

**UNIVERSITY OF MEDICINE AND PHARMACY “CAROL DAVILA”
BUCHAREST
FACULTY OF DENTAL MEDICINE
DISCIPLINE OF ORTHODONTICS AND DENTO-FACIAL ORTHOPEDICS**

**CONTRIBUTIONS TO THE STUDY UPON THE
ESTIMATION OF THE SKELETAL AGE THROUGH THE
ANALYSIS OF THE CERVICAL VERTEBRAE
DEVELOPMENT ON LATERAL CEPHALOGRAMS**

SUMMARY OF THE PHD THESIS

PhD Coordinator:

PROFESSOR IONESCU ECATERINA, PHD

PhD Student:

ELENA GALAN

2022

List of contents

Contents	iii
List of the published scientific papers	vii
List of tables	viii
List of figures	xi
List of the abbreviations used in the text	xvi
Introduction	xviii
I. General part	1
Chapter 1. Introductory notions of growth and cranio-facial development	2
1.1. Growth, development, modeling	2
1.2. General growth of the organism	4
1.3. Growth periods	7
1.4. Growth of the cranio-facial complex	10
1.5. Puberty. The peak moment of pubertal growth	11
1.6. Factors that influence puberty	14
1.7. Therapeutic aspects regarding the growth periods	18
Chapter 2. Indicators of the biological age	22
2.1. Morphological age	24
2.2. Endocrine age	29
2.3. Dental age	33
2.4. Skeletal age	38
2.4.1. Estimating the skeletal age using the hand and wrist x-ray	39
Chapter 3. Estimation of the skeletal age through the analysis of the cervical vertebrae development on the lateral cephalogram	48
3.1. Introductory notions of the cervical vertebrae anatomy	48
3.2. Development of the CVM indexes	49
3.3. Radiology notions	64

3.3.1. Hand and wrist x-ray	65
3.3.2. Lateral cephalogram	66
3.4. Growth studies	70
II. Personal research	72
Chapter 4. Objectives and coordinates of the scientific research	73
4.1. Objectives, research directions	74
4.2. The study group	75
4.3. Material and method	79
4.3.1. Interpretation of the hand and wrist x-rays	80
4.3.2. Analysis of the development of the cervical vertebrae on the lateral cephalograms	83
4.3.3. Cephalometric analysis	85
4.4. Repeatability of the study	88
4.4.1. Repeatability of the study for interpreting the hand x-ray and the analysis of the cervical vertebrae of the lateral cephalogram	88
4.4.2. Repeatability of the study for the cephalometric data	92
4.4.3. Conclusions	95
Chapter 5. Transvers study regarding the correspondence of the SMI and CVMS indexes of bone maturation during the stages of pubertal growth	96
5.1. Objectives	96
5.2. The study group	97
5.3. Method	97
5.4. Statistical analysis	97
5.5. Results	98
5.5.1. Comparative analysis of the average age for reaching the SMI stages within the study group	98
5.5.2. Prediction of age for reaching the SMI stages using the linear regression equations	107

5.5.3. Comparative analysis of the average age for reaching the CVMS stages within the study group	111
5.6. Limitations of the study	116
5.7. Conclusions	117
Chapter 6. Verification of the concordance of the SMI/CVMS indexes during the pubertal growth stages	119
6.1. Transverse study regarding the concordance of the SMI/CVMS indexes for bone maturation during the stages of pubertal growth	119
6.1.1. Objectives	120
6.1.2. Materials and method	120
6.1.3. Results	122
6.1.4. Discussions	127
6.1.5. Conclusions	128
6.2. Longitudinal study regarding the concordance of the SMI/CVMS indexes of bone maturation during the growth process	129
6.2.1. Objectives	130
6.2.2. Materials and method	130
6.2.3. Results	132
6.2.4. Discussions	135
6.2.5. Conclusions	137
Chapter 7. Transversal study regarding the comparison of the accuracy of the SMI/CVMS indexes in estimating the moment of maximal pubertal growth using the ROC analysis	138
7.1. The ROC analysis (Receiver Operating Characteristics)	138
7.2. Estimating the moment of maximal pubertal growth using the cephalometric parameters	141
7.2.1. Objectives	142
7.2.2. The study group	142
7.2.3. Materials and method	143
7.2.4. Statistical analysis	143
7.2.5. Results	145
7.2.6. Discussions	151

7.2.7 Conclusions	153
7.3. Transversal study regarding the comparison of the accuracy of the SMI/CVMS indexes in estimating the moment of maximal pubertal growth using ROC analysis	154
7.3.1. Objectives	154
7.3.2. The study group	154
7.3.3. Materials and method	154
7.3.4. Statistical analysis	155
7.3.5. Results	156
7.3.5.1. ROC analysis for the SMI indexes within the girls study group	156
7.3.5.2. ROC analysis for the CVMS indexes within the girls study group	158
7.3.5.3. Comparison of the results for the ROC analysis for the SMI/CVMS indexes within the girls study group	159
7.3.5.4. ROC analysis for the SMI indexes within the boys study group	162
7.3.5.5. ROC analysis for the CVMS indexes within the boys study group	164
7.3.5.6. Comparison of the results for the ROC analysis for the SMI/CVMS indexes within the boys study group	165
7.3.6. Discussions	167
7.3.7. Conclusions	170
III. Personal conclusions and contributions	171
Bibliographical references	177
Annexes	198

Introduction

The evaluation of the cranio-facial growth and development is an important part of the diagnosis stage, playing an essential role in planning the orthodontic treatment for young patients, as it is a known fact that starting the orthodontic appliances around the moment of maximal pubertal growth has a high therapeutic efficiency. Knowing the growth stages, the preferred directions in which they manifest at a certain period of time, helps the clinician in elaborating an efficient therapeutic strategy that uses the individual growth potential in order to shorten the active treatment period.

The orthodontic treatments done within the pubertal growth period are more efficient, either when using orthodontic appliances that generate mechanical forces, or functional ones (*Graber, 1994; Baccetti and Franchi, 2000 a,b; Proffit, 2002; Pancherz and Von Bremen, 2002*). The existing studies in the specialty literature suggest that treatments aiming to influence the maxillary growth should start before the moment of maximum growth for the maxilla, while for the mandible it is recommended to start the conventional orthodontic appliances during the moment of maximal mandibular growth and not prior to it (*Panchez și Hägg, 1985; Baccetti, 2000, 2001, 2005; Faltin și col., 2003; Westwood, 2003*).

Along the time, a series of methods have been elaborated in order to identify the growth and development stages, to predict the starting moment of puberty and to determine the existent growth potential. These methods used the chronological age, the mandibular development (Mitani and col., 1992), the height development (*Hunter, 1966; Björk and Helm, 1967; Bergersen, 1972; Van der Beek, 1996*), the appearance of the secondary sexual characters (*Hägg și Taranger, 1980a*), the dental age, the estimation of the skeletal age through the analysis of the hand and wrist x-ray (*Bergersen, 1972; Fishman, 1982*) or the analysis of the cervical vertebrae development on the lateral cephalogram (*Lamparski, 1972*). Out of the indicators of the biological age, the skeletal age is considered by most authors as having the greatest accuracy in determining the biological moment in which the patient is situated (*Gutierrez Muñoz and col., 2006*). Its estimation through the interpretation of the hand and wrist x-ray is a consecrated method, frequently used at the end of the previous century and there are numerous studies in the specialty literature proving the clinical applicability of the method upon different population groups (*Grave and Brown, 1976; Fishman, 1982; Hägg and Taranger, 1982; Flores –Mir and col., 2004; Turchetta, 2007*). The main disadvantage is the necessity of additional irradiation of the patient in order

to make the radiological investigation. Furthermore, it is necessary for the practitioner to master the interpretation technique and have the knowledge regarding the development of the hand bones, an anatomical area with which the orthodontist is not familiar.

During the last decades, as the effects of the radiations have been studied more and more, a series of norms have been set, indicating a limitation of the radiation dosage for the medical investigations of a patient. This context led to the development of methods for estimating the skeletal age using the existent radiological investigations in the initial orthodontic file. In this category one could also find the estimation of the skeletal age through the analysis of the cervical vertebrae on the lateral cephalogram, a frequently used radiological investigation in orthodontics. During the last years, there has been noticed an increase of orthodontists' interest for the analysis of the cervical area and comparative studies have been made in order to verify whether the skeletal age could be determined using this method. Most of them reached the conclusion that the analysis of the cervical vertebrae represents a valid indicator in estimating the skeletal age and at present it is used more and more (*O'Reilly and Yanniello, 1988; Hassel and Farman, 1995; Franchi and col., 2000, 2002; Baccetti and col., 2002, 2005; San Roman and col., 2002; Grave and Townsend, 2003a,b; Flores-Mir and col., 2006*).

The studies quoted in the specialty literature have been conducted upon population groups that are different from the population in our country, some of them using historical data. From here it emerged the necessity to conduct this research upon a heterogeneous, actual group, selected from the population of Bucharest and the adjacent areas. In this context, the theme of the PhD thesis is an actual one, which is situated among the national and international preoccupations of the scientists regarding orthodontics, seeking the estimation of the skeletal age along the stages of pubertal growth.

The thesis is structured in three main parts: the general part, consisting of 3 chapters, the personal part, consisting of 4 chapters and the last part represented by the chapter of conclusions and personal contributions.

The research hypothesis: it has been sought whether the estimation of the skeletal age for the patients in the study group could be done using the analysis of the cervical vertebrae development, thus avoiding an additional radiological exposure.

Objectives

The main objective of the research was to contribute to the study of the skeletal age estimation, by comparatively analyzing two methods for estimating the skeletal age: the

analysis of the SMI indexes for bone maturation on the hand and wrist x-ray and the CVMS analysis of the cervical vertebrae development of the lateral cephalogram.

Research directions

I hereby specify the difficulty met in realizing the comparison between the SMI and CVMS indexes, as they describe two different anatomical regions and have a different number of classes: 11 and respectively 5. From here emerged the impossibility to make a direct comparison. In two out of the three research directions, the two methods for estimating the skeletal age have been indirectly compared, by relating to a new parameter. Thus, in the second research direction (Chapter 6), the SMI and CVMS indexes were related to the periods of pubertal stages and the concordance of the two indexes in estimating the pubertal periods was statistically calculated using the kappa Cohen coefficient. This has been verified both in a transversal study and in a longitudinal study, upon a group for which serial investigations existed.

Within the third research direction (Chapter 7), the peak moments of growth were determined, regarding certain cephalometric parameters and, related to them and using the ROC (Receiver Operating Characteristics) analysis, the accuracy of the two indexes was determined for correctly classifying the subjects into individuals who have not yet reached the moment of maximal pubertal growth and others who reached it or even went past it.

The study group

In order to reach the mentioned objectives, a transversal study was conducted upon a heterogeneous group selected from children and youths from Bucharest and adjacent areas, consisting of 150 patients, 89 girls and 61 boys, ages between 8.1 and 18, patients with dento-maxillary anomalies who came for orthodontic treatment, the investigations included in the study being done in the same day, prior to starting the orthodontic treatment.

Methodology for the research

For the subjects participating in the study, the hand and wrist x-ray and the lateral cephalogram were done with diagnostic purpose and evaluated, in the same day, prior to the beginning of the orthodontic treatment. The SMI indexes for bone development were determined according to the Grave/Brown and Fishman methods, while the indexes for the cervical vertebrae development were determined according to the Hassel/Farman and Baccetti methods (2002). There was a selection of five cranio-facial parameters in order to

determine the development of the maxilla and the mandible (Nsa-Nsp, Nsa-Gn, Go-Gn, Ar-Gn și Ar-Go) and these parameters were measured on the lateral cephalograms.

The statistical analysis was different according to each direction of research, this being described in the chapters about the personal contribution (Chapters 4-7).

The repeatability of the study (Chapter 4)

Following the repeatability tests, good values were obtained for the kappa Cohen coefficient for the SMI indexes (Fishman) and the CVMS indexes (Baccetti), which justifies the use of these indexes in the main study for estimating the skeletal age. Good values for the repeatability tests were also obtained for the measured cephalometric parameters. These were analyzed using the t test for paired measurements, the Bland/Altman test and the Lin correlation coefficient for concordance, the obtained values justifying the use of the obtained data following the measurements in the main study.

Based upon the results obtained in the repeatability test, for each method, the methods used in the main study were chosen, the Fishman method for interpreting the hand x-ray and the Baccetti (2002) method for analyzing the development of the cervical vertebrae on the lateral cephalogram.

Chapter 5

The main objective of this study was to investigate the SMI stages of bone development, determined for the children and the youths in the study group, by analyzing the hand and wrist x-ray using the Fishman method and the CVMS indexes by analyzing the development of the cervical vertebrae on the lateral cephalogram, according to the Baccetti (2002) method.

The aim was to determine the synergy or the asynergy of the chronological and the biological age within the studied group. Also, the average age was determined for the appearance of the SMI and the CVMS stages for the subjects in the research group, the results obtained being analyzed and compared both within the studied group, taking into account the sexual dimorphism, and the existing data in the specialty literature, obtained following similar studies upon different population groups.

For the SMI indexes, using the linear regression equations there has been determined the mathematical model to show the existing relation between the SMI stages and the chronological age for the participants in the study.

Conclusions

- The research proved the great variability of the chronological age when the SMI and CVMS stages are reached both in the studied groups (girls and boys) and in comparison with the subjects in the comparison groups. This proves that the chronological age is not a valid indicator for estimating the biological age of the patient during the stages of diagnostic and treatment.
- There have been differences between the two sexes regarding reaching the SMI/CVMS stages for skeletal maturation; within the studied group, the girls had a 1.04-year advanced evolution compared to the boys for the SMI stages and a 1.25-year one for the CVMS stages.
- By comparing the results of the study with the studies quoted in the specialty literature, there was found a great variation of the moments for reaching the stages of skeletal maturation, due to the different population characteristics, the different environmental and socio-economic factors. Another reason could be the age of the studies with which the comparison was made and of the data used in those studies, most of them using historical data.
- The subjects in the study group reached the stages of skeletal development prior to the subjects in the comparison studies, which shows the decrease of the average age when the girls and the boys start their puberty as the time passes, thus confirming the “secular tendency”. Within the study group, for both sexes, the biggest variations were registered in the pre-pubertal stage.
- From the comparative analysis of the SMI and CVMS indexes in the studied group there emerged the fact that the moment of maximal pubertal growth, indicated on the hand x-ray by the SMI 6 stage (MP3Cap), corresponds on the lateral cephalogram to the CVMS 3 stage.
- The research proved the strong correlation existing between the SMI and CVMS indexes, the correlation degree obtained for the girls ($r=0.90$) being bigger than the one for the boys ($r=0.87$). The similitudes observed between the charts showing the evolution of the two indexes, the similar value of the average difference between the moments for reaching certain stages by the girls and the boys in the studied group, show that the skeletal age may be evaluated also using the CVMS indexes, not only the analysis of the SMI indexes.

- For the regression equations, the obtained R² determination coefficient was 0.85 for the girls and 0.91 for the boys, this indicating a strong association between the SMI stages and the chronological age.

Chapter 6

The studies done in this chapter aimed to statistically verify the concordance of the SMI/CVMS indexes in evaluating the stages of pubertal growth. Two studies were conducted, a transversal and a longitudinal one, both of them studying the statistical validation of the following hypothesis:

- the pre-pubertal stage corresponds to the SMI 1, 2, 3, 4 and the CVMS 1, 2 indexes;
- the pubertal stage corresponds to the SMI 5, 6, 7 and the CVMS 3 indexes;
- the post-pubertal stage corresponds to the SMI 8, 9, 10, 11 – CVMS 4, 5 indexes.

For the interpretation of the obtained data, three statistical analyses were done:

- the Pearson parametric test for correlation, to analyze the degree of association of the obtained values;
- the t test for paired measurements, in order to determine whether there exist systematic errors within the analyzed data;
- the kappa Cohen coefficient, to determine the degree of concordance of the SMI/CVMS indexes in evaluating the pubertal stages.

Conclusions

- The studies in Chapter 6 proved the correlation and concordance existing between the SMI/CVMS indexes, related to the stages of pubertal period. In both studies (transversal and longitudinal) the tested hypothesis was confirmed. The obtained values for the kappa Cohen coefficient show, for the transversal study, the existence of an almost perfect accord for the girls ($k=0.83$) and a substantial accord for the boys ($k=0.67$). The values obtained for the longitudinal study were superior to those from the transversal study, indicating an almost perfect accord for both sexes ($k=0.84$ for the girls and $k=0.85$ for the boys).
- The results from the longitudinal study indicate a possible clinical applicability of the SMI/CVMS indexes along the treatment, after starting the orthodontic appliances. These showed that the method could be clinically used, offering the

orthodontist information about the biological stage in which the patient is situated, in order to be able to evaluate the remanent growth for the duration of the orthodontic treatment.

- The research showed that both SMI and CVMS indexes could be statistically used to determine the biological moment in which the patient is situated, this allowing the orthodontist to regularly use the lateral cephalogram in order to estimate the skeletal age, saving the patient from a supplementary irradiation necessary for a hand x-ray.

Chapter 7

The main study had as an objective to compare the two methods of estimating the skeletal age, using the ROC analysis (Receiver Operating Characteristics), in order to determine the accuracy of the two methods in identifying the subjects who haven't yet reached the peak moment of pubertal growth and those who have reached it or even went past it. As a reference test, the study used the peak moments of growth registered for the cephalometric parameters chosen to describe the development of the maxilla and the mandible.

Secondary, comparative analyses were made for the peak moments registered for the analyzed cranio-facial parameters, both within the study group (taking into account the sexual dimorphism) and the results quoted in the specialty literature, obtained following similar studies, done upon different population groups, in different periods.

Conclusions

- Following the ROC analysis there has been proven that for both groups, both the SMI and the CVMS indexes have a good capacity in indicating the subjects that have not yet reached the moment of maximal pubertal growth and those who reached it or when past it. In all cases, for all the analyzed parameters, the values for the AUC (the area underneath the ROC curve) were over 0.8, which indicates that the diagnostic accuracy is very good or excellent.
- The study showed that the SMI indexes have a better accuracy than the CVMS indexes, but both methods may be successfully used.
- The study in chapter 7 regarding the selected cephalometric parameters confirms the sexual dimorphism in reaching the peak moments of growth registered for these parameters, the girls getting there sooner than the boys. For both sexes there exist a difference of approximately two years, significantly lower for the girls, between the moment of maximal growth of the maxilla and of the mandible. For both sexes, with

no exception, the peak moment registered for the maxillary growth for the subjects in the study group is sooner than the one registered for the subjects in the comparison studies.

- For the analyzed maxillary parameters of the subjects in the study, there has been proved that the moment of maximal pubertal growth takes place between the SMI 1-3 stages and CVM 1-2 stages. For the mandibular parameters, the moment of maximal pubertal growth takes place between the SMI 5-7 stages and CVM 2-3 stages. Thus is confirmed the recommendation that the expansion treatments for the maxilla be done before the moment of maximal pubertal growth, while those for the mandibular growth should start during the stage of maximal pubertal growth or shortly after that.
- The research proved the existence of individual variability, both within the study group and in relation with the comparison groups.

Personal conclusions and contribution

The study showed that both methods for estimating the skeletal age are valid from a statistical point of view, allowing them to be used during the diagnostic stage, in order to evaluate the biological moment in which the patient is situated, but also along the orthodontic treatment, to estimate the patient's growth potential. It has been proved that interpreting the skeletal age through the analysis of the SMI indexes according to Fishman's method has a greater accuracy, but comes along with an apparent disadvantage: the necessity of having additional x-rays. It has been showed that from a statistic point of view, the estimation of the skeletal age using the analysis of the cervical vertebrae development on the lateral cephalogram could be successfully used. Even if its accuracy is significantly smaller, it offers the practitioner enough data for the estimation of the biological moment of the patient and comes along with the advantage that the necessary radiological investigation is already in the initial orthodontic file, thus saving the patient from an additional irradiation.

Which method is better? The statistical analyses showed that both techniques could be successfully used, but here intervenes a series of variables belonging to the doctor's capacity to do the necessary interpretations: learning the methods, the clinical experience with the respective technique, the popularization of the methods, the existence of some guides with

clear schemes allowing a facile understanding of them, but also the therapeutic moment in which the growth evaluation is wanted.

Fishman's method, using the hand x-ray, comes with the advantage of having more classes (11 stages), which allows identifying more growth moments, the stages being clearly defined in the classification and easily seen of the x-ray. Nevertheless, due to the necessity of having additional x-rays, the decision to ask for a radiological investigation should be well thought for each patient, weighing the benefit of the investigation against the prejudice of the irradiation to which the patient is subjected. Taking into consideration the great individual variability in what regards the stages of the pubertal period, none of the analyzed methods offers total guaranty for the data collected from the interpretations. Therefore, the results of this research should be carefully interpreted. They offer certain guide lines that may orient the doctor in evaluating the biological moment of the patient, but aside these methods, the individual diversity is a constant. Due to this diversity, it is necessary that for evaluating the biological moment of the patient to corroborate the data from the analysis of the indicators for the biological age (morphological, endocrine, dental and skeletal).

Taking into consideration the present norms for reducing the irradiation dosage for the patients, it is advisable that in the diagnostic stage, the practitioner do certain estimations regarding the biological moment of the patient, by analyzing the cervical vertebrae development on the lateral cephalogram existing in the initial file and corroborating the data with the results from the analysis of the other indicators of the biological age. On the other hand, there are certain clinical cases of patients with growth disorders, for which it is necessary to have a more elaborated investigation in what concerns the estimation of the skeletal age along the orthodontic treatment. In these cases, it is useful to have a hand x-ray or an additional lateral cephalogram in order to investigate the present moment in which the patient is situated.

Taking into account the necessary irradiation dosage for the investigation, the scale leans towards using the hand x-ray, the effective irradiation dosage for it being $0.16 \mu\text{Sv}$, while for the lateral cephalogram done without a protective shield in order to correctly show the cervical vertebrae is $5.03 \mu\text{Sv}$. Even if for the lateral cephalogram the protective shield would be used (the specialists having mixed opinions in what regards the visibility of the cervical vertebrae), the irradiation dosage ($3.3 \mu\text{Sv}$) would still be bigger than the one for the hand x-ray (*Patcas, 2012*).

In conclusion, it would be optimal that initially the doctor evaluate the growth using the data from the orthodontic file and evaluate the patient's biological moment by analyzing the development of the cervical vertebrae on the lateral cephalogram, knowing the growth and development stages and corroborating the results obtained with the other indicators of the biological age. Later on, along the treatment, should any growth problems or deviations from the normal growth patterns be identified, the skeletal age could be investigated using a hand and wrist x-ray. This implies that the doctor masters both methods for investigating the skeletal age, each of them offering certain benefits according to the treatment stage in which it is used.

An important contribution of the thesis comes from the fact that the studies were done upon a heterogeneous group selected from our country, from Bucharest and its adjacent areas, using current investigations, from the period 2004-2019, most of them being done after 2010.

Selective bibliography:

Baccetti, T., Franchi, L., Toth., L.R. and McNamara, J.A. (2000,a) Treatment timing for Twin-block therapy. *Am. J. Orthod. Dentofacial Orthop.* 118: 159-170.

Baccetti, T., Franchi, L. and McNamara, J.A. (2000,b) Treatment and post-treatment craniofacial changes after rapid maxillary expansion and facemask therapy. *Am. J. Orthod. Dentofacial Orthop.* 118: 404-413.

Baccetti, T., Franchi, L., Cameron, C.G. and McNamara, J.A. (2001) Treatment timing for rapid maxillary expansion. *The Angle Orthod.* 71: 343-350.

Baccetti, T., Franchi, L. and McNamara, J.A. (2002) An improved version of the cervical vertebral maturation (CVM) method for the assessment of mandibular growth. *The Angle Orthod.* 72: 316-323.

Baccetti, T., Franchi, L. and McNamara, J.A. (2005) The cervical vertebral maturation (CVM) method for the assessment of optimal treatment timing in dentofacial orthopedics. *Semin. Orthod.* 11: 119-129.

Bergersen, E.O. (1972) The male adolescent facial growth spurt: its prediction and relation to skeletal maturation. *The Angle Orthod.* 42: 319-336.

Björk, A., Helm, S. (1967) Prediction of the age of maximum pubertal growth in body height. *Angle Orthod.* 37: 134-143.

Faltin, K., Faltin, R.M., Baccetti, T., Franchi, L., Ghiozzi, B. and McNamara, J.A. (2003) Long-term effectiveness and treatment timing for bionator therapy. *The Angle Orthod.* 73: 221-230.

Fishman, L.S. (1982) Radiographic Evaluation of Skeletal Maturation: A Clinically Orientated Method Based on Hand Wrist Films. *Angle Orthodontics* 52, 88-112.

Flores-Mir, C., Burgess, C.A., Champney, M., Jensen, R.J., Pitcher, M.R. and Major, P.W. (2006) Correlation of skeletal maturation stages determined by cervical vertebrae and hand-wrist evaluations. *The Angle Orthod.* 76: 1-5.

Franchi, L., Baccetti, T. and McNamara Jr., J.A. (2000) Mandibular Growth as Related to Cervical Vertebral Maturation and Body Height. *American Journal of Orthodontics & Dentofacial Orthopedics* 118, 335-340, <https://doi.org/10.1067/mod.2000.107009>.

Franchi, L. and Baccetti, T. (2002) The use of maturational indices for the identification of optimal treatment timing in dentofacial orthopaedics, (p. 151-170) In: McNamara, J.A. Jr. and Kelly, K.A. (ed.) Treatment timing: orthodontics in four dimensions. Craniofacial Growth Series, Vol. 39. Ann Arbor, Michigan: Center for Human Growth and Development, The University of Michigan.

Graber, T.M., Vanarsdall R.L. jr. (1994) Orthodontics: Current Principles and Techniques, Mosby, St. Louis.

Grave, K.C., Brown, T. (1976) Skeletal ossification and the adolescent growth spurt. *Am J Orthod.* 69:611-619, [https://doi.org/10.1016/0002-9416\(76\)90143-3](https://doi.org/10.1016/0002-9416(76)90143-3).

Grave, B., Brown, T. and Townsend, G. (1999) Comparison of cervicovertebral dimensions in Australian Aborigines and Caucasians. *Eur. J. Orthod.* 21: 127-135.

Grave, K. and Townsend, G. (2003a) Cervical vertebral maturation as a predictor of the adolescent growth spurt. *Aust. J. Orthod.* 19: 25-31.

Gutiérrez Muñiz, JA., Berdasco Gómez, A., Esquivel Lauzurique, M., Jiménez Hernández, JM., Posada Lima, E., Romero del Sol, JM. et al. (2006) Growth and Development. In: Pediatrics, Collective of Authors, T1. [online]. 14.02.2007. Editorial Medical Sciences Havana Cuba Available from:
http://www.bvs.sld.cu/libros_texto/pediatria_tomoi/paritei_cap06.pdf.

Hassel, B. and Farman, A.G. (1995) Skeletal Maturation Evaluation Using Cervical Vertebrae. *American Journal of Orthodontics. & Dentofacial Orthopedics* 107, 58-66, [https://doi.org/10.1016/S0889-5406\(95\)70157-5](https://doi.org/10.1016/S0889-5406(95)70157-5).

Hägg, U. and Taranger, J. (1980,a) Menarche and voice changes as indicators of the pubertal growth spurt. *Acta Odontol. Scand.* 38: 179-186.

Hägg, U., Taranger, J. (1982) Maturation indicators and the pubertal growth spurt. *Am J Orthod.* 1982;82:299–309, [https://doi.org/10.1016/0002-9416\(82\)90464-X](https://doi.org/10.1016/0002-9416(82)90464-X).

Hunter, C.J. (1966) The correlation of facial growth with body height and skeletal maturation at adolescence. *The Angle Orthod.* 36: 44-54.

Lamparski, D.G. (1972) Skeletal Age Assessment Utilizing Cervical Vertebrae. Master of Science Thesis, University of Pittsburgh, Pittsburgh.

Mitani, H., Sato, K. (1992) Comparison of mandibular growth with other variables during puberty. *Angle Orthod.* 62: 2171222.

O'Reilly, M. and Yanniello, G.J. (1988) Mandibular Growth Changes and Maturation of Cervical Vertebrae: A Longitudinal Cephalometric Study. *Angle Orthodontist* 58, 179-184.

Pancherz, H., Hagg, U. (1985) Dentofacial orthopedics in relation to somatic maturation. *Am J Orthod.* 88: 273–287.

Pancherz, H. and Von Bremen, J. (2002) Efficiency of class II division 1 therapy in relation to treatment timing and modality, (p. 25-53) In: McNamara, J.A. Jr. and Kelly, K.A. (ed.) Treatment timing: orthodontics in four dimensions. Craniofacial Growth Series, Vol. 39. Ann Arbor, Michigan: Center for Human Growth and Development, The University of Michigan.

Patcas, R., Signorelli, L., Peltomäki, T., Schätzle, M. (2012) Is the use of the cervical vertebrae maturation method justified to determine skeletal age? A comparison of radiation dose of two strategies for skeletal age estimation. *European Journal of Orthodontics* 35 604–609, doi:10.1093/ejo/cjs043, July.

Proffit, W.R. and Fields, H.W. (2000) Contemporary Orthodontics. (3rd Ed.) St. Louis: Mosby Inc., 4, 25-42, 91-92.

San Roman, P., Palma, J.C., Oteo, M.D. and Nevado, E. (2002) Skeletal maturation determined by cervical vertebrae development. *Eur. J. Orthod.* 24: 303-311.

Turchetta, B.J., Fishman, L.S. and Subtelny, D.J. (2007) Facial Growth Prediction: A Comparison of Methodologies. *American Journal of Orthodontics. & Dentofacial Orthopedics* 132, 439-449, <https://doi.org/10.1016/j.ajodo.2005.10.026>.

Van der Beek, M.C., Hoeksma, J.B., Prahl Andersen, B. (1996) Vertical facial growth and statural growth in girls: A longitudinal comparison. *Eur. J. Orthod.* 18: 549-555.

Westwood, P.V., McNamara, J.A., Baccetti, T., Franchi, L. and Sarver, D.M. (2003) Long-term effects of Class III treatment with rapid maxillary expansion and facemask therapy followed by fixed appliances. *Am. J. Orthod. Dentofacial Orthop.* 123: 306-320.

List of the published scientific papers:

1. **Galan, E.**, Hlatcu, A.R., Bencze, A., Teodorescu, E., Păcurar, M., Chibeleian, M., Ionescu, E. (2021) Concordance of SMI and CVMS bone maturation indices in pubertal growth stages – cross-sectional study. *Ro J Stomatol.*67(3), p186-192, DOI: 10.37897/RJS.2021.3.10
https://rjs.com.ro/articles/2021.3/RJS_2021_3_Art-10.pdf
2. **Galan, E.**, Hlatcu, A.R., Milicescu, Ș. Jr., Teodorescu, E., Neagoe, S., Ionescu, E. (2022) The Verification of the Degree of Concordance of the SMI/CVMS Indexes in Evaluating the Pubertal Growth Stages - Longitudinal Study. *Appl. Sci.* 12, (6) 2783, (IF=2.679). <https://doi.org/10.3390/app12062783>
<https://www.mdpi.com/2076-3417/12/6/2783/pdf>