a deep learning network to automatically predict the	ResNet34, with convolution blocks stacked	accuracy, sensitivity, and specificity.	More studies should be encouraged to achieve public confidence.	Involves only Korean patients from only one hospital and	Exploited a deep learning framework to automatically predict the	accuracy, sensitivity, and specificity were 0.954,	DL can standardize the decision process and

CEPHALOGRAM IN KOREAN INDIVIDUALS			149) (Male: 461, Female: 379)				need for orthodontic surgery using cephalogram.	hierarchically (CNN)		small number of cases.	need for orthognathic surgery based on the cephalogram of the patients	0.844, and 0.993, respectively	help orthodontists	
DETERMINATION OF GROWTH AND DEVELOPMENT PERIODS IN ORTHODONTICS WITH ARTIFICIAL NEURAL NETWORK	Kök et al., 2021, Turkey	Retro spect ive	419 patients (CVM1:70, CVM2:70, CVM3:69, CVM4:70, CVM5:70, CVM6:70	8 to 17y	Lateral and hand-wrist radiographs		Determine the growth-development periods and gender from the cervical vertebrae using the artificial neural network (ANN).	Twenty-four ANN models were obtained and seven with success level and clinically applicable were selected	Accuracy, Sensitivity, Specificity and F1 score	Using all the information from cephalometric radiograph in addition to linear measurements can provide better results	Hand-wrist age determination is more advanced than cephalometry and cervical vertebra.	If the ANN models could determinate patient's cervical vertebral stage and gender.	The accuracy for the testing set was: 71.4% (ANN-1), 49.2% (ANN-2), 76.1% (ANN-3), 50.7% (ANN-4), 69.8% (ANN-5), 81% (ANN-6), 90.4% (ANN-7), 90.5% (ANN-Gender)	The growth-development periods and gender were determined from the cervical vertebrae by using ANN with satisfactory success
EARLY PREDICTION OF THE NEED FOR ORTHOGNATHIC SURGERY IN PATIENTS WITH REPAIRED UNILATERAL CLEFT LIP AND PALATE USING MACHINE LEARNING AND LONGITUDINAL LATERAL CEPHALOMETRIC ANALYSIS DATA	Lin et al., 2021, Korea	Retro spect ive	56 patients	T0: 6.3y and T1: 16.7y	Lateral radiographs		Determine the cephalometric predictors of the future need for orthognathic surgery in patients with repaired unilateral cleft lip and palate (UCLP) using machine learning.	Boruta method to identify the most relevant features out of the cephalometric predictors at T0 and XGBoost algorithm to predict the future need for orthognathic surgery	10-fold cross-validation accuracy with F1-score	Multi-center study to increase the sample.	Small sample size.	The most important features of the cephalogram and the need for orthognathic surgery	The prediction model had 87.4% accuracy and when ANB, PP-FH, CF and FCA variables are inserted	At age of 6 years, it was possible to predict the future need for orthognathic surgery using cephalometric predictors with a good accuracy

INFLUENCE OF THE DEPTH OF THE CONVOLUTIONAL NEURAL NETWORKS ON AN ARTIFICIAL INTELLIGENCE MODEL FOR DIAGNOSIS OF ORTHOGNATHIC SURGERY	Kim et al., 2021, Korea	Retro spect ive	960 patients (non-surgical: 640, surgical: 320)	24.6 ± 4.9	Lateral radiographs	investigate the relationship between image patterns in cephalometric radiographs and the need for orthognathic surgery, and report on a method for improving the accuracy of predictive models according to the depth of the neural network	CNN models (ResNet-18, 34, 50 and 101)	AUC, Accuracy, Sensitivity and Specificity	Multi-center data to improve the model's performance.	Single center study.	Predict the need of orthognathic surgery using cephalometric radiographs	AUC: 0.979 (ResNet-18), 0.974 (ResNet-34), 0.945 (ResNet-50), 0.944 (ResNet-101). Accuracy: 0.938 (ResNet-18), 0.936 (ResNet-34), 0.911 (ResNet-50), 0.913 (ResNet-101). Sensitivity: 0.882 (ResNet-18), 0.876 (ResNet-34), 0.806 (ResNet-50), 0.824 (ResNet-101). Specificity: 0.966 (ResNet-18), 0.966 (ResNet-34), 0.964 (ResNet-50), 0.958 (ResNet-101).	ResNet-18 and 34 had better performance than ResNet-50 and 101 models.
ON CONSTRUCTION OF TRANSFER LEARNING FOR FACIAL SYMMETRY ASSESSMENT BEFORE AND	Lin et al., 2021, Taiwan	Retro spect ive	71 patients	-	CBCT	A CNN model with a transfer learning	CNN models (VGGNet16, VGGNet19,	Accuracy	Larger number of data and more effective NN architectures can enhance the accuracy	The model can only be used for small data sets and	Predict facial symmetry scores using	The accuracy for VGG16, VGG19, ResNet50	The most suitable model for the transfer

AFTER ORTHOGNATHIC SURGERY						approach for facial symmetry assessment based on 3-dimensional (3D) features to assist physicians in enhancing medical treatments.	ResNet50 and Xception)			can't be trained by new DL architecture.	the trained model.	and Xception was: 80%, 86%, 83% and 90%, respectively.	learning was Xception model
PREDICTION OF HAND-WRIST MATURATION STAGES BASED ON CERVICAL VERTEBRAE IMAGES USING ARTIFICIAL INTELLIGENCE	Kim et al., 2021, Koreal	Retro spect ive	499 images from 455 patients	9.9 ± 2.6	Lateral and hand-wrist radiographs	Predict the hand-wrist maturation stages based on the CV images observed in lateral cephalograms, and to analyse the accuracy of the proposed algorithms.	Various combinations of regression models were used	Mean Absolute Error (MAE), round MAE, Root Mean Square of Error (RMSE) and Accuracy	Further studies with a larger sample with na even distribution of sex, chronological age and skeletal maturation. More features can also improve the prediction accuracy.	Small sample size and imbalanced data with a great number of patients whose SMI stage was 0.	Patients hand-wrist maturation based on CV images and its accuracy.	The final ensemble model consisted of eight machine learning models. The MAE, round MAE and RMSE were 0.90, 0.87 and 1.20, respectively.	Chronological age and sex increased the accuracy. CV images can be used to predict hand-wrist SMI using machine learning.
USAGE AND COMPARISON OF ARTIFICIAL INTELLIGENCE ALGORITHMS FOR DETERMINATION OF GROWTH AND DEVELOPMENT BY CERVICAL VERTEBRAE STAGES IN ORTHODONTICS	Kök et al., 2019, Turkey	Retro spect ive	300 patients	8 to 17y	Lateral radiographs	determine cervical vertebrae stages (CVS) for growth and development periods by the frequently used seven artificial intelligence classifiers, and to compare the performance of these	Seven algorithms were selected:k-nearest neighbors (k-NN), Naive Bayes (NB), decision tree, ANN, SVM, Random forest and logistic regression	AUC, Accuracy, Precision, F1 score and Recall	There are no author suggestions or recommendations for future studies.	The author's did not mentioned any limitations over the study	Use seven different algorithms to determine cervical vertebrae stages from cephalometric radiograph and compare their performance	Decision tree had the highest accuracy for CVS1 to CVS4 (97.1%, 90.5%, 73.2%, 58.5%, respectively) and kNN for CVS5 (60.9%) and CVS6 (78.7%). ANN had the second-highest	ANN is the preferred method for determining CVS because it was the most stable algorithm

algorithms
with each
other.

accuracy,
except for
CVS5.

Results of individual studies and Synthesis of results

Orthognathic surgery: Five studies were included regarding the application of AI to predict the need for orthognathic surgery or conventional orthodontics^{21–25} (Chart 2). Shin *et al.*²¹, demonstrated that the DL network proposed by them can standardize the decision process for orthognathic surgery and help orthodontists's using posterior and lateral radiographs. Their results for accuracy, sensitivy, and specificity were 0.954, 0.844, and 0.993, respectively. Lin *et al.*²², was the only study that showed results lower than 90% for accuracy or success rate in predicting the need for orthognathic surgery. However, they evaluated that ANB, facial convexity angle, and the maxillary plan to Frankfurt plane angle were the main parameters to define the need for surgery. Lin *et al.*²³, used four different CNN models to predict facial symmetry after orthognathic surgery using CBCT images. Xception model was the most suitable for this purpose with 90% accuracy. Kim *et al.*²⁴, showed that ResNet-18 and 34 showed better performance than Resnet-50 and 101 to predict the need for orthognathic surgery using lateral radiographs. The results for the four CNN models test were: AUC: 0.979 (ResNet-18), 0.974 (ResNet-34), 0.945 (ResNet-50), 0.944 (ResNet-101). Accuracy: 0.938 (ResNet-18), 0.936 (ResNet-34), 0.911 (ResNet-50), 0.913 (ResNet-101). Sensitivity: 0.882 (ResNet-18), 0.876 (ResNet-34), 0.806 (ResNet-50), 0.824 (ResNet-101). Specificity: 0.966 (ResNet-18), 0.966 (ResNet-34), 0.964 (ResNet-50), 0.958 (ResNet-101). Lee *et al.*²⁵, showed that DCNN can be applied to predict orthognathic surgery and show which structure is the most important for diagnosis. Modified-Alexnet showed higher AUC and accuracy (0.969 and 0.919) than MobileNet (0.908 and 0.838) and ResNet-50 (0.923 and 0.838). The algorithm architecture used for all studies in this section was deep learning based^{21–25}.

Skeletal maturation/development: Four studies regarding the application of AI to assess development or skeletal maturation^{31,40–42} (Chart 2). Kim *et al.*³¹, showed that cervical vertebrae (CV) images can be used to predict hand-wrist SMI by presenting a model consisted of eight ML models. Also, age and sex can increase the accuracy. Kök *et al.*⁴⁰, concluded that growth development periods and gender can be predicted using ANN. The higher accuracy (0.942) was

present by ANN-7 (composed by all 32 linear measurements) followed by ANN-Gender (ANN7+gender). K k *et al.*⁴¹, results showed that ANN was the most stable algorithm to predict CV stages (CVS1-CVS6) with accuracy results of 93%, 89.7%, 68.8%, 55.6%, 47.4% and 78%, respectively. All studies used lateral radiographs and more than one DL model. However, only Seo *et al.*⁴² didn't use hand-wrist radiographs as a comparison method. They evaluated and compared six different CNN-based DL models to classify CVM maturation. All of them had accuracy higher than 90% and also AUC higher than 90% for all CVM stages. All studies showed that AI can be used to predict skeletal maturation.

Skeletal classification: One study was included regarding the application of AI to classify patients' skeletal patterns (Chart 2). Yu *et al.*⁴³, evaluated sagittal and vertical discrepancies on lateral radiographs using CNN. It showed results higher than 90% for both skeletal classifications and presented heat maps for a better understanding of the region that influences the most to distinguish skeletal patterns.

TMJ osteoarthritis (TMJOA): One study was included regarding the application of AI to detect TMJ osteoarthritis. Lee *et al.*⁴⁴, showed that sagittal CBCT images and deep learning are capable to predict TMJOA. The DL used was a single-shot detector. The authors evaluated accuracy, precision, recall, and F1 score. The results were 0.86, 0.85, 0.84, and 0.84, respectively. The authors suggested that additional imaging modalities should improve the performance of the DL and provide more information on the TMJ inflammation (Chart 2).

Obstructive Sleep Apnea: One study was included regarding the application of AI to detect obstructive sleep apnea. Tsuiki *et al.*⁴⁵, showed that DCNN model (VGG-19) can accurately identify OSA using lateral radiographs (Chart 2). The authors divided the sample images into three groups according to the area that was evaluated: full images (original images), main region (facial profile, the upper airway, and craniofacial soft and hard tissues), and head only (occipital region). The main region had the best results for sensitivity, specificity, and AUC (0.84, 0.81, 0.92) followed by full image (0.9, 0.77, and 0.89), and head

only (0.71, 0.63, and 0.7). The authors suggested that demographic characteristics and anthropometric features could improve the diagnostic OSA.

DISCUSSION

Summary of evidence

To our knowledge, this is the first systematic review to present X-ray imaging-based AI models applied to diagnosis and treatment planning. As a limitation, we have excluded manuscripts that used panoramic images because the studies were not focused on the orthodontics' diagnosis or planning. In most reviewed papers, authors divided AI applications in orthodontics based on radiographic images into two groups: diagnosis and treatment planning.

Diagnosis. Diagnosis' is probably the most important aspect of orthodontic treatment. Assessing development and skeletal maturation is needed for patients still growing and present skeletal alterations. With that is possible to provide the best treatment for each developmental period^{46–48}. The cervical vertebrae method⁴⁹ is commonly used to identify maturation stages because it can be assessed in lateral radiographs. However, due to its subjectivity and the chance of distortion depending on the patient positioning, clinicians need to have specific training to use this method. That's one of the reasons why hand-wrist radiographs are still the gold standard for assessing the development stage of a patient⁵⁰. However, AI can be used to help orthodontists to identify the CVM stages. All the studies assessed here showed that AI had good results assessing the development stage of patients using lateral radiographs when compared to gold standard or to humans' evaluation. Furthermore, the different studies showed that ANN model had best results when compared to other AI models^{31,40–42}.

Facial analysis and skeletal classification play an important role in orthodontics' diagnosis. All the growth deviations that the patient had will produce a skeletal alteration, and the orthodontist must classify the patient properly in all 3 planes^{51–53}. However, lateral radiographs can only classify vertical and sagittal relationships. Yu et al.⁴³, aimed to use DL to assess skeletal classification and, unlikely previous studies, they didn't use CNN models to perform cephalometric landmarks. The authors justified that eliminating this process would improve the

classification performance. For assessing vertical relationships, it was used the Bjork's Sum and Jarabak's Ratio and the results showed 96,4% accuracy. For sagittal relationships, the ANB angle and Witts' appraisal were used and a 95,7% accuracy was obtained.

Patients with obstructive sleep apnea usually present a retrognathic mandible and/or a lower hyoid position with causes a more crowded oropharynx. Patients with OSA can be diagnosticated in lateral radiographs, mainly when it's a severe case. However, 3D images still provide better and more qualified data. Tsuike et al.⁴⁵, evaluated 3 types of images: full lateral radiographs images, the main airway region (including facial profile, teeth, cervical bones, maxilla, and mandible), and the occipital region. Best results were obtained for the main region, and the worst were at the occipital region. Also, their results are comparable with the manual cephalometric analysis. It shows that the use of DL models can be applied as an objective additional diagnosis method to OSA patients.

TMJ osteoarthritis is a multi-system disease. CBCTs allow dentists to diagnose the TMJ bone by finding irregular contour, osseous defects, cortical loss or flattening of the condyles⁵⁴. Early diagnosis can be the best chance to minimize the damage caused by osteoarthritis, since there is no treatment available yet. Lee et al.⁴⁴, evaluate if AI could detect TMJOA in CBCT sagittal images. The results showed that using only the CBCT sagittal images had results higher than 80% like Bianchi et al.⁵⁵, that used CBCT, clinical and biological data.

Treatment Planning. Once the diagnosis is placed, treatment planning is the next step in orthodontic treatment. It's important to enhance that treatment planning needs radiographic images, facial evaluation, and models to be made, mainly for borderline patients. The proper decision to treat with orthodontic treatment or orthognathic surgery usually requires more experience from the orthodontist^{51,56,57}. All studies presented here had results higher than 90% when studied adult patients that need surgical treatment. Lin et al.²², was the only study that used young patients with unilateral cleft lip and palate and had 87,4% accuracy and was the only one to use cephalometric measures. The other studies^{21,23-25} used deep convolutional neural networks (DCNN) to extract features and identify the structures that play an important role in the decision. The authors justify that by saying that the marking and measurement values can

be a bias. This model resembles an orthodontist's subjective or morphological analysis. Previous studies^{19,58} compared the orthodontists' impression and cephalometric values and have concluded that there is the correlation between both analyses.

Limitations. The main limitation of this systematic review was that most studies that apply AI to orthodontics usually needs multi-source data, rather than x-rays-based image alone. For this reason, we retrieve only 12 manuscript that meets our PICO's criteria. Also, we have not assessed the BIAS of each AI model due to the lack of standardized tools for this purpose. Also, the lack of general applicability is a major limitation in AI models because most of the data are from the same center.

CONCLUSIONS

AI can be used to improve the performance to assess diagnostic and treatment planning using X-ray-based images. The best applications were over temporomandibular joint osteoarthritis, skeletal maturation, and classification, OSA and the need for orthognathic surgery.

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3.2 Publicação 2*

Title of the article: Artificial intelligence as a prediction tool for orthognathic surgery assessment.

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* Artigo escrito conforme as normas bibliográficas da revista *American Journal of Orthodontics and Dentofacial orthopedics* para a qual foi submetido.

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Abstract

Introduction: An ideal orthodontic treatment involves qualitative and quantitative measurements of dental and skeletal components to evaluate patient's discrepancies, such as facial, occlusal, and functional characteristics. The decision between orthodontics and orthognathic surgery is still challenging, especially in borderline patients. The advances in technology are helping the clinical decision in orthodontics. The increased available data and the big data era make possible to use artificial intelligence to guide the clinician's diagnosis. This study aimed to test different machine learning (ML) models' capacity to predict orthognathic surgery or orthodontics treatment using soft and hard tissue cephalometric values. **Methods:** 920 lateral radiographs from patients previously treated with conventional orthodontics or associated with orthognathic surgery were used, n=558 class II and n=362 class III, respectively. Thirty-two measurements were obtained from each cephalogram at the initial appointment. The subjects were randomly split into training (n=552), validation (n=183), and test datasets (n=185) as an entire sample and divided into class II and class III sub-groups. The data extracted were evaluated by 10 machine learning models and by 4 experts panel of orthodontists (n=2) and surgeons (n=2). **Results:** The combined prediction with 10 models showed top-ranked performance in the testing-set for accuracy, F1-score and AUC (entire sample: 0.707, 0.706, 0.791; Class II: 0.759, 0.758, 0.824; Class III: 0.822, 0.807, 0.89). **Conclusions:** The proposed combined 10 ML approach model accurately predicted the needs for orthognathic surgery, showing a better performance in class III patients.

Introduction

Correct diagnosis is essential to choose the right treatment plan in orthodontic treatment. For that, it's necessary to have qualitative and quantitative diagnostical factors in evaluating discrepancies, such as facial, occlusal, and cephalometric analysis¹⁻⁸. It will help orthodontists to understand better where the patient's problem is, its etiology and how severe the patient's discrepancy is. These items, added to the patient's facial esthetics and self-perception can better guide the treatment plan and prognosis⁹⁻¹¹.

Orthodontic treatment for adult patients can be mainly divided in three major groups: corrective orthodontic treatment, compensatory orthodontic treatment, and decompensatory orthodontic treatment for orthognathic surgery^{2,9,12}. The last one is destined for patients who skeletal discrepancy is severe enough that compensatory orthodontic treatment wouldn't be able to improve the patients' complaints and problems. It's essential that the treatment of choice improve not only the patient's occlusion, but also its profile, aesthetic, function, airways, and self-stem^{9,13,14}.

New techniques and technologies, such as CBCT and skeletal anchorage, can be applied to expand the compensatory horizons^{15–17}. However, borderline patients may still be the biggest challenge for orthodontists. In these cases, clinical experience plays an essential role in the diagnostic decision^{9,18}.

The large amount of data is produced daily in orthodontics treatments all over the world thanks to digitalization and the search for better results, enabling new technologies such as artificial intelligence (AI), more specifically machine learning (ML) models, to assist the diagnosis decision-making process, through formulas, equations, and data integration^{19–28}.

Unlike traditional statistical approaches, AI is not based on a hypothesis or depends on restricted parameters. It uses datasets and is capable of using several variables simultaneously and making iterations. It makes it possible for the machine to create patterns and rules, resembling human learning^{20,28–30}.

Accurate AI models require a high number of features, and in orthodontics, the cephalogram is an exam that is present and standardized in the entire world and generates variables that can be easily extracted by clinicians^{22,23,30,31}.

This study aimed to test different machine learning models' capacity to predict if a patient needs orthognathic surgery using cephalometric values of soft and hard tissue obtained from lateral radiographs, compared to clinicians' diagnosis and treatment performed. Also, verify if the ML results in better accuracy for class II or class III patients and the most important features in the decision-making. The hypothesis of this study is that AI can predict accurately the need for orthognathic surgery.

Material and methods

Datasets

Ethical approval for the study was obtained from the Ethics Committee on Human Research of the School of Dentistry at Araraquara, São Paulo State University (UNESP) – number 47379021.2.0000.541. The sample used in this retrospective study consists of 920 patients previously treated with conventional orthodontics or associated with orthognathic surgery in three different centers between the years of 2000 and 2018. Inclusion criteria were pre-treatment lateral radiographs of skeletal class II ($ANB \geq 4$ or $Witts > 0$) and class III ($ANB \leq 0$ or $Witts < 0$) patients that were indicated for orthognathic surgery or orthodontic

treatment, with or without premolars extractions, older than 16 years old, and on stages CS5 or CS6 of vertebral maturation^{18,32,33}. Exclusion criteria were anodontias, syndromic patients, and patients that are still growing. 32 cephalometric values were obtained from each lateral radiograph based on Steiner, Mcnamara and Tweed's analysis^{32,34} (Table I). Those measures were made on Studio 3 (Radiomemory, Belo Horizonte, MG – Brasil), and on 5% of the sample the cephalometric tracing was redone for calibration and method error (Fig 1).

Consensus and true treatment diagnosis

We used two different sample population diagnostics. The first one was the true treatment plans that were the final decisions determined by the orthodontists with the patients, which is more complex and noisier to predict: it not only depends on the clinical diagnosis but also on other unseen confounders, such as the psychology, socioeconomic status, etc., of the patients. The second one, was the consensus diagnosis performed by a 4 experts panel composed of orthodontists (n=2) and surgeons (n=2). The lateral radiograph with the cephalometric values were randomly presented to each one of the experts that should give the diagnosis if the patient needed orthognathic surgery or orthodontics. If the consensus didn't make a majority, the true treatment was considered as the final decision. By that, it was possible to minimize the bias of the true treatment decision and train the machine with more accurate data. On this paper, the results were focused mainly on the consensus diagnosis.

Machine learning details

The subjects were randomly split into training, validation, and test datasets with a sample size of 552, 183, and 185, respectively. 10 machine learning were used, including: Bayesian logistic generalized linear model (bayesglm)³⁵, glmboost³⁶, elastic net (glmboost)³⁷, high-dimensional discriminant analysis(hdda)³⁸, linear discriminant analysis (lda2)³⁹, naïve bayes (naïve_bayes)⁴⁰, single-hidden-layer neural networks (nnet)⁴¹, random forest (RF)⁴², Kernel-based support vector machine (svmLinear)⁴³, XGBoost (xgbTree)⁴⁴. All tuning parameters such as the learning rate, iterations, and regularization parameters, were optimized from the 10-fold cross validation

based on the training dataset. The 10 trained models were applied to the validation set to obtain the predicted responses (Fig.2).

Furthermore, a logistic regression was used to fit the true responses based on the validation dataset using a weighted average of the 10 models to find the optimal weights of each method for model ensemble. The prediction accuracy, precision and recall rate for the surgical group, precision, and recall rate for the orthodontic group, F1 score, and areas under the Receiver Operating Characteristic Curve (AUC) of the 10 methods and the combined model were calculated on the validation datasets to evaluate their prediction performance and make a comparison. Furthermore, to avoid overfitting the 10 methods trained on the training data and the combined model trained on the validation data were applied to the independent test set to make a comparison. Class II and Class III patients were also evaluated separately, and all prediction models' performances were assessed.

Feature importance scores were used to evaluate the importance of each cephalometric variable, to determine the proper diagnosis for orthognathic surgery. Two feature importance scores were calculated, including the permutation feature importance for random forest and the gain metric for XGBoost, through the R wrapper varImp. All statistical and machine learning predictive modeling were carried out through R package caret, software R/4.1.0.

Results

Consensus diagnosis performance

Entire sample

The top machine learning approaches for accuracy for consensus diagnosis were nnet on the validation test (0.78) and xgbTree on the testing set (0.712).

The overall performance of the combined model was the best with the highest AUC (0.871), F1-score (0.788), and accuracy (0.797) on the validation set and second-best AUC (0.791), F1-score (0.706), and accuracy (0.707) on the testing set (Table II).

Class II patients

Performance of the 11 methods for validation and testing dataset to predict the consensus diagnosis were shown in Table III and Fig. 3.

The best machine learning methods predicting consensus diagnosis for class II patients was the combined ML with accuracy of 0.855 followed by RF and xgbTree with accuracy of 0.782 for both methods on the validation set. For the testing set, the highest accuracy for consensus diagnosis for class II was performed by RF (0.768) followed by glmboost (0.723).

The combined machine learning model presented the highest scores for all metrics in validation set and for F1-score (0.853) and AUC (0.905) in testing set. Accuracy of 0.759 was second ranked for the testing set (Table III).

Class III patients

Performance of the 11 methods for validation and testing dataset to predict the consensus diagnosis were shown in Table IV and Fig. 4.

Naïve Bayes and RF presented the best performance for consensus diagnosis, with accuracy 0.863 and 0.849 in the testing set, respectively. The combined model presented the best prediction metrics in all metrics for validation set with accuracy of 0.873, AUC of 0.923, and F-1 score of 0.87. For the testing set, third best AUC (0.89), F1-score (0.807), and accuracy (0.822) (Table IV).

Real treatment performance

The true treatment diagnosis was subject to more bias which made it harder for the models to perform. The performances of real treatment for entire sample, class II, and class III patients are shown in the supplementary tables I-IV.

Discussion

The decision to refer a patient to orthodontic treatment associated with orthognathic surgery can demand some empirical knowledge. For that reason, ML models can be applied with less human bias. Once the AI is fed with labeled or unlabeled data, it creates patterns, models, and relationships between the data that resemble the human learning process, making it possible to translate empirical knowledge into scientific knowledge. For that reason, in this study, it

was preferred to use ML models that were based on cephalometric variables as input values rather than models that used deep learning for image processing and pattern recognition procedures^{29,45–48}. By using cephalometric variables, it was possible to expose which cephalometric measurements are the most relevant in the decision-making. However, Lee et al.²⁹, showed that the region of interest of their gradient-weighted class activation mapping evolves upper and lower incisor, mandibular and maxillary symphysis, and occlusal plane, which coincides with the Witts feature that was the most important feature for most predictions in our results (Fig 5).

Also, the machine learning methods were trained, validated, and tested in two different ways: by the true treatment that was proposed, and the consensus diagnosis results from 4 clinical expert-based diagnoses. With that, it was possible to exclude subjective decision biases that could occur during the true treatment decision, like the patient's fear of the surgery, the lack of experience of the orthodontist, and the patient's self-perception^{2,9,49,50}. The orthodontists showed higher accuracy than surgeons for all groups to predict which treatment was conducted to each patient (Supplementary tables V-VII). It may have occurred because the orthodontists are more trained to know how far they can go to make a orthodontic dentoalveolar compensation. Meanwhile, surgeons would have the bias to refer surgery more to borderline patients.

The importance score bar plots imply that the top features most important in machine learning methods are similar in association with clinicians' consensus diagnosis and real treatments. Features Witts and ANB are both the most important in prediction of the real treatments and consensus diagnosis, respectively, corroborating with previous studies^{51,52}. The circular plots imply that the top features that are most significant are different between the association with consensus diagnosis and real treatments. For the entire sample, CO-A is the most significant for real treatments while F.plan.occl is the most significant for consensus diagnosis. For Class II patients, ANB, SNB, and Witts are the most significant for real treatments, while ANB and HNB are the most significant for consensus diagnosis, different than the proposed by Proffit et al. that suggested that incisor overjet, Pog-NPerp, AFPI and AFAI are the most significant variables⁵⁵.

The most significant feature for consensus diagnosis for class II patients was the feature Wits, while Kerr et al.⁵⁶ suggested that ANB and IMPA were the most significant and Lee et al.⁵² supported that Wits appraisal, lower incisor angulation, and Holdaway H angle were the strongest predictors. This may also indicate the difference between complex machine learning methods and naïve association tests. Enhanced machine learning methods can capture those important features with complex nonlinear relationships with the responses which cannot be captured by the association t-tests (Fig 6).

The feature Wits was the most significant for all groups rather than other anteroposterior analysis, such as ANB angle. It probably happened because the Wits appraisal isn't as influenced by different structures like ANB angle that can be influenced by cranial base alteration or any maxillary rotation that would impact the anteroposterior discrepancies^{53,54}.

From the above results, it's possible to see that the prediction of consensus diagnosis has higher prediction accuracy, implying that consensus diagnosis is easier to predict. A limitation of this study was that subjective features such as patient's anxiety, needs, and fears were not included, and it's well known that it takes an important place in the final decision for an orthodontic treatment. So, it's important to enhance that ML models can be used to assist and improve the decision-making process but should not be the final decision.

Conclusion

The machine learning methods proposed in this study can accurately predict the need for orthognathic surgery in patients with class II and class III pattern. The performance was better when consensus diagnosis was used rather than the true treatment because of the lack of subjectiveness human bias. Wits and ANB were the most important features to predict which would be the best treatment for the patient. Class III patients showed the best results, mainly with the combine machine learning method for the validation dataset.

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Figure Captions

Figure 1. Cephalometric points, planes, and tracing made with Studio 3.

Figure 2. Methods workflow. Data capture of class II and class III patients. Data processing of cephalometric variables, patients' age and sex. Data analytics divided in true treatment and consensus diagnosis to train and test the machine learning models to predict if the patient needs orthodontics or orthognathic surgery. Important and significant features that were extracted from the cephalometric variables and the performance metrics.

Figure 3. ROC curve of the consensus diagnosis of validation (A) and testing set (B) for class II patients.

Figure 4. ROC curve of the consensus diagnosis of validation (A) and testing set (B) for class III patients.

Figure 5. Most important features for Random Forest and XGBoost consensus diagnosis for entire sample (A and B), class II (C and D) and class III patients (E and F), respectively.

Figure 6. Boxplot for the most important features for consensus diagnosis in class II (A) and class III patients (B). Circunplot for most significant features for consensus diagnosis in class II (C) and class III patients (D)

Figure 1.

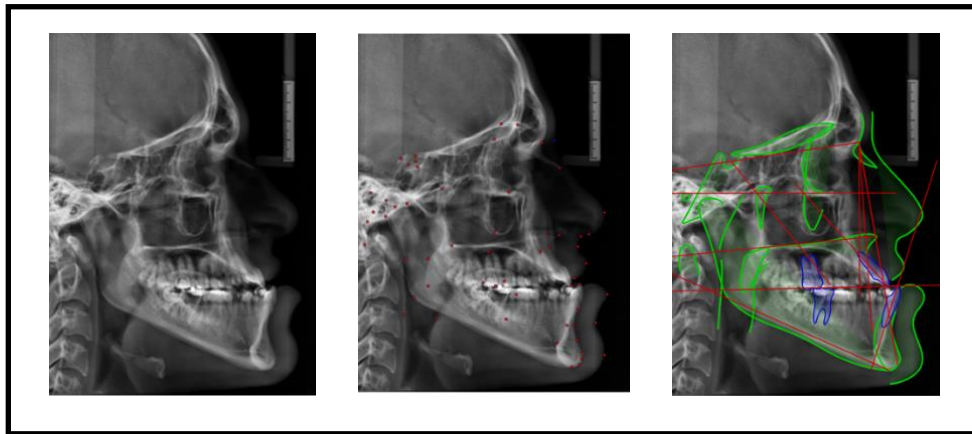


Figure 2.

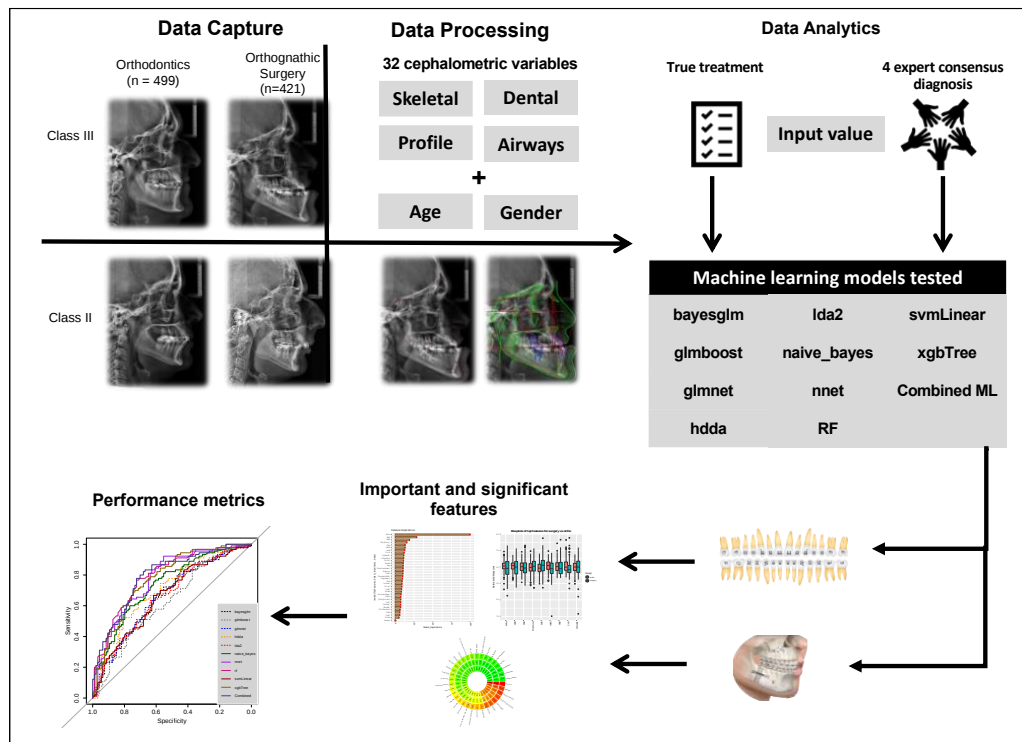


Figure 3.

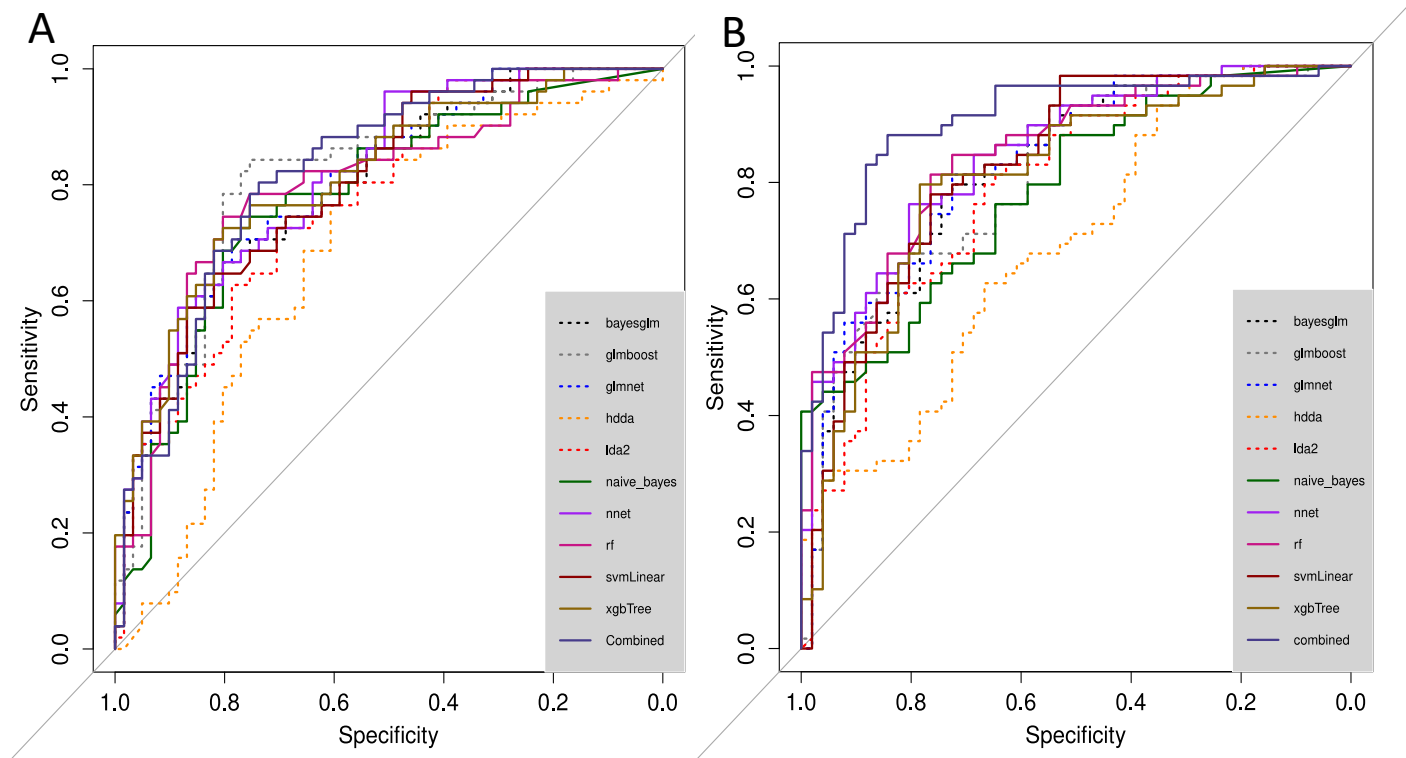


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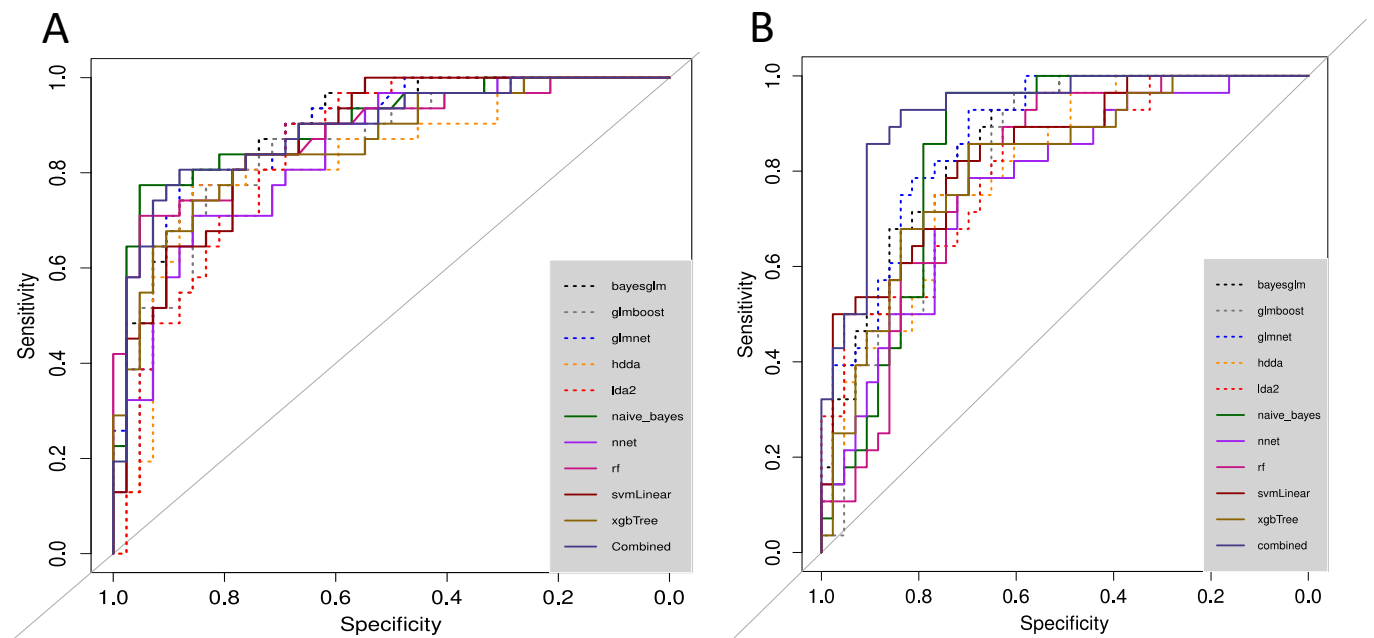


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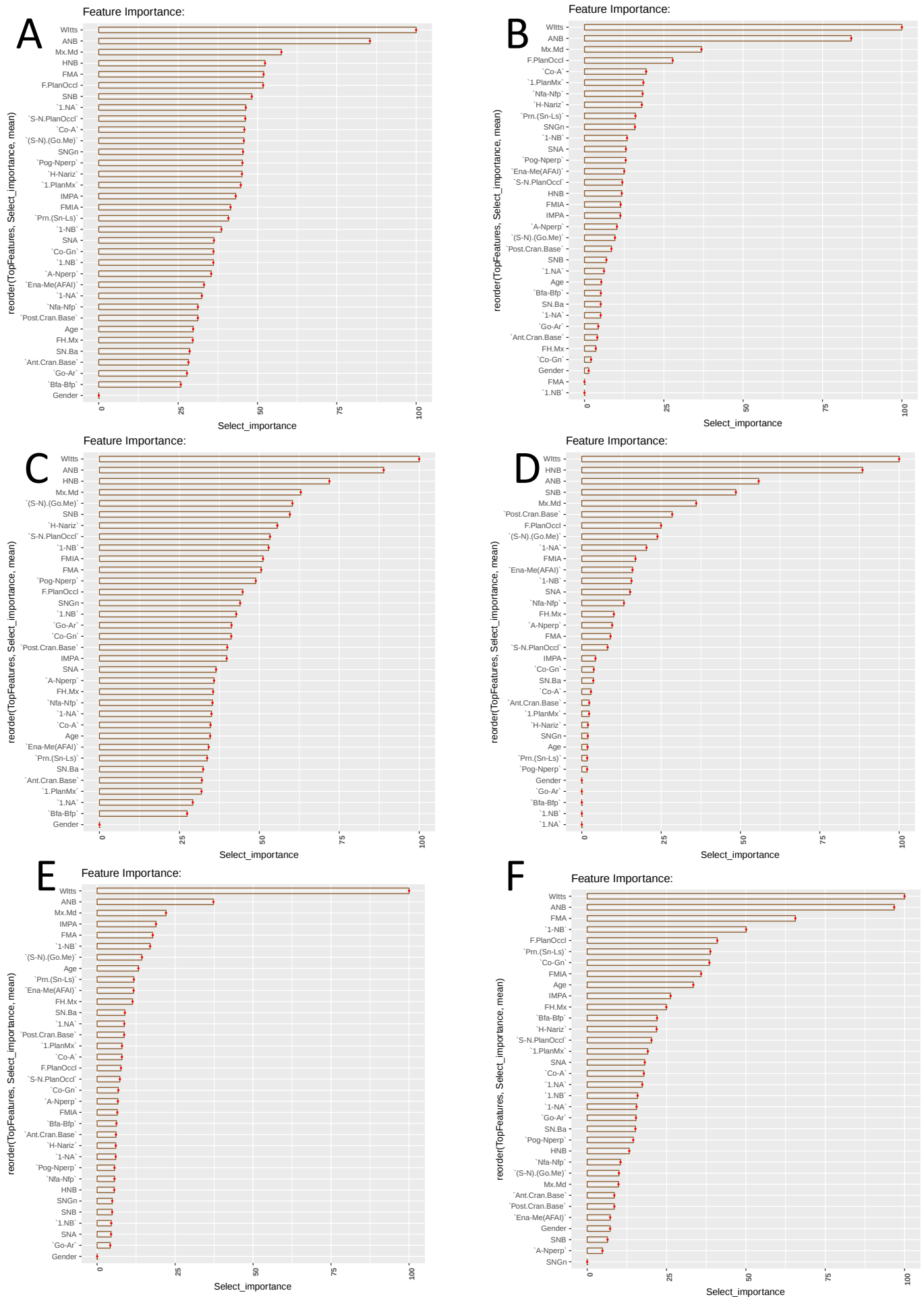
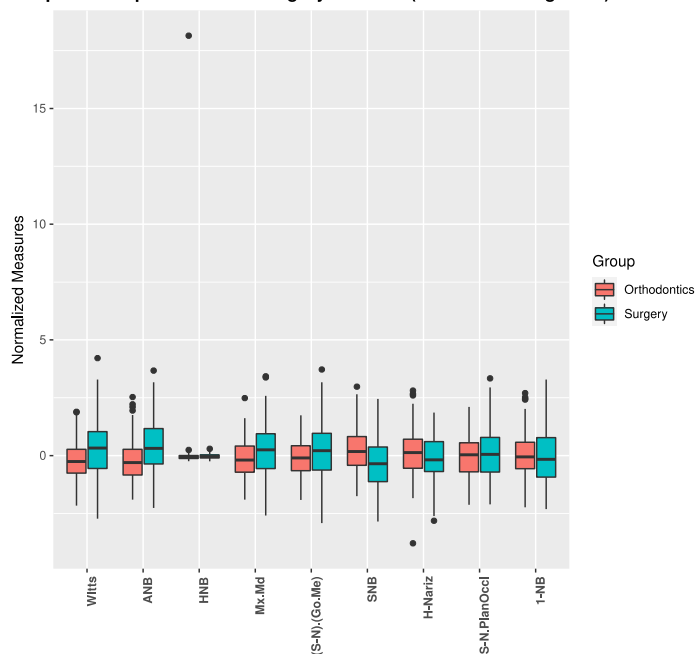


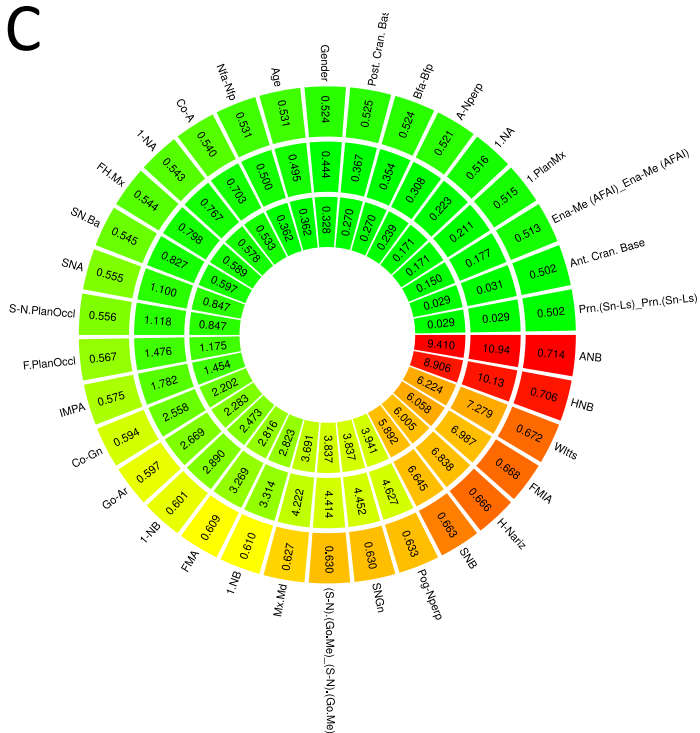
Figure 6.

A

Boxplots of top features for surgery vs ortho (consensus diagnosis)

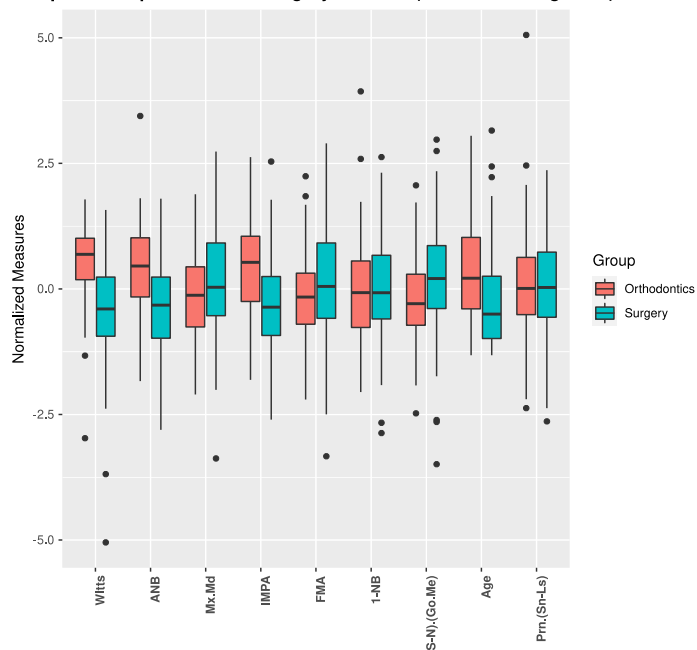


C

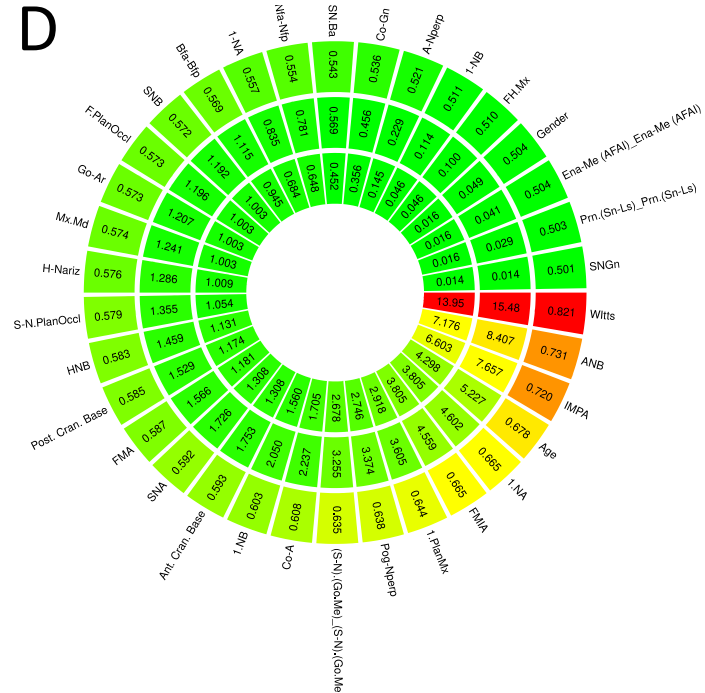


B

Boxplots of top features for surgery vs ortho (consensus diagnosis)



D



Tables

Table I. Cephalometric variables that were measured in lateral radiographs.

Variables	Description
Relation between maxilla and mandible with the cranial base	
SNA	Relation between the maxilla and the cranial base
SNB	Relation between the mandible and the cranial base
A-Nperp	Relation between the maxilla and the cranial base
Pog-Nperp	Relation between the mandible and the cranial base
Cranial base evaluation	
SNBa	Cranial base angle
Ant. Cran. Base	Anterior Cranial Base's length
Post. Cran. Base	Posterior Cranial Base's length
Relation between maxilla and mandible	
ANB	Angular relationship between maxilla and mandible
Witts	Linear relationship between maxilla and mandible
Co-A	Maxilla's length
Co-Gn	Mandible's length
Vertical Analysis	
(S-N).(Go-Me)	Cranial base and mandibular plane angle
S-N.Gn	the cranial base and Gnatium angle
FMA	Frankfurt to mandibular plane angle
Mx.Md	maxillary to mandibular plane angle
FH.Mx	Frankfurt to maxillary plane angle
AFAI	Lower Anterior Facial Height
AFPI	Lower posterior Facial Height
Dental Analysis	
1.NA	Upper incisor's inclination
1-NA	Upper incisor's protrusion
1.NB	Lower incisor's inclination
1-NB	Lower incisor's protrusion
IMPA	Mandibular incisor plane angle
FMIA	Frankfurt mandibular incisor plane angle

1.PlanoMx	Maxilla's incisor to maxillary plane angle
Profile Analysis	
Prn.(Sn-Ls)	Nasolabial angle
H-Nariz	Holdway line distance to pro-nasal point
HNB	Profile's avaliation
Occlusal Plane Analysis	
S-N.Plano Oclusal	Cranial base and occlusal plane angle
F.Plano Oclusal	Frankfurt plane and occlusal plane angle
Airways Analysis	
Nfa-Nfp	Upper airways analisys
Bfa-Bfp	Lower airways analisys

Table II. 10 methods and combined ML model validation and testing set for the entire sample consensus diagnosis.

	10 methods validation set for consensus diagnosis for entire sample						
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.681	0.652	0.699	0.57	0.767	0.67	0.733
glmboost	0.61	0.565	0.633	0.443	0.738	0.589	0.674
glmnet	0.676	0.647	0.693	0.557	0.767	0.663	0.735
hdda	0.681	0.615	0.747	0.709	0.66	0.68	0.749
lda2	0.67	0.634	0.694	0.57	0.748	0.66	0.733
naive_bayes	0.692	0.621	0.77	0.747	0.65	0.692	0.786
nnet	0.78	0.767	0.789	0.709	0.835	0.774	0.842
RF	0.758	0.754	0.761	0.658	0.825	0.747	0.81
svmLinear	0.643	0.63	0.648	0.43	0.806	0.615	0.724
xgbTree	0.758	0.722	0.786	0.722	0.786	0.754	0.798
Combined ML	0.797	0.818	0.784	0.684	0.883	0.788	0.871
	10 methods testing set for consensus diagnosis for entire sample						
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.598	0.611	0.589	0.489	0.702	0.592	0.661
glmboost	0.582	0.594	0.574	0.456	0.702	0.574	0.626
glmnet	0.609	0.625	0.598	0.5	0.713	0.603	0.664
hdda	0.625	0.604	0.651	0.678	0.574	0.624	0.706
lda2	0.598	0.603	0.594	0.522	0.67	0.595	0.659
naive_bayes	0.679	0.65	0.716	0.744	0.617	0.679	0.737
nnet	0.685	0.686	0.684	0.656	0.713	0.684	0.776
RF	0.701	0.74	0.676	0.6	0.798	0.697	0.792

svmLinear	0.598	0.629	0.582	0.433	0.755	0.585	0.661
xgbTree	0.712	0.708	0.716	0.7	0.723	0.712	0.779
Combined ML	0.707	0.714	0.7	0.667	0.745	0.706	0.791

Table III. 10 methods and combined ML model validation and testing set for class II patients consensus diagnosis.

10 methods validation set for consensus diagnosis for class II patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.755	0.742	0.773	0.831	0.667	0.75	0.821
glmboost	0.691	0.687	0.698	0.78	0.588	0.684	0.812
glmnet	0.736	0.721	0.762	0.831	0.627	0.73	0.828
hdda	0.609	0.621	0.591	0.695	0.51	0.602	0.693
lda2	0.736	0.727	0.75	0.814	0.647	0.731	0.79
naive_bayes	0.709	0.68	0.771	0.864	0.529	0.695	0.787
nnet	0.755	0.735	0.786	0.847	0.647	0.749	0.848
RF	0.782	0.787	0.776	0.814	0.745	0.78	0.846
svmLinear	0.755	0.75	0.761	0.814	0.686	0.751	0.83
xgbTree	0.782	0.787	0.776	0.814	0.745	0.78	0.807
Combined ML	0.855	0.852	0.857	0.881	0.824	0.853	0.905
10 methods testing set for consensus diagnosis for class II patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.705	0.661	0.75	0.725	0.689	0.705	0.795
glmboost	0.723	0.652	0.826	0.843	0.623	0.723	0.817
glmnet	0.705	0.655	0.759	0.745	0.672	0.705	0.804
hdda	0.67	0.625	0.714	0.686	0.656	0.669	0.688

	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.795	0.833	0.776	0.645	0.905	0.781	0.894
glmboost	0.726	0.739	0.72	0.548	0.857	0.706	0.847
glmnet	0.767	0.85	0.736	0.548	0.929	0.744	0.884
hdda	0.808	0.815	0.804	0.71	0.881	0.8	0.824
lda2	0.767	0.733	0.791	0.71	0.81	0.761	0.846
naive_bayes	0.863	0.889	0.848	0.774	0.929	0.857	0.898
nnet	0.781	0.759	0.795	0.71	0.833	0.774	0.841
RF	0.849	0.917	0.816	0.71	0.952	0.84	0.882
svmLinear	0.781	0.8	0.771	0.645	0.881	0.768	0.873
xgbTree	0.795	0.864	0.765	0.613	0.929	0.778	0.861
Combined ML	0.822	0.909	0.784	0.645	0.952	0.807	0.89

Supplementary Tables

Supplementary Table I. 10 methods and combined ML model validation and testing set for the entire sample true treatment.

	10 methods validation set for true treatment for entire sample						
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.637	0.657	0.61	0.697	0.566	0.632	0.647
glmboost	0.61	0.635	0.577	0.667	0.542	0.605	0.609
glmnet	0.604	0.626	0.573	0.677	0.518	0.597	0.619
hdda	0.659	0.687	0.627	0.687	0.627	0.657	0.716
lda2	0.637	0.651	0.616	0.717	0.542	0.63	0.652
naive_bayes	0.676	0.685	0.662	0.747	0.59	0.67	0.743
nnet	0.714	0.753	0.674	0.707	0.723	0.713	0.776
RF	0.714	0.737	0.687	0.737	0.675	0.709	0.781
svmLinear	0.654	0.664	0.639	0.737	0.554	0.646	0.658
xgbTree	0.692	0.722	0.659	0.707	0.675	0.69	0.747
	10 methods testing set for true treatment for entire sample						
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.62	0.638	0.595	0.677	0.553	0.615	0.646
glmboost	0.636	0.633	0.641	0.768	0.482	0.622	0.636
glmnet	0.614	0.625	0.597	0.707	0.506	0.606	0.631
hdda	0.679	0.672	0.691	0.788	0.553	0.67	0.71
lda2	0.636	0.645	0.622	0.717	0.541	0.629	0.646
naive_bayes	0.63	0.628	0.635	0.768	0.471	0.616	0.702
nnet	0.652	0.677	0.624	0.677	0.624	0.65	0.712
RF	0.668	0.676	0.658	0.737	0.588	0.663	0.725
svmLinear	0.652	0.647	0.662	0.778	0.506	0.64	0.659

xgbTree	0.62	0.631	0.603	0.707	0.518	0.612	0.712
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Supplementary Table II. 10 methods ML models validation and testing set for class II patients true treatment.

10 methods validation set for true treatment for class II patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.664	0.688	0.606	0.803	0.455	0.63	0.703
glmboost	0.682	0.701	0.636	0.818	0.477	0.65	0.729
glmnet	0.664	0.688	0.606	0.803	0.455	0.63	0.705
hdda	0.691	0.722	0.632	0.788	0.545	0.669	0.736
lda2	0.655	0.675	0.6	0.818	0.409	0.613	0.704
naive_bayes	0.673	0.692	0.625	0.818	0.455	0.638	0.76
nnet	0.682	0.691	0.655	0.848	0.432	0.641	0.723
RF	0.682	0.701	0.636	0.818	0.477	0.65	0.777
svmLinear	0.664	0.667	0.652	0.879	0.341	0.603	0.705
xgbTree	0.736	0.74	0.727	0.864	0.545	0.71	0.713
10 methods testing set for true treatment for class II patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.777	0.769	0.794	0.896	0.6	0.756	0.847
glmboost	0.777	0.769	0.794	0.896	0.6	0.756	0.828
glmnet	0.777	0.769	0.794	0.896	0.6	0.756	0.848
hdda	0.661	0.738	0.569	0.672	0.644	0.654	0.729
lda2	0.768	0.766	0.771	0.881	0.6	0.747	0.83
naive_bayes	0.732	0.753	0.692	0.821	0.6	0.714	0.782
nnet	0.732	0.728	0.742	0.881	0.511	0.701	0.834

RF	0.688	0.695	0.667	0.851	0.444	0.649	0.748
svmLinear	0.75	0.735	0.793	0.91	0.511	0.717	0.847
xgbTree	0.688	0.722	0.625	0.776	0.556	0.668	0.755

Supplementary Table III. 10 methods ML models validation and testing set for class II patients true treatment.

10 methods validation set for true treatment for class III patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.789	0.718	0.875	0.875	0.718	0.789	0.78
glmboost	0.746	0.675	0.839	0.844	0.667	0.746	0.782
glmnet	0.817	0.757	0.882	0.875	0.769	0.817	0.787
hdda	0.69	0.639	0.743	0.719	0.667	0.69	0.76
lda2	0.746	0.667	0.862	0.875	0.641	0.746	0.758
naive_bayes	0.676	0.636	0.711	0.656	0.692	0.674	0.758
nnet	0.662	0.654	0.667	0.531	0.769	0.65	0.777
RF	0.662	0.611	0.714	0.687	0.641	0.661	0.707
svmLinear	0.789	0.718	0.875	0.875	0.718	0.789	0.796
xgbTree	0.634	0.6	0.659	0.562	0.692	0.628	0.707
10 methods testing set for true treatment for class III patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
bayesglm	0.863	0.897	0.841	0.788	0.925	0.86	0.904
glmboost	0.822	0.857	0.8	0.727	0.9	0.817	0.879
glmnet	0.863	0.926	0.826	0.758	0.95	0.859	0.899
hdda	0.836	0.818	0.85	0.818	0.85	0.834	0.888
lda2	0.795	0.781	0.805	0.758	0.825	0.792	0.852
naive_bayes	0.808	0.828	0.795	0.727	0.875	0.804	0.865

nnet	0.781	0.84	0.75	0.636	0.9	0.771	0.825
RF	0.726	0.76	0.708	0.576	0.85	0.714	0.809
svmLinear	0.863	0.871	0.857	0.818	0.9	0.861	0.9
xgbTree	0.836	0.92	0.792	0.697	0.95	0.828	0.905

Supplementary Table IV. 10 methods and combined ML model validation and testing set for the entire sample true treatment.

Expert prediction for true treatment for validation set for the entire sample.							
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.67	0.767	0.606	0.566	0.795	0.669	0.68
Surgeon.B	0.533	0.585	0.49	0.485	0.59	0.533	0.538
Ortho C	0.72	0.75	0.686	0.727	0.711	0.718	0.719
Surgeon D	0.654	0.781	0.585	0.505	0.831	0.65	0.668
Expert prediction for consensus diagnosis for validation set for the entire sample							
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.879	0.89	0.872	0.823	0.922	0.876	0.873
Surgeon.B	0.61	0.549	0.66	0.57	0.641	0.605	0.605
Ortho C	0.819	0.74	0.907	0.899	0.757	0.818	0.828
Surgeon D	0.819	0.859	0.797	0.696	0.913	0.81	0.804
Expert prediction for true treatment for testing set for the entire sample.							
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.707	0.753	0.663	0.677	0.741	0.706	0.709
Surgeon.B	0.451	0.486	0.429	0.354	0.565	0.448	0.459
Ortho C	0.668	0.683	0.65	0.717	0.612	0.665	0.664
Surgeon D	0.674	0.775	0.611	0.556	0.812	0.672	0.684

	Expert prediction for consensus diagnosis for testing set for the entire sample.						
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.864	0.865	0.863	0.856	0.872	0.864	0.864
Surgeon.B	0.533	0.528	0.536	0.422	0.638	0.526	0.53
Ortho C	0.837	0.788	0.9	0.911	0.766	0.836	0.839
Surgeon D	0.864	0.958	0.805	0.756	0.968	0.862	0.862

Supplementary Table V. Performance metrics based on 4 experts predictions for true treatments and consensus diagnoses for validation and testing set for class II patients

	Expert prediction for true treatment for validation set for class II patients						
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.673	0.812	0.565	0.591	0.795	0.672	0.693
Surgeon.B	0.482	0.6	0.4	0.409	0.591	0.482	0.5
Ortho C	0.664	0.723	0.578	0.712	0.591	0.651	0.652
Surgeon D	0.664	0.774	0.561	0.621	0.727	0.661	0.674
	Expert prediction for consensus diagnosis for validation set for class II patients						
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.845	0.937	0.774	0.763	0.941	0.845	0.852
Surgeon.B	0.6	0.667	0.554	0.508	0.706	0.599	0.607
Ortho C	0.782	0.769	0.8	0.847	0.706	0.778	0.777
Surgeon D	0.855	0.906	0.807	0.814	0.902	0.854	0.858
	Expert prediction for true treatment for testing set for class II patients						
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.661	0.837	0.551	0.537	0.844	0.661	0.691
Surgeon.B	0.402	0.5	0.31	0.403	0.4	0.398	0.599

Ortho C	0.67	0.734	0.583	0.701	0.622	0.66	0.662
Surgeon D	0.58	0.763	0.486	0.433	0.8	0.579	0.616
Expert prediction for consensus diagnosis for testing set for class II patients							
	Accuracy	Precision surgery	Precision ortho	Recall surgery	Recall ortho	F1score	AUC
Ortho A	0.857	0.907	0.826	0.765	0.934	0.853	0.85
Surgeon.B	0.491	0.444	0.534	0.471	0.508	0.489	0.489
Ortho C	0.759	0.687	0.854	0.863	0.672	0.759	0.767
Surgeon D	0.777	0.842	0.743	0.627	0.902	0.767	0.765

Supplementary Table VI. Performance metrics based on 4 experts predictions for true treatments and consensus diagnoses for validation and testing set.

Expert prediction for true treatment for validation set for class III patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
Ortho A	0.718	0.75	0.702	0.562	0.846	0.705	0.704
Surgeon.B	0.437	0.357	0.488	0.312	0.538	0.423	0.425
Ortho C	0.69	0.632	0.758	0.75	0.641	0.69	0.696
Surgeon D	0.69	0.778	0.66	0.437	0.897	0.66	0.667
Expert prediction for consensus diagnosis for validation set for class III patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
Ortho A	0.915	0.958	0.894	0.821	0.977	0.909	0.899
Surgeon.B	0.549	0.429	0.628	0.429	0.628	0.528	0.528
Ortho C	0.859	0.737	1	1	0.767	0.858	0.884
Surgeon D	0.803	0.889	0.774	0.571	0.953	0.775	0.762
Expert prediction for true treatment for testing set for class III patients							
	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC

Ortho A	0.767	0.767	0.767	0.697	0.825	0.763	0.761
Surgeon.B	0.479	0.414	0.523	0.364	0.575	0.467	0.469
Ortho C	0.685	0.625	0.758	0.758	0.625	0.685	0.691
Surgeon D	0.726	0.783	0.7	0.545	0.875	0.71	0.71

Expert prediction for consensus diagnosis for testing set for class III patients

	Accuracy	Precision_surgery	Precision_ortho	Recall_surgery	Recall_ortho	F1score	AUC
Ortho A	0.932	0.933	0.93	0.903	0.952	0.93	0.928
Surgeon.B	0.534	0.448	0.591	0.419	0.619	0.519	0.519
Ortho C	0.822	0.725	0.939	0.935	0.738	0.822	0.837
Surgeon D	0.863	0.957	0.82	0.71	0.976	0.853	0.843

4 CONCLUSÃO

Essa dissertação demonstrou que a inteligência artificial pode ser utilizada como auxílio na tomada de decisão para tratamento ortodôntico e cirúrgico. O primeiro artigo concluiu que a IA pode ser utilizada para melhorar diagnósticos e planos de tratamentos utilizando imagens radiográficas, sendo que as melhores aplicações foram para osteoartrite nas articulações temporomandibulares, maturação e classificação esquelética, síndrome da apnéia obstrutiva do sono e necessidade de cirurgia ortognática. Já o segundo artigo concluiu que o modelo proposto pode auxiliar o processo de tomada de decisão do ortodontista para definir se um paciente necessita ou não de cirurgia ortognática. Além disso, o modelo apresentou melhores resultados quando treinado por diagnósticos obtidos em consenso entre experts e em pacientes com padrão esquelético classe III.

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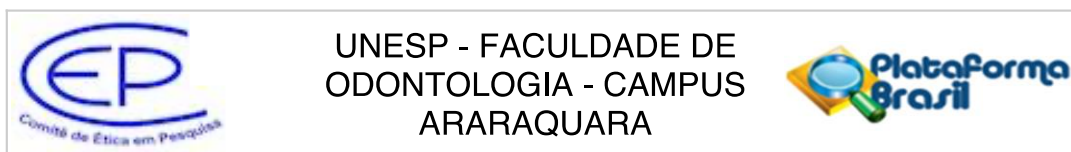
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ANEXO A – APROVAÇÃO DO COMITÊ DE ÉTICA



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: APLICAÇÃO DA INTELIGÊNCIA ARTIFICIAL NA PREDIÇÃO DE CIRURGIA ORTOGNÁTICA OU ORTODONTIA CONVENCIONAL

Pesquisador: Jonas Bianchi

Área Temática:

Versão: 2

CAAE: 47379021.2.0000.5416

Instituição Proponente: Faculdade de Odontologia de Araraquara - UNESP

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.905.916

Apresentação do Projeto:

Trata-se apresentação do projeto de pesquisa cujo resumo consta: "O correto diagnóstico e planejamento são de fundamental importância para que o tratamento ortodôntico tenha sucesso. A capacidade de tomar decisão se um paciente deverá ser tratado ortodonticamente ou com auxílio de cirurgia ortognática cabe a uma série de fatores como análise facial, oclusal e cefalométrica. Esta última, por ser amplamente estudada e ter a capacidade de quantificar erros esqueléticos e dentários, é imprescindível para o ortodontista e cirurgiões bucomaxilo faciais. Com o avanço tecnológico computacional e aumento do número de exames e dados, existe a possibilidade de incluir a inteligência artificial no processo diagnóstico. Por ser uma análise quantitativa, os dados fornecidos podem ser facilmente extraídos e utilizados em técnicas de aprendizado de máquina (machine learning) para auxiliar ortodontistas e cirurgiões na tomada de decisão. Desta forma, o objetivo desse estudo será de desenvolver e avaliar diferentes modelos de inteligência virtual capazes de prever se um paciente necessita ou não de cirurgia ortognática a partir dos valores obtidos de telerradiografias laterais avaliando tanto tecido duro e mole, e avaliar se este modelo é preciso em suas tomadas decisões. Para isso, serão utilizados 1000 telerradiografias laterais de pacientes previamente tratados com ortodontia ou cirurgia ortognática e divididos em dois grupos: cirúrgicos e não cirúrgicos. Dentro destes grupos serão subdivididos de acordo com seu padrão esquelético (classe II ou classe III). Serão traçadas as análises cefalométricas destes pacientes no tempo inicial (T1) previamente ao tratamento ortodôntico

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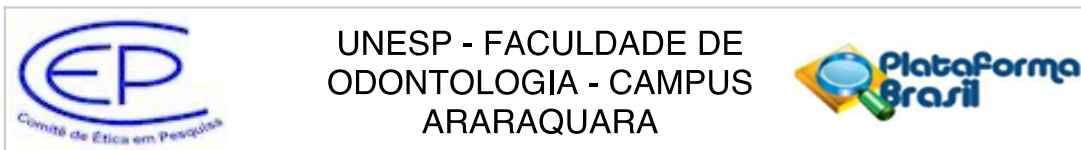
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convencional e/ou preparo cirúrgico e os dados alimentarão um sistema de inteligência artificial para predição se um paciente é classificado como cirúrgico ou tratamento ortodôntico convencional.”

Objetivo da Pesquisa:

O objetivo deste trabalho é desenvolver e avaliar diferentes modelos de inteligência virtual capazes de prever se um paciente necessita ou não de cirurgia ortognática a partir dos valores obtidos em telerradiografias laterais, previamente ao tratamento (T1) avaliando tanto tecido duro e mole, e avaliar se este modelo é preciso em suas tomadas decisões.

Avaliação dos Riscos e Benefícios:

Riscos: segundo os pesquisadores, haverá exposição de dados dos pacientes, mas o risco será minimizado pelo uso de códigos, que impossibilitem a identificação dos exames.

Benefícios: Os pacientes não se beneficiarão diretamente com este estudo, porém os resultados obtidos serão utilizados para melhora do diagnóstico cirúrgico de outros pacientes, no futuro.

Comentários e Considerações sobre a Pesquisa:

Estudo Nacional e unicêntrico, retrospectivo, não randomizado, de caráter acadêmico para obtenção de título de mestrado para o aluno PEDRO HENRIQUE JOSÉ DE OLIVEIRA, cujo orientador é o Profº Drº Jonas Bianchi. Não haverá patrocinador. Serão incluídos 1.000 telerradiografias provenientes do arquivo de uma clínica de Campinas, do período de 2000 a 2014.

“Os critérios de inclusão serão telerradiografias mostrando Classe II esquelético, definido pelo ângulo ANB4 e/ou Witts>0, classe III esquelético, definido pelo ângulo ANB0e/ou Witts”.

Os pesquisadores propõem a dispensa do TCLE, porque não possuem o contato direto com os pacientes e afirmam não conseguir realizar a busca desses pacientes para poder pedir autorização. Sendo assim, o estudo irá trabalhar com banco de dados que já estão em posse do pesquisador responsável. Todos os pacientes receberão um código para preservar a identidade dos mesmos. Segundo os pesquisadores, “A clínica particular em Campinas irá ceder em forma de arquivo de excel (.xlsx) os dados cefalométricos dos pacientes já desidentificados e catalogados, em forma de ID (001, 002, 003...).

Outras informações a respeito do paciente que serão fornecidos são: “idade, sexo e se o paciente passou ou não por cirurgia ortognática, para que possa ser feita análise estatística descritiva destes dados.”

A partir dessas telerradiografias serão realizadas análises por inteligência artificial utilizando algoritmos de machine learning para avaliação dos dados. Para isso, as telerradiografias dos

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pacientes, que já receberam cirurgia ou ortodontia, serão adicionadas aos modelos de algoritmos junto com seus valores cefalométricos. Por meio da cross-validation e processamento estatístico a inteligência artificial irá prever se um paciente é do tipo cirúrgico ou ortodôntico, com base nos valores apresentados na cefalometria inicial e na classificação pelo exame clínico. Serão avaliados a acurácia, sensibilidade, especificidade, área sobre a curva (ROC curve) e score “F1” dos modelos computacionais gerados. A previsão de início e término do projeto é de: 02-09-2021 a 30-03-2023.

Considerações sobre os Termos de apresentação obrigatória:

Os seguintes documentos foram inseridos na Plataforma Brasil:

- 1 - Autorização da chefia do departamento de Odontopediatria da FOAr-UNESP e da clínica Melchhiades de Odontologia, em Campinas, portadora das telerradiografias.
 - 2 – Cronograma
 - 3 – Orçamento
 - 4- Protocolo PB
 - 5 - Projeto de pesquisa em arquivo word
 - 6 - Folha de rosto
 - 7 - Termo de compromisso de utilização de dados sigilosos (TCUD)
 - 8 - Termo de concordância com a resolução 466/12 e com as normas do CEP da FOAr-UNESP.
- Os pesquisadores solicitaram dispensa do TCLE.

Recomendações:

Vide campo Conclusões ou Pendências e Lista de Inadequações.

Conclusões ou Pendências e Lista de Inadequações:

Todas as pendências anteriores foram atendidas e atualizadas na plataforma Brasil, de acordo com o que segue:

Pendência 1

No documento intitulado Orçamento, submetido em 27/05/2021, solicita-se que seja esclarecido que o recurso será do próprio pesquisador, pois somente está escrito custeio.

RESPOSTA: Foi anexado novo documento (24/06/2021) com alteração seguindo a solicitação.

ATENDIDA

Pendência 2

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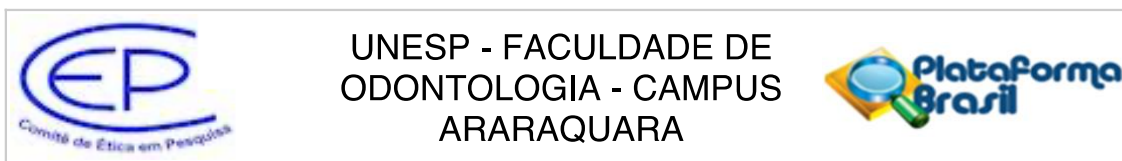
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Nos documentos intitulados PB Informações Básicas do Projeto, Projeto de Pesquisa Pedro HJ Oliveira, submetidos em 27/05/2021, a seleção das imagens compreenderá o período de 1980 a 2021 e outras de 2000 a 2014 e no documento de Termo de Dispensa TCLE Signed, submetido em 16/04/2021, a seleção das imagens compreenderá o período de 2000 a 2014, no documento intitulado Termo de Compromisso de Utilização de Dados TCUD Signed submetido em 16/04/2021, a seleção das imagens compreenderá o período de 2000 a 2018, esclarecer essas inconsistências e adequar todos os documentos para um único período.

RESPOSTA: A princípio a ideia seria que abrangendo um período de tempo maior, acreditou-se que facilitaria na seleção dos dados e também em um número amostral maior. No entanto, para manter maior qualidade de imagem e buscar padronização, optou-se selecionar as imagens compreendendo o período de 2000 a 2014, pois desta forma visamos abranger apenas telerradiografias digitais. Os documentos que estavam com a data errada foram alterados seguindo a solicitação.

ATENDIDA

Pendência 3

No documento intitulado PB Informações Básicas do Projeto, submetido em 27/05/2021, adequar o item critérios de inclusão: Os critérios de inclusão serão TELERRADIOGRAFIAS mostrando Classe II esquelético, definido pelo ângulo ANB4 e/ou Witts > 0, classe III esquelético, definido pelo ângulo ANB0 e/ou Witts < 0 [16,37], com ou sem extrações de pré-molares, pacientes maiores de 16 anos e estágio de maturação vertebral CS 5 ou CS 6.

RESPOSTA: O documento foi alterado seguindo a solicitação ("Os critérios de inclusão serão telerradiografias mostrando Classe II esquelético, definido pelo ângulo ANB4 e/ou Witts > 0, classe III esquelético, definido pelo ângulo ANB0 e/ou Witts < 0 [16,37], com ou sem extrações de pré-molares, pacientes maiores de 16 anos e estágio de maturação vertebral CS 5 ou CS 6 [38].")

ATENDIDA

Pendência 4

Nos documentos intitulados PB Informações Básicas do Projeto, submetido em 27/05/2021, no Termo de Dispensa TCLE Signed, submetido em 16/04/2021, no Termo de Compromisso de Utilização de Dados TCUD Signed submetido em 16/04/2021, no Projeto de Pesquisa Pedro HJ Oliveira, submetido em 27/05/2021 é comentado que os dados

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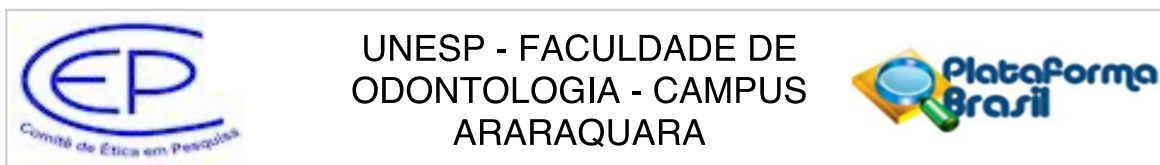
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utilizados serão DESIDENTIFICADOS, solicita-se esclarecer como será feita a seleção de idade.

RESPOSTA: A clínica particular em Campinas irá ceder em forma de arquivo de excel (.xlsx) os dados cefalométricos dos pacientes já desidentificados e catalogados, em forma de ID (001, 002, 003...). Além destes dados, as outras informações a respeito do paciente serão fornecidos: teleradiografias, idade, sexo e se o paciente passou ou não por cirurgia ortognática, para que possa ser feita análise estatística descritiva destes dados.

ATENDIDA

Pendência 5

Nos documentos intitulados PB Informações Básicas do Projeto, Projeto de Pesquisa Pedro HJ Oliveira, submetidos em 27/05/2021, Cronograma Signed, submetido em 16/04/2021, solicita-se que seja adequado o cronograma para início em 02/09/2021. Caso outro documento apresente o cronograma o mesmo deverá ser alterado.

RESPOSTA: Os documentos foram alterados seguindo a solicitação.

ATENDIDA

Considerações Finais a critério do CEP:

Protocolo APROVADO em reunião de 13 de agosto de 2021.

O pesquisador deverá apresentar um relatório parcial no meio do período da pesquisa e um relatório final.

Deve ser apresentado somente o relatório final em pesquisas com duração de até 1 ano.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1728957.pdf	09/07/2021 17:10:09		Aceito
Declaração de Pesquisadores	TermoCompromissoUtilizacaoDadosTCUDsigned.pdf	09/07/2021 17:09:57	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Outros	CartaRespostaCEPSigned.pdf	09/07/2021 17:09:38	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Parecer Anterior	PB_PARECER_CONSUBSTANCIADO_CEP_4769075.pdf	24/06/2021 22:10:43	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Orçamento	Orcamento2.pdf	24/06/2021 22:10:24	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Projeto Detalhado / Brochura	ProjetoPesquisaPedroHJOliveira.pdf	24/06/2021 22:09:39	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito

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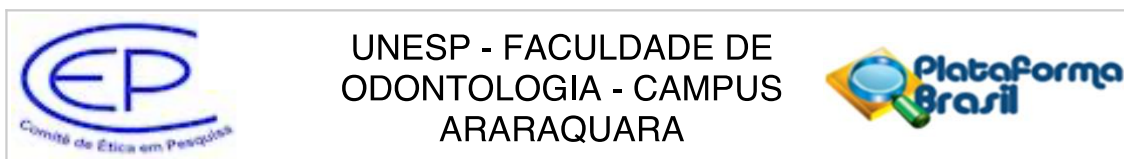
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Investigador	ProjetoPesquisaPedroHJOliveira.pdf	24/06/2021 22:09:39	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Cronograma	Cronogramav2.pdf	24/06/2021 22:08:34	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Declaração de Instituição e Infraestrutura	AutorizacaoUsoDependenciasDepto.pdf	27/05/2021 20:38:53	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Declaração de Instituição e Infraestrutura	AutorizacaoDeUsoDependenciasCMO.pdf	27/05/2021 20:37:49	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TermoDeDispensaTCLESigned.pdf	16/04/2021 16:49:30	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Declaração de concordância	TermoDeConcordanciaSigned.pdf	16/04/2021 16:49:02	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito
Folha de Rosto	FolhadeRostoAssinada.PDF	16/04/2021 16:42:27	PEDRO HENRIQUE JOSE DE OLIVEIRA	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

ARARAQUARA, 14 de Agosto de 2021

Assinado por:
Andréa Gonçalves
(Coordenador(a))

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Não autorizo a publicação deste trabalho pelo prazo de 2 anos.

(Direitos de publicação reservado ao autor)

Araraquara, 26 de Janeiro de 2023.

Pedro Henrique José de Oliveira