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TITLE

**USE OF DIGITAL TECHNOLOGIES IN THE DIAGNOSIS,
TREATMENT PLANNING AND THERAPY OF
ORTHODONTIC PATIENTS.**

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Handwritten signature of Prof. Vincenzo D'Antò in black ink.

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SUMMARY

The current definition of being “digital” is the “re-imagining of processes to be by default a fully online, fully automated process from end user interaction to back office processing, with no or minimal need for human intervention”[1].

Digital technology has begun to be a fundamental part of our daily life, starting from the use of smartphones to its use in medical diagnosis, treatment modalities, teaching and learning tools, and surgical techniques [2].

Digital technology in a dental practice started in 1974 with the introduction of computerized scheduling [3]. At the beginning, the approach of using digital technology was to increase the accuracy of the diagnosis; as a result, the workflow was simplified [4].

In the last thirty years, most dental offices and dental schools have begun to use clinical records, photographs and digital radiographs. Moreover, digital technology has evolved from two-dimensional visualization, based on photographs or drawings, to the possibility of exploring a patient in his three dimensions. Also, soft tissue analysis using 3D stereophotogrammetry (3D photos), intra-oral scans and three-dimensional radiography are rapidly replacing study casts and two dimensional radiography [2]. One of the benefit of the digitalization is the opportunity to have high resolution images with low radiation obtained through the cone beam computed tomography, that is currently considered the preferred imaging modality in orthodontics [4].

In addition, digital technology in orthodontics allows to perform virtual treatment planning, as well as translate the plans into treatment execution with digitally driven appliance manufacture and placement using various CAD/CAM techniques from printed models, indirect bonding trays and custom made brackets to robotically bent wires. Moreover, it is also becoming possible to remotely monitor treatment and control it [2].

The virtual treatment planning not only allows the clinician to explore a number of treatment options in a simple manner, it also facilitates better communication with other dental professional especially in cases that require combined orthodontic and restorative treatment. Furthermore, it provides an effective communication with patients and allows them to visualize the treatment outcome and also understand the treatment process [2].

The aim of this PhD project was to study the use of digital technologies in the diagnosis, treatment planning and therapy of orthodontic patients.

This thesis is composed of four studies.

The aim of the first study was to perform a collaborative web service to support orthodontic treatments, using a collective of models, automatically generated, on the basis of different

datasets, made by different scholars and practitioners at the School of Orthodontics of the University of Naples “Federico II”, in order to help in the diagnosis of the orthodontic patient. In chapter 2, it is reported a research on the association between gingival biotype and facial typology evaluated by means of a cephalometric and 3D facial analysis, in patients seeking an orthodontic treatment.

The third study aimed to determine the distribution of the $CoGoMe^\wedge$, and its relationship with age, sagittal jaw relationship ($ANPg^\wedge$) and mandibular inclination ($SN^\wedge GoGn$) in a population of patients from Southern Italy.

In chapter 4, it is described a research on the periodontal health of patients undergoing fixed orthodontic and clear aligner therapy with a supportive periodontal therapy after a 3-month follow-up.

References

1. Hmeid, R. What does “being digital” actually mean?.
<https://www.infoq.com/articles/meaning-being-digital/>. Last assessed on 05 to october 2018.
2. Tarraf, N.E., Ali, D.M. (2018). Present and the future of digital orthodontics☆. *Seminars in Orthodontics*. 24:376–85.
3. Reisman, A., Emmons, H., Green, E.J., Occhionero, R., Mehta, S., Morito, S., Dadachanji, K. (1974). Computer simulation of scheduling in a dental practice involving expanded duty dental auxiliaries. *Technical memorandum*.
4. Vaid, N.R. (2018). Digital technologies in orthodontics—An update. *Seminars in Orthodontics*. 24:373–5.

CHAPTER 1

A Collaborative Web Service Exploiting Collective Rules and Evidence Integration to Support Orthodontic Decisions.

Abstract

Despite the growing demand for orthodontic care, there is lack of unanimity in the interpretation of orthodontic data and in the diagnostic and therapeutic orthodontic choices. In order to support orthodontic decision-making, this article proposes a collaborative web-service that generates a collective model for orthodontists in their daily practice. The platform is bi-directional: on the one hand it is able to deliver the collective model to orthodontists, using different friendly visualization tools; on the other hand, it is able to update the dataset, thus generating new models. The web service is based on decision trees algorithms, modeled using cephalometric and orthodontic cast measurements as features. A clinical evaluation shows that, whereas there is a low level of agreement within and between orthodontists, decision trees may result beneficial in supporting clinical decision-making.

This chapter is based on “Adinolfi P., D’Antò V., D’Avanzo E., Pango Madariaga A. C., Martina R., Michelotti A., Zanolli R. A Collaborative Web Service Exploiting Collective Rules and Evidence Integration to Support Orthodontic Decisions. *Journal of Cleaner Production* 176 (2018):813-826”.

1.1. Introduction.

Dental malocclusions are highly prevalent pathologies in the general population [1–3] and the increasingly great attention to aesthetic and functional problems [4,5] has driven to a larger demand of orthodontic treatments in the last years [6]. As evidenced by a survey of the American Association of Orthodontists (AAO), “The survey titled “The Economics of Orthodontics,” asked members of the AAO in the United States and Canada information about patients they were treating in 2012), in 2012 AAO members have treated a total of 5,876,000 patients, with an increase of 20% as compared to 2010. Another survey, still conducted on behalf of the AAO, shows how adults, who have undergone orthodontic care, support that their treatment contributed to meaningful improvements in both their professional and personal lives. 75% of subjects surveyed reported about their increased self-confidence, while 92% of the whole sample of respondents would feel able to suggest the orthodontic treatment to other adults.

Despite the growing demand for orthodontic care [7,8], with a real paradigm shift also in its marketing strategies [9], orthodontic diagnosis may be difficult to be drawn [10], due to the subjective interpretation of the diagnostic records [11], demonstrating that a minimal configuration of a record set for orthodontic diagnosis and treatment planning could not be defined. On the other side, treatment planning is a decisive and critical moment for the clinician, especially in the case of *extraction*, which is a non-reversible procedure, mainly based on the practitioner's experiences. For instance, Ribarevski et al. [12], in their investigation, demonstrated that the level of agreement for the *extraction/non-extraction* decision within the orthodontists was moderate, as well as a poor agreement between the orthodontists exists. More recent inquiries show that this trend, about poor agreement *within* and *among* orthodontists, still holds [13–15]. On the whole, these findings show the subjective aspects of orthodontic diagnoses [16], the lack of universality and unanimity in the interpretation of orthodontic data [17] and, consequently, in the choice of treatment [18,19], also suggesting that treatment planning is derived from weak levels of scientific evidence [20].

In the light of the above evidence, a referencing framework for orthodontic data evaluation would be desirable and beneficial for a diagnostics treatment selection [21] particularly as regards controversial cases, where subjective data interpretation could generate incorrect decisions [22]. The main objective of this work is the realization of a collaborative web service to support orthodontic treatments, using a collective of models, automatically generated, on the basis of different datasets, made by different scholars and practitioners at the School of Orthodontics of the University of Naples “Federico II”. The proposed approach aims to fulfill two subtasks:

- 1) generating individual models that can be compared, and validated, to the strategies adopted by scholars from the School of Orthodontics and, based on these individual models, building a collective model, according to a specific configuration of the orthodontic features;
- 2) creating a “bi-directional” web platform. In one direction, the platform is able to deliver these models, using different friendly visualization tools and rules, to scholar and practitioners in their daily working practice, including refresher courses and training for orthodontic schools. In the other direction, the platform is able to benefit from the contribution of its users in order to update the dataset and, as a consequence, to generate new models.

The engine behind the web service is based on *decision trees* algorithms [23] that are modeled using cephalometric and orthodontic cast measurements as features.

Decision tree (hereafter DT) is a classification scheme that generates a tree and a set of rules from a given dataset [24]. It has been widely employed both to represent and to run decision processes [25,26]. Considering that medical, and as such orthodontic, decisions are made for various purposes including screening, diagnosing, and treatment prescription/suggestion, the decision problem becomes difficult to visualize and implement [27].

Decision tree represents also a useful and indispensable graphical tool in such settings, as it allows for intuitive understanding about the problem and can aid the decision adoption since it is interpretable through *if-then rules* by any orthodontist, even if not trained in using computer applications. Furthermore, the “robustness” of the proposed approach [28,29] goes far beyond the simplification of the orthodontic decision process, since models extracted from data, through decision trees, can guarantee a major “objectivity” asked by the interpretation of the orthodontic data [30,31], as cited above, and, as a consequence, can allow for the suggestion of the most appropriate therapy, based on the collective of models, previously validated by experts and scholars. Such an approach represents a further attempt, along with the others, towards the foundation of a common framework aiming at reducing, as much as possible, the subjectivity in the interpretation of orthodontic data [32].

Seok-Ki & Tae-Woo [33] propose an approach for the diagnosis of teeth extractions through neural networks, providing the evaluation of their model. The authors employed a dataset of 156 patients made of 12 cephalometric variables and 6 additional indexes. Extraction patterns, useful for diagnosis, were obtained applying four neural networks that make use of a back-propagation

algorithm. Experimental results show that success rates of the models generated were 93% for the diagnosis of extraction vs. non-extraction and 84% for the detailed diagnosis of the extraction patterns.

Xie, Wang & Wang [34] used a neural network, for the orthodontic treatment of patients between 11 and 15 years old, in order to determine extraction treatment. Experimental settings employed a dataset made of 200 subjects, using 23 indices as features. The experiments allowed to estimate the contributions of the 23 input indices to the final output (i.e., extraction vs. non-extraction). For instance, "Anterior teeth uncovered by incompetent lips" and "IMPA (L1-MP)" resulted to be the two indices that give the biggest contributions sequentially. According to the authors, when the clinicians are predicting whether an orthodontic treatment requires extraction, the indices "anterior teeth uncovered by incompetent lips" and "IMPA (L1-MP)" should be taken into consideration first.

Martina, Teti, D'Addona & Iodice [18] developed a decision support system, based on neural networks, in order to aid clinical decision making for orthodontic extractions. The employed neural network makes use of a feed-forward back-propagation paradigm trained on a dataset made of 48 cases, exploiting, overall, 32 cephalometric and orthodontic cast measurements as features. The 32 features made up a 32-component input vector and the extraction therapeutic option represented the corresponding 1-component output vector, classified as belonging to one of two categories: extraction vs not-extraction. As for the evaluation, the system output was considered correct if its decision (i.e. extraction or not-extraction) coincided with the decision for the patient at the moment of the orthodontic treatment. In both cases, the performance of the system achieved an accuracy level of more than 75%.

1.2. Material and methods

1.2.1. Dataset

This work exploits the application of DT for orthodontics treatments to detect and visualize the most relevant combinations of features pertaining to the orofacial system. The preliminary dataset consists of 290 medical records of patients, from 8 to 53 years of age (with a *mean* of 15.59 years), in the permanent dentition, without previous orthodontic intervention. Subjects' characteristics were divided according to *skeletal class*, *clinical*, *radiographic*, and *functional* features. Table A.1, in Appendix A, reports a complete classification of the features employed.

The dataset is the fruit of the contribution of different scholars working in the School of Orthodontics at the University of Naples “Federico II”. In other words, each scholar/practitioner builds its own dataset by detecting, for each patient, 39 common features, shared by all scholars, used to describe the cases (including the *class label*, that is *teeth extraction* or *non-extraction*). The dataset counts 232 *negative* examples (i.e. medical records about patients classified as *not extraction* cases) and 58 *positive* examples (i.e. medical records about patients classified as *extraction* cases), so there is a situation of unbalanced distribution of data (i.e., *skewed* as is said in statistical terms) with respect to the *class label/target value* (i.e. *teeth extraction* or *non-extraction*) that you want to model. This state of affairs will require certain steps during the training of the algorithm, in order to take account of the lower weight, played by the *positive* examples, within the entire economy of the dataset. The experimentation, and the testing, delivered through the web service, will be designed to support treatments for Class I malocclusion.

1.2.2. Implementation

Experiments introduced in the following, and the corresponding web service prototype based on them, employ J48 DT, a WEKA implementation [35] of C4.5 DT algorithm, developed by Ross Quinlan [36], which, in turn, is an extension of the ID3 tree, the early algorithm version of the same author [23]. Turning to the definition provided by Mitchell [37], DT’s, such as ID3 and C4.5, classify instances, that is, orthodontic medical records, by sorting them down from the root to some leaf nodes, providing the classification of the instances (i.e., *extraction*=1 vs. *not-extraction*=0). Nodes of the DT’s specify tests of some *features* (or *attributes*) describing the instances, such as *dentobasalDiscrepancy* at the *root* node of the DT in Figure B.1 of Appendix B. *Branches* descending from nodes correspond to one of possible values the attribute may assume; for instance, *dentobasalDiscrepancy* in Figure B.1 may assume two sets of possible values, ≤ -3.5 and > -3.5 . Any instance (i.e., medical record) is classified by starting from the root node of the tree, on the top, where the attribute of the node is tested; then, DT moves down through the tree branches, looking for the *feature* value of the given example. The same process will be repeated for the sub-tree rooted at the new node. For instance, always looking at Figure B.1, after testing *dentobasal Discrepancy* at the root node, J48 jumps on the right and left branches, based on the two sets of value the root feature may assume, and tests, respectively, *Canine Class Malocclusion Right* and *Canine Class Malocclusion Left*. The feature/attribute selection (that is, which feature to test at each node of the tree), plays a chief role for DT’s. In the experiments introduced in the

following, two *feature selection* methods have been employed: *Information Gain* and *GainRatio* [35,37], whose calculation is reported in Appendix A, respectively in Eq. A.2 and A.3. *InfoGain* is strictly related to the *Entropy* [23,37], an index of the purity of a dataset, since it just represents the expected reduction in entropy that results by the partition of the examples according to this attribute, as can be seen from the Eq. A.1. For instance, for the orthodontic dataset, the *Entropy* is about 0.22, a value that indicates the unbalancing of the distribution towards the *non-extraction target/class label* (i.e., 0). Table B.2 in the Appendix B reports the *ranked list of features*, obtained from the orthodontic dataset after employing the *InfoGain* mechanism, just described above, for the experiment one described in Section 4. One drawback of *InfoGain*, however, is that it tends to prefer attributes with many values. *GainRatio* (Quinlan, 1986; Mitchell, 1997) is a possible remedy to this issue, since it levels the playing field by penalizing the multiple-valued attributes. Table C.2 and Table D.2 report on a comparison among the two feature selection strategies, respectively for the experiments 2 and 3, also detailed in Section 4.

1.2.3. Evaluation

Experiments performed for this work have been tested using different evaluation metrics [38,39]. As first evaluation metrics, *accuracy* has been employed, that measures how often DT makes the correct prediction, calculating the ratio between the number of *correct predictions* and the *total number of predictions* (Eq. A.4). However, this metrics suffers from an important drawback since it does not make distinction between classes; correct answers for each class are treated equally. For instance, how many examples failed for each class? This is the case of the skewed distribution of the orthodontic dataset. Furthermore, it does not distinguish those cases in which the patient was subjected to *extraction* when, instead, should not have (i.e., *false positive*), or other cases where the extraction was not made but it was necessary (i.e., a *false negative*). For such a kind of evaluation the *confusion matrix* (Eq. A.5) was employed, showing a detailed breakdown of *correct* and *incorrect* classifications for each class. The *matrix* returns a better overview of which class is best identified by the model; such a kind of information would otherwise be lost only looking at the overall *accuracy*.

Out of the cases that the DT predicted to be true (i.e., the DT assigned an *extraction* target value), how many of them actually need it? *Precision* score (Eq. A.6) answers the question, while *recall* (Eq. A.7) allows for determining how many cases are found to be true by the DT, out of all the cases that are true. *Precision* and *recall* can be read in the light of their harmonic mean, F_1 score

(Eq. A.8), a single metric that, unlike the arithmetic mean, tends toward the smaller of the two elements, resulting small if either *precision* or *recall* is small. In machine learning the term *learning curve* represents the generalization performance of the model as a function of the size of the training set [40]; in other words, it depicts improvement in performance on the vertical axis when there are changes in another parameter (on the horizontal axis), that is, the training set size. A chief role in this experimentation is played by the clinical validation. Indeed, the clinical validation has a twofold objective. First, it aims to measure decisions *within* and *between* orthodontists where, as demonstrated by the previous work, reported in Section 1, the former seem to be *poor/moderate*, whereas the latter resulted to be *poor*. Second, the clinical control aims at validating the automatically generated DT's and their rules. Since, as said, orthodontists' decisions suffer from a lack of objectivity, DT's aim to support them with trees/rules that must be shared as much as possible by physicians who have such a low rate of agreement, with themselves and between them.

1.3. Results/Experiments/Discussion

Three runs of experiments were performed, in order to generate different types of DT to be submitted to medical validation and, therefore, testing their “goodness” and efficiency from a clinical point of view. All details about the results of the experiments are reported, respectively, in Appendix B, Appendix C and Appendix D. Each Appendix contains the DT generated for the experiment, a table reporting details on the *learning curve*, and a table reporting the *attribute ranked list* that compares attributes selected through *InfoGain* and *GainRatio*. To build the DT model out of the orthodontic dataset, for all the experiments performed, J48 has been run employing *Leave-One-Out Cross-Validation* (LOOCV), in order to estimate the generalization capability of models created by the procedure (i.e. DT's), rather than of the model itself [35,37]. LOOCV estimates the generalization performance of a model trained on $n-1$ samples of data, which is a pessimistic estimate of the performance of a model trained on n samples. Rather than choosing one model, the thing to do is to fit the model to all the data, and use LOOCV to provide a conservative estimate of the performance of the model.

Table 1 . Overall accuracy for the first experiment expressed in %

Classification Summary		
Correctly Classified		
Instances	207	71.34
Incorrectly Classified		
Instances	83	28.62
Total Number of Instances	xx	

Table 2 . Detailed accuracy for the first experiment expressed in %

	Precision	Recall	F1
Weighted Average	70.8	71.4	71.1
Class: 0	81.7	82.8	82.2
Class: 1	27.3	25.9	26.5

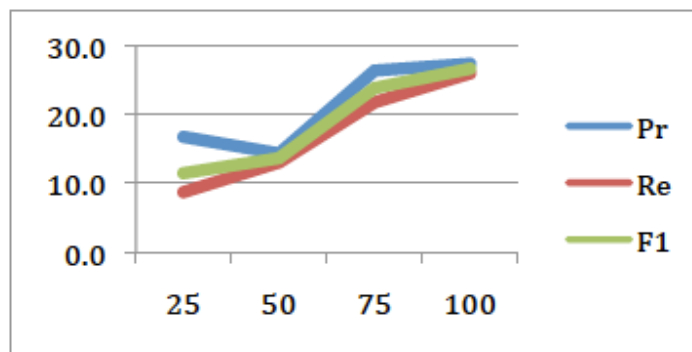


Figure 1. Graph of the learning curve for the first experiment

Table 3. Detailed accuracy for the first experiment but with SMOTE expressed in %

	Precision	Recall	F1
Weighted Average	72.8	73.1	72.9
Class: 0	82.9	83.6	83.3
Class: 1	32.1	31.0	31.6

Using this setting for the first run, J48 generated the DT shown on Figure B.1 (Appendix B), performing with an *overall accuracy* of 71.37%, as reported in Table 1. To get a better overview for both *extraction* (i.e., 1) and *not-extraction* (i.e., 0) class labels, Table 2 shows a detailed *accuracy*, for each class, in terms of *precision*, *recall* and F_1 . Even if these results could appear satisfying as for the basic setting, since they outperform the performance of the *baseline* (i.e., a *trivial acceptor* whose *precision*, *recall* and F_1 were, respectively, 20%, 100% and 33%), two “singularities” were noted on learning curve, as can be seen in Figure 1. In fact, although it showed an increasing trend, two local falls were visible, in terms of performance, towards 50% and 75% of the model training. This behavior suggested employing a new experimental setting. However, before doing this, it has been tested the capability of J48 to address the skewed distribution of the orthodontic dataset towards *not-extraction* class. This is non-trivial from a clinical point of view for two reasons. First of all because in recent years a common trend has emerged from experience, to treat patients with orthodontic appliances, rather than resorting to the extraction. So, as new medical records will be collected to update DT’s models, a tendency to collect a greater number of *non-extraction* with respect to *extraction* cases is expected. Secondly, *extraction* treatment planning is a decisive and critical moment for the clinician, since it is a non-reversible procedure, and tends to be mainly based on the practitioner's experiences. For these reasons, it is of fundamental importance that J48 is equipped with a mechanism capable of balancing the distribution towards the *extraction* cases and give them a greater characterization. To this end it has been preferred to choose the first configuration of J48, so to get in the most unfavorable situation. In order to resample the dataset, it has been employed the SMOTE methodology [41,42]. Results of the experiments are reported in Table 3. As you can see, there is a general and noticeable improvement, both in terms of *weighted average* and for the individual classes, demonstrating the feasibility of the approach also for better settings of J48

With regard to the second experiment, it has been requested to J48 to return all “difficult cases”, that is, those that could be difficult or impossible to classify. J48 returned a list of 15 medical records, reported in Table C.3. Among the reported records, 5 cases belong to the *non-extraction* class while 10 belong to the *extraction* class. With this new configuration, J48 showed an overall improvement of all its performance. As reported in Table 4, the *overall accuracy* increased from 71.37% of the first setting to 85.4545% of the new one. The *detailed accuracy*, per classes, also confirms the improvement, as showed in Table 5. This table shows a general increase in terms of the *weighted average* F_1 , from 71.1 % of the previous configuration to 84.8% of the new one.

Looking at the individual classes, J48 exhibits the same order of magnitude in the improvement: F_1 for the *extraction* class (i.e., 1) increases from 26.5 % of the previous setting to 53.5% of the new one, whereas for the *non-extraction* (i.e., 0) class F_1 increased from 82.2 to 91.4%. As for the learning curves, Figure 2 clearly shows how the singularities, exhibited in the previous configuration, have disappeared, showing an increasing linearity of the learning curve that suggests a certain reliability in improving the model, and to generalize, where new medical records appear.

This configuration setting represents the first intersection point between the automatic evaluation of the generated DT's and the clinical evaluation that will be introduced shortly. In fact, the DT generated at this step, showed in Figure B.1, is given to the members of the Orthodontic School in order to evaluate its "goodness" and efficiency. Another intersection point between this configuration setting and the clinical evaluation is provided by the "difficult cases". All these cases were given to the physicians in order to test their difficulties to classify them. This second trial allows also to evaluate orthodontist *within* and *between* agreement. However, before introducing the clinical evaluation, it is interesting watching at the last configuration setting of J48. The third configuration was set exploiting C4.5, and its implementation J48, inner capability of post-pruning [37]. The technique allows reducing the size of the tree. As for the orthodontic decision-making problem it allows to provide clinicians with a different visualization of the tree, as well as with little change in the rules generated, and the same performance. The third tree generated after the pruning step is showed in Figure D.1. As can be noted, unlike the tree generated in the second configuration, this one comes in a "lean" and "elongated" shape. The performance of the new tree does not change, at least in terms of *overall* and *detailed* accuracy, as demonstrated by the results reported in Table 4 and Table 5. Be recorded only a slight decrease in the learning curve, however, it continues to grow with linearity, and in the absence of drop points, as reported in more detail in the Table D.1

Table 4. Overall accuracy for the second experiment expressed in %

Classification Summary		
Correctly Classified Instances	235	85.4545
Incorrectly Classified Instances	40	14.5455
Total Number of Instances	275	

Table 5. Detailed accuracy for the second experiment expressed in %.

	Precision	Recall	F1
Weighted Average	84.4	85.5	84.8
Class: 0	89.5	93.4	91.4
Class: 1	60.5	47.9	53.5

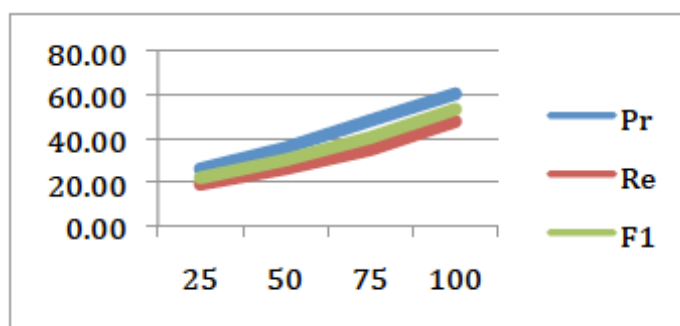


Figure 2. Graph of the learning curve for the second experiment.

Table 6. Overall accuracy for the third experiment expressed in %

Correctly Classified instances	235	85.4545
Incorrectly classified instances	40	14.5455
Total number of instances	275	

Table 7. Detailed accuracy for the third experiment expressed in %

	Precision	Recall	F1
Weighted average	84.4	85.5	84.8
Class 0	89.5	93.4	91.4
Class 1	60.5	47.9	53.5

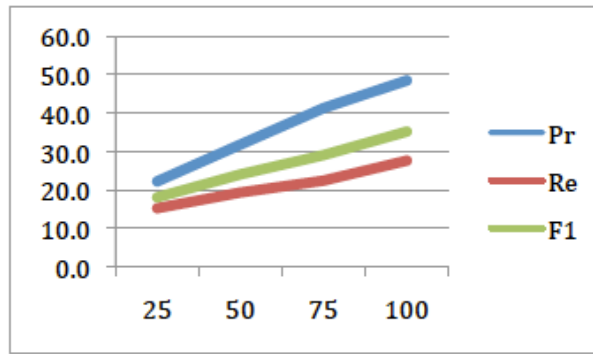


Figure 3. Graph of the learning curve for the third experiment

The clinical evaluation has a twofold objective. First, it aims to know how the physicians at the Orthodontic School classify the 15 “difficult cases”. Here it has been conjectured that the cases rejected by J48 were so complicated that the medical experts cannot even classify them. The second objective was to evaluate, from a clinical point of view, the “goodness” and the efficiency of the generated DT’s. DT’s come with their own rationale, that are candidate “best practices” under form of *if then rules*, or as readable *paths* on the branches of the DT visualization, from the *root* to the *leaf* nodes, as in Figure 4 and Figure 5.

As for the first experiment, in order to get the classification of the 15 “difficult cases”, 20 orthodontists were given a blinded excel table with all 15 medical records, that is, where record ID’s were removed as well as the earlier classification (i.e., *extracted* or *not-extracted*). During the administration of the test, physicians were told to classify the records, generated randomly from a DT, looking at only the 38 out 39 features (without class label that was removed) describing the case. In the first round, a set of 10 orthodontists annotated 15 medical records. In the second round, when the annotation was blind, only 4 records registered the same annotation of the first round, spread on 4 different physicians from the first round. On the whole, these results show a *within* moderate/poor agreement (i.e., about 26%). Then, it was tested the agreement *between* annotation/physicians looking at how other physicians shared the decision that their colleague took at the first round. For one patients belonging to *not-extraction* class the decision was shared by 19 colleagues; for another patient, always belonging to *not-extraction*, the decision was shared by 18 colleagues; for one patient belonging to class 1 (i.e., *extraction*), the decision was shared by 18 physicians. Seven cases were shared by less than 3 physicians, demonstrating an overall moderate *between* agreement, in line with the previous body of knowledge.

As for the second clinical experiment, DT’s generated by J48 in the second and third experimental setting, and showed in Figure 4 and Figure 5, were submitted to clinicians in order to test their

“goodness” to support physicians’ decisions. During the administration of the test, physicians were required to trace, on the printed tree, all possible paths that were considered useful and plausible to take a positive decision (i.e., *extraction*), even if the path ended in a leaf node with 0 (i.e., *non-extraction*).

Results for the tree reported on Figure 4 show that only eight rules have been traced. Rule 2 is the most frequently suggested by physicians. It gets to the leaf node employing only 4 features on the upper part of the tree. Also Rule 1, shared by 9 physicians, employs only 4 features out of 38 to take a decision. Five physicians share rule 3 and 4. Whereas the former uses 4 features, the latter takes, even, only 2 features to make a decision. Only one path (i.e., rule 6) employed more than 6 features and it has been suggested by only one physician.

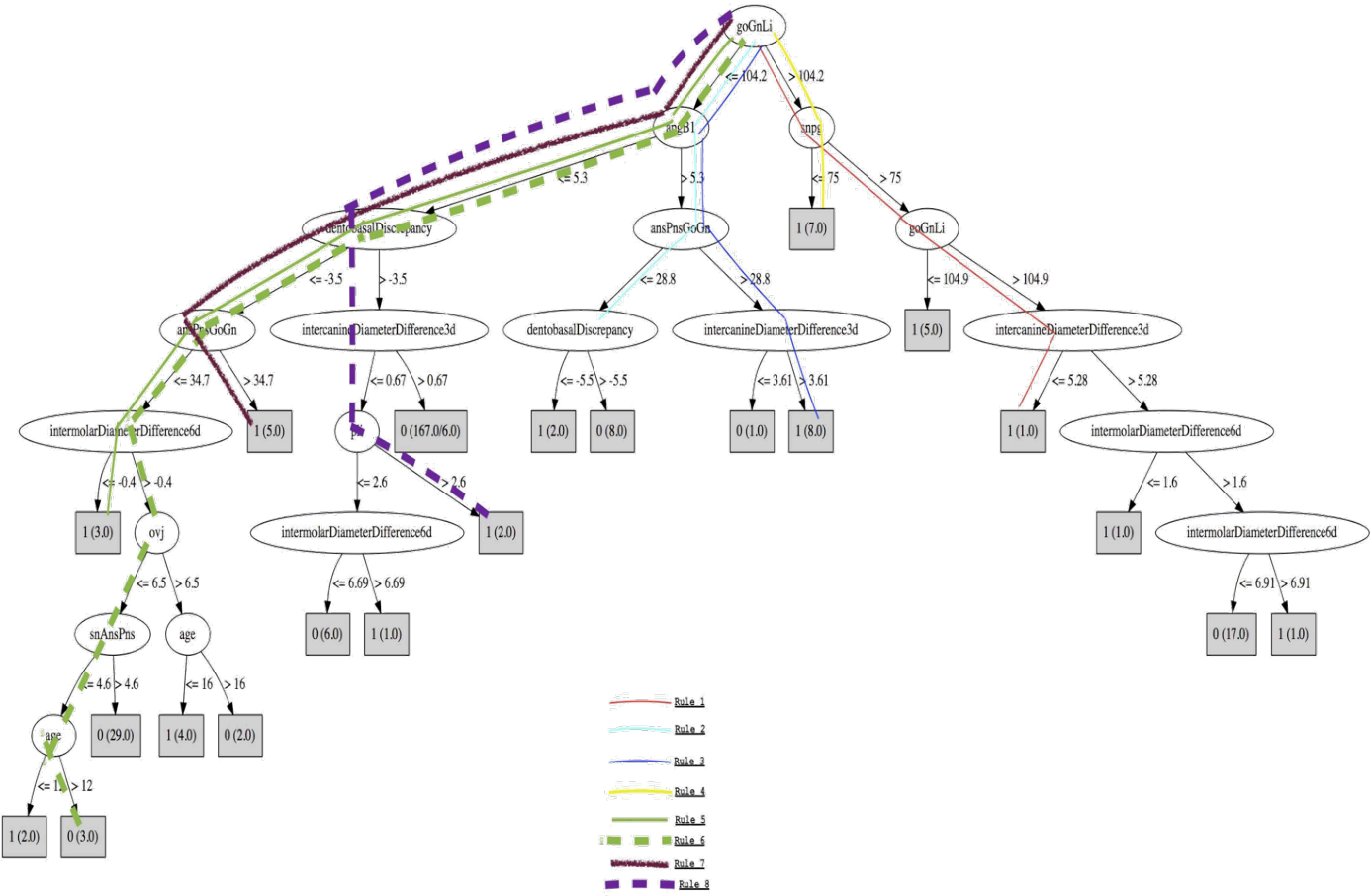


Figure 4. DT generated with the second experimental setting and validated with the rules annotated from physicianFigure 4 – DT generated with the second experimental setting and validated with the rules annotated from physicians.

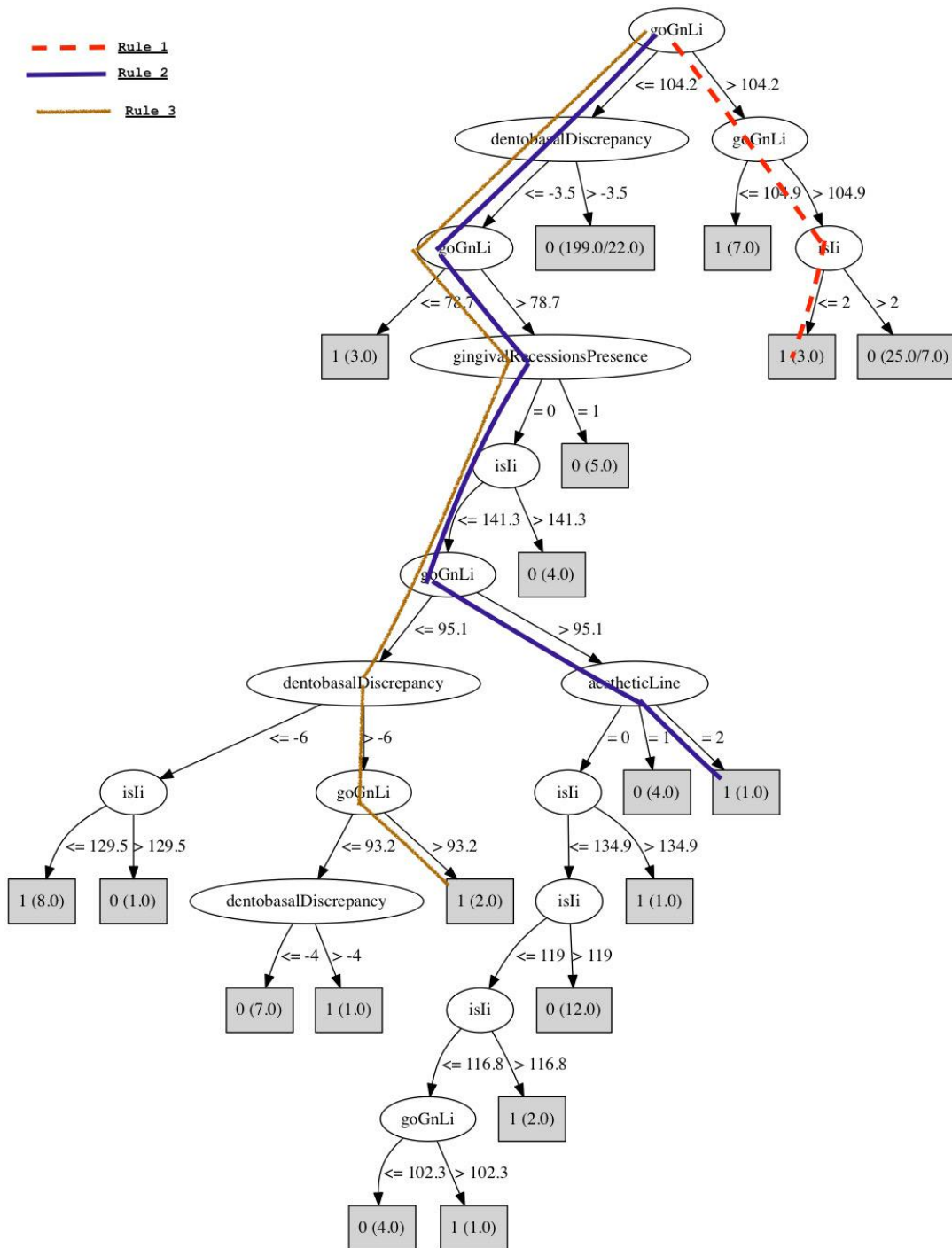


Figure 5. DT generated with the third experimental setting and validated with the rules annotated from physicians.

Turning to the DT generated with the third setting and showed in Figure 5, it resulted with three main rules considered plausible by physicians. Rule 1, in red, is the most frequent, since it has been suggested by 12 clinicians. This rule makes use of only 3 features and is located on the upper

side of the tree. Rule 2 is suggested by 10 physicians and it takes a longer path, so to speak, since it uses 5 features. Finally, rule 3, that employs 7 features, is suggested by 2 physicians. The good news is that all the rules chosen by the clinicians, with the exception of a particular case, ended in the positive class label, that is, they were extraction decisions. The two clinical evaluations, that earlier appeared to be autonomous from each other, indeed converge towards a common rationale: physicians, that in the first clinical evaluation exhibited low *within* and *between* agreement, when given a set of candidate “best practices”, through a DT that shows them possible decision under the form of paths on the tree, show agreement, demonstrating the benefit of employing such a model to support orthodontic decision-making. All the rules chosen are located in the upper side of the DT and make use of a small number of features with respect to the complete list of 38 features that describe each medical record. In other words, orthodontists seem to apply Occam’s razor, preferring the simplest hypothesis that fits the data and, as such, behaving such as other scientists, they have inductive bias towards simple explanations over more complex ones. In this sense, this is an argument against that supported by Turpin and Huang [20] who claim the lack of scientific evidence.

Mitchell [37] argues that the preference for shorter hypothesis is that it is less likely to deal with them to fit the training data with respect to very complex hypotheses that even fitting current data, however, they fail to generalize, correctly, on new data.

1.4. Conclusion

There is an increasing interest in the decision support systems that may assist physicians, scholars and practitioners in orthodontics for their decision-making regarding the treatment to be adopted for their patients. These mechanisms aim at reducing the subjective interpretation of the features considered in the decision making and, as a consequence, improving the “best practice” adopted. The framework proposed in this work represents a further step towards the foundation of a social mechanism, aiming at generating models, delivered through a web service, that are the product of the contribution of several individual models. This mechanism, for its part, will benefit from the collaboration of various professionals and/or scholars that, through the web service, can help to integrate new evidence to update the models generated which, in this sense, are never to be final. Other sets of features could be easily tested through the web service available at www.coltho.org. It is planned to integrate these datasets with further demographic, ecological and aesthetic *features* that, as said above, seem to contribute, implicitly or explicitly, to the orthodontic decision-making.

Experiments performed to generate DT's models show that they outperform the state of the art provided by other approaches in terms of common evaluation metrics used in the field, even if related works employed more "optimistic" metrics to evaluate their approaches that cannot be compared with ours at all. A clinical evaluation demonstrated that whereas a poor *within* and *between* agreements for the physicians, the use of the DT's as a mean to support clinical decisions may result beneficial for the task. Other clinical evaluations are planned as future work. In particular, subsets of random medical records will be evaluated to verify the rate of *within* and *between* agreements. A more structured annotation will be requested to physicians, using a Likert scale for each extraction decision. The results of this annotation scheme will be processed by a SEM model [43,44] that will help to identify the role of specific features with respect to a final model of constructs that is conjectured to exist in the orthodontic practice. In one direction the platform is able to deliver these models, using different friendly visualization tools and rules, to scholar and practitioners in their daily working practice, including refresher courses and training for orthodontic schools, establishing a collaboration among them and, as such, providing a learning value and a paradigm in helping them to become more sustainable [45].

References

1. Proffit, W., Fields, H., Moray LJ. (1998). Prevalence of malocclusion and orthodontic treatment need in the United States: estimates from the N-HANES III survey. *Int J Adult Orthod Orthogn Surg.* 13:97–106.
2. Dhar, V., Jain, A., Van Dyke, T.E., Kohli, A. (2007). Prevalence of gingival diseases, malocclusion and fluorosis in school-going children of rural areas in Udaipur district. *Journal of Indian Society of Pedodontics and Preventive Dentistry.* 25:103–5.
3. Choi, S.H., Kim, B. Il, Cha, J.Y., Hwang, C.J. (2015). Impact of malocclusion and common oral diseases on oral health-related quality of life in young adults. *American Journal of Orthodontics and Dentofacial Orthopedics.* 147:587–95.
4. de Paula Júnior, D.F., Santos, N.C.M., da Silva, É.T., Nunes, M.F., Leles, C.R. (2009). Psychosocial impact of dental esthetics on quality of life in adolescents. *The Angle Orthodontist.* 79:1188–93.
5. Abanto, J., Tello, G., Bonini, G.C., Oliveira, L.B., Murakami, C., Bönecker, M. (2015). Impact of traumatic dental injuries and malocclusions on quality of life of preschool children: A population-based study. *International Journal of Paediatric Dentistry.* 25:18–

- 28.
6. Lin, F., Ren, M., Yao, L., He, Y., Guo, J., Ye, Q. (2016). Psychosocial impact of dental esthetics regulates motivation to seek orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*. 150:476–82.
 7. Jawad, Z., Bates, C., Hodge, T. (2015). Who needs orthodontic treatment? Who gets it? and who wants it? *British Dental Journal*. 218:99–103.
 8. Vig, K.W.L., Mercado, A.M. (2015). Overview of orthodontic care for children with cleft lip and palate, 1915-2015. *American Journal of Orthodontics and Dentofacial Orthopedics*. 148:543–56.
 9. Kravitz, N.D., Bowman, S.J. (2016). A Paradigm Shift in Orthodontic Marketing. *Seminars in Orthodontics*. 22:297–300.
 10. Chua, E.S.L., Felicita, A.S. (2015.). The orthodontic extraction of permanent molars: a literature review. Vol. 31, *Australian orthodontic journal*. p. 69–77.
 11. Rischen, R.J., Breuning, K.H., Bronkhorst, E.M., Kuijpers-Jagtman, A.M. (2013). Records Needed for Orthodontic Diagnosis and Treatment Planning: A Systematic Review. *PLOS ONE*. 8:1–8.
 12. Ribarevski, R., Vig, P., Vig, K.D., Weyant, R., O'Brien, K. (1996). Consistency of orthodontic extraction decisions. *European Journal of Orthodontics*. 18:77–80.
 13. Hu, Z., Yin, X., Liao, J., Zhou, C., Yang, Z., Zou, S. (2015). The effect of teeth extraction for orthodontic treatment on the upper airway: a systematic review. *Sleep and Breathing*. 19:441–51.
 14. Edwards, R., Alsufyani, N., Heo, G., Flores-Mir, C. (2015). Agreement among orthodontists experienced with cone-beam computed tomography on the need for follow-up and the clinical impact of craniofacial findings from multiplanar and 3-dimensional reconstructed views. *American Journal of Orthodontics and Dentofacial Orthopedics*. 148:264–73.
 15. Berk, N.W., Bush, H.D., Cavalier, J., Kapur, R., Studen-Pavlovich, D., Sciote, J., Weyant, R.J. (2002). Perception of Orthodontic Treatment Need: Opinion Comparisons of Orthodontists, Pediatric Dentists, and General Practitioners. *Journal of Orthodontics*. 29:287–91.
 16. Cotrim, E.R., Vasconcelos Júnior, Á.V., Haddad, A.C.S.S., Reis, S.A.B. (2015). Perception of adults' smile esthetics among orthodontists, clinicians and laypeople. *Dental Press*

- Journal of Orthodontics*. 20:40–4.
17. Auconi, P., Scazzocchio, M., Cozza, P., McNamara, J.A., Franchi, L. (2015). Prediction of class III treatment outcomes through orthodontic data mining. *European Journal of Orthodontics*. 37:257–67.
 18. Martina, R., Teti, R., D'Addona, D., Iodice, G. (2006.). - Neural network based system for decision making support in orthodontic extractions. In: *Pham DT, Eldukhri EE, Soroka AJ, editors. Intelligent Production Machines and Systems. Oxford: Elsevier Science Ltd*; p. 235–40.
 19. Nouri, M., Asefi, S., Baghban, A.A., Ahmadvand, M., Shamsa, M. (2016). Objective vs subjective analyses of arch form and preformed archwire selection. *American Journal of Orthodontics and Dentofacial Orthopedics*. 149:543–54.
 20. Turpin, D.L., Huang, G. (2016.). The role of evidence in orthodontics. In: *Orthodontics-E-Book: current principles and techniques*. p. 200.
 21. Barreto, M.S., Faber, J., Vogel, C.J., Araujo, T.M. (2016). Reliability of digital orthodontic setups. *Angle Orthodontist*. 86:255–9.
 22. Nguyen, T., Proffit, W. (2016.). The decision-making process in orthodontics: Current principles and techniques, 6th edition. 208–244 p.
 23. Quinlan, J.R. (1986). Induction of decision trees. *Machine Learning*. 1:81–106.
 24. Witten, I.H., Frank, E. (2011.). Data mining: Practical machine learning tools and techniques. In *Morgan Kaufmann Inc.*;
 25. López-Vallverdú, J.A., Riaño, D., Bohada, J.A. (2012). Improving medical decision trees by combining relevant health-care criteria. *Expert Systems with Applications*. 39:11782–91.
 26. Anderson, D.R., Sweeney, D.J., Williams, T.A., Camm, J.D., Cochran, J.J. (2015.). An introduction to management science: quantitative approaches to decision making. Cengage learning. Vol. 34, The Journal of the Operational Research Society. 174 p.
 27. Croskerry, P. (2015.). Clinical decision making. In pediatric and congenital cardiac care. In *Springer London*; p. 397–409.
 28. Hasan, M.R., Bakar, N.A.A., Siraj, F., Sainin, M.S., Hasan, M.S. (2015). Single decision tree classifiers ' accuracy on medical data. *Proceedings of the 5th International Conference on Computing and Informatics, ICOCI 2015*. :671–6.
 29. Ghosh, A., Manwani, N., Sastry, P.S. (2017). On the robustness of decision tree learning under label noise. *PAKDD 2017*. 10235 LNAI:685–97.

30. Hammond, J., Keeney, R., Raiffa, H. (2015.). Smart choices: a practical guide to making better decisions. In: *Harvard Business Review Press*.
31. Hunink, M.G.M., Weinstein, M.C., Wittenberg, E., Drummond, M.F., Pliskin, J.S., Wong, J.B., Wong, J.B., Glasziou, P.P. (2014). Decision making in health and medicine: Integrating evidence and values, second edition. *Decision Making in Health and Medicine: Integrating Evidence and Values, Second Edition*. :1–424.
32. Masías, V.H., Krause, M., Valdés, N., Pérez, J.C., Laengle, S. (2015). Using decision trees to characterize verbal communication during change and stuck episodes in the therapeutic process. *Frontiers in Psychology*. 6:379.
33. Jung, S.-K., Kim, T.-W. (2016). New approach for the diagnosis of extractions with neural network machine learning. *American Journal of Orthodontics and Dentofacial Orthopedics*. 149:127–33.
34. Xie, X., Wang, L., Wang, A. (2010). Artificial neural network modeling for deciding if extractions are necessary prior to orthodontic treatment. *The Angle Orthodontist*. 80:262–6.
35. Hall, M., Frank, E., Holmes, G., Pfahringer, B., Reutemann, P., Witten, I.H. (2009). The WEKA data mining software: an update. *SIGKDD Explor Newsl*. 11:10–8.
36. Quinlan, R.J. (1993.). Programs for machine learning. *San Francisco, CA, USA.: Morgan Kaufmann Inc.*; C4.5.
37. Mitchell Tom M. (1997.). Machine learning. [Internet]. *New York, NY, USA.: McGraw Hill*; 421 p.
38. Fürnkranz, J., Flach, P.A. (2003). An analysis of rule evaluation metrics. *Proceedings, Twentieth International Conference on Machine Learning*. 1:202–9.
39. Fawcett, T. (2006). An introduction to ROC analysis. *Pattern Recognition Letters*. 27:861–74.
40. Sammut, C., Webb, G.I. (2011.). Encyclopedic of machine learning. *Springer science and Business media.*;
41. Weiss, G.M. (2004). Mining with Rarity: A Unifying Framework. *SIGKDD Explor Newsl*. 6:7–19.
42. Chawla, N.V., Bowyer, K.W., Hall, L.O., Kegelmeyer, W.P. (2002). SMOTE: Synthetic minority over-sampling technique. *Journal of artificial intelligence research*. 16:321–57.
43. Novo-Corti, I., Barreiro-Gen, M. (2014). Are public policies aimed in the right direction?: Analysis of the true reason of Spanish households for have no internet access.

Int J Knowl Soc Res. 5:33–42.

44. Novo-Corti, I., González-Laxe, F., Pociovalisteanu, D.-M. (2015). The economic analysis of maritime catastrophes in sensitive areas: the assessment and calculation of damages in the environment and population's way of life. *Journal of Cleaner Production.* 107:267–78.
45. Lozano, R., Lukman, R., Lozano, F.J., Huisingh, D., Lambrechts, W. (2013). Declarations for sustainability in higher education: becoming better leaders, through addressing the university system. *Journal of Cleaner Production.* 48:10–9.

Table A.1. Feature set with names, values and category division of the features (Skeletal, clinical, radiographic, and personal data).

Appendix A

ID	Feature category	Feature full name	Feature name/acronym	Feature value
1	Personal data		Age	Years
2	Personal data		Sex	Binary (Male = 1, Female = 0)
3	clinical	Dentobasal discrepancy	dentobasal discrepancy (DBD)	Millimetres
4	clinical (assessment models cass)	Inter canine diameter difference	inter canine diameter difference (3 diameter)	Millimetres
5	clinical (assessment models cass)	Inter molar diameter difference	inter molar diameter difference (6 diameter)	Millimetres
6	clinical	Palate rotation of upper molars	Molars rotation	Binary (absence=0; presence=1)
7	clinical	Canine class malocclusion right	Canine class malocclusion right	first=0; second=1; third=2
8	clinical	Canine class malocclusion left	Canine class malocclusion left	first=0; second=1; third=2
9	clinical	Molar class malocclusion right	Molar class malocclusion right	first=0; second=1; third=2
10	clinical	Molar class malocclusion left	Molar class malocclusion left	first=0; second=1; third=2
11	radiographic, skeletal	Sella–nasion–A point angle	SNA	Degree
12	radiographic, skeletal	Sella–nasion–B point angle	SNPg	Degree
13	radiographic, skeletal	Angle formed by the NA floor with NPG plane. Sagittal intermaxillary relationship	ANPg	Degree
14	radiographic, skeletal	Angle formed by sellar plane with the palatal plane ANS-PNS	SN ^Ans-Pns	Degree
15	radiographic, skeletal	Angle formed by the saddle plan SN with mandibular plan Go- Gn	SN^Go-Gn	Degree
16	radiographic, skeletal	Angle formed by the palatine plan ANS – PNS with mandibular plan Go- Gn	Ans-Pns^Go-Gn	Degree
17	radiographic, skeletal	Angle formed by the palatine plan ANS – PNS with the incisor upper axis Is	Ans-Pns^Is	Degree
18	radiographic, skeletal	Angle formed by the mandibular plan Go- Gn with the lower incisor axis Ii.	Go-Gn^Li	Degree
19	radiographic, skeletal	Distance between the dental plan Apg and lower incisor edge B1	Apg-B1	Millimeters
20	radiographic, skeletal	Lower Incisor position	LIP	Millimeters
21	radiographic, skeletal	Upper Incisor position	UIP	Millimeters
22	clinical	Overjet	Ovj	Millimeters
23	clinical	Overbite	OVB	Millimeters
24	radiographic, skeletal	Interincisal Angle Is^Ii	Is^Ii	Degree
25	radiographic, skeletal	Protrusion lower lip	PLI	Millimeters
26	radiographic, skeletal	Co-Go-Me angle	Co-Go-Me	Degree
27	clinical (assessment models cass)	Anterior 12olton index	Anterior Bolton index	(normal=0; increased=1; decreased=2)
28	clinical	Kind of gingival	Gingival tipology (Geng Tip)	Binary (thick=0; thin=1)
29	clinical	Gingival recessions	Gingival recessions' presence (Rec)	Binary (absence=0; presence=1)
30	clinical	Labial incompetence	Labial incompetence (Lab incompet)	(absence=0; mild=1; severe=2)
31	clinical	Aesthetic line	Aesthetic line	(orthognathic=0; retrusive= 1; protruded=2)
32	clinical	Smile teeth exposure	Smile teeth exposure	(Good= 0; scarce=1)
33	clinical	Coincidence of the facial midline with the dental midline	Midline coincidence	(Coinciding=0; not coinciding=1)
34	clinical	Angle formed by a tangent line to the point subnasal and one tangent to labial filter	Nasolabial angle	(normal=0; closed=1; open=2)
35	clinical	Trend of the profile that can be normal, concave or convex	Facial profile	(normal=0, concave=1; convex=2)
36	clinical	Distance between the chin and neck	Chin-neck distance	(Normal=0; increased= 1; decreased=2)
37	clinical	Fixed, functional and fixed lingual	Treatment of orthodontic with extractions	(no=0; yes D=1, yes P=2)
38	clinical (class label)	Teeth extracted	Teeth extracted	yes=1, no=0

Entropy – Mitchell (1997) defines the *Entropy* as follows: given a collection of S samples (the orthodontics dataset with its 290 examples), containing *positive* (58 teeth *extracted*) and *negative* (232 teeth *not extracted*) examples, for a given target concept (i.e., *extraction* vs. *no-extraction*), the entropy of S , relative to this Boolean classification, is

$$\text{Entropy}(S) = p_+ \log_2 p_+ + p_- \log_2 p_- \quad (\text{A.1})$$

where p_+ and p_- are, respectively, the proportion of *positive* and *negative* examples in S . *Entropy* is 0 if all members of S belong to the same class; it is 1 when S contains an equal number of *positive* and *negative* examples. Finally, *Entropy* assumes values from 0 to 1 when the collection S contains unequal numbers of positive and negative examples. In the case of the orthodontic dataset $\text{Entropy} \approx 0.22$, confirming a distribution of skewed towards *negative* examples.

Information Gain – Mitchell (1997) defines the *InfoGain* of an attribute A , with respect to a collection of examples S as

$$\text{Gain}(S, A) = \text{Entropy}(S) - \sum_{v \in \text{Values}(A)} \frac{|S_v|}{|S|} \text{Entropy}(S_v) \quad (\text{A.2})$$

Where $\text{values}(A)$ is the set of all possible values for an attribute A , and S_v is the subset of the collection of examples S for which the attribute A has value v . The first term of Equation (A.2) is just the entropy of the original collection S , whereas the second term is the expected value of the entropy after S is partitioned using A .

GainRatio - Mitchell (1997) defines the *GainRatio* as the ratio between the earlier *Gain* measure and the *SplitInformation*

$$\text{GainRatio}(S, A) = \frac{\text{Gain}(S, A)}{\text{SplitInformation}(S, A)} \quad (\text{A.3})$$

The term *SplitInformation* discourages the employing of attributes with many uniformly distributed values. **Accuracy** - Accuracy easily states how often the DT makes the correct prediction and it is expressed as

$$\text{Accuracy} = \frac{\# \text{ of correct predictions}}{\# \text{ of total predictions}} \quad (\text{A.4})$$

The metric makes no distinction among classes, treating equally correct answers for each class. This metric is adopted by related work reported in Section 2.1.

Confusion matrix – A *confusion matrix* (Stehman, 1997) is a table with two rows and two columns that reports the number of *false positives*, *false negatives*, *true positives*, and *true negatives*, allowing a detailed analysis with respect to the proportion of correct guesses given by *accuracy*, because it will yield misleading results if the data set is unbalanced as for the orthodontic dataset.

(A.5)

Confusion Matrix

a	b	classified as
TP	FN	a=0
FP	TN	b=1

Precision and recall - The precision score (Powers 2011) quantifies the ability of a DT to not label a *negative* example as *positive* and it is defined as follows

$$\text{Precision} = \frac{\# \text{ of true positive}}{\# \text{ of true positive} + \# \text{ of false positive}} \quad (\text{A.6})$$

and *recall* as how many correct hits were found

$$\text{Recall} = \frac{\# \text{ of true positive}}{\# \text{ of true positive} + \# \text{ of false negative}} \quad (\text{A.7})$$

F1 score - The F1-score (Powers 2011) is a single metric that combines both precision and recall via their harmonic mean, and it is defined as

$$F1 = \frac{2 \text{precision} \times \text{recall}}{\text{precision} + \text{recall}} \quad (\text{A.8})$$

Appendix B

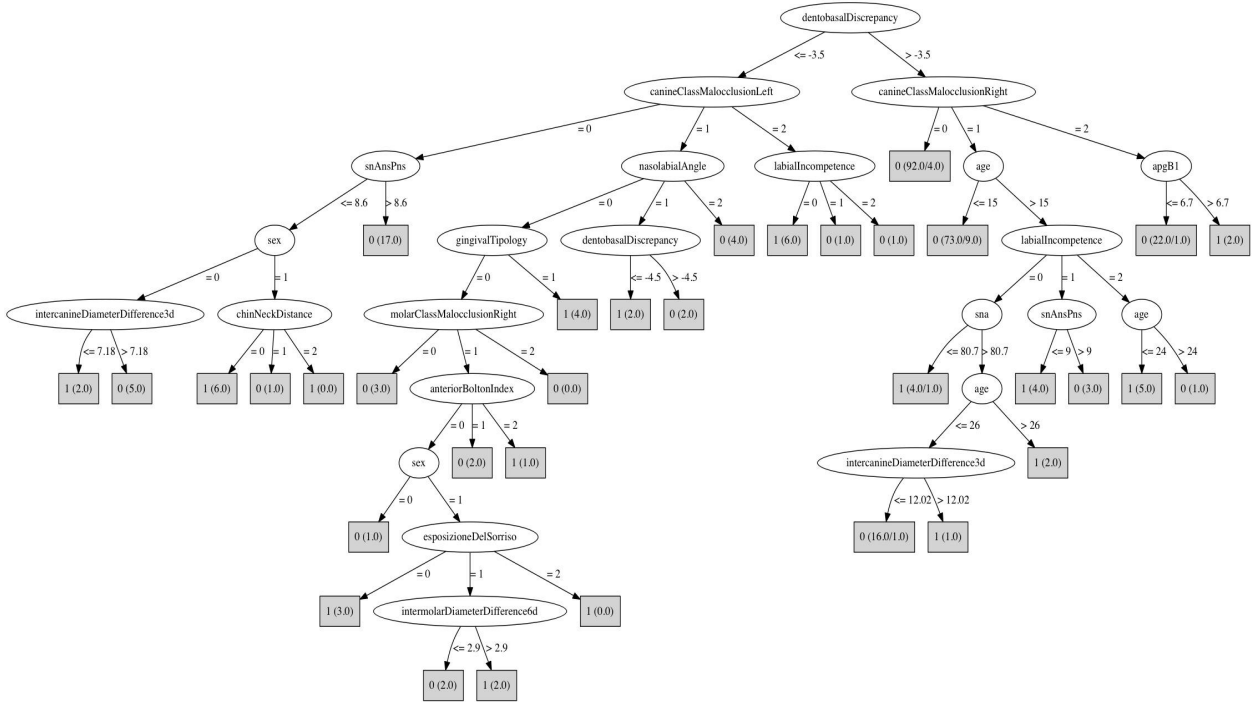


Figure B1. DT of the first experimental setting.

Table B.1 - Learning curve of the first experimental setting.

	Precision	Recall	F-Measure	% of training examples
Weighted Avg.	0.708	0.714	0.711	100%
class: 0	0.817	0.828	0.822	
class: 1	0.273	0.259	0.265	
Weighted Avg.	0.649	0.670	0.659	75%
class: 0	0.769	0.811	0.789	
class: 1	0.263	0.217	0.238	
Weighted Avg.	0.596	0.608	0.602	50%
class: 0	0.737	0.757	0.747	
class: 1	0.143	0.130	0.136	
Weighted Avg.	0.614	0.680	0.641	25%
class: 0	0.753	0.865	0.805	
class: 1	0.167	0.087	0.114	

Table B.2. Attribute ranking comparison for the first experimental setting.

Info Gain Ranked attributes			Gain Ratio feature evaluator (used by decision tree)		
Feature ID	weight	attribute name	Feature ID	weight	attribute name
18	0.0717399	goGnLi	18	0.115996	goGnLi
3	0.04652	dentobasalDiscrepancy	3	0.0606004	dentobasalDiscrepancy
24	0.0404195	isLi	24	0.0424348	isLi
9	0.0290591	molarClassMalocclusionRight	6	0.0376848	molarsRotation
7	0.0281632	canineClassMalocclusionRight	9	0.0204002	molarClassMalocclusionRight
8	0.0257698	canineClassMalocclusionLeft	7	0.0203799	canineClassMalocclusionRight
30	0.0188856	labialIncompetence	8	0.0182366	canineClassMalocclusionLeft
10	0.0158049	molarClassMalocclusionLeft	30	0.0180311	labialIncompetence
32	0.0049656	esposizioneDelSorriso	10	0.0111847	molarClassMalocclusionLeft
34	0.0044037	nasolabialAngle	29	0.0071296	gingivalRecessionsPresence
28	0.0036951	gingivalTipology	28	0.0056385	gingivalTipology
29	0.0032651	gingivalRecessionsPresence	32	0.0049993	esposizioneDelSorriso
35	0.0027168	facialProfile	34	0.0032921	nasolabialAngle
6	0.0022397	molarsRotation	35	0.0021865	facialProfile
31	0.002228	aestheticLine	36	0.0020418	chinNeckDistance
36	0.0021304	chinNeckDistance	31	0.0018946	aestheticLine
33	0.0008209	midlineCoincidence	33	0.000936	midlineCoincidence
27	0.0002618	anteriorBoltonIndex	27	0.0002232	anteriorBoltonIndex
2	0.0000791	Sex	2	0.0000805	sex

Appendix C

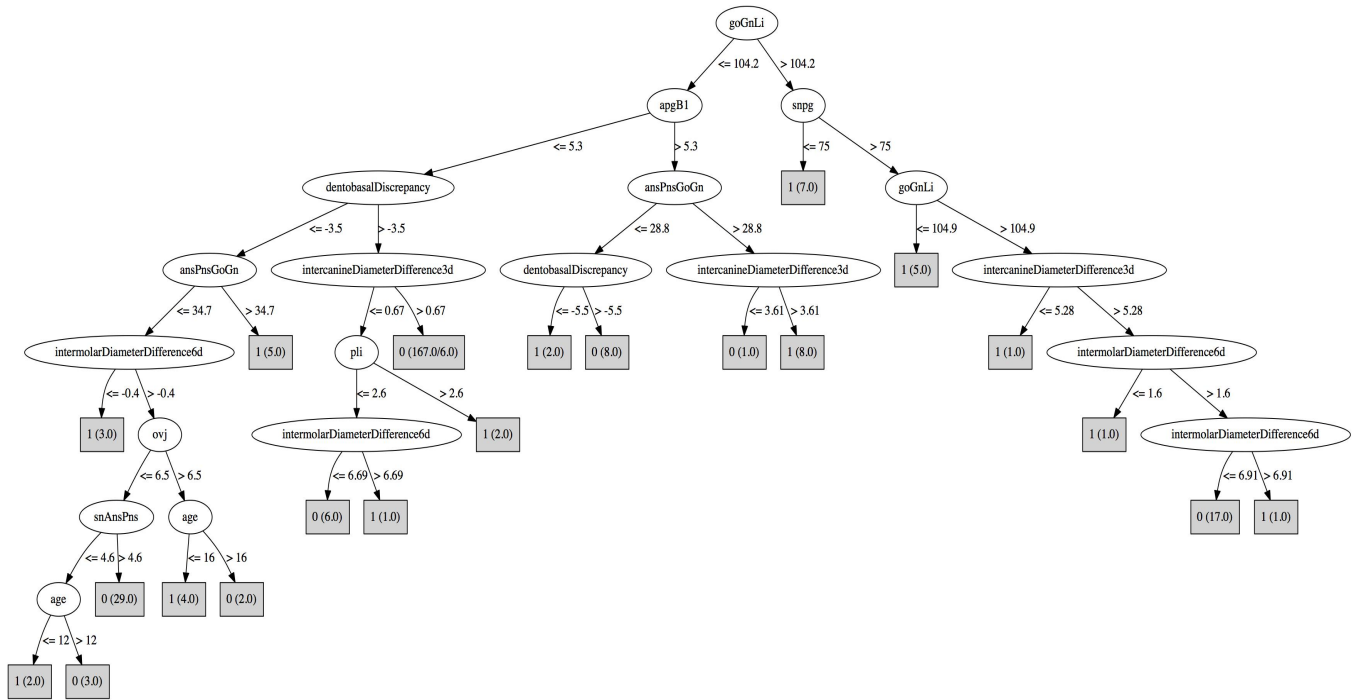


Figure C.1 DT of the second experimental setting.

Table C.1. Learning curve; Pr, Re, and F1 calculated on the positive examples.

	Pr	Re	F1
25	26.20	19.20	22.16
50	35.80	26.30	30.32
75	48.30	35.00	40.59
100	60.50	47.90	53.47

Table C.2. Attribute ranking for the second experimental setting.

ID Feature	Gain Ratio weight	Feature name	ID Feature	IGE weight	Feature name
18	0.130698	goGnLi	18	0.079335	goGnLi
3	0.077879	dentobasalDiscrepancy	3	0.059458	dentobasalDiscrepancy
22	0.048539	Ovj	9	0.039253	molarClassMalocclusionRight
6	0.047002	molarsRotation	7	0.038204	canineClassMalocclusionRight
20	0.034437	Lip	22	0.035736	ovj
7	0.027657	canineClassMalocclusionRight	8	0.034526	canineClassMalocclusionLeft
9	0.027529	molarClassMalocclusionRight	20	0.031279	lip
8	0.024423	canineClassMalocclusionLeft	30	0.024269	labialIncompetence
30	0.023093	labialIncompetence	10	0.022014	molarClassMalocclusionLeft
10	0.015598	molarClassMalocclusionLeft	32	0.007142	esposizioneDelSorriso
28	0.010565	gingivalTipology	28	0.006883	gingivalTipology
32	0.007185	esposizioneDelSorriso	34	0.005469	nasolabialAngle
34	0.004112	nasolabialAngle	35	0.004798	facialProfile
31	0.003878	aestheticLine	31	0.004503	aestheticLine
35	0.003818	facialProfile	6	0.00292	molarsRotation
33	0.001881	midlineCoincidence	33	0.00167	midlineCoincidence
27	0.001122	anteriorBoltonIndex	27	0.001292	anteriorBoltonIndex
29	0.000714	gingivalRecessionsPresence	36	0.000485	chinNeckDistance
36	0.000474	chinNeckDistance	29	0.000314	gingivalRecessionsPresence
2	0.000226	Sex	2	0.000221	sex

Table C.3. Data filtering of the original dataset.

Data Filtering			
Original data set		Filtered data set	
232	negative	227	
58	positive	48	
		Examples removed from the original dataset	
		ID4	
		ID26	
		ID35	
		ID112	
		ID145	
		ID146	
		ID166	
		ID167	
		ID170	
		ID178	
		ID192	
		ID235	
		ID263	
		ID275	
		ID288	

Appendix D

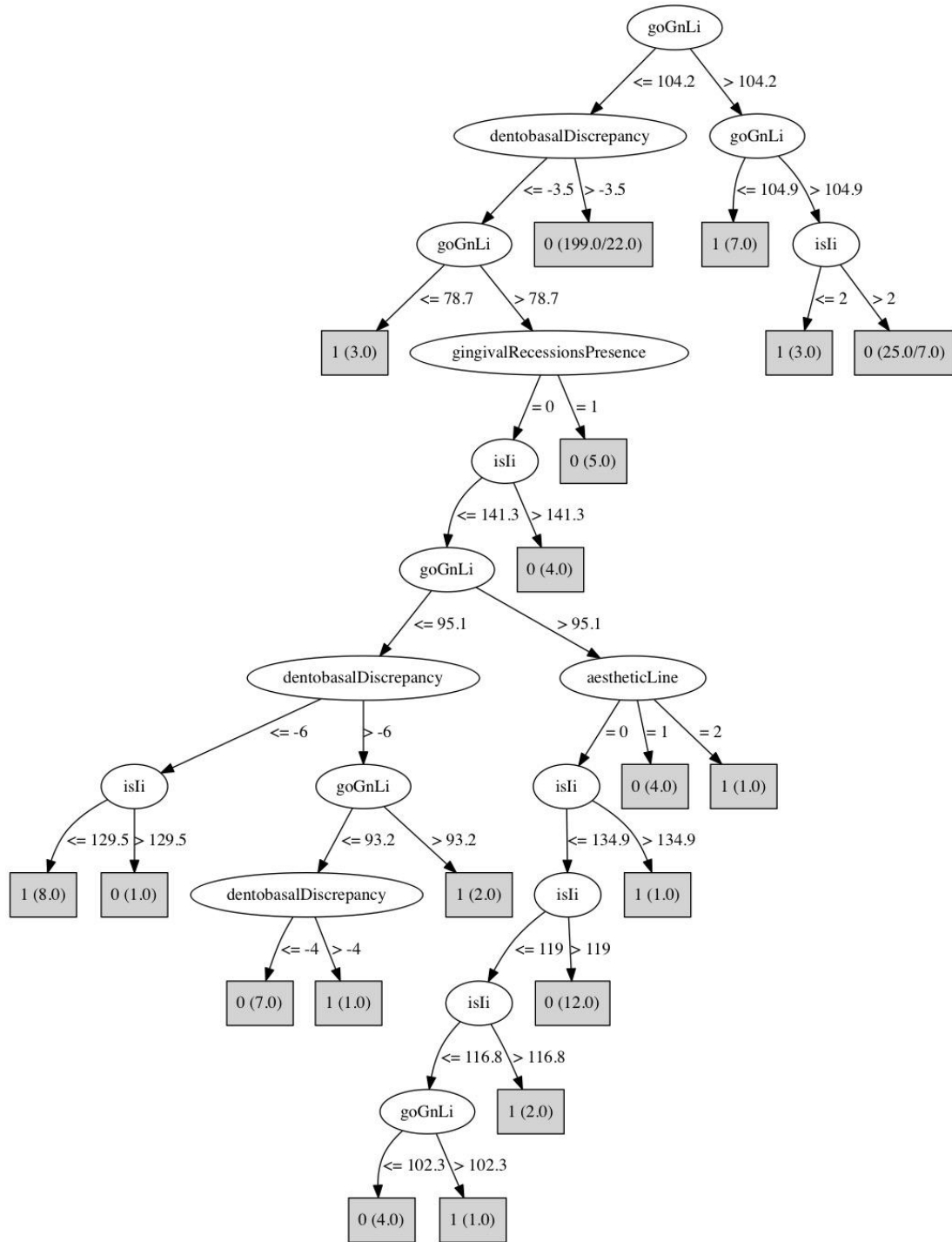


Figure D.1. DT of the third experimental setting.

Table D.1. Learning curve; Pr, Re, and F1 calculated on the positive examples.

Partition	Pr	Re	F1
25	22.2	15.2	18.0
50	31.8	19.3	24.0
75	41.3	22.4	29.0
100	48.5	27.6	35.2

Table D.2. Attribute ranking comparison for the third experimental setting.

Info Gain Ranked attributes			Gain Ratio feature evaluator (used by decision tree)		
Feature ID	weight	attribute name	Feature ID	weight	attribute name
18	0.0717399	goGnLi	18	0.115996	goGnLi
3	0.04652	dentobasalDiscrepancy	3	0.0606004	dentobasalDiscrepancy
24	0.0404195	isLi	24	0.0424348	isLi
9	0.0290591	molarClassMalocclusionRight	6	0.0376848	molarsRotation
7	0.0281632	canineClassMalocclusionRight	9	0.0204002	molarClassMalocclusionRight
8	0.0257698	canineClassMalocclusionLeft	7	0.0203799	canineClassMalocclusionRight
30	0.0188856	labialIncompetence	8	0.0182366	canineClassMalocclusionLeft
10	0.0158049	molarClassMalocclusionLeft	30	0.0180311	labialIncompetence
32	0.0049656	Smile teeth exposure	10	0.0111847	molarClassMalocclusionLeft
34	0.0044037	nasolabialAngle	29	0.0071296	gingivalRecessionsPresence
28	0.0036951	gingivalTipology	28	0.0056385	gingivalTipology
29	0.0032651	gingivalRecessionsPresence	32	0.0049993	Smile teeth exposure
35	0.0027168	facialProfile	34	0.0032921	nasolabialAngle
6	0.0022397	molarsRotation	35	0.0021865	facialProfile
31	0.002228	aestheticLine	36	0.0020418	chinNeckDistance
36	0.0021304	chinNeckDistance	31	0.0018946	aestheticLine
33	0.0008209	midlineCoincidence	33	0.000936	midlineCoincidence
27	0.0002618	anteriorBoltonIndex	27	0.0002232	anteriorBoltonIndex
2	0.0000791	sex	2	0.0000805	sex

CHAPTER 2

Association between gingival biotype and facial typology through cephalometric evaluation and three-dimensional facial scanning.

Abstract

In dentistry, the assessment of periodontal biotype is considered one of the most important parameters to plan the treatment, and craniofacial morphology might affect it. The aim of this study was to investigate the association between facial typology and gingival biotype in patients by means of two-dimensional and three-dimensional evaluations of facial typology. This study included 121 participants searching for orthodontic treatment (43 M, 78 F; 20.4±10.4). The gingival biotype was evaluated based on the transparency of the periodontal probe through the gingival margin of the mid-buccal sulcus for both upper (UGB) and lower (LGB) anterior teeth. SellionNasion[^]GonionGnation (SN[^]GoGn) and CondylionGonionMenton (CoGoMe[^]) angles were measured on two-dimensional cephalograms. Three-dimensional face scans were acquired by means of a three-dimensional facial scanner (3dMD system) and successively analysed to assess the facial typology using the ratio between lower facial height (SNMe) and total facial height (NMe). Chi-square test and regression analysis were used to evaluate the associations between gingival biotype and facial morphology (P<0.05). The chi-square test showed that there was not statistically significance association between facial typology and gingival biotype (UGB P=0.83; LGB P=0.75). The logistic regression showed an association between SNMe/NMe and the UGB (P=0.036), and SNMe/NMe and LGB (P=0.049). The decreased ratio of SNMe/NMe might be a protective factor for thin gingival biotype.

This chapter is based on “Valletta R., Pango Madariaga A. C., Tortora G., Rongo R., Simeon V., Spagnuolo G., D’Antò V. Association between gingival biotype and facial typology through cephalometric evaluation and three-dimensional facial scanning. Appl. Sci. 2019, 9(23), 5057”.

2.1. Introduction

Orthodontic patients have an increased risk of developing gingivitis mainly due to an inflammatory reaction following the accumulation of bacterial plaque [1–5].

Many authors have shown that gingival recessions can develop during or after orthodontic treatment [6–10]. Indeed, at the end of orthodontic therapy, the reported prevalence of gingival recessions ranges between 5% to 12% and this prevalence increases up to 47% in long-term observations (5years) [9,11–13].

A recent systematic review has established that the direction of dental movements and the buccal-lingual thickness of the gingiva can play an important role in altering soft tissues during orthodontic treatment. There is a high probability of recession during tooth movement in areas with less than 2 mm of gingival thickness [14]. This could affect the integrity of periodontal tissues and represent a risk factor when orthodontic treatments [15], implants [16] and restorative treatments are performed [17]. Gingival biotype is defined as the thickness of the gingiva in the labiolingual direction [16]. Studies reported that gingival biotype is an important parameter that must be evaluated to reduce the risk of gingival recession [18].

Therefore, the assessment of periodontal biotype is considered one of the most important parameter for outcomes focused on the dental planning according to the classification of periodontal and peri-implant diseases and conditions [19].

Many features of gingival phenotype are genetically determinate; others seem to be influenced by age, sex, growth, tooth shape, and tooth position. [20]. Moreover, it has been shown that there is an intra and inter-individual variation in width [21] and thickness of the vestibular gingiva [22].

Facial typology is classified as: dolichofacial, mesofacial, and brachyfacial. Dolichofacial has excessive vertical facial growth, it is usually associated with increased SellaNasion[^]GonionGnathion (SN[^]GoGN) angle, and increased maxillary/mandibular planes angle (AnsPns[^]GoGn) [23,24]. Brachyfacial has reduced vertical growth, it is usually accompanied by reduced SN[^]GoGn, reduced AnsPns[^]GoGn, and decreased lower facial height (SNMe) total facial height (NMe) ratio [25].

The cephalometric evaluation of the facial type is essential for orthodontic diagnosis, because the amount and direction of jaw growth will significantly alter the need for orthodontic biomechanics [26].

Craniofacial morphology may also affect the gingival phenotype [20,27]. Some studies have evaluated the relationship of bone morphology to facial typology [28–30], a correlation between facial and alveolar bone has already been demonstrated [31]. Indeed, in dolichofacial

patients, the mandibular symphysis is high and thin, while in brachyfacial patients, the symphysis is low and thick [32]. In consequence, before starting an orthodontic treatment it is important to evaluate and to diagnose both the gingival biotype and the facial typology in order to reduce the risk of damage to the periodontium [33]. Only few studies, instead, have evaluated the association between gingival thickness and craniofacial morphology [33].

Various methods have been applied to register facial soft tissue; among them the most representative methods, to obtain three-dimensional (3D) scans, are laser scanner and 3D stereophotogrammetry [34,35]. Soft tissue analysis using 3D stereophotogrammetry is reproducible and reliable [36–39]. Hence, this is a valid method to analyse facial soft tissues, avoiding any X-ray exposure to the patient.

The aim of this study was to investigate the association between gingival biotype and facial typology evaluated by means of a cephalometric and 3D facial analysis, in patients seeking an orthodontic treatment.

The null hypothesis was that there is no association between gingival biotype and facial typology.

2.2. Materials and Methods

2.2.1. Subjects

The study sample comprised 121 patients (43 males, 78 females; from 8 to 56 years old, median 17.04; IQR 13.7-22.1) recruited among patients who had to start the orthodontic treatment at the Section of Orthodontics and Temporomandibular Disorders of the University of Naples “Federico II”.

All patients were fully informed about the nature of the study and signed an informed consent. The research protocol was approved by the Ethics Committee of the University of Naples Federico II (58/19).

The following selection criteria were applied: 1) patients > 8 years, 2) pre-orthodontic treatment, 3) upper and lower permanent anterior teeth and 4) good oral hygiene.

Exclusion criteria included diseases requiring premedication to perform periodontal probing; systemic diseases that can influence the activity of periodontal disease; individuals taking drugs that affect the periodontal status; patients with removable prostheses and pregnant or breastfeeding women.

2.2.2. Periodontal assessment and clinical procedure

The gingival biotype was evaluated based on the transparency of the periodontal probe through the gingival margin of the mid-buccal sulcus of both central, lateral incisors and

canine, both maxillary and mandibular. If the outline of the probe could be seen through the gingival margin, it was categorized as “thin” (Figure 1); if not, it was categorized as “thick” (Figure 2) [40]

All the variables were recorded by one expert operator (periodontist), using a millimetre periodontal probe (15-mm North Carolina probe), inserted in the gingival sulcus with a force of about 0.25 Newton.



Figure 1. Thin Biotype with North Carolina Probe

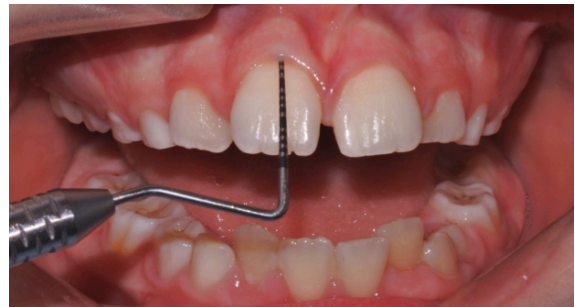


Figure 2. Thick Biotype with North Carolina Probe

2.2.3. Facial typology assessment with cephalometric evaluation

Delta-Dent software (Outside format, Milan, Italy) was used to perform two-dimensional cephalometric tracings to evaluate facial typology.

For this study, the cephalometric analysis was performed as shown in Figure 3a-b. Briefly, two cephalometric variables were assessed: the $SN^{\wedge}GoGn$ (average value \pm SD $33^{\circ} \pm 2.5^{\circ}$) determined jaw divergence, which is the angle between the anterior cranial base (Sella-Nasion) and the mandibular plane (Gonion-Gnathion), and the $CoGoMe^{\wedge}$ (average value \pm SD $132^{\circ} \pm 6.0^{\circ}$) measured the mandibular structure, which is the angle between the condylar axis (Condylion-Gonion) and the mandibular base (Gonion-Menton).

The sample was divided into three types of craniofacial morphology: brachyfacial, with a $SN^{\wedge}GoGn$ equal to or lower than 27° , mesofacial with a $SN^{\wedge}GoGn$ between 27° and 37° , and dolichofacial with a $SN^{\wedge}GoGn$ equal to or greater than 37° .

The following landmarks (Figure 3a) were identified and traced on lateral cephalogram in order to evaluate facial typology: ‘Sella’ (S, the centre of sella turcica), ‘Nasion’ (N, external point of the junction between nasal and frontal bone), ‘Gonion’ (Go, the most inferior posterior point of the mandibular angle), ‘Gnathion’ (Gn, point of the mandibular symphysis on the facial axis) ‘Menton’ (Me, the most inferior point of the mandibular symphysis), ‘Condylion (Co, the highest and most posterior point on the contour of the mandibular condyle).

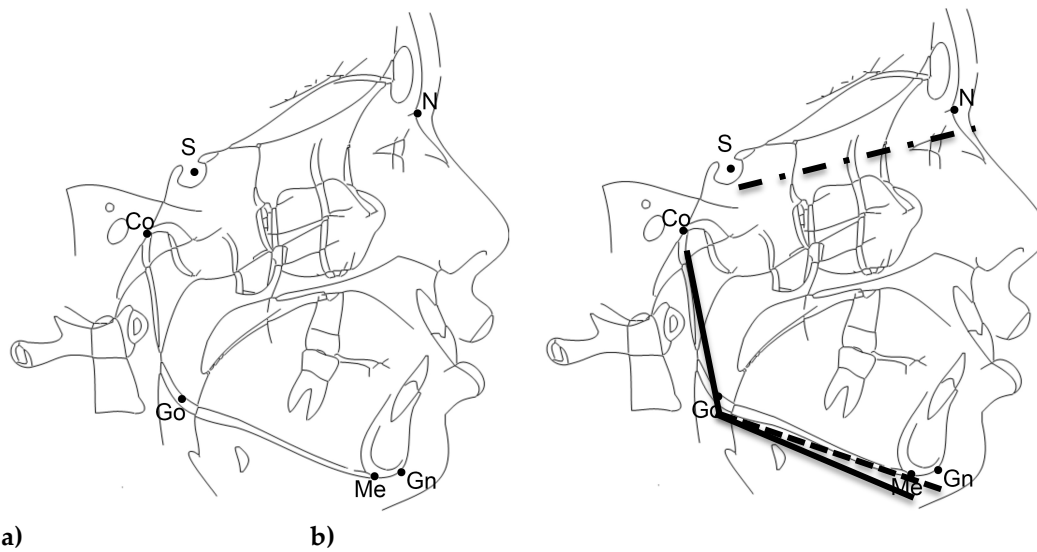


Figure 3 a-b. Cephalometric points, planes and angles. a) Sellion' (S, the centre of sella turcica), 'Nasion' (N, external point of the junction between nasal and frontal bone), 'Gonion' (Go, the most inferior posterior point of the mandibular angle, 'Gnathion' (Gn, point of the mandibular symphysis on the facial axis) 'Menton' (Me, the most inferior point of the mandibular symphysis), 'Condylion (Co, the highest and most posterior point on the contour of the mandibular condyle); b) SN plane, GoGn plane and CoGoMe Angle.

2.2.4. 3D Facial scans

2.2.4.1. Acquisition Process

The facial scanner 3dMD (3dMD LLC, Atlanta, GA, USA) was used in this study. The scanner was installed in a specific setting, with no lighting, neither natural nor artificial, during the acquisition.

The scanner configuration consisted of three pairs of stereo-cameras, two texture cameras and four geometric cameras with lenses slightly convergent; two projectors and three led panels, positioned on right and on the left.

The calibration of the system was the first step of the protocol acquisition. The operator invited the patient to look straight ahead with the head in natural head position (NHP) for all scanning time. The teeth were taken together with eyes opened. After the participant has been properly positioned, 90 cm away from the scanner, a video with the six cameras was recorded.

Successively, the scans were exported from the video as .obj images and analysed through the 3dMDVultus (3dMD LLC, Atlanta, GA, USA). All images were stored on secure computer in the School of Dentistry at University of Naples.

2.2.4.2. 3D Cephalometric Analysis

Once that the images were registered and analysed using 3dMDVultus Software, three landmarks were identified: N ('Soft Tissue Nasion' is the midpoint on the soft tissue contour of the base of the nasal root at the level of the frontonasal suture); SN ('SubNasion' is the midpoint on the nasolabial soft tissue contour between the columella crest and the upper lip) and Me ('Soft Tissue Menton' is the most inferior midpoint on the soft tissue contour of the chin). Among these three points, two linear measurements were constructed for the analysis: NMe (Total facial height) and SNMe (Inferior facial height), as shown in Figure 4.

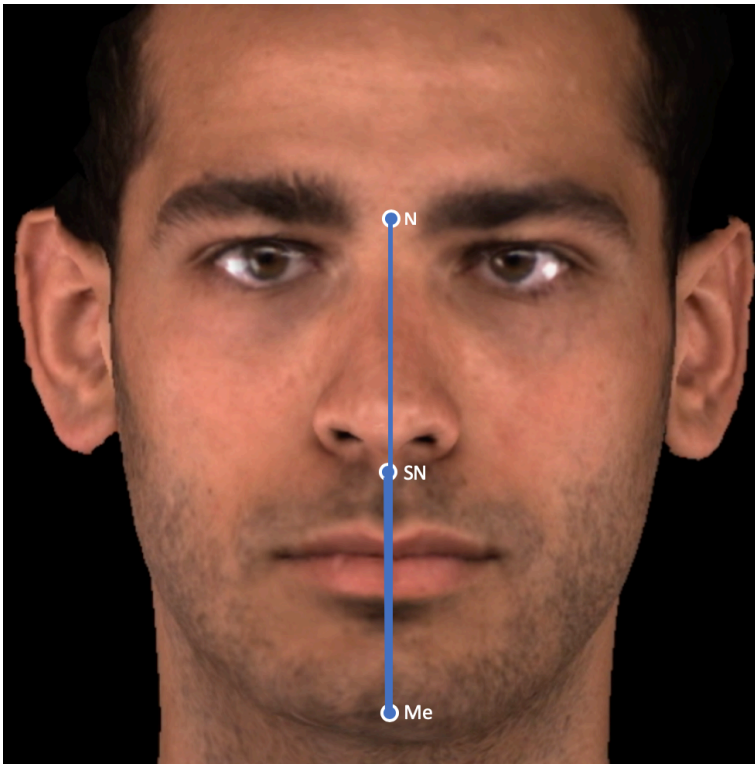


Figure 4. Facial typology assessment with Facial Scanner

2.2.5. Sample size

The sample size was established based on the fact that a sample size of 100 patients reaches 80% of power (1-beta) to detect an effect size (W) of 0.31 (medium-large effect size) using a chi square test with 2 degrees of freedom and a significance level (alpha) of 0.05.

2.2.6. Statistical analysis

Descriptive statistics on age, gender, gingival biotype and baseline characteristics were performed (Table 1). Continuous variables were reported as mean and standard deviation (SD) or median and inter-quartile range (IQR) according to distribution Shapiro-Wilk test was performed to evaluate variable distribution. Categorical variables were reported as count and

percentage and were compared using the chi-square (gingival biotype vs facial typology). Logistic regression analysis was used to assess the association between continuous variables (CoGoMe[^] and SNMe/NMe) and dichotomous variable (thin or thick biotype) used as dependent variable. The level of statistical significance was set at P<0.05. Statistical analysis was performed using STATA version 14.0 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP, USA).

2.3. Results

The total sample consisted of 121 pre-orthodontic patients, 43 males and 78 females, median age 17.04 (IQR 13.7-22.1). Table 1 showed description of the sample regarding age, sex, gingival biotype, facial typology. Two-dimensional and 3D cephalometric data are reported in table 2, and all were normally distributed.

The sample was divided into 3 groups according to SN[^]GoGn: and there were 33 (27.27%) brachyfacial patients, 59 (48.76%) mesofacial patients and 29 (23.97%) dolichofacial patients, as shown in Table 1.

Regarding the gingival biotype most patients presented a thick gingival biotype (UGB 86.78%; LGB 52.07%), as seen in Table 1.

The chi-square test showed that there was not statistically significance association between SN[^]GoGn and gingival biotype (UGB P=0.83; LGB P=0.75; and gingival biotype P=0.77, Table 3).

Similarly, the logistic regression analysis showed that CoGoMe[^] was not associated with any variables of gingival biotype (UGB, P=0.340; LGB, P=0.065).

Finally, logistic regression analysis showed a statistically significant association of SNMe/NMe with the UGB (Odds Ratio=0.843; 95% CI 0.719-0.989; P=0.036), and of SNMe/NMe with LGB (Odds Ratio=0.904; 95% CI 0.899-1.003; P=0.049) showing that when the ratio of SNMe/NMe decreased, there is a minor risk to find a thin biotype (Table 4).

Table 1. Characteristics of study subjects according to age, gender, gingival biotype and facial typology.

Variables	N	Mean ± SD
age	121	20.39 ± 10.40
	Frequency	Percentage %
Gender		

Male	43	35.54
female	78	63.64
Upper gingival biotype		
Thick	105	86.78
Thin	16	13.22
Lower gingival biotype		
Thick	63	52.07
Thin	58	47.93
Facial typology SN^GoGn		
Brachyfacial	33	27.27
Mesofacial	59	48.76
Dolichofacial	29	23.97

Data are presented as mean and standard deviation (SD) or frequencies and percentages.

Table 2. Descriptive variables of the sample size

Variables	Mean + SD	P50	P25	P75
SN^Go-Gn	32.7°±8°	32.7°	28.1°	36.3°
CoGoMe^	123.2°±6.6°	122.8°	118.7°	127.4°
SNMe/SMe	0.514±0.042	0.51	0.497	0.530

Data are presented as mean, standard deviation (SD) and interquartile range (IQR).

Table 3. Classification of gingival biotype in patients with different facial typology using the 15-mm North Carolina probe.

Facial Typology	Upper Gingival Biotype		Mean	P value	
	Thick	Thin			
Brachyfacial	29 (27.62%)	4 (25.00%)	33 (27.27%)	0.83	
Mesofacial	50 (47.62%)	9 (56.25%)	59 (48.76%)		
Dolichofacial	26 (24.76%)	3 (18.75%)	29 (23.97%)		
Total	105 (100%)	16 (100%)	121 (100%)		
	Lower Gingival Biotype				
	Thick	Thin	Mean	P value	
Brachyfacial	16 (25.40%)	17 (29.31%)	33 (27.27%)	0.75	
Mesofacial	33 (52.38%)	26 (44.83%)	59 (48.76%)		
Dolichofacial	14 (22.22%)	15 (25.86%)	29 (23.97%)		
Total	63 (100%)	58 (100%)	121 (100%)		
	Gingival Biotype				
	Thick/Thick	Thick/Thin	Thin/Thin	Mean	P value
Brachyfacial	16 (25.40%)	13 (30.95%)	4 (25%)	33 (27.27%)	0.77
Mesofacial	33 (52.38%)	17 (40.48%)	9 (56.25%)	59 (48.76%)	
Dolichofacial	14 (22.22%)	12 (28.57%)	3 (18.75%)	29 (23.97%)	
Total	63 (100%)	42 (100%)	16 (100%)	121 (100%)	

Data are presented as numbers, percentages, mean and P-value.

Table 4. SnMe (Inferior facial height) and NMe (Total facial height): ratio SNMe/NMe

SNMe/NMe	P value	Odds Ratio (OR)	95%IC
Upper Biotype	0.036*	0.843	0.888-1.042
Lower Biotype	0.049*	0.904	0.899-1.003

Data are presented as odds ratio (OR) and interquartile range (IQR). * Indicates statistically significant value ($P < 0.05$).

2.4. Discussion

The aim of this study was to investigate the association between facial typology and gingival biotype in pre-orthodontic patients, in order to guarantee a better diagnosis and planning of orthodontic treatment.

We tested if the facial typology measured on two-dimensional cephalograms (SN[^]GoGn and CoGoMe[^]) or on three-dimensional facial scans (SNMe/NMe) could affect the gingival biotype. This study did not find any association between facial typology assessed on two-dimensional angles SN[^]GoGn or CoGoMe[^] and maxillary and mandibular gingival biotype of the anterior regions. There is one study that correlates the craniofacial morphology using a magnetic resonance imaging (MRI) with gingival recession and clinical attachment loss. The study used the ratio of facial width and length (facial index) for describing the craniofacial morphology, and showed that patients with long narrow face were associated with higher loss of attachment [41].

A recent study performed by Kaya et al. investigated the relationship between gingival phenotype and craniofacial morphology in the sagittal and vertical direction. In contrast to the present study, the gingival phenotype was determined with an endodontic file namely transgingival probing (<1mm and >1mm, thin and thick phenotype respectively). These results demonstrated that there is no association between gingival thickness and craniofacial typology [33].

In this study the facial typology was evaluated also with three-dimensional facial scans, to assess the association between SNMe/NMe and the gingival thickness. This analysis showed that the facial proportions have a statistically significant association with the gingival biotype. In particular, when the ratio of SNMe/NMe is decreased, there is a minor risk to find a thin gingival biotype either in the maxillary and mandibular anterior region.

This is the first study that evaluated the gingival thickness through the transparency of the periodontal probe (thin and adequate gingival biotype) with the different vertical facial heights and it showed that there is no correlation between facial morphology and gingival thickness on

lateral cephalograms [24]. Gingival thickness can be assessed by transgingival probing [42], ultrasonic measurement [43] or through the visibility of the probe [44,45]. Transgingival probing was not used because of the need of local anaesthesia, which could induce a local volume increase and discomfort for the patients [42]. Also ultrasonic measurement was not preferred because of its repeatability with a coefficient of 1,20 mm [46]. Instead, the transparency of the probe through the gingival margin was found to have a high reproducibility by De Rouck et al showing 85% inter-examiner repeatability (k value = 0.7, P value = 0.002) [44]. Therefore, this study used the periodontal probe visible through the gingiva after its placement in the facial sulcus of the anterior teeth [44].

Orthodontic treatment can have important role in periodontal changes [47]. The thickness of the gingiva are supposed to represent an indicator for reducing the risk of bone loss and gingival recession [7]. In fact, there are two studies that have a statistically significant relationship between facial biotype and alveolar height and thickness with a greater risk of moving incisors beyond the anatomic limits of the alveolar bone by application of uncontrolled forces. [12,13].

This uncontrolled movement can bring to alveolar bone fenestrations increasing the susceptibility to gingival recession [48,49] and to a recession in case of less than 2 mm of gingival thickness [14].

The current study presents several strengths. First, the periodontal assessments were performed in all of patients at the beginning of orthodontic treatment. This allows an accurate diagnosis and treatment planning. In order to avoid bias due to differences in operator performance, only two trained clinicians did the periodontal charting. Moreover, a new method to evaluate craniofacial morphology was introduces without exposure for the patients of further radiation. The study also has some limitations. First, the sample size was relatively small to achieve a more reliable result. Second, only few patients presented a thin UGB, however this was in accordance with the normal prevalence of this biotype [33]. Further longitudinal studies are necessary to evaluate the long-term effects of orthodontic treatment on gingival biotype in different facial typology.

2. 5. Conclusions

Within the limits of this study, it is possible to conclude that:

1. There is no association between facial typology (evaluated with SN[^]GoGn and CoGoMe) and gingival biotype.

2. When the ratio of SNMe/NMe is decreased, it represented a protective factor and a minor risk to find a thin gingival biotype.

References

1. Liu, P.; Liu, Y.; Wang, J.; Guo, Y.; Zhang, Y.; Xiao, S. Detection of fusobacterium nucleatum and fadA adhesin gene in patients with orthodontic gingivitis and non-orthodontic periodontal inflammation. *PLoS One* **2014**, *9*, 3–7.
2. Bollen, A.; Cunha-cruz, J.; Bakko, W.; Huang, G.J.; Hujoel, P.P. The Effects of orthodontic therapy on periodontal health: a systematic review of controlled evidence. *J. Am. Dent. Assoc.* **2008**, *139*, 413–422.
3. Liu, H.; Sun, J.; Dong, Y.; Lu, H.; Zhou, H.; Hansen, B.F.; Song, X. Periodontal health and relative quantity of subgingival porphyromonas gingivalis during orthodontic treatment. *Angle Orthod.* **2011**, *81*, 609–615.
4. Tanner, A.C.R.; Sonis, A.L.; Lif Holgerson, P.; Starr, J.R.; Nunez, Y.; Kressirer, C.A.; Paster, B.J.; Johansson, I. White-spot lesions and gingivitis microbiotas in orthodontic patients. *J. Dent. Res.* **2012**, *91*, 853–858.
5. Cardoso-Silva C, Barbería E, Ramos Atance JA, Maroto M, Hernández A, G.-G.F. Microbiological analysis of gingivitis in pediatric patients under orthodontic treatment. *Eur J Paediatr Dent* **2011**, *12*, 210–4.
6. Vanarsdall, R.L.; Corn, H. Soft-tissue management of labially positioned unerupted teeth. *Am. J. Orthod.* **1977**, *72*, 53–64.
7. Maynard, J.G. The rationale for mucogingival therapy in the child and adolescent. *Int. J. Periodontics Restorative Dent.* **1987**, *7*, 36—51.
8. Hall, W.B. The Current Status of Mucogingival Problems and Their Therapy. *J. Periodontol.* **2012**, *52*, 569–575.
9. Renkema, A.M.; Navratilova, Z.; Mazurova, K.; Katsaros, C.; Fudalej, P.S. Gingival labial recessions and the post-treatment proclination of mandibular incisors. *Eur. J. Orthod.* **2015**, *37*, 508–513.
10. Renkema, A.M.; Fudalej, P.S.; Renkema, A.A.P.; Abbas, F.; Bronkhorst, E.; Katsaros, C. Gingival labial recessions in orthodontically treated and untreated individuals: A case - Control study. *J. Clin. Periodontol.* **2013**, *40*, 631–637.
11. Aziz T, F.-M.C. A systematic review of the association between appliance-induced labial movement of mandibular incisors and gingival recession. *Aust Orthod J.* **2011**, *27*, 33–39.
12. Renkema, A.M.; Fudalej, P.S.; Renkema, A.; Kiekens, R.; Katsaros, C. Development of

- labial gingival recessions in orthodontically treated patients. *Am. J. Orthod. Dentofac. Orthop.* **2013**, *143*, 206–212.
13. Morris, J.W.; Campbell, P.M.; Tadlock, L.P.; Boley, J.; Buschang, P.H. Prevalence of gingival recession after orthodontic tooth movements. *Am. J. Orthod. Dentofac. Orthop.* **2017**, *151*, 851–859.
 14. Kim, D.M.; Neiva, R. Periodontal soft tissue non-root coverage procedures: a systematic review from the AAP regeneration workshop. *J. Periodontol.* **2015**, *86*, S56–S72.
 15. Joss-Vassalli, I.; Grebenstein, C.; Topouzelis, N.; Sculean, A.; Katsaros, C. Orthodontic therapy and gingival recession: A systematic review. *Orthod. Craniofacial Res.* **2010**, *13*, 127–141.
 16. Kois JC Predictable single-tooth peri-implant esthetics: five diagnostic keys. *Compend Contin Educ Dent.* **2004**, *25*, 895–6, 898, 900 passim; quiz 906–7.
 17. Ahmad, I. Anterior dental aesthetics: Gingival perspective. *Br. Dent. J.* **2005**, *199*, 195–202.
 18. Grover, V.; Bhardwaj, A.; Mohindra, K.; Malhotra, R. Analysis of the gingival biotype based on the measurement of the dentopapillary complex. *J. Indian Soc. Periodontol.* **2014**, *18*, 43.
 19. Papapanou, P.N.; Sanz, M.; Buduneli, N.; Dietrich, T.; Feres, M.; Fine, D.H.; Flemmig, T.F.; Garcia, R.; Giannobile, W. V.; Graziani, F.; et al. Periodontitis: consensus report of workgroup 2 of the 2017 world workshop on the classification of periodontal and peri-Implant diseases and conditions. *J. Clin. Periodontol.* **2018**, *89*, s173-S182.
 20. Vandana, K.L.; Savitha, B. Thickness of gingiva in association with age, gender and dental arch location. *J. Clin. Periodontol.* **2005**, *32*, 828–30.
 21. Seibert, J.; Lindhe, J. Aesthetics and periodontal therapy. In *Textbook of Clinical Periodontology. 2nd ed.*; 1989; pp. 477–514.
 22. Olsson, M.; Lindhe, J. Periodontal characteristics in individuals with varying form of the upper central incisors. *J. Clin. Periodontol.* **1991**, *18*, 78–82.
 23. Fields, H.; Proffit, W.; Nixon, W.; Phillips, C.; Stanek, E. Facial pattern differences in long-faced children and adults. *Am. J. Orthod.* **1984**, *85*, 217–223.
 24. Cangialosi, T.J. Additional criteria for sample division suggested. *Am. J. Orthod. Dentofac. Orthop.* **1989**, *96*, A24.
 25. Opdebeeck, H.; Bell, W. The short face syndrome. *Am. J. Orthod.* **1978**, *73*, 499–511.
 26. Schudy FF The Rotation of the mandible resulting from growth: its implications in orthodontic treatment. *Angle Orthod.* **1964**, *34*, 75–93.

27. Matarese, G.; Isola, G.; Ramaglia, L.; Dalessandri, D.; Luchesse, A.; Alibrandi, A.; Fabiano, F.; Cordasco, G. Periodontal biotype: characteristic, prevalence and dimension related to dental malocclusion. *Minerva Stomatol* **2016**, *65*, 231–8.
28. Al-Zo'ubia, I.A.; Hammadb, M.M.; Abu Alhaijac, E.S.J. Periodontal parameters in different dentofacial vertical patterns. *Angle Orthod.* **2008**, *78*, 1006–1014.
29. Hornera, K.A.; Behrents, R.G.; Beom Kim, K.; Buschang, P.H. Cortical bone and ridge thickness of hyperdivergent and hypodivergent adults. *Am. J. Orthod. Dentofac. Orthop.* **2012**, *142*, 170–178.
30. Esfahanizadeh, N.; Daneshparvar, N.; Askarpour, F.; Akhoundi, N.; Panjnoush, M. Correlation Between Bone and Soft Tissue Thickness in Maxillary Anterior Teeth. *J. Dent. (Tehran)*. **2016**, *13*, 302–308.
31. Sadek, M.M.; Sabet, N.E.; Hassan, I.T. Alveolar bone mapping in subjects with different vertical facial dimensions. *Eur. J. Orthod.* **2014**, *37*, 194–201.
32. Björk A. Prediction of mandibular growth rotation. *Am. J. Orthod.* **1969**, *55*, 585–99.
33. Kaya, Y.; Alkan, Ö.; Alkan, E.A.; Keskin, S. Gingival thicknesses of maxillary and mandibular anterior regions in subjects with different craniofacial morphologies. *Am. J. Orthod. Dentofac. Orthop.* **2018**, *154*, 356–364.
34. Baik, H.S.; Kim, S.Y. Facial soft-tissue changes in skeletal class III orthognathic surgery patients analyzed with 3-dimensional laser scanning. *Am. J. Orthod. Dentofac. Orthop.* **2010**, *138*, 167–178.
35. Kau, C.H.; Richmond, S.; Incrapera, A.; English, J.; Xia, J.J. Three-dimensional surface acquisition systems for the study of facial morphology and their application to maxillofacial surgery. *Int J Med Robot. Comput Assist Surg* **2007**, *3*, 97–110.
36. Aynechi, N.; Larson, B.E.; Leon-Salazar, V.; Beiraghi, S. Accuracy and precision of a 3D anthropometric facial analysis with and without landmark labeling before image acquisition. *Angle Orthod.* **2011**, *81*, 245–252.
37. Plooij, J.M.; Swennen, G.R.J.; Rangel, F.A.; Maal, T.J.J.; Schutyser, F.A.C.; Bronkhorst, E.M.; Kuijpers-Jagtman, A.M.; Bergé, S.J. Evaluation of reproducibility and reliability of 3D soft tissue analysis using 3D stereophotogrammetry. *Int. J. Oral Maxillofac. Surg.* **2009**, *38*, 267–273.
38. Toma, A.M.; Zhurov, A.; Playle, R.; Ong, E.; Richmond, S. Reproducibility of facial soft tissue landmarks on 3D laser-scanned facial images. *Orthod. Craniofacial Res.* **2009**, *12*, 33–42.
39. De Menezes, M.; Rosati, R.; Ferrario, V.F.; Sforza, C. Accuracy and reproducibility of a 3-dimensional stereophotogrammetric imaging system. *J. Oral Maxillofac. Surg.* **2010**,

- 68, 2129–2135.
40. Kan, J.Y.K.; Rungcharassaeng, K.; Umezu, K.; Kois, J.C. Dimensions of peri-implant mucosa: an evaluation of maxillary anterior single implants in humans. *J. Periodontol.* **2003**, *74*, 557–562.
 41. Salti, L.; Holtfreter, B.; Pink, C.; Habes, M.; Biffar, R.; Kiliaridis, S.; Krey, K.F.; Bülow, R.; Völzke, H.; Kocher, T.; et al. Estimating effects of craniofacial morphology on gingival recession and clinical attachment loss. *J. Clin. Periodontol.* **2017**, *44*, 363–371.
 42. Ronay, V.; Sahrman, P.; Bindl, A.; Attin, T.; Schmidlin, P.R. Current status and perspectives of mucogingival soft tissue measurement methods. *J. Esthet. Restor. Dent.* **2011**, *23*, 146–156.
 43. Eger, T.; Müller H.-P.; Heinecke, A. Ultrasonic determination of gingival thickness subject variation and influence of tooth type and clinical features. *J. Clin. Periodontol.* **1996**, *23*, 839–845.
 44. De Rouck, T.; Eghbali, R.; Collys, K.; De Bruyn, H.; Cosyn, J. The gingival biotype revisited: transparency of the periodontal probe through the gingival margin as a method to discriminate thin from thick gingiva. *J. Clin. Periodontol.* **2009**, *36*, 428–433.
 45. Cortellini, P.; Bissada, N.F. Mucogingival conditions in the natural dentition: narrative review, case definitions, and diagnostic considerations. *J. Clin. Periodontol.* **2018**, *45*, S190–S198.
 46. Müller, H.P.; Könönen, E. Variance components of gingival thickness. *J. Periodontol. Res.* **2005**, *40*, 239–244.
 47. Alfuriji, S.; Alhazmi, N.; Alhamlan, N.; Al-Ehaideb, A.; Alruwaithi, M.; Alkatheeri, N.; Geevarghese, A. The effect of orthodontic therapy on periodontal health: A review of the literature. *Int. J. Dent.* **2014**, *2014*.
 48. Holmesa, H.D.; Tennantb, M.; Goonewardene, M.S. Augmentation of faciolingual gingival dimensions with free connective tissue grafts before labial orthodontic tooth movement: An experimental study with a canine model. *Am. J. Orthod. Dentofac. Orthop.* **2005**, *127*, 562–572.
 49. Wennström, J.L.; Lindhe, J.; Sinclair, F.; Thilander, B. Some periodontal tissue reactions to orthodontic tooth movement in monkeys. *J. Clin. Periodontol.* **1987**, *14*, 121–129.

CHAPTER 3

Distribution of the Condylion-Gonion-Menton (CoGoMe[^]) angle in a population of patients from Southern Italy.

Abstract

The condylion-gonion-menton angle (CoGoMe[^]) is commonly used as a pre-treatment indicator of responsiveness in Class II patients treated with functional appliances. The distribution of this angle in the Caucasian population is still unknown. This study aimed to determine the distribution of the CoGoMe[^] and its relationship with age, sagittal jaw relationship (ANPg[^]), and mandibular inclination (SN[^]GoGn) in patients from Southern Italy. The sample included 290 subjects (median 14 years of age; Interquartile range, IQR, 12–17) with lateral cephalograms taken before the orthodontic treatment. The distribution of the CoGoMe[^] was assessed with the Shapiro–Wilk test, and the differences according to the ANPg[^] and the SN[^]GoGn were estimated using onewayANOVA. Linear regression analysis was performed to evaluate how the CoGoMe[^] varied according to age. The statistical significance was set at $P < 0.05$. The results showed that the CoGoMe[^] was normally distributed ($P = 0.290$) with a mean value of $127.2^\circ \pm 7.7^\circ$. The distribution of the CoGoMe[^] in groups with different SN[^]GoGn angles was significantly different ($P < 0.001$). These angles showed a positive association (Beta coefficient $B = 0.6$; 95% CI: 0.51, 0.67; $P < 0.001$). In growing patients, the CoGoMe[^] decreased every year by 0.6° ($B = -0.6$; 95% CI: -1.05, -0.12; $P = 0.014$). In conclusion, the CoGoMe[^] was associated with mandibular inclination and could be considered to be a predictor of vertical growth patterns.

This chapter is based on “D’Antò V., Pango Madariaga A.C., Rongo R., Bucci R., Simeon V., Franchi L. and Valletta R. Distribution of the Condylion-Gonion-Menton (CoGoMe[^]) angle in a population of patients from Southern Italy. *Dent. J.* 2019, 7, 104”.

3.1. Introduction

The purpose of orthodontic treatment is to achieve an aesthetic improvement and provide functional occlusion and balanced facial features [1]. A precise diagnosis is essential for choosing the correct therapy and determining the prognosis adequately. Therefore, orthodontic treatment planning requires an accurate prediction of the amount and direction of craniofacial development [2–4]. Since Broadbent [5] introduced lateral cephalometric radiography in 1931, studies on craniofacial growth and development have increased in number, and many researchers suggested definitions and norms for the normal occlusion. Hence, radiographic cephalometry has become one of the most important instruments of clinical and research orthodontics [6].

The appropriate interpretation of any cephalometric analysis requires norms that are calculated from populations and adjusted according to age, gender, and ethnic group [5,6]. The cephalometric value norms represent a valuable aid for clinicians to determine the measure of deviations from the population average, or what is considered “healthy”. Currently, orthodontic patients in clinical practice range from children to adults, and they belong to a variety of ethnic groups; therefore, a wide range of representative standards would ideally be needed to perform an individualised orthodontic treatment plan [7,8].

Mandibular growth prediction is a factor of utmost importance in orthodontic/orthopaedic treatment planning [9]. Indeed, it seems crucially important to identify the mandibular growth pattern before treatment, as patients with signs of posterior mandibular growth rotation (hyperdivergent growth pattern) are assumed to be more difficult to treat than those with an anterior mandibular rotation (hypodivergent growth pattern) [10–12]. The most widely used method for establishing the jaw growth rotation is cephalometric analysis. Several different analyses have been introduced to evaluate a patient’s divergency, such as Ricketts analysis or Jarabak analysis [13,14].

The $SN^{\wedge}GoGn$ is a very useful diagnostic parameter to consider before starting an orthodontic treatment because it evaluates the facial pattern of a subject, and it reflects the variability of the mandibular plane in relation to the anterior cranial base [15].

Another important morphological characteristic of the lower jaw related to the anterior/posterior rotational growth pattern is the angle formed by the condylar axis (CoGo) and the mandibular base (GoMe), i.e., the Condylion-Gonion-Menton angle ($CoGoMe^{\wedge}$) [10,11]. Although this angle has been proposed as a possible predictor of responsiveness during orthopaedic therapies [16], there are no studies on the distribution of the $CoGoMe^{\wedge}$ and its relationship with classical cephalometric vertical ($SN^{\wedge}GoGn$) and sagittal measurements ($ANPg^{\wedge}$).

Finally, ANPg[^] is an angle useful for the sagittal classification of the malocclusion, Class I, Class II or Class III skeletal relationship, it is formed by NA (Nasion-point A line) line through N and A and NPg (Nasion-Pogonion line) line through N and Pg.

Therefore, the aim of this study was to determine the distribution of the CoGoMe[^], and its relationship with age, sagittal jaw relationship (ANPg[^]) and mandibular inclination (SN[^]GoGn) in a population of patients from Southern Italy. The null hypothesis was that there is no relationship between the CoGoMe[^] and the SN[^]GoGn.

3.2. Materials and Methods

3.2.1. Subjects

This research protocol was approved by the Ethics Committee of the University of Naples Federico II (121/19; 18-03-2019).

For this retrospective study, the lateral cephalograms of patients treated at the Section of Orthodontics at the University of Naples Federico II, were screened. Due to the retrospective design of the study, it was not possible to obtain the informed consent from all the participants, however before orthodontic treatment, all patients provide authorization to use their clinical records for research purposes.

The lateral cephalograms were selected based on the following inclusion criteria:

- age \geq 8
- a good quality lateral x-ray

The following conditions were considered as exclusion criteria:

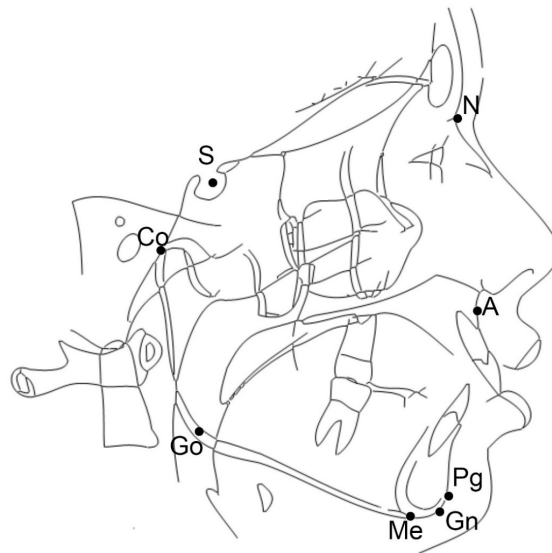
- patients with systemic diseases
- patients with genetic syndromes
- previous orthodontic treatment

All the lateral radiographs were taken before the orthodontic treatment in natural head position [17,18]. One operator traced all lateral cephalograms with a cephalometric software program (Dolphin, Chatsworth, CA, USA).

For this study, the cephalometric analysis was performed as shown in Figure 1a-b. Briefly, three cephalometric variables were assessed: the CoGoMe[^] measured the mandibular structure, which is the angle between the condylar axis (Condylion-Gonion) and the mandibular base (Gonion-Menton); the SN[^]GoGn determined jaw divergence, which is the angle between the anterior cranial base (Sella-Nasion) and the mandibular plane (Gonion-Gnathion); the ANPg[^] assessed sagittal jaw discrepancy, which is the angle between the Nasion-point A line and the Nasion-Pogonion line [19].

The sagittal malocclusion was classified into three groups according to the ANPg[^]: Class III with an ANPg[^] equal to or lower than -1°, Class I with an ANPg[^] between -1° and 5°, and Class II with an ANPg[^] equal to or greater than 5°. Similarly, the sample was divided into three groups according to their vertical malocclusion: Hypodivergent with a SN[^]GoGn equal to or lower than 27°, Normodivergent with a SN[^]GoGn between 27° and 37°, and Hyperdivergent with a SN[^]GoGn equal to or greater than 37°, as seen Figure 2a, 2b and 2c.

Figure 1a. Cephalometric analysis and landmarks. Landmarks: A (Point A), more posterior point of the frontal concavity of the maxillary between the anterior nasal spine and the alveolar processes; N (Nasion), more anterior point of the junction of the nasal and frontal bone (frontonasal suture); S (Sella), centre of the



hypophyseal fossa; Go (Gonion), midpoint of the curvature at the angle of the mandible; Co (Condylion) the highest and most posterior point on the contour of the mandibular condyle; Pg (pogonion), the most anterior point of the symphysis, Gn (Anatomical gnathion), point of the mandibular symphysis on the facial axis; Me (Menton), most inferior point of the mandibular symphysis;

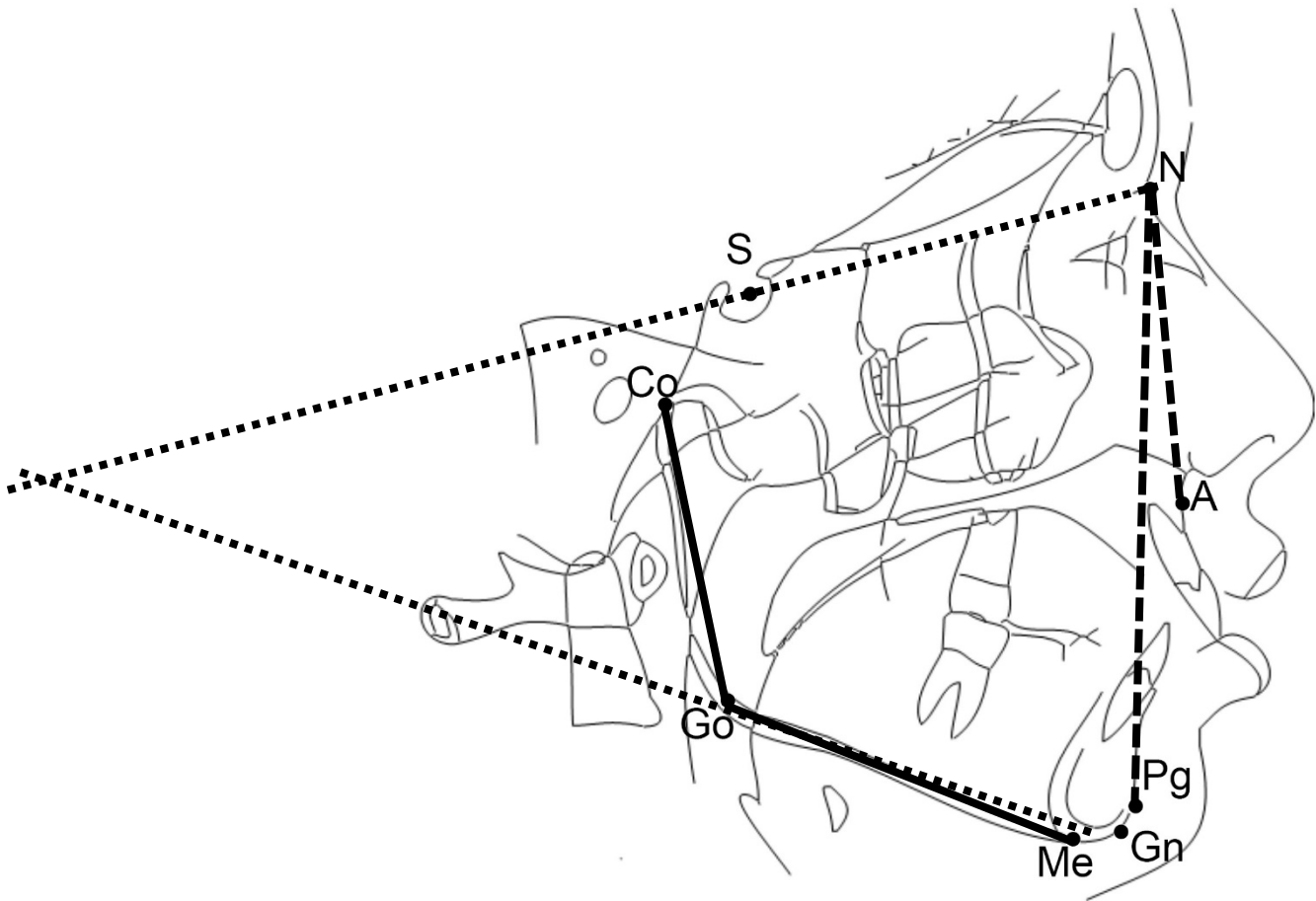


Figure 1b. Reference: NA (Nasion-point A line) line through N and A; NPg (Nasion-Pogonion line) line through N and Pg; SN (Sella-Nasion line) line through S and N; GoGn (Mandibular plane) line through Go and Gn; CoGo (condylar axis) line through Co and Go; GoMe (Mandibular base) line through Go and Me

- SN[^]GoGn
- CoGoMe[^]
- - - - ANPg[^]

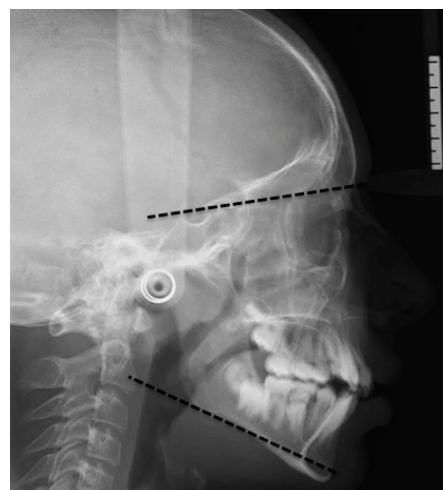


Figure 2a- 2b. Hypodivergent and hyperdivergent patients according to SN[^]GoGn.

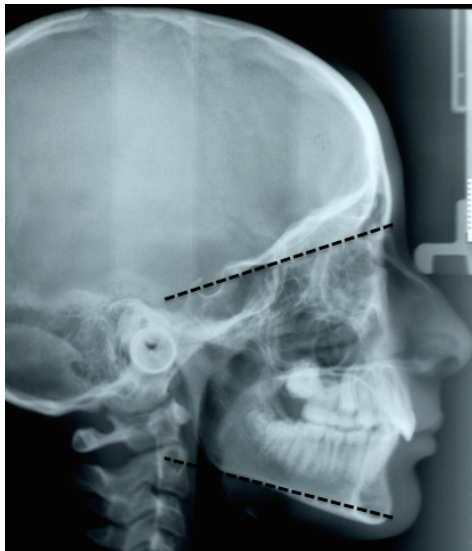


Figure 2c. Normodivergent patient according to SN^GoGn.

3.2.2. Statistical analysis

The technical errors of measurement were calculated from 101 randomly selected lateral cephalograms. The CoGoMe^ was reassessed by the same examiner after a memory washout period of at least 8 weeks. The method error for all measurements was calculated using Dahlberg's formula [20]. Systematic differences between duplicated measurements were tested using a paired Student's t-test with the type I error set at .05.

Categorical variables were reported as frequencies and percentages, and continuous variables were reported as means and standard deviations if data distribution was normal or as medians and interquartile range if the data showed a skewed distribution. The Shapiro-Wilk (SW) test was used to evaluate normality assumption.

The Pearson correlation analysis was used to assess the relationship between continuous variables, when requested.

Differences in the CoGoMe^ among individuals with different ANPg^ and SN^GoGn were estimated as appropriate by using one-way Analysis of Variance (ANOVA).

Linear regression analysis was performed to evaluate (1) how the CoGoMe^ (used as dependent variable) changed according to the age and (2) how the CoGoMe^ (used as independent variable and adjusted for age) was able to predict the SN^GoGn. For the first issue, two models for linear regression analysis were performed. One model included growing patients younger than 17 years and the other included patients aged 17 years and older. Beta coefficients and 95% confidence intervals were calculated.

The level of statistical significance was set at $P < 0.05$. Statistical analysis was performed using STATA version 14.0 (StataCorp LP, Stata Statistical Software, College Station, TX, USA).

3.3. Results

The sample included 290 subjects: 122 males (42.1%) and 168 females (57.9%), aged 8 to 53 years (median 14; IQR 12-17).

The method error for the three angles assessed in the study was $ANP_g^\wedge=0.4^\circ$, $SN^\wedge GoGn=0.9^\circ$ and $CoGoMe^\wedge=1.3^\circ$ and there were no systematic errors for any measurements ($P>0.05$).

In the total sample of 290 patients, the $CoGoMe^\wedge$ resulted normally distributed (SW test, $P=0.290$), with a mean value of $127.2^\circ\pm 7.7^\circ$ as seen in Table 1 and Figure 2. The ANP_g^\wedge and the $SNGoGn^\wedge$ presented a mean value of $2.6^\circ\pm 3.2^\circ$ and $31.9^\circ\pm 6.8^\circ$, respectively (Table 1).

Table 1. Cephalometric values in the study sample.

Variables	Mean	Median	Standard Deviation
ANP_g^\wedge	2.6°	2.9°	3.2°
$SN^\wedge GoGn$	31.9°	32°	6.8°
$CoGoMe^\wedge$	127.2°	127.5°	7.7°

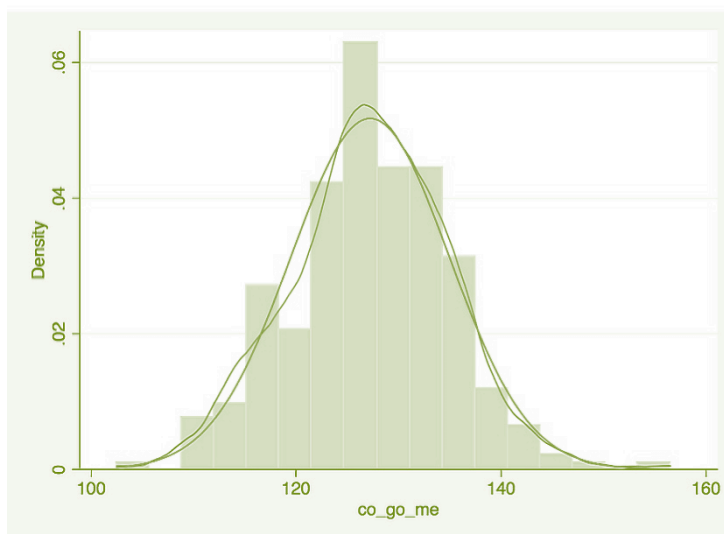


Figure 3. Graph describing the distribution of the $CoGoMe^\wedge$ in the study population ($N=290$; mean \pm SD= $127.2^\circ\pm 7.7^\circ$ [CI 95% 112.1 $^\circ$ -142.3 $^\circ$]).

After dividing the sample into three groups according to the ANP_g^\wedge , the $CoGoMe^\wedge$ showed no statistically significant difference ($P=0.560$). In particular, Class III ($ANP_g^\wedge\leq -1^\circ$) included 32 patients and showed a mean $CoGoMe^\wedge$ of $128.59^\circ\pm 7.8^\circ$; Class I ($-1^\circ < ANP_g^\wedge < 5^\circ$) included 196 patients and presented a mean $CoGoMe^\wedge$ of $127.09^\circ\pm 7.8^\circ$; Class II ($ANP_g^\wedge\geq 5^\circ$) included 62 patients and showed a mean $CoGoMe^\wedge$ of $126.9^\circ\pm 7.2^\circ$, as seen in Table 2.

When the sample was divided into three groups according to the $SN^\wedge GoGn$, statistically significant difference in the $CoGoMe^\wedge$ was observed ($P<0.001$). In particular, 60 patients were

Hypodivergent ($SN^{GoGn} < 27$) and presented a mean $CoGoMe^{\wedge}$ of $120.1^{\circ} \pm 6.63^{\circ}$; 166 patients were Normodivergent ($27 \leq SN^{GoGn} \leq 37$) and presented a mean $CoGoMe^{\wedge}$ of $127.1^{\circ} \pm 6.11^{\circ}$; 64 patients were Hyperdivergent ($SN^{GoGn} > 37$) and presented a mean $CoGoMe^{\wedge}$ of $134.02^{\circ} \pm 6.18^{\circ}$, as shown in Table 2 and Figure 4.

Table 2. Distribution of the $CoGoMe^{\wedge}$ according to the $ANPg^{\wedge}$ and the SN^{GoGn} . Differences in $CoGoMe^{\wedge}$ among individuals with different $ANPg^{\wedge}$ and SN^{GoGn} were estimated as appropriate using one-way ANOVA. Bold text indicates statistically significant differences.

Variables	Groups	N	Mean	Sd	P50	P25	P75	ANOVA
$ANPg^{\wedge}$	Class III ($\leq -1^{\circ}$)	32	128.59°	7.8°	129.2°	123.65°	133.5°	F(2, 287)=0.58, P=0.56
	Class I ($-1^{\circ} < x < 5^{\circ}$)	196	127.09°	7.8°	127.4°	122.45°	132.85°	
	Class II ($\geq 5^{\circ}$)	62	126.9°	7.2°	125.9°	121.8°	130.8°	
SN^{GoGn}	Hypodivergent ($\leq 27^{\circ}$)	60	120.1°	6.63°	120.4°	102.5°	134°	F(2, 287)=77.04, P<0.001
	Normodivergent ($27^{\circ} < x < 37^{\circ}$)	166	127.1°	6.11°	127.1°	110.2°	143.8°	
	Hyperdivergent ($\geq 37^{\circ}$)	64	134.02°	6.18°	133.7°	121.7°	156.5°	

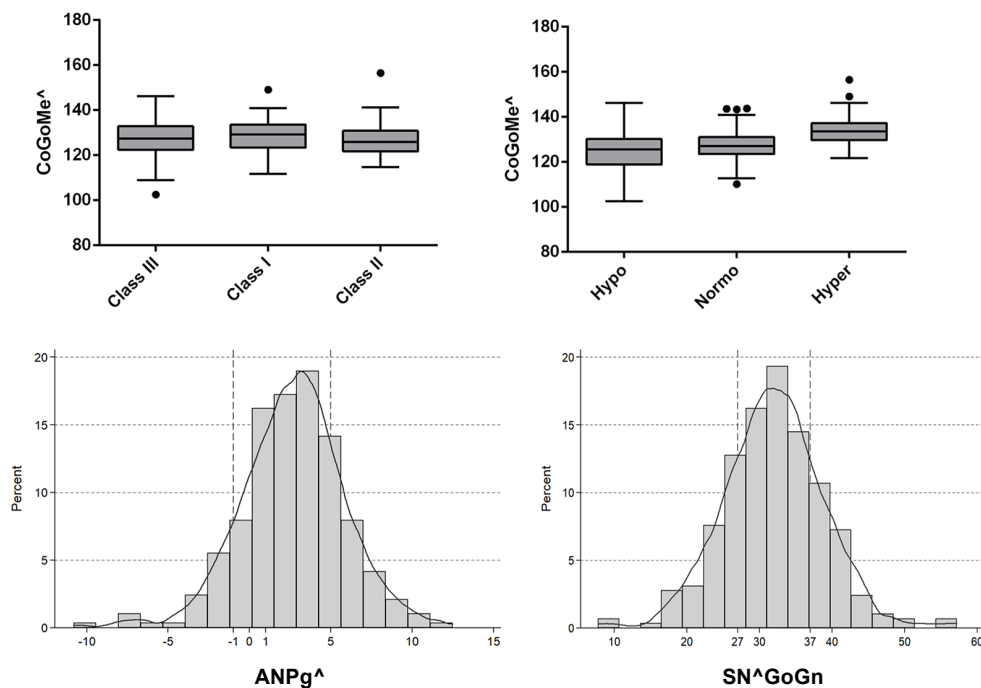


Figure 4. Box-and-whiskers plots (upper panel) of the $CoGoMe^{\wedge}$ angle by $ANPg^{\wedge}$ and SN^{GoGn} . Line in the box: median value. Box hinges: 25–75th percentiles; ends of the segments: 5–95th percentiles; dots: outliers. Histograms with kernel distribution (lower panel) were presented to describe $ANPg^{\wedge}$ and SN^{GoGn} variables. Cut-off value were highlighted with dashed line (-1 and 5).

The correlation between the $CoGoMe^{\wedge}$ and the SN^{GoGn} was moderate ($R=0.6$, $P<0.0001$). On the other hand, the correlation between the $CoGoMe^{\wedge}$ and the $ANPg^{\wedge}$ was

absent ($R=-0.02$, $P=0.74$) while a weak correlation was observed between the $SN^{\wedge}GoGn$ and the $ANPg^{\wedge}$ ($R=0.21$, $P=0.0003$).

In the linear regression analysis performed on patients under 17 years of age ($N=210$), a clear decrease of the $CoGoMe^{\wedge}$ during growth was observed ($b=-0.6$; 95% CI:-1.05,-0.12; $P=0.014$), as shown in Table 3. However, in the linear regression performed on subjects older than 17 years of age ($N=80$), this association disappeared and the angle remained stable over time ($b=0.004$; 95% CI:-0.31, 0.32; $P=0.98$), as seen in Table 3.

Finally, the results of the regression model with the $SN^{\wedge}GoGn$ as dependent variable reported that for each degree of increase of the $CoGoMe^{\wedge}$ resulted in an increase of $SN^{\wedge}GoGn$ by 0.6° ($b=0.6$; 95% CI: 0.51, 0.67; $P<0.001$, Table 3).

Table 3. Distribution of the $CoGoMe^{\wedge}$ according to the $ANPg^{\wedge}$ and the $SN^{\wedge}GoGn$. Differences in $CoGoMe^{\wedge}$ among individuals with different $ANPg^{\wedge}$ and $SN^{\wedge}GoGn$ were estimated as appropriate using one-way ANOVA. Bold text indicates statistically significant differences.

	Models	B	CI 95%	P
1	$CoGoMe^{\wedge}/Age$ younger than 17 years ($N=210$)	-0.6	-1.05,-0.12	0.014
2	$CoGoMe^{\wedge}/Age$ 17 years and older ($N=80$)	0.004	-0.31,-0.32	0.98
3	$SN^{\wedge}GoGn/ CoGoMe^{\wedge}*Age$ ($N=290$)	0.6	0.51, 0.67	<0.001

3.4. Discussion

The aim of this study was to determine the distribution of the $CoGoMe^{\wedge}$ in a population of patients from Southern Italy and to assess the association of this mandibular angle with vertical and sagittal cephalometric parameters. The results showed that the $CoGoMe^{\wedge}$ was normally distributed in the studied population, and it was correlated to the vertical facial type ($SN^{\wedge}GoGn$), however, it was not influenced by the anteroposterior jaw relationship ($ANPg^{\wedge}$).

Our study is the first to report a strong association between the $CoGoMe^{\wedge}$ and the $SN^{\wedge}GoGn$ with these two angles positively correlated. Indeed, each degree of increase of the $CoGoMe^{\wedge}$ resulted in an increase of the $SN^{\wedge}GoGn$ by 0.6° . Moreover, the mean value of the $CoGoMe^{\wedge}$ was statistically significant different according to the identified subgroups of the $SN^{\wedge}GoGn$. Hence, the $CoGoMe^{\wedge}$ could help to identify mandibular growth patterns, and therefore clinicians are suggested to consider this variable carefully at the beginning of the orthodontic therapy. Indeed, $CoGoMe^{\wedge}$ might be useful to understand the mandibular rotational pattern, giving more accurate information than the $SN^{\wedge}GoGn$, that is influenced also

by the inclination of the anterior cranial base [15]. The CoGoMe^\wedge is a variable related only to mandibular structure (condylar axis and mandibular base), hence its evaluation is not affected by any other external structures. This strong correlation between CoGoMe^\wedge and $\text{SN}^\wedge\text{GoGn}$ is related both to an anatomical consideration, both angles evaluate the mandibular base, and to a functional consideration, usually hyperdivergent patients have a lower muscles thickness and a lower bite force, that might have a less control on the vertical growth pattern [21,22].

In the current study, the CoGoMe^\wedge decreased with growth, up to 17 years of age. Björk and co-workers [23,24] studied mandibular rotation and distinguished 2 types of rotation, internal and external, by superficial remodelling. From the age of 4 years to adulthood, the internal rotation is about 15° forward, while the external rotation is about $11^\circ/12^\circ$ backward, producing a $3^\circ/4^\circ$ total decrease of the mandibular angle during growth [23,24]. Hence, the natural backward rotation of the mandible during growth might be responsible for the reduction of the CoGoMe^\wedge observed in the current study.

The clinical significance of this study is related to the importance of growth predictors for the orthodontic diagnosis and treatment planning, with possible implications on the success rate and the duration of the orthodontic treatment for each specific malocclusion [25]. During the orthodontic diagnosis and treatment planning the possibility to correctly identify the mandibular rotational pattern during growth is a fundamental factor [16]. It is well recognised that patients with a hyperdivergent mandibular growth pattern are more difficult cases [9,10,17]. Not only the cephalometric analysis but also anatomical characteristics were used to identify the mandibular rotational pattern. Already in the early 60s, Björk and Skieller underlined the possibility of predicting the mandibular growth pattern by looking at some specific anatomic mandibular structures in longitudinal lateral cephalograms with the purpose of identifying facial morphology and the progression of mandibular rotation [18–20]. They introduced seven mandibular morphological signs that identified hyperdivergent and hypodivergent mandibular patterns [20]. Although, the CoGoMe^\wedge is a cephalometric angle, it is strongly related to the mandibular anatomy and, due to its correlation with the $\text{SN}^\wedge\text{GoGn}$, it might improve the accuracy of the cephalometric diagnosis.

Class II malocclusion is one of the most prevalent orthodontic problems in the Caucasian population [26–28]. It might cause detrimental aesthetic effects and social impairment in children's daily lives, it affects their oral-health related quality of life, and it is a risk factor for dental traumas [29]. In growing subjects, one treatment option to correct skeletal Class II malocclusions uses functional/orthopaedic appliances, [30] but still great variability in the achievable mandibular advancement has been observed across literature due to numerous factors. One factor that might be responsible for different growth potential is mandibular

morphology. Petrovic pointed out that the individual mandibular growth potential and the responsiveness to the functional orthopaedic treatment were strongly influenced by the mandibular growth pattern [10,11]. The CoGoMe[^] was proposed as a pre-treatment indicator of lower jaw responsiveness in Class II patients treated with functional appliances at the mandibular growth spurt [16]. Hence, it was suggested that the CoGoMe[^] could be used for an efficient discrimination between good (CoGoMe[^] < 125.5°) and bad (CoGoMe[^] > 125.5°) responders to functional treatment of skeletal Class II malocclusion due to mandibular retrusion. This is the first study that evaluated the distribution and the associations of the CoGoMe[^] with the SN[^]GoGn and the ANPg[^] in a large population from Southern Italy, providing cephalometric norms for Caucasian patients.

The limitation of this study was that, due to ethical issues, it was not possible to collect an untreated longitudinal sample.

3.5. Conclusions

In conclusion, this study showed the following:

- In the studied sample, the CoGoMe[^] presented a mean value of 127.2°±7.7°.
- Skeletal sagittal jaw discrepancies did not influence the CoGoMe[^].
- From 8 to 17 years of age, the CoGoMe[^] decreased 0.6° per year.
- For each degree of increase of the CoGoMe[^], the SN[^]GoGn increased by 0.6°.
- The CoGoMe[^] can be considered a useful cephalometric parameter for the diagnosis of the vertical facial growth pattern.

References

1. Bae EJ, Kwon HJ, Kwon OW. Changes in longitudinal craniofacial growth in subjects with normal occlusions using the Ricketts analysis. *Korean J Orthod.* 2014;44:77-87. DOI: 10.4041/kjod.2014.44.2.77
2. Sadowsky PL. Craniofacial growth and the timing of treatment. *Am J Orthod Dentofacial Orthop.* 1998;113:19-23. DOI: 10.1016/S0889-5406(98)70272-0
3. Rongo R, D'Antò V, Bucci R, Polito I, Martina R, Michelotti A. Skeletal and dental effects of Class III orthopaedic treatment: a systematic review and meta-analysis. *J Oral Rehabil.* 2017;44:545-562. DOI: 10.1111/joor.12495
4. Rongo R, Valleta R, Bucci R, Bonetti GA, Michelotti A, D'Antò V. Does clinical

- experience affect the reproducibility of cervical vertebrae maturation method? *Angle Orthod.* 2015;85:841-847. DOI: 10.2319/080414-544.1
5. Broadbent Holly B. A new x-ray technique and its application to orthodontia. *Angle Orthod.* 1931;1:45-66.
 6. Athanasiou A. *Orthodontic Cephalometry.* London, England: Mosby-Wolf.; 1997.
 7. Koski K. The norm concept in dental orthopedics. *Angle Orthod.* 1955;25:113-117.
 8. Obloj B, Fudalej P, Dudkiewicz Z. Cephalometric standards for polish 10-year-olds with normal occlusion. *Angle Orthod.* 2008;78:262-269. DOI: 10.2319/011207-14.1
 9. Fleming PS, Qureshi U, Pandis N, Dibiasi A, Lee RT. An investigation of cephalometric and morphological predictors of successful twin block therapy. *Aust Orthod J.* 2012;28:190-196.
 10. Petrovic AG, Stutzmann J. The concept of mandibular tissue-level growth potential and the responsiveness to a functional appliance. In: Graber WL, Ed. *Orthodontics: States of Art, Essence of the Science.* St. Louis, Mo:CV Mosby Co.; 1986.
 11. Petrovic A, Stutzmann J, Lavergne J. Mechanism of craniofacial growth and modus operandi of functional appliances: a cell.level and cybernetic approach to orthodontic decision making. In: Carlson DS, Ed. *Craniofacial Growththeoryand Orthodontic Treatment.* Ann Arbor, Mich: Center for Human G.; 1990.
 12. Petrovic AG. A cybernetic approach to craniofacial growth control mechanisms. *Nov Acta Leopoldina.* 1986;58:27-67.
 13. Ricketts RM. Cephalometric analysis and synthesis. *Angle Orthod.* 1961;31:141-156.
 14. Jarabak. Joseph R. Animal cephalometry. *Angle Orthod.* 1942;12:87-93.
 15. DeVincenzo JP. Changes in mandibular length before, during, and after successful orthopedic correction of Class II malocclusions, using a functional appliance. *Am J Orthod Dentofac Orthop.* 1991;99:241-257. DOI: 10.1016/0889-5406(91)70006-I
 16. Franchi L, Baccetti T. Prediction of individual mandibular changes induced by functional jaw orthopedics followed by fixed appliances in class ii patients. *Angle Orthod.* 2006;76:950-954. DOI: 10.2319/110205-385
 17. Solow B, Tallgren A. Natural head position in standing subjects. *Acta Odontol Scand.* 1971;29:591-607.
 18. Siersbæk-Nielsen S, Solow B. Intra- and interexaminer variability in head posture recorded by dental auxiliaries. *Am J Orthod.* 1982;82:50-57. DOI: 10.1016/0002-9416(82)90546-2
 19. Riolo W, Moyers R, McNamara JA, Hunter W. An atlas of craniofacial growth: cephalometric standards from university school growth study. Ann Arbor Mich: The

- University of Michigan, Center for Human Growth and Development.; 1974.
20. Dahlberg G. Statistical methods for medical and biological students. Stat methods Med Biol students. 1940.
 21. Raadsheer MC, Kiliaridis S, Van Eijden TM, Van Ginkel FC, Prahl-Andersen B. Masseter muscle thickness in growing individuals and its relation to facial morphology. Arch Oral Biol. 1996;41:323-332. DOI: 10.1016/0003-9969(95)00136-0
 22. Raadsheer MC, van Eijden TM, van Ginkel FC, Prahl-Andersen B. Contribution of jaw muscle size and craniofacial morphology to human bite force magnitude. J Dent Res. 1999;78:31-42. DOI: 10.1177/00220345990780010301
 23. Bjork A, Skieller V. Facial development and tooth eruption. An implant study at the age of puberty. Am J Orthod. 1972;62:339-383.
 24. Bjork A. Facial growth rotation-reflections on definition and cause. proc finn dent soc. 1991;87:51-58.
 25. Popowich K, Nebbe B, Heo G, Glover KE, Major PW. Predictors for class II treatment duration. Am J Orthod Dentofac Orthop. 2005;127:293-300. DOI: 10.1016/j.ajodo.2003.12.025
 26. Paduano S, Bucci R, Rongo R, Silva R, Michelotti A. Prevalence of temporomandibular disorders and oral parafunctions in adolescents from public schools in Southern Italy. Cranio. December 2018:1-6. DOI: 10.1080/08869634.2018.1556893
 27. Paduano S, Rongo R, Bucci R, Aiello D, Carvelli G, Ingenito A, Cantile T, Ferrazzano GF. Is there an association between various aspects of oral health in Southern Italy children? An epidemiological study assessing dental decays, periodontal status, malocclusions and temporomandibular joint function. Eur J Paediatr Dent. 2018;19:176-180. DOI: 10.23804/ejpd.2018.19.03.2
 28. Perrotta S, Bucci R, Simeon V, Martina S, Michelotti A, Valletta R. Prevalence of malocclusion, oral parafunctions and temporomandibular disorder-pain in Italian schoolchildren: An epidemiological study. J Oral Rehabil. 2019;46:611-616. DOI: 10.1111/joor.12794
 29. Cunningham SJ, Hunt NP. Quality of life and its importance in orthodontics. J Orthod. 2001;28:152-158. DOI: 10.1093/ortho/28.2.152
 30. D'Anto V, Bucci R, Franchi L, Rongo R, Michelotti A, Martina R. Class II functional orthopaedic treatment: a systematic review of systematic reviews. J Oral Rehabil. 2015;42:624-642. DOI: 10.1111/joor.12295

CHAPTER 4

Impact of fixed orthodontic appliance and clear aligners on the periodontal health: a prospective clinical study.

Abstract

This study aimed to evaluate the periodontal health of orthodontic patients with supportive periodontal therapy in a 3-month follow-up. The sample comprised 20 patients (mean age 20.6 ± 8.1 years) in treatment with multibracket fixed appliances (fixed group-FG), and 20 patients (mean age 34.7 ± 12.5 years) in treatment with clear aligners (clear aligners group-CAG). At baseline (T0) and after 3 months (T1) probing depth (PD), plaque index (PI), bleeding on probing (BOP) and gingival recession (REC) were measured. Patients were trained to perform an individualized tooth brushing technique and every 2-weeks they were re-called to reinforce the oral hygiene instructions. The intra-group comparisons (T1 vs T0) were calculated with the Wilcoxon signed rank test, while a linear regression model was used for the inter-group comparisons (FG vs CAG). The significance level was set at $P < 0.05$. Statistically significant decrease in both groups were found for PD (FG: $\Delta -9.2$ IQR $-22.5, -5.5$; CAG: $\Delta -12.6$ IQR $-25.4, -4.8$), BOP (FG: $\Delta -53.5$ IQR $-70.5, -37$; CAG: $\Delta -37.5$ IQR $-54.5, -23$) and PI (FG: $\Delta -17.5$ IQR $-62.5, 14.5$; CAG: $\Delta -24$ IQR $-49.5, -5$). The result of the linear regression models suggested that the type of appliance did not have any effects on the improvement of periodontal variables. Therefore, patients undergoing orthodontic treatment with fixed appliances and clear aligners did not show differences in gingival health when followed by a dental hygienist.

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4.1. Introduction

The main etiological factor in the development of gingivitis is the supragingival dental plaque along the gingival margin. Gingivitis is the inflammatory response of the gingival tissues to the metabolic products and pathogenic toxins of bacteria found in the oral biofilm. The inflammatory change of supragingival plaque is a strong predisposing factor for disease progression. Although gingivitis does not always progress to periodontitis, periodontitis is always preceded by gingivitis [1,2].

Periodontal diseases are very common problems in children, adolescents and adults. Among school-children from primary school, almost 55% of individuals experienced some periodontal problems [3]. Also, epidemiological studies revealed a prevalence range of 35-41% for moderate periodontitis and of 10-41% for severe periodontitis [4,5]. Furthermore, it has been reported that the prevalence of aggressive and advanced forms of periodontitis is 10-14% and it increases in the age groups from 35-44 years. [6,7] Accordingly, more than 70% of adults presented some form of periodontal disease. Therefore, periodontal treatment is a crucial step, before starting any orthodontic treatment, to restore and maintain the health of the supporting periodontal tissues [8].

Malocclusion is a frequent findings among adolescents and adult, [9,10], and fixed orthodontic therapy is the most common approach for treating different types of malocclusions. However, despite the effectiveness of the multibracket fixed therapy, this type of treatment makes the dental hygiene procedures more difficult due to the presence of brackets, bands and arch-wires [11]. Therefore, it prevents optimal hygiene of the oral cavity and it promotes the accumulation of dental biofilm, which in turn can lead to the development of white spot lesions, caries and can seriously damage the periodontium [8]. In particular, it has been shown that patients wearing fixed orthodontic appliances present the highest accumulation of bacterial plaque in the gingival margin and behind the arch-wires of the maxillary lateral incisors and canines. The frequency of tooth brushing and the motivation for the orthodontic treatment is significantly associated with a reduction of dental biofilm in subjects undergoing fixed orthodontic therapy [12].

Clear aligner treatment has been introduced in the last decades to satisfy the aesthetic and comfort requirements of adult orthodontic patients. This treatment is based on removable thermoplastic splints covering all the teeth and part of the marginal aspects of the gingiva, which progressively move the teeth into an ideal position [13]. Thanks to the satisfactory mechanical proprieties of these devices and to the valuable progresses of the aligners technology, nowadays these therapy is suitable for the correction of a wide spectrum of malocclusions [14]. Results from a systematic review revealed that periodontal indices, as well

as the quantity and quality of plaque, are better during clear aligner treatment than during fixed orthodontic therapy [15].

During the orthodontic treatment, the dental hygienist must provide the patient with adequate tools to perform regular and satisfactory home oral hygiene. Since the development of a patient's oral hygiene skills requires teaching and close guidance during repeated visits, dental hygienists have a primary role in the acquisition of such skills [16]. Furthermore, to achieve continuous patient compliance throughout the treatment, dental hygienists should perform periodic check-ups and reinforce the home hygiene techniques by means of auxiliary dental products [16,17]. The available scientific evidence shows that the intervals of periodontal support therapy should be individualized to the patient's need. For example, a recall interval every 3 months for all patients after periodontal therapy is weak [18]. Finally, individualized education, and clinical and motivational strategies should be adopted to raise the awareness of the importance of brushing teeth regularly to maintain a healthy condition for teeth and gingiva, which is crucial for orthodontic patients [8,19].

The aim of this study was to evaluate the periodontal health of patients undergoing fixed orthodontic and clear aligner therapy with a supportive periodontal therapy after a 3-month follow-up. The null hypothesis was that there was not difference in the periodontal health of patients with fixed orthodontic and clear aligner therapy, even after the intervention of the dental hygienist.

4.2. Materials and Methods

4.2.1 Subjects

The study sample comprised 40 consecutive patients (age >12 years) with permanent dentition (26 females, 14 males, mean age 27.6±12.6) recruited among patients already undergoing the orthodontic treatment at the Section of Orthodontics and Temporomandibular Disorders of the University of Naples Federico II (Naples, Italy). All the patients were treated by post-graduate students of the School of Orthodontics. Twenty patients (mean age 20.6±8.1 years) presented ongoing multibracket fixed therapy (Fixed Group–FG), whereas 20 patients (mean age 34.7±12.5 years) were in treatment with clear aligners (Clear Aligners Group–CAG). For the FG, metal brackets (Mini Sprint, Forestadent®, Pforzheim, Germany) and .016” NiTi archwire (Biostarter®, Pforzheim, Germany) were used. For the CAG, aligners were made of polyethylene terephthalate glycol copolyester (PET-G), 0.75mm thick (AirNivol S.r.l, Navacchio, Pisa, Italy). Exclusion criteria included diseases requiring premedication to perform periodontal probing, systemic diseases that can influence the activity of periodontal

disease, individuals taking drugs that affect the periodontal status, patients with removable prostheses, and pregnant or breastfeeding women.

All patients were fully informed about the nature of the study and signed an informed consent. The investigations were carried out following the rules of the Declaration of Helsinki of 1975, revised in 2013, and obtained an approval from an ethics committee before undertaking the research by the Ethics Committee of the University of Naples Federico II (protocol and acceptance number 119/19).

4.2.2. Periodontal assessment and clinical procedure.

T0: Periodontal charting was performed, recording gingival biotype, plaque index (PI), bleeding on probing (BOP), probing depth (PD) and gingival recessions (REC). The gingival biotype was evaluated, based on the transparency of the periodontal probe through the gingival margin of the tooth while probing the mid buccal sulcus of both central, lateral incisors and canine, both maxillary and mandibular. If the outline of the probe could be seen through the gingival margin, it was categorized as “thin”; if not, it was categorized as “thick” [20]. All the variables were recorded by one expert operator (periodontist), using a millimeter periodontal probe (15-mm North Carolina probe), inserted in the gingival sulcus with a force of about 0.25 Newton. Subsequently, one trained dental hygienist performed supra- and sub-gingival scaling, to remove the dental biofilm and calculus. Finally, all patients were trained to perform an individualized tooth brushing technique. Every two weeks, the patients were re-called to reinforce the home oral hygiene instructions. Motivation and oral hygiene instructions and reinforcement were provided by the same professional dental hygienist.

T1: The periodontal health check-up was repeated after 3 months using the same indices.

4.2.2. Sample size.

A sample size analysis was performed before recruitment. The primary outcome measure of this study was the PI. Based on a previous investigation [21], it was assumed that a clinical significant difference in PI was 5% and that the two groups share a common standard deviation of 5%. A sample size including 17 subjects per group was sufficient to detect between-group differences in PI ($\alpha=0.05$ and $1-\beta=0.8$). To avoid underpowered study due to drop out the sample size was increased to 20 patients for each group.

4.2.3. Statistical Analysis

Descriptive statistics on age, gender, number of sites, gingival biotype and baseline characteristics were performed at baseline. Shapiro-Wilk test was performed to evaluate

variable distribution. According to the distribution, continuous variables were reported as mean (M) and standard deviation (SD) or median and inter-quartile range (IQR), and the between-groups difference (CAG vs. FG) was computed with unpaired Student's t-test or Mann-Whitney test. Categorical variables were reported as absolute number and percentages and the between-groups difference (CAG vs. FG) was computed with chi-square test or Fisher exact test. The comparisons between T1 vs T0 (the difference T1-T0 was named delta Δ), in each specific treatment group, for PD, PI, BOP and REC variables were performed with a paired test for asymmetric distribution (Wilcoxon signed rank test). To test if the difference Δ of each periodontal variable was influenced by type of treatment or by other variables, a linear regression model was performed. The beta coefficient, with 95% confidence interval (95% CI), of CAG vs FG was reported. Four different models were proposed: Model 1, CAG vs FG unadjusted; Model 2, model 1 + adjustment according to the baseline values; Model 3, model 2 + adjustment according to age and number of sites; Model 4, model 2 + adjustment according to propensity score. The propensity scores were estimated by fitting the logistic regression model with different treatment method (CAG or FG) as dependent variable. The level of statistical significance was set at $P < 0.05$. Statistical analysis was performed using STATA version 14.0.

4.3. Results

At the baseline (T0), a statistically significant difference between the two groups was found regarding the age ($P = 0.0001$), with patients belonging to the CAG being older than those belonging to the FG (CAG 34.7 ± 12.5 years; FG 20.6 ± 8.1 years). Moreover, the number of sites examined was statistically different ($P = 0.03$) as shown in Table 1. In addition, 75% of all individuals examined had a thick gingival biotype. Furthermore, BOP was significantly increased in the FG as compared to CAG (FG= Median 77 (IQR 56.5, 85); CAG= Median 55.5 (IQR 39.5, 70); $P = 0.006$), while REC was more present in the CAG (CAG= Median 22.2 (IQR 7.1, 32.9) than in FG (FG= Median 4.4 (IQR 0, 14.7); $P = 0.016$).

Table 1. Characteristics of the patients included in the study for FG and CAG.

	Total	FG	CAG	P-value
<i>Age (years)</i>				
M \pm SD	27.6 \pm 12.6	20.6 \pm 8.1	34.7 \pm 12.5	0.0001
<i>Sex</i>				
Female	26 (65%)	11 (55%)	15 (75%)	0.18
<i>Number of sites</i>				
M \pm SD	168 \pm 9.1	165 \pm 9.8	171 \pm 7.4	0.03
<i>Gingival biotype</i>				
<i>thick</i>	30 (75%)	16 (80%)	14 (70%)	0.46

<i>Gingival biotype upper thick</i>	33 (82.5%)	18 (90%)	15 (75%)	0.21
<i>Gingival biotype lower thick</i>	31 (77.5%)	16 (80%)	15 (75%)	0.70

FG: fixed group; CAG: clear aligners group; M: mean; SD: standard deviation. Statistically significant differences are reported in bold.

The intra-group comparisons (T1 vs T0) showed statistically significant decreases in both groups for PD (FG:Δ-9.2 IQR -22.5,-5.5; P=0.0001; CAG:Δ-12.6 IQR -25.4,-4.8; P=0.0002), BOP (FG:Δ-53.5 IQR -70.5,-37; P=0.0001; CAG:Δ-37.5 IQR -54.5,-23; P=0.0002) and PI (FG:Δ-17.5 IQR-62.5,14.5; P=0.04; CAG: Δ -24 IQR -49.5,-5; P=0.002) (Table 2). REC increased significantly only in the FG (Δ1.3 IQR 0,3.4; P=0.006) as shown in Table 2 and Figure 1.

Table 2. Intra-group differences after a 3-month follow-up (T1-T0).

	FG				CAG			
	T0	T1	Δ	P	T0	T1	Δ	P
<i>PD, %</i>								
median	10.4	0	-9.2	0.0001	13.9	0.25	-12.6	0.0002
IQR	6.1, 24.2	0, 1.2	-22.5, -5.5		4.8, 31.1	0, 2.9	-25.4, -4.8	
<i>PI, %</i>								
median	30.5	14.5	-17.5	0.04	41.5	10.5	-24	0.002
IQR	5, 73	3.5, 24	-62.5, 14.5		25, 53	2, 23	-49.5, -5	
<i>BOP, %</i>								
median	77	13.5	-53.5	0.0001	55.5	13.5	-37.5	0.0001
IQR	56.5, 85	6, 28	-70.5, -37		39.5, 70	5, 17.5	-54.5, -23	
<i>REC, %</i>								
median	4.4	5.2	1.3	0.006	22.2	24.3	1.25	0.38
IQR	0, 14.7	2.3, 18.4	0, 3.4		7.1, 32.9	6.5, 44.5	-5.7, 7.3	

IQR: inter-quartile range; FG: fixed group; CAG: clear aligners group; PD: probing depth, PI: plaque index, BOP: bleeding on probing; REC: gingival recession. Statistical analysis was performed using a paired test for asymmetric distribution (Wilcoxon signed rank test). Statistically significant differences are reported in bold.

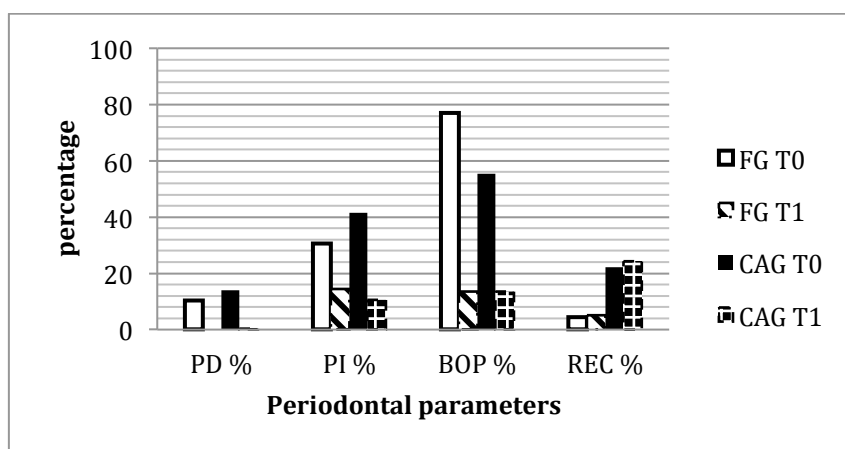


Figure 1. Graph describing the mean % of the four periodontal parameters assessed at baseline (T0) and at 3-months follow-up (T1) in the two groups. FG: fixed group; CAG: clear aligners group; PD: probing depth, PI: plaque index, BOP: bleeding on probing; REC: gingival recession.

The four linear regression models of difference Δ confirmed that the type of orthodontic appliances did not have any effects on the improvement of each periodontal variables (Model 2: Δ PD, β 1.2, 95%CI -1.8 to 4.1, P=0.43; Δ PI, β -0.6, 95%CI -12.9 to 11.7, P=0.92; Δ BOP, β -0.45, 95%CI -10.6 to 9.7, P=0.93; Δ REC, β -0.45, 95%CI -6.2 to 5.2, P=0.87). This finding was not affected by differences between groups such as patient's age and number of sites. (Model 3: Δ PD, β 2.9, 95%CI -0.8 to 6.7, P=0.12; Δ PI, β -3.1, 95%CI -18.5 to 12.3, P=0.68; Δ BOP, β -2.03, 95%CI -11.3 to 15.4, P=0.76; Δ REC, β -4.03, 95%CI -10.2 to 2.1, P=0.19) as shown in Table 3.

Table 3. Linear regression models of difference delta (Δ) for each periodontal variable.

Outcome	Model	Beta	95%CI	P
Δ %PD	1	-1.8	-10.7, 7.1	0.69
	2	1.2	-1.8, 4.1	0.43
	3	2.9	-0.8, 6.7	0.12
	4	2.8	-0.9, 6.5	0.14
Δ %PI	1	-3.8	-27.6, 19.9	0.75
	2	-0.6	-12.9, 11.7	0.92
	3	-3.1	-18.5, 12.3	0.68
	4	-5.0	-20.3, 10.3	0.51
Δ %BOP	1	14.9	-0.01, 29.9	0.07
	2	-0.5	-10.6, 9.7	0.93
	3	2.0	-11.3, 15.4	0.76
	4	0.6	-12.4, 13.6	0.92
Δ %REC	1	-2.0	-7.2, 3.3	0.45
	2	-0.5	-6.2, 5.2	0.87
	3	-4.0	-10.2, 2.1	0.19
	4	-4.1	-10.1, 1.9	0.18

PD: probing depth; PI: plaque index; BOP: bleeding on probing; REC: gingival recessions, CI: confidence interval.

4.4. Discussion

The present study aimed to evaluate the periodontal health of patients undergoing fixed orthodontic and clear aligner therapy with a supportive periodontal therapy after a 3-month follow-up. The results confirm the null hypothesis, as no difference was observed in the periodontal health the two groups of patients when followed by a dental hygienist for 3 months. Indeed, these findings showed that the patients' periodontal status improved in both groups after the intervention of the professional dental hygienist and no significant effect of the appliance was found.

The oral cavity is colonized by a complex ecosystem of oral microbiota [22]. The problem of the lack of adequate microbial plaque removal takes on greater dimensions when undergoing orthodontic treatment [23,24]. Therefore, the orthodontic patient not only requires greater professional assistance, but also precise and individualized instructions for home oral hygiene, which must be continuous and rigorous, given the presence of orthodontic devices that lead to

a potential worsening of conditions of the oral cavity until the onset of diseases. In fact, the present study showed that patients undergoing orthodontic treatment presented gingivitis associated to dental plaque, in accordance to the new classification of periodontal and peri-implant diseases and conditions [25].

In the scientific literature, there is still debate on the influence of clear aligners on oral hygiene. Miethke and co-workers showed that the plaque index of patients treated with clear aligners was significantly lower than that of patients with conventional fixed orthodontics, at the different time points. Nevertheless, the oral hygiene improved in both groups during the entire course of the study [26]. A study by Levrini and co-workers pointed out that patients undergoing orthodontic treatment with clear aligners prompted a lower total biofilm mass accumulation in the short-term when compared to patients in treatment with fixed orthodontic appliances, suggesting the use of clear aligners as a first treatment option in patients who are at risk of developing periodontal diseases [27]. Two recent meta-analyses, underlined that clear aligners should be used in patients with high risk of gingival inflammation, but the level of evidence was very low and more high-quality studies are required to corroborate these results [28,29]. Interestingly, in the current survey the patients were enrolled in the study as they were already undergoing on orthodontic treatment (both multibracket therapy or clear aligners therapy), and they were naive from any individualized oral hygiene instruction. The comparison at the baseline (T0) showed increased BOP in the fixed orthodontic group, supporting that when no adequate information are provided to the patients, poorer oral hygiene can be observed in patients wearing multibracket appliances. However, the supportive therapy provided by the professional dental hygienist determined a dramatic improvement in the periodontal health of both groups of patients, independently from the kind of appliance. These results suggest that when appropriate oral hygiene instruction and motivation are offered to the patients, the type of orthodontic treatment has no effect on periodontal health. Furthermore, these findings are in accordance with a recent prospective randomized control trials by Chhibber and co-authors, that pointed out no evidence of differences in oral hygiene levels among clear aligners, self-ligated brackets, and conventional elastomeric ligated brackets after 18 months of active orthodontic treatment [30].

Differently from the previous studies, the current survey gave great importance not only to professional oral hygiene, but also to the motivation of the patients' home hygiene with regular check-ups (every 2 weeks) and by personalizing home-hygiene techniques. This result agrees with previous studies in which the importance of motivation in orthodontic patients was addressed [31,32]. Furthermore, regular check-ups are crucially important to perform appropriate differential diagnosis in presence of gingival bleeding [33].

Interestingly, in the current study changes of REC were observed only in the FG groups. One possible explanation was the higher degree of dental expansion due to the fixed orthodontic treatment related to the standard arch-form of the wire [19].

The current study presents several strengths. First, periodontal assessments, professional hygiene and motivation, training and check-ups were given to the patients by only two trained clinicians. This avoided bias due to differences in operator performance. Second, since the first step toward improving oral hygiene is patient compliance, monitoring gingival health and reinforcing the patient's individualized tooth brushing techniques were performed every 2 weeks to increase patient awareness of the importance of good oral hygiene. The study also has some limitations. First, the baseline age of patients was statistically significant different between the two groups due to the increasing number of adult patients asking for aesthetic orthodontic therapy. Moreover, no data on the smoking status were collected. Finally, the reported data have been collected with a short follow-up (3 months). Further longitudinal studies are necessary to evaluate the long-term effects of professional hygiene on the periodontal status of patients undergoing different types of orthodontic appliances.

4.5. Conclusions

In accordance with the null hypothesis, within the limits of the current study, it can be concluded that no evidence of difference was observed in the periodontal health of patients undergoing fixed orthodontic therapy and clear aligner therapy, when a dental hygienist provided regular check-ups and adequate oral hygiene instructions. Therefore professional oral hygiene associated with motivation and reinforcement for the adequate control of dental biofilm during the orthodontic treatment allows the patients to prevent the onset of periodontal disease and achieve good periodontal health, despite the type of orthodontic appliance used.

References

1. Machtei, E.E., Hausmann, E., Dunford, R., Grossi, S., Ho, A., Davis, G., Chandler, J., Zambon, J., Genco, R.J. (1999). Longitudinal study of predictive factors for periodontal disease and tooth loss. *Journal of clinical periodontology*. 26:374–80.
2. Listgarten, M.A., Schifter, C.C., Laster, L. (1985). 3-Year Longitudinal Study of the Periodontal Status of an Adult Population With Gingivitis. *Journal of Clinical Periodontology*. 12:225–38.
3. Paduano, S., Rongo, R., Bucci, R., Aiello, D., Carvelli, G., Ingenito, A., Cantile, T., Ferrazzano, G.F. (2018). Is there an association between various aspects of oral health in

- Southern Italy children? An epidemiological study assessing dental decays, periodontal status, malocclusions and temporomandibular joint function. *European journal of paediatric dentistry*. 19:176–80.
4. Strohmeier L, Cerati M, Brambilla E, Malerba A, V.G. (1991). Periodontal epidemiology in Italy by CPITN. *International dental Journal*. 41:313–5.
 5. Aimetti, M., Perotto, S., Castiglione, A., Mariani, G.M., Ferrarotti, F., Romano, F. (2015). Prevalence of periodontitis in an adult population from an urban area in North Italy: Findings from a cross-sectional population-based epidemiological survey. *Journal of Clinical Periodontology*. 42:622–31.
 6. Kassebaum, N.J., Bernabé, E., Dahiya, M., Bhandari, B., Murray, C.J.L., Marcenes, W. (2014). Global burden of severe periodontitis in 1990-2010: A systematic review and meta-regression. *Journal of Dental Research*. 93:1045–53.
 7. Sheiham, A., Netuveli, G.S. (2002). Periodontal diseases in Europe. *Periodontology 2000*. 29:104–21.
 8. Marini, I., Bortolotti, F., Incerti Parenti, S., Gatto, M.R., Alessandri Bonetti, G. (2014). Combined effects of repeated oral hygiene motivation and type of toothbrush on orthodontic patients: A blind randomized clinical trial. *Angle Orthodontist*. 84:896–901.
 9. Perrotta, S., Bucci, R., Simeon, V., Martina, S., Michelotti, A., Valletta, R. (2019). Prevalence of malocclusion, oral parafunctions and temporomandibular disorder-pain in Italian schoolchildren: An epidemiological study. *Journal of oral rehabilitation*. 46:611–6.
 10. Bucci, R., Koutris, M., Lobbezoo, F., Michelotti, A. (2019). Occlusal sensitivity in individuals with different frequencies of oral parafunction. *The Journal of prosthetic dentistry*.
 11. Liu, H., Sun, J., Dong, Y., Lu, H., Zhou, H., Hansen, B.F., Song, X. (2011). Periodontal health and relative quantity of subgingival porphyromonas gingivalis during orthodontic treatment. *Angle Orthodontist*. 81:609–15.
 12. Mei, L., Chieng, J., Wong, C., Benic, G., Farella, M. (2017). Factors affecting dental biofilm in patients wearing fixed orthodontic appliances. *Progress in Orthodontics*. 18:0–5.
 13. Martina, S., Rongo, R., Bucci, R., Razionale, A.V., Valletta, R., D’Antò, V. (2019). In vitro cytotoxicity of different thermoplastic materials for clear aligners. *The Angle Orthodontist*. :091718-674.1.
 14. Bucci, R., Rongo, R., Levate, C., Michelotti, A., Barone, S., Razionale, A.V., D’Antò, V. (2019). Thickness of orthodontic clear aligners after thermoforming and after 10 days

- of intraoral exposure: a prospective clinical study. *Progress in orthodontics*. 20:36.
15. Rossini, G., Parrini, S., Castroflorio, T., Deregibus, A., Debernardi, C.L. (2015). Efficacy of clear aligners in controlling orthodontic tooth movement: a systematic review. *The Angle orthodontist*. 85:881–9.
 16. Huang, J., Yao, Y., Jiang, J., Li, C. (2018). Effects of motivational methods on oral hygiene of orthodontic patients: A systematic review and meta-analysis. *Medicine*. 97:e13182.
 17. Nassar, P.O., Bombardelli, C.G., Walker, C.S., Neves, K.V., Tonet, K., Nishi, R.N., Bombonatti, R., Nassar, C.A. (2013). Periodontal evaluation of different toothbrushing techniques in patients with fixed orthodontic appliances. *Dental Press Journal of Orthodontics*. 18:76–80.
 18. Farooqi OA, Wehler CJ, Gibson G, Jurassic MM, J.J. (2015). Appropriate recall interval for periodontal maintenance: a systematic review. *J Evid Based Dent Pract*. 15:171–81.
 19. Antoun JS, Mei L, Gibbs K, F.M. (2017). Effect of orthodontic treatment on the periodontal tissues. *Periodontology 2000*. 74:140–57.
 20. Kan, J.Y.K., Rungcharassaeng, K., Umezu, K., Kois, J.C. (2003). Dimensions of peri-implant mucosa: an evaluation of maxillary anterior single implants in humans. *Journal of Periodontology*. 74:557–62.
 21. Newbrun, E. (1996). Indices to measure gingival bleeding. *Journal of periodontology*. 67:555–61.
 22. Mohammed, H., Varoni, E.M., Cochis, A., Cordaro, M., Gallenzi, P., Patini, R., Staderini, E., Lajolo, C., Rimondini, L., Rocchetti, V. (2018). Oral dysbiosis in pancreatic cancer and liver cirrhosis: A review of the literature. *Biomedicines*. 6:1–18.
 23. Davis, S.M., Plonka, A.B., Fulks, B.A., Taylor, K.L., Bashutski, J. (2014). Consequences of orthodontic treatment on periodontal health: Clinical and microbial effects. *Seminars in Orthodontics*. 20:139–49.
 24. Sifakakis, I., Papaioannou, W., Papadimitriou, A., Kloukos, D., Papageorgiou, S.N., Eliades, T. (2018). Salivary levels of cariogenic bacterial species during orthodontic treatment with thermoplastic aligners or fixed appliances: a prospective cohort study. *Progress in Orthodontics*. 19.
 25. G. Caton, J., Armitage, G., Berglundh, T., Chapple, I.L.C., Jepsen, S., S. Kornman, K., L. Mealey, B., Papapanou, P.N., Sanz, M., S. Tonetti, M. (2018). A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification. *Journal of Clinical Periodontology*. 45:S1–8.
 26. Miethke, R.R., Brauner, K. (2007). A Comparison of the periodontal health of patients

- during treatment with the invisalign® system and with fixed lingual appliances. *Journal of Orofacial Orthopedics / Fortschritte der Kieferorthopädie*. 68:223–31.
27. Levrini, L., Mangano, A., Montanari, P., Margherini, S., Caprioglio, A., Abbate, G.M. (2015). Periodontal health status in patients treated with the Invisalign® system and fixed orthodontic appliances: A 3 months clinical and microbiological evaluation. *European Journal of Dentistry*. 9:404–10.
 28. Lu, H., Tang, H., Zhou, T., Kang, N. (2018). Assessment of the periodontal health status in patients undergoing orthodontic treatment with fixed appliances and Invisalign system. *Medicine (United States)*. 97.
 29. Jiang, Q., Li, J., Mei, L., Du, J., Levrini, L., Abbate, G.M., Li, H. (2018). Periodontal health during orthodontic treatment with clear aligners and fixed appliances: A meta-analysis. *Journal of the American Dental Association*. 149:712-720.e12.
 30. Chhibber, A., Agarwal, S., Yadav, S., Kuo, C.L., Upadhyay, M. (2018). Which orthodontic appliance is best for oral hygiene? A randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics*. 153:175–83.
 31. Lalic, M., Aleksic, E., Gajic, M., Milic, J., Malesevic, D. (2012). Does oral health counseling effectively improve oral hygiene of orthodontic patients? *European journal of paediatric dentistry*. 13:181–6.
 32. Acharya, S., Goyal, A., Utreja, A.K., Mohanty, U. (2011). Effect of three different motivational techniques on oral hygiene and gingival health of patients undergoing multibracketed orthodontics. *Angle Orthodontist*. 81:884–8.
 33. Patini, R., Staderini, E., Gallenzi, P. (2016). Multidisciplinary surgical management of Cowden syndrome: Report of a case. *Journal of Clinical and Experimental Dentistry*. 18:472–4.

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