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STRÎȘCA Stanislav

VIRTUAL PLANNING TECHNOLOGY IN THE ASSESSMENT OF ANATOMICAL BALANCE IN PATIENTS WITH DENTO-MAXILLARY ANOMALIES

323.01 STOMATOLOGY

Summary of the Doctoral Thesis in Medical Sciences

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The thesis was developed at the Department of oral and maxillofacial surgery and oral implantology „Arsenie Guțan" State University of Medicine and Pharmacy „Nicolae Testemițanu".

Scientific coordinator
Sîrbu Dumitru, PhD med. sci., associate professor

Scientific Co-adviser
Șontea Victor, PhD physics and mathematics sci., university professor

Guidance committee members:
Trifan Valentina, PhD med. sci., associate professor
Mostovei Andrei, PhD med. sci., associate professor
Suharschi Ilie, PhD med. sci., assistant professor

The defense will take place on 24.01.24, at 14:00, in the premises of USMF „Nicolae Testemițanu", bd. Ștefan cel Mare și Sfânt, 165, office 204, in the meeting of the Commission for public defense of the doctoral thesis, approved by decision of the Scientific Council of the Consortium of 05.10.23 (minutes no. 22).

The composition of the Commission for public defence of the defence of the doctoral thesis:

President:
Chele Nicolae,
Dr. habil., med. sci., university professor

Members:

Sîrbu Dumitru,
PhD med. sci., associate professor

Șontea Victor,
PhD teh. sci., university professor

Solomon Oleg,
PhD med. sci., associate professor

Official references:

Tatarciuc Silvia,
Dr. habil., med. sci., university professor

Trifan Valentina,
PhD med. sci., associate professor

Cirimpei Vasile,
PhD med. sci.,

Author
Strîșca Stanislav

SUMMARY

INTRODUCTION

Relevance and importance of the topic: Dento-maxillary anomalies are characterized by growth and developmental disturbances, whether primary or acquired, of the dental system or maxillary bone bases, resulting in significant imbalances within the dental-alveolar and occlusal arches [1].

Most studies underscore the importance of orthodontic treatment in conjunction with orthognathic surgery, as this combined approach is currently the worldwide standard for effectively correcting these anomalies through surgical interventions on dental arches and/or maxillary bones, substantially improving the quality of life [2].

Traditional treatment planning for these anomalies traditionally relies on clinical examinations, patient photographs, two-dimensional radiological images (2D), and study models made of plaster mounted in articulators and transferred using a facebow. Hsu et al. have identified several issues associated with traditional planning for gnato-surgical interventions, mainly due to the inability to visualize the facial skeleton as a whole [3].

The success of orthognathic surgical interventions greatly depends on the surgical technique and precise execution of the preoperative surgical plan. Virtual surgical planning allows the simulation of various surgical techniques.

Processing three-dimensional images using planning software enables us to virtually simulate osteotomies, reposition bone fragments into the desired position, control intercuspation, manage interference between osteotomized fragments, and visualize postoperative results in real-time. Innovations in orthognathic surgery have significantly reduced the risks associated with surgical procedures, both during surgery and in the postoperative period, including the risk of relapse. However, authors like Brodie et al. have suggested that tongue volume (TV), in addition to posture and function, plays a notable role in the development of dento-facial anomalies [4]. Hence, to gain a better understanding of the tongue's influence on occlusal stability after orthognathic surgery, it is important to calculate the volume of the oral cavity (OC) and tongue (TV) to determine the volumetric balance between TV and OC, as well as changes in the position of the hyoid bone.

Goal: The aim of this study is to ascertain anatomical balance in patients with dento-maxillary anomalies and assess postoperative changes to optimize surgical treatment through the application of virtual planning technology.

Objectives:

1. Studying the existing virtual surgical planning technology in the diagnosis and treatment of dento-maxillary anomalies.
2. Performing three-dimensional evaluations of oral cavity volume, tongue volume, upper airways, and hyoid bone position to elucidate the correlation between tongue volume and other parameters.
3. Conducting a comparative assessment of oral cavity volume, tongue volume, and anatomical balance among different classes of dento-maxillary pathologies.
4. Analyzing the comparative anatomical balance and assessing volumetric changes in the oral cavity, upper airways, and hyoid bone position in the pre- and postoperative periods.
5. Interpreting the results and formulating recommendations.

Research hypothesis

The main research hypothesis, derived from the study's objective, posits that anatomical balance is dependent on the class of dento-maxillary anomalies. Within the research, three hypotheses have been formulated to be either supported or rejected:

The first hypothesis assumes that there is no correlation between tongue volume, oral cavity volume, hyoid bone position, and maxillo-mandibular relationships depending on the class of dento-maxillary anomaly.

Minimum axial cross-sectional oropharyngeal area is correlated with high values of anatomical balance.

Anatomical balance will change in the postoperative period by decreasing in Class II and increasing in Class III.

The null hypothesis posits that anatomical balance in the postoperative period will not undergo statistically significant changes.

The synthesis of scientific research methodology and the justification of the chosen research methods are as follows:

In the development of this study, we utilized research methods and conducted a bibliographic analysis of international and national literature sources that address the use of virtual surgical planning technology in the diagnosis and treatment of dento-maxillary anomalies.

To achieve our proposed objectives, we chose to conduct a serial trial research, where each patient included in the research group simultaneously serves as their own control. Within the study, digital methods of virtual planning were employed for diagnosing and treating dento-maxillary anomalies. Furthermore, we studied the volume of the oral cavity, tongue, upper airways, hyoid bone position, and the changes resulting from orthognathic surgery interventions using contemporary analysis software, both pre- and post-operatively. The same measurements were taken during the one-month follow-up visits. A total of 105 patients were included in the research, with 35 in each group.

The approval for the thesis topic was obtained during a meeting of the Scientific Council of Nicolae Testemițanu State University of Medicine and Pharmacy, documented in the minutes of meeting number 10 dated September 17, 2019. Positive ethical approval for conducting the study was granted during meetings number 23 on April 12, 2019, and number 17 on March 26, 2023, by the Research Ethics Committee.

The scientific novelty and originality:

1. For the first time, a comprehensive three-dimensional volumetric assessment of oral cavity anatomical structures has been conducted within the population of the Republic of Moldova, using contemporary software programs.
2. For the first time, mathematical-statistical analysis has identified correlations between tongue volume and other anatomical structures, as well as various cephalometric landmarks.
3. Objective assessment of anatomical balance requires a volumetric evaluation of anatomical structures such as tongue volume, oropharyngeal volume, oral cavity volume, and residual oral cavity volume.

4. Preoperative and postoperative DICOM data overlay was performed using a contemporary "voxel-based" protocol for comparative evaluation of the obtained results.
5. It was demonstrated for the first time that increased tongue volume values are correlated with mandibular prognathism, and furthermore, anatomical balance remains consistent regardless of the class of dento-maxillary anomaly.
6. Virtual planning of orthognathic surgery was proposed for the first time, taking into consideration the parameters of anatomical balance.

Practical significance:

The practical significance of this study lies in the fact that the planning of orthognathic surgery must be undertaken with caution, taking into consideration not only cephalometric and aesthetic parameters but also tongue volume, oropharyngeal volume, and the remaining space of the oral cavity. This is especially important in cases where there is a planned posterior displacement of the mandible, as this could potentially lead to airway constriction and increase the risk of relapse.

The scientific findings have been implemented into the research, methodological, and clinical activities within the Department of Oro-Maxillofacial Surgery and Oral Implantology „Arsenie Guțan” at USMF „Nicolae Testemițanu”.

The scientific results have been presented through active participation in 25 national and international scientific forums, including: 24th Congress of the European Association for Cranio Maxillo Facial Surgery (2018, Munich, Germany); International Conference Bredent Group Days (2018, Chișinău, Republic of Moldova); Nicolae Testemițanu State University of Medicine and Pharmacy Days (2018, 2019, Chișinău, Republic of Moldova; Mention – First Degree Diploma); UNAS Congress XXII (2018, Bucharest, Romania); UNAS International Congress XXIII (2019, Bucharest, Romania); 1st BaSS (Balkan Stomatological Society) Symposium (2019, Iași, Romania); Technical-Scientific Conference of UTM Students, Master's, and PhD Students (2019, Chișinău, Republic of Moldova; Mention – Third Degree Diploma); International Implantology Congress ImplantoDays (2018, 2019, Chișinău, Republic of Moldova); Annual Scientific Conference of Young Specialists at IMSP IMU (2019, Chișinău, Republic of Moldova); 28th Annual Congress EAO (Lisbon, Portugal); Connect Dentistry Summit (2021, Bucharest, Romania); 25th Congress of the European Association for Cranio Maxillo Facial Surgery (2021, Paris, France); International Exhibition of Scientific Research, Innovation, and Inventions, 18th Edition, Pro Invent (2020, Cluj-Napoca, Romania; Mention – Gold Medal); International Exhibition of Scientific Research, Innovation, and Inventions, 18th Edition, Pro Invent (2020, Cluj-Napoca, Romania; Mention – Bronze Medal); International Exhibition INVENTICA, 25th Edition (2021, Iași, Romania; Mention – Silver Medal); Traian Vuia Invention Salon (2022, Timișoara, Romania; Mention – Bronze Medal); Euro Invent 13th Edition, European Exhibition of Creativity and Innovation (2021, Iași, Romania; Mention – Bronze Medal).

Keywords: dento-maxillary anomalies, orthognathic surgery, virtual surgical planning, virtual segmentation, anatomical balance.

1. VIRTUAL PLANNING TECHNOLOGY IN THE DIAGNOSIS OF DENTO-MAXILLARY ANOMALIES. STUDY 1

Dento-maxillary anomalies (DMAs) are defined in specialized literature as disorders affecting the growth and development of the dental system, maxillary bone bases, and facial soft tissues [5]. Patients with this condition may experience a decrease in masticatory efficiency, aesthetic, and phonetic disturbances [6]. Consequently, these disorders lead to significant imbalances, which often have repercussions on the patient's psycho-emotional well-being, creating feelings of imperfection and impacting their quality of life [7].

Anatomic balance in the oral cavity refers to the harmonious state of its anatomical structures. This state indicates that all elements of the stomatognathic system are proportionally and functionally arranged, contributing to the overall health and functionality of the oral cavity. Anatomic balance is also represented as the ratio between tongue volume and oral cavity volume, multiplied by 100, with the result expressed as a percentage. It's worth noting that according to specialized literature, lower values of anatomic balance are positively correlated with a reduced risk of developing sleep apnoea syndrome [8].

2. MATERIALS AND METHODS OF STUDY 1

2.1. General study information

The study was conducted following the principles of the Declaration of Helsinki and was approved by the ethics committee number 43 on March 16, 2018.

The research was multicentric, enrolling patients seeking orthodontic and surgical treatment at the Department of oro-maxillofacial surgery and oral implantology „Arsenie Guțan" and the university clinical base SRL „Omni Dent" from 2018 to 2022.

The minimum number of patients was calculated based on the following parameters: z test – means: two independent samples; Analysis: A priori: required sample size calculation; Distribution = Normal; Effect size dz = 0.5; Power (1-β err prob) = 0.8 α err prob = 0.05; Output: Noncentral distribution parameters δ = 2.5854415; Critical z = 1.7062592 Df = 25.7380304; Sample size = 29. Applying this formula, we obtained a minimum of 29 patients for each group.

Therefore, the current study focused on 105 patients divided into 3 groups based on their malocclusion. The first study group included 35 patients with Class II malocclusion, characterized by distalized molar relationships, comprising 28 females and 7 males.

The second study group included 35 patients with Class III malocclusion, characterized by mesialized molar relationships and a negative overjet, comprising 23 females and 12 males.

The control group included 35 patients with orthognathic occlusion, Class I molar relationships, and normal overjet and overbite, comprising 26 females and 9 males (average age 36.6 years).

The inclusion criteria were as follows: healthy somatic patients with Class I, II, and III Angle malocclusion; age of 18 years and above.

The exclusion criteria included: the presence of craniofacial developmental anomalies; trauma to the lower face region; temporomandibular joint disorders; previous orthodontic treatment; history of orthognathic surgery.

Diagnostic methods used in the research from Study 1 included: Radiological images: Lateral Cephalometric Radiographs (TRG), Cone Beam Computed Tomography (CBCT); Direct and indirect scanning of dental arches; Three-dimensional volumetric analysis of anatomical structures.

The acquisition of CBCT and TRG images was standardized following the manufacturer's protocol for the Dentsply Sirona Orthophos SL CT scanner (85 kV at 12 mA, exposure time of 14.18 seconds, volume size 11x10, isotropic voxel size 0.16mm; Sirona, Bensheim, Germany). The acquisition followed the ALADA principles (As Low As Diagnostically Achievable) and the protocol of the International Commission on Radiological Protection for minimizing radiation dose.

The intraoral scanning was performed individually for each patient using the Trios 3 intraoral scanner (precision - 4.5 ± 0.9 µm; accuracy - 6.9 ± 0.9 µm; 3Shape; Copenhagen; Denmark), and subsequently exported in .stl format.

Volumetric analysis:

The DICOM data from the CBCT and .stl files of virtual models were imported into the freely licensed software Slicer 3D 4.10.1. The volume of the oral cavity (figure 1) represents the sum composed of the tongue volume, oropharyngeal airway volume, and the remaining endobucal airway volume.

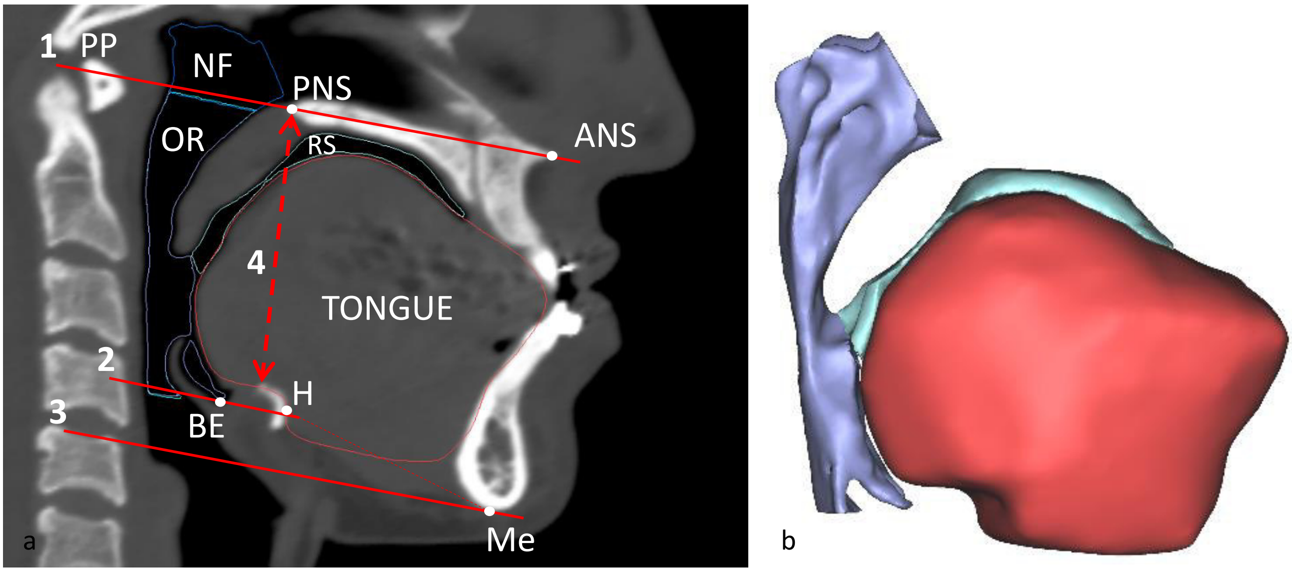

Figure 1. Calculation of the oral cavity, nasopharynx, oropharynx, tongue, and residual air space volumes. a) Anatomical landmarks (NF-nasopharynx; OR-oropharynx; BE-base of epiglottis; RS-residual space; PNS-posterior nasal spine; ANS-anterior nasal spine; H-hyoid bone; Me-menton) and sagittal section planes of computer tomography: 1 – palatal plane PP; 2 – epiglottis base plane; 3 – mandibular plane; 4 – hyoid bone height. b) Surface reconstruction.

The volume of the tongue, segmented based on the grayscale range, includes the region laterally and anteriorly to the dental arches, superiorly to the hard palate, and inferiorly to the plane formed by Me through BE via H. The volume of the oropharyngeal airways was limited superiorly by the PP plane and inferiorly by the BE plane. The minimum value of the oropharyngeal surface area was calculated in the axial plane and expressed in mm2. The volume of the endobucal airways included the space between the mucosa of the hard palate and the tongue. The height of the hyoid bone was determined by measuring the distance from the PNS (posterior nasal spine) to the hyoid bone, both in the native sagittal plane section and in the three-dimensional model. The distance from the hyoid bone was calculated from the anterior margin of the hyoid bone to the Me point, both in the native sagittal plane section and in the three-dimensional model. Anatomic balance represents the ratio of the tongue volume to the oral cavity volume, multiplied by 100. To reduce segmentation errors, additional segmentation of the upper airways was performed, and a Boolean subtraction mathematical procedure was carried out.

2.2. Statistical analysis of Study 1

The data collected were processed using RStudio and IBM SPSS Statistics 26.0. For continuous (quantitative) variables, the mean values with standard deviation, median with interquartile range, minimum, and maximum values were estimated. Comparative evaluations among the groups (three in total) were performed using non-parametric tests according to the relationships between groups for independent samples (Kruskal-Wallis test for independent samples with post-hoc analysis, Bonferroni correction). Visualization was done using box plots. Correlational analysis was conducted using the Spearman's ρ test, supplemented by estimating 95% confidence intervals. Visualization included correlation diagrams showing the distribution of the analysed data and correlation coefficient values. For the statistical tests, an α value of 0.05 was considered as the threshold.

3. RESULTS OF STUDY 1

Virtual planning technology was used to calculate the volume of the structures of interest in 105 patients (28 males, 77 females), with 35 patients in each of the Class I, II, and III groups. In total, 1155 anatomical structures were segmented, including the facial skeleton, upper jaw, lower jaw, hyoid bone, airway volume, nasopharyngeal volume, oropharyngeal volume, tongue volume, oral cavity volume, residual space of the oral cavity, and the minimum axial surface area of the oropharynx. Additionally, 525 cephalometric landmarks were marked, and 420 anatomical values were calculated.

3.1. The characterization of the groups

The patients were divided into 3 study groups based on the type of dento-maxillary anomaly. In total, 28 males and 77 females were included in this study, with an average age of 29 years (Median 27 years, IQR = 13). Within Class I, the average age was 30 years (Median 29 years, IQR = 10), Class II had an average age of 28 years (Median 28 years, IQR = 13), and Class III had an average age of 27 years (Median 24 years, IQR = 16). The application of the Kruskal-Wallis test did not identify statistically significant differences (p = 0.206) among these classes, indicating that the age at which patients sought treatment was similar regardless of the class of anomaly.

The mean value of the SNA angle in Class I was 80.490 (Median 800, IQR = 4), in Class II it was 81.230 (Median 820, IQR = 5), and in Class III it was 80.340 (Median 800, IQR = 4). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.296) among these classes.

The mean value of the SNB angle in Class I was 78.510 (Median 780, IQR = 3), in Class II it was 75.030 (Median 75.000, IQR = 5), and in Class III it was 83.660 (Median 820, IQR = 5). The Kruskal-Wallis test identified statistically significant differences (p < 0.001). Post-hoc analysis revealed that the SNB angle in Class I was statistically significantly different from the SNB angle in Class II (p = 0.003) and Class III (p < 0.001).

The mean value of the ANB angle in Class I was 1.940 (Median 20, IQR = 2), in Class II it was 6.140 (Median 60, IQR = 3), and in Class III it was -3.290 (Median -30, IQR = -5). The Kruskal-Wallis test identified statistically significant differences (p < 0.001). Post-hoc analysis revealed that the ANB angle in Class I was statistically significantly different from the ANB angle in Class II (p < 0.001) and Class III (p < 0.001).

The mean Wits value in Class I was 0.37 (Median 0.15, IQR = 0), in Class II it was 4.54 (Median 5, IQR = 3), and in Class III it was -7.6 (Median -7, IQR = -15). The Kruskal-Wallis test identified statistically significant differences (p < 0.001). Post-hoc analysis revealed that the Wits value in Class I was statistically significantly different from the Wits value in Class II (p < 0.001) and Class III (p < 0.001).

The mean value of the FMA angle in Class I was 19.940 (Median 200, IQR = 6.8), in Class II it was 23.230 (Median 230, IQR = 13), and in Class III it was 22.060 (Median 230, IQR = 8). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.262) among these classes.

The mean volume of the tongue was 81.30 cm3, with 79.86 cm3 in Class I (Median 80.01 cm3, IQR = 20), 74.50 cm3 in Class II (Median 70.79 cm3, IQR = 13), and 89.57 cm3 in Class III (Median 86.62 cm3, IQR = 20). The Kruskal-Wallis test identified statistically significant differences (p = 0.001). Post-hoc analysis revealed that the tongue volume in Class I did not significantly differ from Class II (p = 0.266) and Class III (p = 0.090), but Class II and III showed significant differences (p < 0.001).

The mean volume of the airways was 23.04 cm3, with 22.99 cm3 in Class I (Median 21.65 cm3, IQR = 8.95), 23.25 cm3 in Class II (Median 23.25 cm3, IQR = 13.86), and 22.89 cm3 in Class III (Median 22.92 cm3, IQR = 9.52). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.894) among these classes.

The mean volume of the oropharynx was 15.84 cm3, with 15.42 cm3 in Class I (Median 13.98 cm3, IQR = 7.4), 15.94 cm3 in Class II (Median 15.85 cm3, IQR = 7.42), and 16.17 cm3 in Class III (Median 15.93 cm3, IQR = 8.34). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.652) among these classes.

The mean minimum axial surface area of the oropharynx was 170.74 mm2, with 174.74 mm2 in Class I (Median 156 mm2, IQR = 6), 172.54 mm2 in Class II (Median 140 mm2, IQR = 151), and 164.94 mm2 in Class III (Median 174.74 mm2, IQR = 148). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.772) among these classes.

The mean distance from the posterior nasal spine to the hyoid bone was 58.37 mm, with 57.89 mm in Class I (Median 57 mm, IQR = 9), 57.91 mm in Class II (Median 56 mm, IQR = 9), and 59.31 mm in Class III (Median 58 mm, IQR = 13). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.902).

The mean distance from the hyoid bone to the menton was 42.30 mm, with 42.46 mm in Class I (Median 43 mm, IQR = 9), 40.69 mm in Class II (Median 42 mm, IQR = 9), and 43.77 mm in Class III (Median 43 mm, IQR = 13). The Kruskal-Wallis test did not identify statistically significant differences (p = 0.166).

The mean volume of the oral cavity was 99.16 cm3, with 97.13 cm3 in Class I (Median 94.55 cm3, IQR = 26), 91.42 cm3 in Class II (Median 88 cm3, IQR = 12), and 108.95 cm3 in Class III (Median 107.58 cm3, IQR = 34). The Kruskal-Wallis test identified statistically significant differences ($p = 0.001$). Post-hoc analysis revealed that the volume of the oral cavity in Class I was significantly different from Class III ($p = 0.049$) and not significantly different from Class II ($p = 0.540$). Additionally, this comparative evaluation showed significant differences between Class II and III ($p < 0.001$).

The mean value of the anatomical balance was 81.74%, with 82.14% in Class I (Median 82%, IQR = 6), 81.23% in Class II (Median 83%, IQR = 7), and 81.86% in Class III (Median 82%, IQR = 10). The Kruskal-Wallis test did not identify statistically significant differences ($p = 0.771$).

4. DISCUSSION. STUDY 1

4.1. Virtual Segmentation of Anatomical Structures

Virtual segmentation of anatomical structures is the process of accurately separating and defining a specific anatomical region from a medical image, such as a CT scan (or an MRI), based on the range of Hounsfield units' density. Virtual segmentation is a critical technique in medicine that has led to significant advances in the field of medical imaging, aiding in the improvement of patient diagnosis and treatment. This technology is employed in the medical field for a range of applications, including surgical planning, radiation therapy, and computer-aided diagnosis. Virtual segmentation finds utility in various medical domains, including radiology, oncology, neurosurgery, and orthognathic surgery.

4.2. Tongue Volume, Oral Cavity Volume, and Anatomic Balance

The statistical analysis revealed that tongue volume is larger in Class III compared to Class I and II. Correlation analysis elucidated that tongue volume is positively correlated with oral cavity volume, SNB angle, and negatively correlated with ANB angle and Wits value.

Therefore, tongue volume appears to be closely related to the sagittal position of the mandible. In 1965, Köle hypothesized that macroglossia could be a cause of mandibular prognathism development; however, he failed to clarify the role of the tongue in the development of dento-maxillary anomalies. This was due to the lack of quantitative and qualitative objective volume calculation capabilities at that time.

Additionally, Spearman correlation analysis conducted individually for each class indicated a more pronounced negative correlation between tongue volume and the minimum axial section of the oropharynx in Class II. This suggests that Class II patients with larger tongue volumes and a narrowed oropharyngeal lumen should be monitored as they are at risk of developing obstructive sleep apnoea syndrome (OSAS) according to the literature.

Based on the obtained results, oral cavity volume was statistically significantly different among the three groups ($p=0.001$). Specifically, oral cavity volume was 97.13 cm3 in Class I, 91.42 cm3 in Class II, and 108.95 cm3 in Class III. Similar results were found by Iwasaki et al., where oral cavity volume was smaller in Class II and larger in Class III.

However, the difference lies in the anatomic balance value, which in the current research is practically similar across all three classes, while in Iwasaki's study, it differs among the three classes.

Considering that oral cavity volume is larger in Class III and smaller in Class II, while anatomic balance remains similar across all three groups, it can be presumed that this phenomenon is a defence mechanism of the body. Therefore, when orthodontic tooth extraction is performed to camouflage the dento-maxillary anomaly without considering tongue volume, recurrences, or the development of OSAS are possible.

These findings indicate the degree of influence of tongue volume and oral cavity volume on the oropharynx and anatomic balance. Furthermore, based on the obtained results, the second part of the study will analyse how oral cavity volume and anatomic balance values change following orthognathic surgery interventions.

4.3. Oropharyngeal Volume, Minimum Axial Sectional Area, and Obstructive Sleep Apnoea Syndrome (OSAS)

In this study, the Minimum Cross-Sectional Area (MCSA) was calculated by recording the area with the minimum value using CBCT images, which are widely used in daily dental practice. Chaudhry et al. demonstrated that CBCT can be successfully utilized to calculate the oropharyngeal volume and MCSA, and they concluded that dental practitioners play a crucial role in identifying patients at risk of developing Obstructive Sleep Apnoea Syndrome (OSAS). The research results suggested that MCSA and oropharyngeal volume obtained from CBCT are correlated with high STOP-bang scores (≥ 3) used by sleep specialists [9]. For this reason, dental practitioners should be trained in how to calculate oropharyngeal volume and MCSA when analysing CBCT images, so that patients at risk of OSAS can be referred to sleep specialists.

4.4. Conclusions of Study I

Based on the limitations of the current study, we can conclude that, contrary to the main hypothesis, anatomic balance is not dependent on the class of dento-maxillary anomalies. Additionally, the minimum surface area of the oropharynx was strongly correlated with high percentage values of anatomic balance. Therefore, the first hypothesis of the study is rejected, and the second one is accepted.

Concurrently, virtual segmentation of anatomical structures represents an innovative technology that can contribute to improving surgical interventions and treatment, as well as customizing treatment based on each patient's characteristics. Virtual segmentation also plays a crucial role in orthognathic surgery, enabling surgeons to plan surgical procedures more precisely and predictively, significantly enhancing patients' quality of life.

The clinical significance of this study lies in the fact that the posterior displacement of the mandible in orthognathic surgeries must be carefully planned to minimize the risks of relapse and airway constriction.

5. VIRTUAL PLANNING TECHNOLOGY IN THE TREATMENT OF DENTO-MAXILLARY ANOMALIES. STUDY 2

The characteristics of a successful treatment of dento-maxillary anomalies include the restoration of morpho-functional and aesthetic aspects with a favourable long-term prognosis, encompassing several criteria: restoring occlusion, masticatory function, facilitating speech, swallowing, and breathing, primary postoperative wound healing, restoration of the oro-maxillo-facial skeletal contour, and facial physiognomy [10].

The development of new treatment methods, based on modern technologies, aims to rehabilitate patients in the shortest possible time with minimal invasive trauma [11]. The workflow of virtual surgical planning technology (figure 2) depends on the specific field of application but generally includes, and is not limited to, data acquisition; analysis of radiological images and conversion into .stl format; three-dimensional anthropometric analysis; surgical simulation; CAD program-based guide/splint modelling; rapid prototyping CAM-based guide/splint manufacturing; delivery of guides/splints to the operating room; and comparison of achieved results.

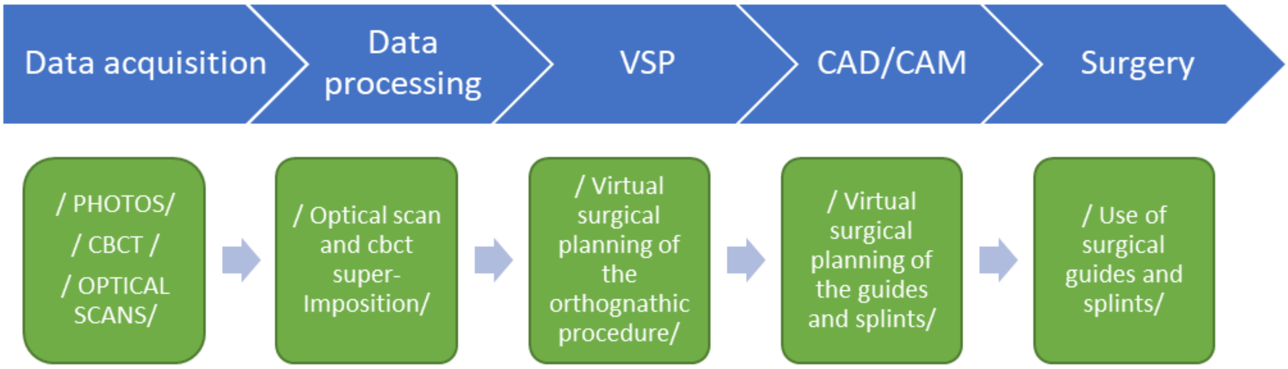

Figure 2. **Schematic representation of the workflow in the digital protocol of virtual surgical planning for orthognathic surgical procedures.**

6. MATERIALS AND METHODS. STUDY 2

6.1. General study information

The study was conducted following the principles of the Declaration of Helsinki and was approved by the Ethics Committee No. 23 on April 12, 2019.

The research was multicentric, involving patients who sought surgical treatment at the Department of Oro-Maxillofacial Surgery and Oral Implantology "Arsenie Guțan" and the University Clinical Base SRL "Omni Dent" from 2018 to 2023.

The minimum number of patients was calculated based on the following parameters: t-test – means: Difference between two dependent means (paired corresponding pairs); Analysis: A priori: required sample size calculation; Distribution = Normal; Effect size dz = 0.6 α err prob = 0.05; Power (1-β err prob) = 0.8; Output: Non-central distribution parameters δ = 2.6153394; Critical t = 1.7340636 Df = 18 Actual power = 0.8079091; Sample size = 19; Therefore, applying the given formula, we obtained a minimum of 19 patients.

As a result, the current study focused on 20 patients who underwent virtual surgical planning technology.

Inclusion criteria were: physically healthy patients with Angle Class II and III malocclusion; age 18 and above.

Exclusion criteria included: the presence of congenital craniofacial anomalies; trauma to the lower face area; temporomandibular joint disorders; prior orthodontic treatment; history of orthognathic surgery.

Diagnostic methods used in the research from Study 2 included: Radiological images: Lateral and Posterior-Anterior Cephalograms, Cone Beam Computed Tomography (CBCT); Facial scanning, direct and indirect scanning of dental arches; Virtual surgical planning.

6.2. Clinical and Paraclinical Examination of Patients

At the patient inclusion stage in the study, a clinical examination was conducted to determine the presence of indications and contraindications for surgical interventions. The clinical examination consisted of both subjective and objective assessments of the patients. During the subjective examination, particular attention was given to general pathologies that might preclude orthognathic surgery. In this regard, a general clinical examination was conducted in collaboration with specialist physicians to assess the compensation or decompensation of concomitant diseases. The standard laboratory diagnosis included: complete blood count, blood biochemistry analysis, blood coagulation time, urinalysis, electrocardiogram, and a COVID-19 test performed 24-28 hours before the surgery.

Radiological examination was performed for each patient using a multislice computed tomography (CT) scanner, specifically the SOMATOM Definition Edge. The acquisition was standardized following the manufacturer's protocol for the SOMATOM Definition Edge/SIEMENS CT scanner (120.00 kV at 209.00 mAs, duration of 12.04 seconds, FOV 23.80, isotropic voxel size 0.4648 mm; Z position -180.50/65.90, Gantry angle (tilt) 0°, Siemens Healthcare GmbH, Erlangen, Germany). The principles of ALADA (As Low As Diagnostically Achievable) and the International Commission on Radiological Protection (ICRP) protocol for radiation protection were adhered to. During the exposure, the patient was in a supine position. Each radiological study comprised 494-602 native axial sections, exported in DICOM digital format for subsequent mathematical processing.

TRG acquisition

The acquisition was standardized according to the manufacturer's protocol for the Dentsply Sirona Orthophos SL cone-beam computed tomography (CBCT) scanner (80 kV at 6 mA, exposure time of 0.5 seconds, volume size 20x18; Sirona, Bensheim, Germany). Cephalometric analysis was performed using the freely licensed Blue Sky Plan 4 software.

Optical scan of the face

The extra-oral optical scanning was performed individually for each patient using the Creality CR 01 extra-oral scanner (precision - 100 ± 0.9 µm; accuracy - 500 ± 0.9 µm; Creality; China). Subsequently, the scans were exported in .obj format using CR Studio software.

Direct scanning of the dental arches.

Intraoral scanning was performed individually for each patient using the Trios 3 intraoral scanner (precision - 4.5 ± 0.9 µm; accuracy - 6.9 ± 0.9 µm; 3Shape; Copenhagen; Denmark), and the scans were subsequently exported in. stl format through the Dental System software.

The three-dimensional assessment of study models involved:

The study models were imported and examined in three dimensions using the Ortho-System software from 3Shape. The following elements were evaluated: Dental Arch Shape; Frenulum and Bridle Insertion and Thickness; Palatal Arch; Palatal Rugae; Dental Misalignments; Pont Analysis; Bolton Analysis:

Virtual surgical planning, digital modeling of occlusal splints, and osteotomy/repositioning guides

Virtual surgical planning of the procedure was performed using Dolphin Imaging 12.0.9.49 software. Following the acquisition of the composite model, as described in study 1, osteotomy lines were placed, and virtual osteotomies were carried out with the repositioning of fragments into the planned position. Subsequently, the fabrication of osteotomy and repositioning guides, as well as intermediate and final occlusal splints, was performed.

The three-dimensional printing of anatomical models, occlusal splints, and osteotomy/repositioning guides.

In the current study, anatomical models were 3D printed using the "extrusion modeling" technology CR-200B (Creality), occlusal splints, and surgical guides were printed from autoclavable resins using the "direct light exposure" technology Halot-Lite (Creality).

6.3. Surgical Procedures Protocol

The orthognathic surgical procedures were performed in a hospital setting, under general anaesthesia, by the same surgical team, using the "mandible-first" protocol described by Professor J. Reyneke and S. Grybauskas. This was facilitated through the use of intermediate and final occlusal splints. Prior to being transferred to the operating room, patients were instructed to brush their teeth and perform oral rinses with a 0.2% chlorhexidine solution for 1 minute. Surgical field preparation was carried out following the standard protocol used in oro-maxillofacial surgery procedures.

The assessment of volumetric changes

To perform an objective evaluation of volumetric changes in the oral cavity, upper airways, and the position of the hyoid bone before and after orthognathic surgery using virtual surgical planning technology, preoperative DICOM data T0 (before starting orthodontic treatment) were compared with postoperative DICOM data T1 (4 weeks postoperative) through a rigid voxel-based overlay technique, as proposed by Cevidanes [12]. The reference used for this comparison was the structures of the cranial base. This analysis was conducted using the Slicer 3D software (version 4.10.2; http://www.slicer.org). Thus, preoperative DICOM data T0 were created and compared with postoperative DICOM data T1.

6.4. Statistical analysis of Study II

The collected data were processed using RStudio and IBM SPSS Statistics 26.0. For continuous (quantitative) variables, the mean with standard deviation, median with interquartile range, minimum, and maximum values were estimated. Comparative evaluation was conducted using non-parametric tests according to the relationships between groups (Wilcoxon test for dependent samples, with a significance level (α) set at 0.05). Data visualization was performed using box plots combined with jitter plots and violin plots, allowing for a comprehensive presentation of the statistical data. Effect size and 95% confidence intervals were also calculated.

7. RESULTS OF STUDY 2

In this study, the virtual planning method was used to analyse and calculate the volume of anatomical structures in cm3 in 20 patients (7 males, 13 females), including 8 patients with Class II malocclusion (average age 30 years) and 12 patients with Class III malocclusion (average age 28 years), before (T0) and after orthognathic surgery (T1). A total of 34 orthognathic surgical procedures were performed (16 in the maxilla, 3 multi-segmental, 18 in the mandible, including two chin-wing osteotomies and 6 genioplasties). There were no postoperative complications or issues during follow-up. Additionally, 220 anatomical formations were virtually segmented, 100 cephalometric landmarks were traced, and 80 mathematical calculations were performed.

Subsequently, a total of 48 anatomical models, 68 occlusal splints, and 136 surgical guides were 3D printed.

7.1. Group characteristics

The study group was divided depending on the time when the segmentation of anatomical structures was performed, so T0 - before the start of orthodontic treatment, and T1 - at 4 weeks postoperatively.

In Class II, the mean values were as follows:

at stage T0: the mean value of SNA was 79.630; SNB - 75.130; ANB - 4.620; Wits value - 1.88; FMA angle - 27.50; distance from the palatal plane to the hyoid bone - 61.25mm; distance from the hyoid bone to Me - 36mm; tongue volume - 81.26cm3; oral cavity volume - 93.34cm3; oropharynx volume - 11.54cm3; minimum value in the axial section of oropharynx volume - 118.38mm2; anatomical balance - 87%.

at stage T1: the mean value of SNA was 81.620; SNB - 78.430; ANB - 1.620; Wits value - 0.86; FMA angle - 19.50; distance from the palatal plane to the hyoid bone - 61.13mm; distance from the hyoid bone to Me - 40.13mm; tongue volume - 81.26cm3; oral cavity volume - 103.43cm3; oropharynx volume - 15.71cm3; minimum value in the axial section of oropharynx volume - 202.38mm2; anatomical balance - 78.5%.

In Class III, the mean values were as follows:

at stage T0: the mean value of SNA was 78.500; SNB - 93.750; ANB - -5.250; Wits value - -9.17; FMA angle - 22.670; distance from the palatal plane to the hyoid bone - 55.67mm; distance from the hyoid bone to Me - 42.58mm; tongue volume - 90.44cm3; oral cavity volume - 107.57cm3; oropharynx volume - 12.42cm3; minimum value in the axial section of oropharynx volume - 126.08mm2; anatomical balance - 83.5%.

at stage T1: the mean value of SNA was 81.57; SNB - 80.430; ANB - 0.880; Wits value - 0.47; FMA angle - 18.340; distance from the palatal plane to the hyoid bone - 58.08mm; distance from the hyoid bone to Me - 43.67mm; tongue volume - 90.44cm3; oral cavity volume - 114.09cm3; oropharynx volume - 16.34cm3; minimum value in the axial section of oropharynx volume - 164.25mm2; anatomical balance - 79%.

So, we observe that there were no differences in tongue volume between the pre and postoperative periods since no surgical interventions were performed on the tongue. Also, statistically significant changes were not observed in the distance from the palatal plane to the hyoid bone, so this distance remained relatively constant. However, all other variables underwent significant volumetric changes, which will be further analysed in detail. Additionally, a detailed analysis of the changes in cephalometric parameters was not performed because the study's purpose is to evaluate volumetric changes in the oropharynx, oral cavity, minimum oropharynx cross-sectional area, anatomical balance, and changes in the distance from the hyoid bone to Me at stage T0 compared to T1.

7.2. Comparative evaluation of the oral cavity volume at stages T0 and T1 in Class II and Class III

The comparative analysis using the Wilcoxon test demonstrated statistically significant differences in the oral cavity volume between T0 (93.34 cm3) and T1 (103.43 cm3) in Class II, with a p-value of 0.014. The effect size was estimated at -1 (95% CI, -1.00, -1.0), indicating a significant increase in the oral cavity volume. Similarly, in Class III, there were statistically significant differences in the oral cavity volume between T0 (107.57 cm3) and T1 (114.09 cm3), with a p-value of 0.003. The effect size was also estimated at -1 (95% CI, -1.00, -1.0), indicating a significant increase in the oral cavity volume. This data shows an increase in the oral cavity volume of 10.8% in Class II and 6.1% in Class III between the two stages (T0 and T1).

7.3. The comparative evaluation of the oropharyngeal volume at stages T0 and T1 in Class II and Class III

The comparative evaluation using the Wilcoxon test varieties showed statistically significant differences in oropharyngeal volume between T0 (11.54 cm3) and T1 (15.71 cm3) in Class II. The effect size was estimated to be -0.89 (95% CI, -0.98 to 0.56), indicating a significant increase in oropharyngeal volume in Class II. Similarly, in Class III, there were statistically significant differences in oropharyngeal volume between T0 (12.42 cm3) and T1 (16.34 cm3). The effect size was estimated to be -0.97 (95% CI, -0.99 to -0.91), indicating a significant increase in oropharyngeal volume in Class III. In both Class II and Class III, there was a substantial increase in oropharyngeal volume, with a 36.1% increase in Class II and a 31.3% increase in Class III.

7.4. The comparative evaluation of the minimum cross-sectional area of the oropharynx at stages T0 and T1 in Class II and Class III

The comparative study using the Wilcoxon test varieties demonstrated the presence of statistically significant differences in the minimum cross-sectional area of the oropharynx at stage T0 (118.38 mm2) compared to T1 (202.38 mm2) in Class II. This difference was statistically significant (Wilcoxon test V = 0.00, p = 0.014), with an effect size estimated at -1 (95% CI, -1.00, -1.00). Similarly, in Class III, at stage T0, the minimum cross-sectional area of the oropharynx in the axial section was 126.08 mm2, and at stage T1, it was 164.25 mm2. These differences were also statistically significant (Wilcoxon test V = 0.00, p = 0.004), with an effect size estimated at -1.00 (95% CI, -1.00, -1.00). Therefore, there was an increase in the minimum cross-sectional area of the oropharynx in the axial section by 71.1% in Class II and 30.3% in Class III. Please note that the effect size is -1 in both cases, which indicates a large effect size, indicating a substantial change in the minimum cross-sectional area.

7.5. he comparative evaluation of the distance from the hyoid bone to Me at stages T0 and T1 in Class II and Class III

The comparative analysis, using the Wilcoxon test, demonstrated the presence of statistical differences in the distance from the hyoid bone to Me at stage T0 (36 mm) compared to T1 (47 mm) in Class II. Although statistically non-significant, it was clinically significant (Wilcoxon test V = 6.00, p = 0.106), with an effect size estimated at -0.67 (95% CI, -0.92, -0.03). In Class III, this trend was not observed, as the distance from the hyoid bone to Me at stage T0 was 42.58 mm, and at stage T1, it was 43.67 mm, statistically non-significant (Wilcoxon test V = 34.00, p = 0.723), with an effect size estimated at -0.13 (95% CI, -0.65, -0.47). Thus, there was an increase in the distance from the hyoid bone to Me of 30.6% in Class II and only 2.6% in Class III.

7.6. The comparative evaluation of anatomic balance at stages T0 and T1 in Class II and Class III

The comparative evaluation using the Wilcoxon test demonstrated the presence of statistically significant differences in anatomic balance at stage T0 (87%) compared to T1 (78.5%) in Class II, with a significant effect size (Wilcoxon test V = 36.00, p = 0.014), and the effect size estimated at 1.00 (95% CI, 1.00, 1.00). The same trend was observed in Class III, where at stage

T0, the anatomic balance was 83%, and at stage T1, it was 79%, and this was statistically significant (Wilcoxon test V = 78.00, p = 0.002), with an effect size estimated at 1.00 (95% CI, 1.00, 1.00). Therefore, the third hypothesis as well as the null hypothesis of the study is rejected because the value of anatomic balance has undergone statistically significant changes by decreasing in both classes.

8. DISCUSSION OF STUDY 2

The virtual surgical technology employed in this study proved to be highly successful. It allowed for the simulation and planning of surgical procedures in both a virtual environment and on 3D-printed anatomical models, as illustrated in Figure 3.

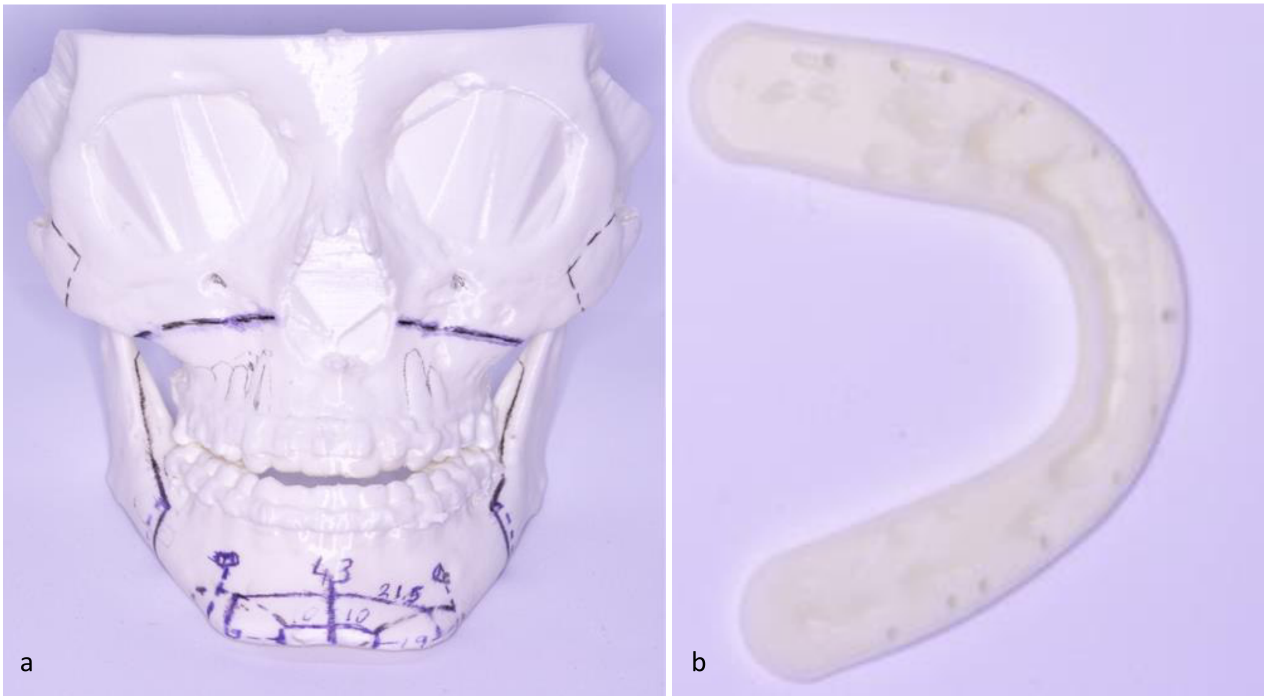

Figura 3. **a) Model anatomic obținut prin modelare prin extrudare. b) Splinturi ocluzale obținute prin expunerea digitala a luminii.**

The 3D-printed anatomical models were created using extrusion modelling technology. The advantage of this technology lies in its ability to provide a high level of precision at a reasonable cost. Consequently, these anatomical models can be used for a variety of medical purposes, including surgical planning, educational purposes, and medical training for students.

In the specialized literature, a series of advantages of these models are described, such as: customization (models can be customized according to the specific needs of the patient or medical case, allowing doctors to better plan surgical interventions or understand the specific anatomy of the patient); education and training (3D-printed anatomical models can be used to train students in the medical field, explain medical procedures to patients, or help patients better understand their condition); risk reduction and increased surgical precision (3D-printed anatomical models can help surgeons better plan surgical interventions and reduce risks, as they can simulate procedures before they are performed on real patients); cost-effectiveness.

In conclusion, 3D-printed anatomical models are an innovative and promising technology that can have a significant impact in the medical field, by improving surgical planning and medical education. Surgical guides for osteotomy and repositioning, together with occlusal splints, were manufactured using 3D printing technology with direct light exposure. The advantage of this technology lies in its high precision, albeit at a slightly higher cost compared to extrusion technology.

These osteotomy guides allowed for intraoperative placement of the osteotomy line in accordance with preoperative digital planning, while positioning guides assisted occlusal splints in moving the osteotomized fragments to their planned positions. These guides were used for both the upper and lower jaws, resulting in increased surgical precision and reduced operation time.

8.1. Conclusion of the study 2

Based on the limitations of the current study, we can conclude that contrary to the third and null hypotheses, anatomical balance underwent statistically significant changes with a decrease in values in both groups.

The clinical importance of this study lies in the fact that the planning of orthognathic surgery interventions must be carried out with caution, considering not only cephalometric and aesthetic parameters but also tongue volume, oropharyngeal volume, and the remaining space in the oral cavity.

Furthermore, the use of high-resolution medical images, 3D models, and virtual simulations allows medical professionals to make more informed decisions and provide a wider range of treatment options. However, virtual surgical planning technology is still relatively new and requires proper training and experience for its correct use. It's also important for the physician to consider that virtual planning is an additional method of surgical preparation, and final decisions must be made during the actual surgical procedure, taking into account all patient variables and characteristics.

In conclusion, virtual surgical planning technology represents a revolution in the medical field, bringing increased precision in surgical procedures, personalized treatments, and reduced risks for patients. This innovation facilitates communication between doctors and patients, enhancing understanding and procedure outcomes, all while saving time and resources in the operating room. However, it is essential to use it in conjunction with proper clinical expertise to achieve the best results.

GENERAL CONCLUSIONS

1. Virtual surgical planning technology, as reviewed in the specialized literature, demonstrates its increasing significance in the medical field. The use of high-resolution medical images, 3D models, and virtual simulations enables medical professionals to make more informed decisions and provide a broader range of treatment options. Additionally, this technology can reduce operating time while enhancing precision and efficiency.

2. Virtual segmentation of anatomical structures is the process by which a specific anatomical structure is precisely separated and defined in a medical image, such as a CT or MRI scan. Three-dimensional assessment using virtual segmentation of the volume of the oral cavity, tongue, upper airways, and the position of the hyoid bone aims to elucidate the correlations between tongue volume and other parameters. The study demonstrates that tongue volume is positively correlated with oral cavity volume, oropharyngeal volume, SNB angle and negatively correlated with ANB angle and Wits. Thus, we can conclude that increased tongue volume is correlated with mandibular prognathism.

3. Comparative evaluation of oral cavity and tongue volume and anatomical balance among different classes of dentomaxillofacial pathologies revealed statistically significant differences in 2 out of 3 parameters. Oral cavity and tongue volume are larger in Class III compared to Class I and Class II, while anatomical balance is relatively consistent across all three classes.

4. Comparative analysis of anatomical balance and volumetric changes in the oral cavity, upper airways, and hyoid bone position in the pre- and postoperative periods demonstrated statistically significant differences in all 4 parameters. Postoperatively, the volume of the oral cavity and oropharynx increased, the distance from the hyoid bone to Me decreased in Class III and increased in Class II, and anatomical balance values decreased in both classes.

5. In light of the limitations of the current study, we can conclude that anatomical balance underwent statistically significant changes, with a decrease in values in both classes.

Bibliography

1. Trifan V., Lupan I., Calfa S. Morbiditatea prin anomaliile dento-maxilare în Republica Moldova. *Medicina stomatologică*, vol. 1, no. 34, 2015.

2. Lin H.-H., Lonic D., Lo L.-J. 3D printing in orthognathic surgery - A literature review. *J Formos Med Assoc*, vol. 117, no. 7, pp. 547–558, Jul. 2018, doi: 10.1016/j.jfma.2018.01.008.

3. Hsu S. *et al.* Accuracy of a computer-aided surgical simulation protocol for orthognathic surgery: a prospective multicenter study. *J Oral Maxillofac Surg*, vol. 71, no. 1, pp. 128–142, Jan. 2013, doi: 10.1016/j.joms.2012.03.027.

4. Brodie A. Muscular factors in the diagnosis and treatment of malocclusions. *Angle Orthod*. 1953;23:71–7.

5. Sólya K. *et al.* Clinical aspects of congenital maxillofacial deformities. *Orv Hetil*, vol. 156, no. 37, pp. 1483–1490, Sep. 2015, doi: 10.1556/650.2015.30240.

6. Mostovei M., Solomon O., Chele N., Sinescu C., Duma V., Mostovei A. Electromyographic Evaluation of Muscle Activity in Patients Rehabilitated with Full Arch Fixed Implant-Supported Prostheses. *Medicina (Kaunas)*, vol. 59, no. 2, p. 299, Feb. 2023, doi: 10.3390/medicina59020299.

7. Mendes de Paula Gomes A., Adas Saliba Garbin C., W. da Silva Ferraz F., Adas Saliba T., Isper Garbin A. J. Dentofacial Deformities and Implications on Quality of Life: A Presurgical Multifactorial Analysis in Patients Seeking Orthognathic Surgical Treatment. J Oral Maxillofac Surg, vol. 77, no. 2, p. 409.e1-409.e9, Feb. 2019, doi: 10.1016/j.joms.2018.09.023.

8. Sankri-Tarbichi A. G. Obstructive sleep apnea-hypopnea syndrome: Etiology and diagnosis. *Avicenna J Med*, vol. 2, no. 1, pp. 3–8, Jan. 2012, doi: 10.4103/2231-0770.94803.

9. Chaudhry U., Cohen J. R., Al-Samawi Y. Use of cone beam computed tomography imaging for airway measurement to predict obstructive sleep apnea. *Cranio*, vol. 40, no. 5, pp. 418–424, Sep. 2022, doi: 10.1080/08869634.2020.1765602.

10. Bell R. B. A History of Orthognathic Surgery in North America. *J Oral Maxillofac Surg*, vol. 76, no. 12, pp. 2466–2481, Dec. 2018, doi: 10.1016/j.joms.2018.09.006.

11. Bahmanyar S., Namin A. W., Weiss R. O., Vincent A. G., Read-Fuller A. M., Reddy L. V. Orthognathic Surgery of the Mandible. *Facial Plast Surg*, vol. 37, no. 6, pp. 716–721, Dec. 2021, doi: 10.1055/s-0041-1735309.

12. Cevidanes L. H. S. *et al.* Superimposition of 3D cone-beam CT models of orthognathic surgery patients. *Dentomaxillofac Radiol*, vol. 34, no. 6, pp. 369–375, Nov. 2005, doi: 10.1259/dmfr/17102411.