UNIVERSIDADE DE SÃO PAULO
HOSPITAL DE REABILITAÇÃO DE ANOMALIAS CRANIOFACIAIS

RODRIGO BARBOZA NUNES

Three-dimensional analysis and airflow simulation using computational fluid dynamics of the upper airways in Treacher-Collins Syndrome

Análise tridimensional e simulação do fluxo de ar por meio de fluidodinâmica computacional das vias aéreas superiores na Síndrome de Treacher-Collins

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Dissertação constituída por artigo apresentada ao Hospital de Reabilitação em Anomalias Craniofaciais da Universidade de São Paulo para obtenção do título de Mestre em Ciências da Reabilitação, na área de concentração Fissuras Orofaciais e Anomalias Relacionadas.

Orientador: Prof. Dr. Cristiano Tonello

BAURU

2021

UNIVERSIDADE DE SÃO PAULO
HOSPITAL DE REABILITAÇÃO DE ANOMALIAS CRANIOFACIAIS

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DEDICATÓRIA

Aos meus amados pais, Otacir (in memoriam) e Gleide, à minha amada esposa Camila e aos meus amados filhos…

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“Não trabalhe apenas arduamente; não trabalhe por 5 ou 10 anos em um problema...
Meu conselho é um trabalho árduo e contínuo por 30 anos.”

Paul Tessier

Discurso de abertura do Presidente no Primeiro Congresso Internacional da
Sociedade Internacional de Cirurgia Crânio-Maxilo-Facial (1987)

RESUMO

RESUMO

Nunes, RB. Análise tridimensional e simulação do fluxo de ar por meio de fluidodinâmica computacional das vias aéreas superiores na síndrome de Treacher-Collins [dissertação]. Bauru: Hospital de Reabilitação de Anomalias Craniofaciais, Universidade de São Paulo; 2021.

Introdução: A síndrome de Treacher-Collins frequentemente está associada a obstrução da via aérea superior e comprometimento respiratório. **Objetivos:** O objetivo do estudo é avaliar tridimensionalmente as vias aéreas superiores de pacientes com a síndrome e analisar a dinâmica respiratória através de simulações com fluidodinâmica computacional. **Métodos:** A amostra consistiu em 14 tomografias computadorizadas de feixe cônico provenientes do arquivo do HRAC-USP; sendo 6 do sexo masculino e 8 do sexo feminino, com idades entre 6-20 anos. Os dados tomográficos foram exportados em DICOM (*Digital Imaging and Communications in Medicine*) para o software MIMICS 21.0 (*Materialism's Software Interactive Medical Image Control System*) e foram gerados e analisados os modelos realistas das vias aéreas superiores. Em seguida, os modelos foram exportados como arquivos de estereolitografia (STL) para o worbench ANSYS e realizadas simulações através do solucionador FLUENT. **Resultados:** A área seccional mínima da orofaringe apresenta valores entre 10,72-201,44 mm^2. Os ângulos formados entre a cavidade nasal/nasofaringe e a orofaringe variam entre 107,65 º-153,56º. O volume da cavidade nasal varia entre 5360.68-13582.96 mm^3, o volume da nasofaringe entre 179.06-3845.89 mm^3 e o volume da orofaringe entre 3338.18-20137.16 mm^3. A distância entre o ângulo da mandíbula e a localização da área seccional mínima varia entre +10.52 mm e -18.10 mm. A simulação fluidodinâmica revelou áreas de aumento da velocidade do ar e pressão dinâmica na orofaringe, grandes diferenças entre os fluxos das narinas na maioria das análises, importante área de constrição na nasofaringe em um caso e tendência a respiração oral em outra análise. **Conclusão:** Dados de volumetria e fluidodinâmica computacional sugerem que na síndrome de Treacher-Collins é comum a redução do volume e obstrução da cavidade nasal e nasofaringe, o que pode induzir o paciente à respiração oral e contribuir para o colapso das vias aéreas e agravamento das deformidades faciais.

Palavras-chave: Síndrome de Treacher-Collins, obstrução na via aérea superior, colapsibilidade da via aérea, volumetria, fluidodinâmica computacional

ABSTRACT

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Nunes, RB. Three-dimensional analysis and airflow simulation using computational fluid dynamics of the upper airways in Treacher-Collins Syndrome [dissertation]. Bauru: Hospital de Reabilitação de Anomalias Craniofaciais, Universidade de São Paulo; 2021.

Introduction: Treacher-Collins syndrome is often associated with upper airway obstruction and respiratory impairment. **Objective**: The objective of the study is to evaluate the upper airways of patients with the syndrome in three dimensions and to analyze the respiratory dynamics through simulations with computational fluid dynamics. **Methods:** The sample consisted of 14 cone beam computed tomographies from the HRAC-USP file; 6 male and 8 female, aged 6-20 years. The tomographic data were exported in DICOM (Digital Imaging and Communications in Medicine) to the software MIMICS 21.0 (Materialism's Software Interactive Medical Image Control System) and realistic models of the upper airways were generated and analyzed. Then, the models were exported as stereolithography (STL) files to the ANSYS worbench and simulations were performed using the FLUENT solver. **Results:** The minimum sectional area of the oropharynx presents values between 10.72-201.44 mm^2. The angles formed between the nasal cavity / nasopharynx and the oropharynx vary between 107.65 º-153.56º. The volume of the nasal cavity varies between 5360.68-13582.96 mm^3, the volume of nasopharynx between 179.06-3845.89 mm^3 and the volume of the oropharynx between 3338.18-20137.16 mm^3. The distance between the angle of the jaw and the location of the minimum sectional area varies between +10.52 mm and -18.10 mm. The fluid dynamics simulation revealed areas of increased air velocity and dynamic pressure in the oropharynx, great differences between the flow of the nostrils in most fluid dynamics analyzes performed, an important area of constriction in the nasopharynx in one case and oral breathing tendency in another analysis. **Conclusion**: Data from volumetry and computational fluid dynamics suggest that in Treacher-Collins syndrome is common the reduction in volume and obstruction of the nasal cavity/nasopharynx, which can induce the patient to mouth breathing and contribute to the collapse of the airways and worsening of facial deformities.

Keywords: Treacher-Collins syndrome, upper airway obstruction, airway collapse, volumetry, computational fluid dynamics.

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SUMMARY

1 INTRODUCTION

1 INTRODUCTION

Treacher-Collins syndrome (TCS) is a genetic disease, defined as a clinical entity from the 1900 report (Collins, 1900), which causes complex craniofacial malformations and is often associated with respiratory complications. The main clinical characteristics of TCS are derived from malformations in the 1st and 2nd branchial arches (Aljerian and Gilardino, 2019; Katsanis et al 2004; Ahmed et ak 2012; Chang et al 2012). Its phenotypic expression is variable, the clinical picture is composed of descending oblique eyelid clefts, malar hypoplasia, maxillary hypoplasia, mandibular hypoplasia and auricular abnormalities (Aljerian and Gilardino, 2019; Katsanis et al 2004; Ahmed et ak 2012; Chang et al 2012).

Patients with the syndrome require special attention from birth, as they may have impaired respiratory function from the first moments of life and require emergency / urgent interventions such as orotracheal intubation or tracheostomy (Aljerian and Gilardino, 2019; Katsanis et al 2004; Chang et al 2012)

The impairment of respiratory function occurs due to obstruction in different anatomical sites. Maxillary hypoplasia, one of the components of the syndrome, produces obstruction in the nasal cavity, nasopharynx. Studies have demonstrated reduced nasal cavity in patients with TCS (Aljerian and Gilardino, 2019; Katsanis et al 2004).

Specifically regarding mandibular involvement, different degrees of hypoplasia may be present in patients with TCS and any component of the mandible may be affected. Characteristically, the growth of the mandible is affected in more than one axis (Aljerian and Gilardino, 2019). In moderate to severe cases, mandibular hypoplasia causes secondary glossoptosis and airway obstruction by the base of the tongue, a finding similar to the airway obstruction observed in patients with Robin Sequence(RS) (Aljerian and Gilardino, 2019; Safi et al 2018).

During growth and development, children with the syndrome may also manifest changes due to impaired respiratory function manifested as obstructive sleep apnea (OSAS). OSAS worsens quality of life and can be fatal, requiring often surgical approaches in the airway such as osteogenic jaw distraction (Aljerian and Gilardino,

2019; Katsanis et al 2004; Safi et al 2018). However, as the airway of patients with TCS has additional challenges in management and worse surgical results when compared to patients with RS alone (Safi et al 2018).

Therefore, the study of upper airways in patients with TCS is of great relevance, both for investigating the obstructed anatomical site and for proposing appropriate treatments and assisting in surgical indication and planning.

2 OBJECTIVES

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The objective of this study is to evaluate the upper airways of patients with the syndrome in three dimensions and to analyze respiratory dynamics through simulations with computational fluid dynamics.

3 ARTICLE

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The article presented in this Dissertation was written according to the instructions and guidelines of The Cleft Palate-Craniofacial Journal.

Manuscript title: **Three-dimensional analysis and airflow simulation using computational fluid dynamics of the upper airways in Treacher-Collins Syndrome**

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ABSTRACT

Introduction: Treacher-Collins syndrome is often associated with upper airway obstruction and respiratory impairment.

Objective: The objective of this study is to evaluate the upper airways of patients with the syndrome in three dimensions and to analyze respiratory dynamics through simulations with computational fluid dynamics.

Methods: The sample consisted of 14 cone-beam computed tomography; 6 male and 8 female, aged 6-20 years. The tomographic data were exported from DICOM (Digital Imaging and Communications in Medicine) to the software MIMICS 21.0 (Materialism's Software Interactive Medical Image Control System), and realistic models of the upper airways were generated and analyzed. Next, the models were exported as stereolithography (STL) files to the ANSYS workbench, and simulations were performed using the FLUENT solver.

Results: The minimum sectional area of the oropharynx presents values between 10.72 and 201.44 mm^2. The angles formed between the nasal cavity / nasopharynx and the oropharynx vary between 107.65º and 153.56º. The volume of the nasal cavity varies between 5360.68 and 13582.96 mm^3, the volume of the nasopharynx between 179.06 and 3845.89 mm^3 and the volume of the oropharynx between 3338.18 and 20137.16 mm^3. The distance between the angle of the jaw and the location of the minimum sectional area varies between +10.52 mm and -18.10 mm. The fluid dynamics simulation revealed areas of increased air velocity and dynamic pressure in the oropharynx, great differences between the flow of the nostrils in most fluid dynamics analyses performed, an important area of constriction in the nasopharynx in one case and oral breathing tendency in another analysis.

Conclusion: Data from volumetry and computational fluid dynamics suggest that in Treacher-Collins syndrome, the reduction in volume and obstruction of the nasal cavity/nasopharynx are common, which can induce the patient to mouth breathing and contribute to the collapse of the airways and worsening of facial deformities.

Keywords: Treacher-Collins syndrome, upper airway obstruction, airway collapse, volumetry, computational fluid dynamics.

INTRODUCTION

Treacher-Collins syndrome is a genetic syndrome that causes craniofacial malformations and is often associated with upper airway obstruction and respiratory impairment. Patients with the syndrome require special attention from birth, as they may have impaired respiratory function from the first moments of life and require emergency or urgent interventions such as orotracheal intubation or tracheostomy. Monitoring during growth and development is also important. Literature reviews show that 54-95% of patients with the syndrome also suffer from obstructive sleep apnea. (Aljerian and Gilardino, 2019; Katsanis and Jabs, 2004)

Maxillary hypoplasia, one of the components of the syndrome, produces obstruction in the nasal cavity, nasopharynx and consequently and can change the breathing pattern. Mandibular hypoplasia, another striking component of the syndrome, produces obstructive effects mainly on the oropharynx, generating a picture similar to that of the Robin sequence, and it may manifest itself with obstructive sleep apnea. (Aljerian and Gilardino, 2019; Katsanis and Jabs, 2004)

Therefore, the assessment of different sites of upper airway obstruction and respiratory dynamics is essential and requires thorough clinical evaluation and complementary imaging tests.

With the advancement of technologies of necessity, the findings of imaging tests such as tomography can be better interpreted and recreate the entire airway in a computational environment and simulate airflow and respiratory dynamics. Thus, the objective of these technologies is to evaluate the upper airways and anatomical sites of obstruction for better planning of therapeutic intervention. (Faizal et al., 2020)

METHODS

This is a retrospective study reviewed and approved by the Research Ethics Committee. The sample consisted of 14 cone-beam computed tomographies; 6 male and 8 female, aged 6-20 years.

The three-dimensional models of the upper airways used for the analysis of volumetry and computational fluid dynamics were developed from tomography data

from tomographic scans. The tomographic data set was exported in DICOM format (Digital Imaging and Communications in Medicine) to MIMICS 21.0 software (Materialism's Software Interactive Medical Image Control System), and realistic models of the upper airways were generated and analyzed.

In MIMICS, the upper airway was recreated through a mesh using the threshold of -1024 and -480 Hounsfield units (HU). To define the reference points of the upper airways, two main planes were drawn: a plane passing through the anterior and posterior nasal spine, which divides the nasal/nasopharynx cavity from the oropharynx; and a plane passing between the anterosuperior border of the fourth vertebra (C4) to the menton. (Zheng et al., 2017) To divide the nasal cavity of the nasopharynx, a plane was drawn passing through the posterior limits of the nasal turbinates (Figure 1). MIMICS analysis and measurement tools were used to calculate the volume of the upper airways and nasal cavity, nasopharynx, and oropharynx; to calculate the minimum sectional area; to locate the minimum sectional area; to calculate the angles between the nasal cavity and the nasopharynx and oropharynx.

Subsequently, stereolithography (STL) models were generated in MIMICS and exported and processed in the Space Claim of the ANSYS workbench to remove noise. Next, the models were exported to ANSYS ICEM-CFD, where meshes were generated, the surface being generated through a triangular mesh, and the internal elements were generated using a predominantly unstructured tetrahedral mesh.

Between 9 and 12 prismatic layers were used close to the contours of the domain in order to keep the y+ less than or equal to 1. The ideal number of volumes to be used, verified in the mesh independence tests, varied between 5 and 7 million according to the dimensions of the case to be studied.

The boundary conditions adopted for the simulations through the Reynolds average simulation code (RANS – from the English Reynolds Average Navier-Stokes) adopted (FLUENT 2020 R2) were of atmospheric pressure in the nostrils and/or at the entrance of the oral cavity and speed prescribed in the pharynx. This speed was calculated considering an air flow of 600 ml/second, a value that corresponds to breathing during the resting state. (Xu et al., 2020; Bates et al., 2019) The other contours were considered rigid and with zero speed.

For flow simulations, the SST k-omega 3.5 turbulence model was used, which presents good numerical results for low flow values, such as the one adopted.

Convective terms were discretized through adoption of a second-order upwind approximation, and diffusive terms were discretized by centered approximations. The resolution scheme adopted was the coupling that solves speed-pressure simultaneously and is more suitable for solving single-phase flows that must reach a steady state. The simulations were interrupted when the continuity residue reached a value of less than 1.10^{-3}.

For analysis of the results, figures were generated where possible to check the speed and pressure at different points of the analyzed geometry. In addition, data were extracted in regions of greatest interest, such as in the region of oropharynx constriction and the nasal/nasopharynx cavity.

RESULTS

The present study showed that the minimum sectional area of the oropharynx is located in the retroglossal region in the 14 tomographies studied (Figure 2). The minimum sectional area of the oropharynx has values that vary between 10.72 mm^2 and 201.44 mm^2 (Figure 2) (Table 1), which represents a variation of up to 20 times in patients of similar age.

The fluid dynamics simulation confirmed the above findings and revealed areas of increased velocity and dynamic pressure, especially in the retroglossal region of the oropharynx (Figure 3).

Analysis of the angles formed between the nasal cavity / nasopharynx and the oropharynx revealed angles ranging between 107.65º and 153.56º (Figure 4) (Table 1).

The analysis of the nasal cavity volume revealed volume variations between 5360.68 mm^3 and 13582.96 mm^3. The analysis of the nasopharynx volume revealed volume variations between 179.06 mm^3 and 3845.89 mm^3 (Figure 4). The analysis of the nasopharynx volume revealed variations between 3338.18 mm^3 and 20137.16 mm^3 (Table 1).

Fluid dynamics simulation also revealed important differences between nostril flows in most dynamics analyses performed (Figure 3).

In the present study, the distance between the angle of the mandible and the location of the minimum sectional area was also evaluated. The distance varies

between +5.18 mm and -18.10 mm. In 3 of the 14 cases analyzed, the angle of the mandible coincides with the location of the minimum sectional area (Figure 4).

In the fluid-dynamic simulation of one of the cases, it was noted that the nasopharynx constriction area is more important than the oropharynx constriction area (Figure 4). An additional fluid-dynamic analysis was also performed comparing nasal breathing and oral breathing, and it was noted that the air flow that can be displaced by oral breathing is greater, but it can generate increased speed and dynamic pressure in the minimum sectional area (Figure 3).

DISCUSSION

Due to the anatomical complexity of the upper airways, it is essential to create accurate models that reproduce the characteristics of this structure. Some advanced software such as MIMICS is able to recreate the geometry of the upper airways in a computational domain and is validated for use in experimental investigations and simulations such as computational fluid dynamics. Some software is validated for fluid dynamics simulations, such as the ANSYS workbench, which contains the FLUENT simulator. (Faizal et al., 2020)

The use of computational fluid dynamics to simulate airflow in the upper airways can help in proposing a guideline for surgical treatment and also increase the cure rate. Computational fluid dynamics also has a benefit in gaining an understanding of the mechanism, treatment, and prevention of obstructive sleep apnea, as reported in a review on the topic. (Faizal et al., 2020) In the present study, the MIMICS and FLUENT tools were used mainly for the analysis of the upper airways.

The analysis of the minimal sectional areas of the oropharynx confirms data from the literature on the location of the minimum sectional area in the retroglossal region of the oropharynx. (Ma et al., 2015) The results of this study related to the minimal sectional area of the oropharynx still demonstrate wide variability in size between the surfaces. In fluid-dynamic simulations, an increase in velocity and dynamic pressure was noted in the region of the minimal sectional area of the oropharynx, and this can cause collapse in the airway.

The collapse of the upper airways is based on the Starling Resistor model, a theoretical model related to Bernoulli's theory. In this model, the oropharynx is

considered a compressible segment with a minimal sectional area. In the minimum sectional area there is an increase in velocity and dynamic pressure. Pressure reduction areas are found downstream and upstream from the minimum sectional area, generating negative intraluminal pressure (negative static pressure). Negative intraluminal pressure can obstruct the airway and stop airflow. (Suzuki and Tanuma, 2020)

Regarding the volume of the nasal airways, the present study is in agreement with the literature data on the reduction of the volume of the nasal cavity/nasopharynx, a study suggests a 38.6% reduction in the volume of the nasal airway in relation to the controls. (Ma et al., 2015) The results of this study show that the difference in size and airflow between nostrils is frequent. In some patients in the present study, the volume of the nasopharynx is also exceptionally low.

The analysis of the angle between the nasal/nasopharynx cavity and the oropharynx suggests that more acute angles hinder the flow of air from the nasal cavity to the oropharynx. However, it is known that the positioning of the cervical region and head can interfere in the analysis, changing permeability, volume, and airway resistance. (Wei et al., 2017)

Regarding the jaw, mandibular involvement is marked in Treacher-Collins syndrome and occurs in more than 78% of patients. Different degrees of mandibular hypoplasia may be present, and any component of the mandible may be affected. (Aljerian and Gilardino., 2019) A point analyzed in the present study is the proximity of the angle of the mandible to the location of the minimum sectional area.

In the literature, some authors suggest that oral breathing is a primary condition for the collapse of the pharyngeal airways based on the concept of the Starling resistor model. (Suzuki and Tanuma, 2020) The present study revealed that nasal obstruction is common in patients with TCS, which can induce mouth breathing in patients and its consequences for respiratory and craniofacial growth. An addition, a fluid dynamics simulation of mouth breathing corroborates the study mentioned above and demonstrates an increase in air velocity and dynamic pressure.

CONCLUSION

In Treacher-Collins syndrome the fluid dynamics simulation of the minimum sectional area demonstrates an increase in air flow velocity and dynamic pressure. Data from volumetry and computational fluid dynamics suggest that the reduction in volume and obstruction of the nasal cavity/nasopharynx are common, and these can induce mouth breathing in a patient and contribute to the collapse of the airways and worsening of facial deformities.

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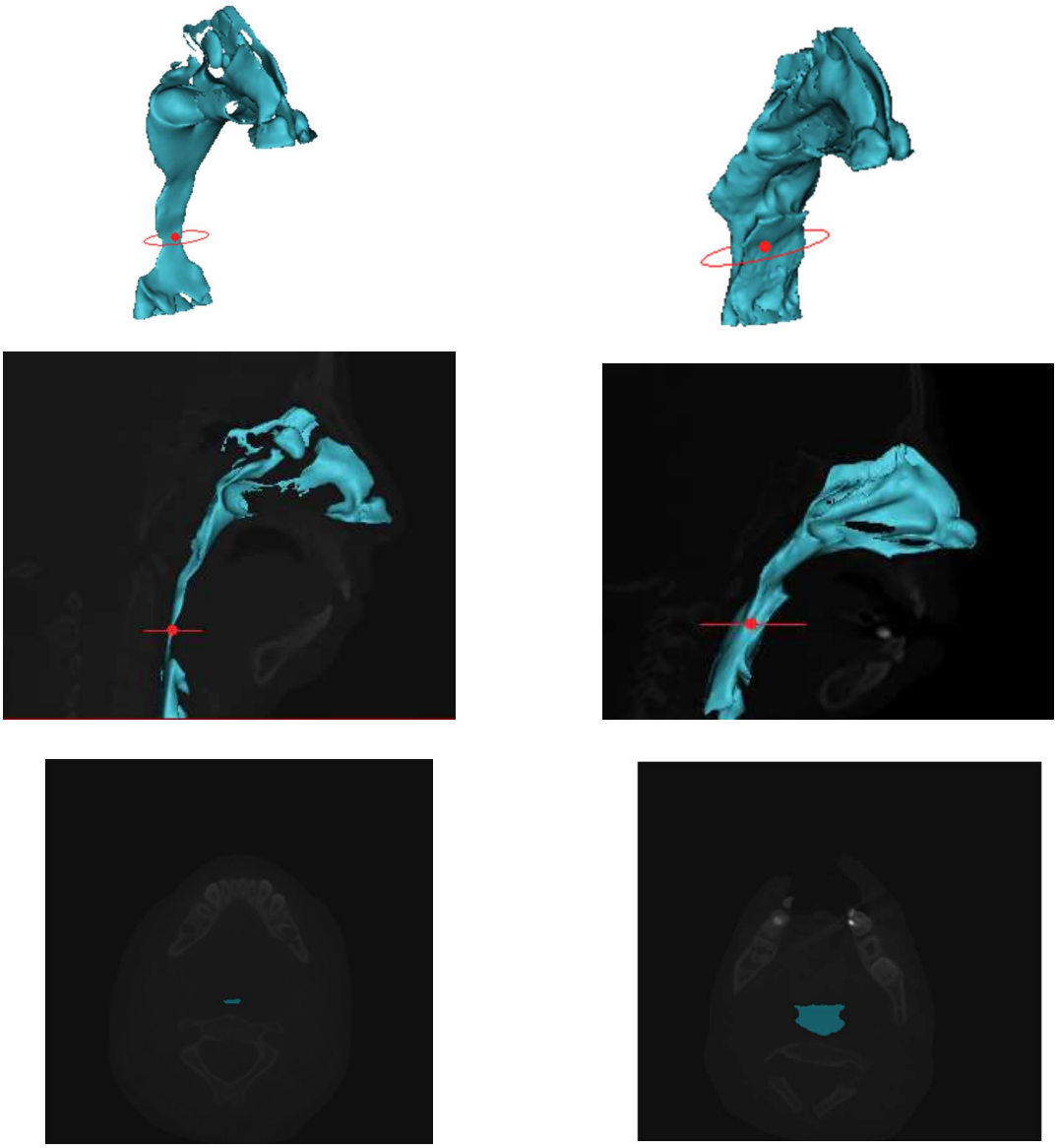
FIGURES

Methodology for three-dimensional reconstruction of the upper airways

Overlapping tomographic image and three-dimensional reconstruction of the upper airway	Representation of upper airway segmentation. The nasal cavity is in purple, the nasopharynx in yellow, the oropharynx in red, and the hypopharynx in blue.	Representation of upper airway segmentation. The nasal cavity is in purple, and the nasopharynx is in yellow.

Figure 1: Methodology for the reconstruction of the upper airways.

Comparison between the airways of Treacher-Collins syndrome patients

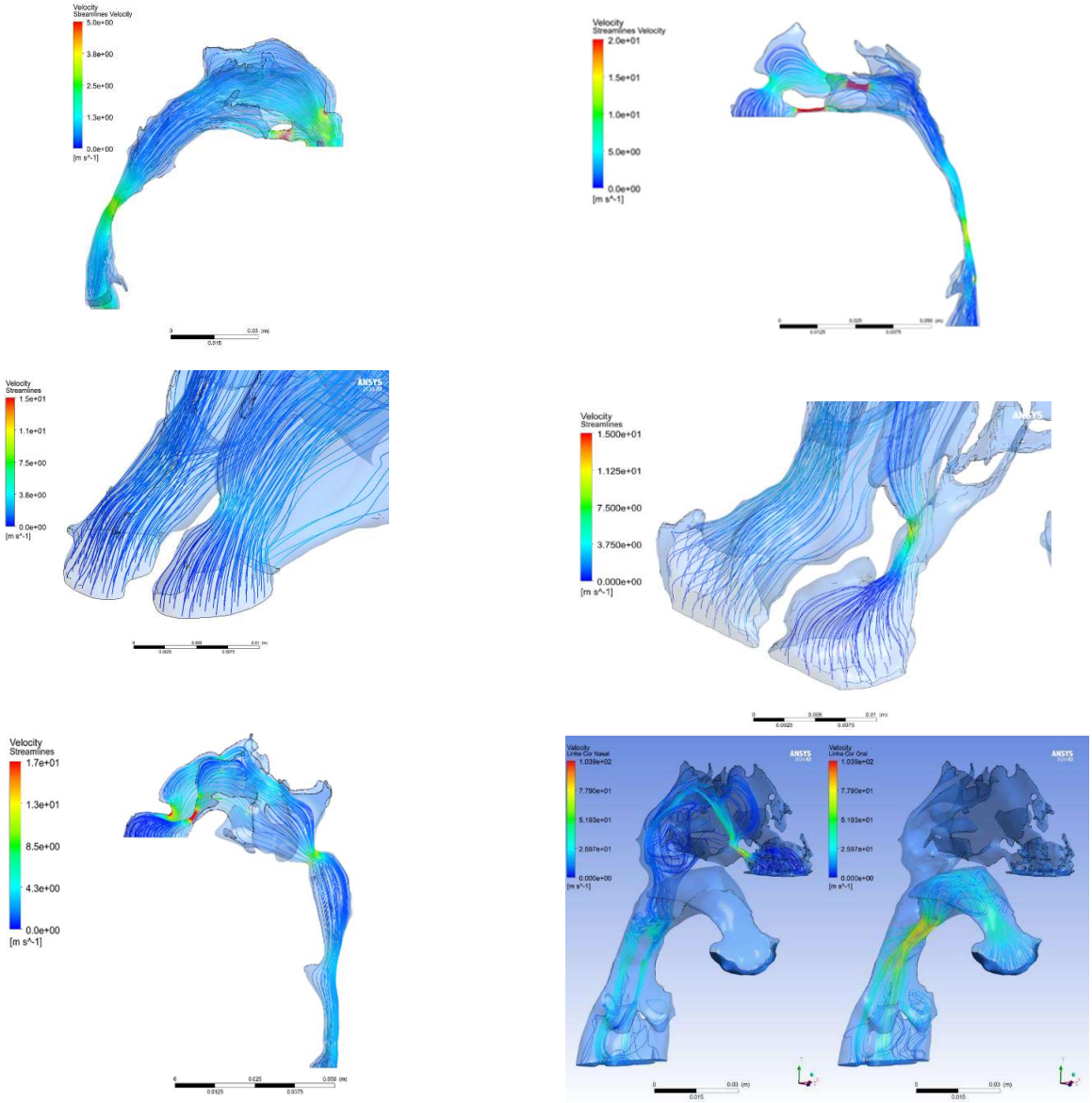


Line 1 – Three-dimensional reconstruction of the upper airway of a patient with Treacher-Collins syndrome aged 8 years and 8 months. Line 2 – Minimum sectional area in the retroglossal region of the oropharynx. Line 3 – Minimum sectional area of the upper airway (10.72 mm2; ~ 7.26 mm x 1.47 mm) seen in an axial section of the cone beam tomography.

Line 1 – Three-dimensional reconstruction of the upper airway of a patient with Treacher-Collins syndrome aged 9 years and 2 months. Line 2 – Minimum sectional area in the retroglossal region of the oropharynx. Line 3 – Minimum sectional area of the upper airway (201.44 mm2; ~ 20.42 mm x 9.86 mm) seen in an axial section of the cone beam tomography.

Figure 2: Comparison between the airways of patients with TSC.

Fluid dynamics simulation of the upper airways

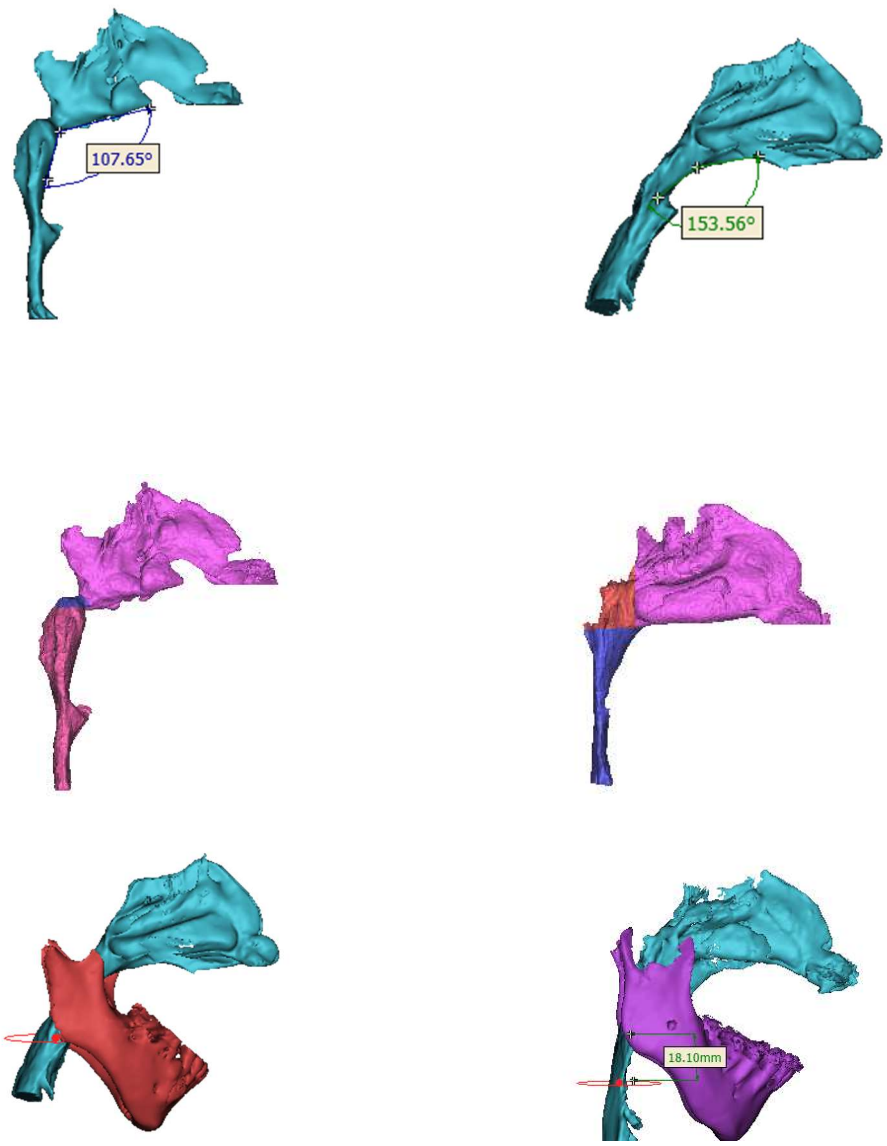


Line 1 – Area of increased speed in the retroglossal region of the oropharynx. Line 2 – Right nostril represents 43.58% of the nasal cavity flow and left nostril 56.42% of the nasal cavity flow. Line 3 – There is a difference in nasal flow and an important area of constriction in the nasopharynx with increased air velocity and dynamic pressure.

Line 1 – Area of increased speed in the retroglossal region of the oropharynx. Line 2 – Right nostril represents 70% of the nasal cavity flow and left nostril 30% of the nasal cavity flow. Line 3 – Representation of nasal and oral breathing. The fluid dynamics simulation demonstrates increased air velocity and dynamic pressure in oral breathing.

Figure 3: Fluid dynamics simulation of the upper airways

Analysis of upper airway volumetry



Line 1 – Representation of the angle (107.65°) between the nasal cavity / nasopharynx and oropharynx. Line 2 – Nasopharynx with very small volume represented in blue. Volume 179.06 mm3. Line 3 – Location coincidence between the angle of the mandible and the minimum sectional area.

Line 1 – Representation of the angle (153.56o) between the nasal cavity / nasopharynx and oropharynx. Line 2 – Nasopharynx of a patient with similar age 21.4 times greater. Volume 3845.89 mm3. Line 3 – Proximity between the angle of the mandible and the minimum sectional area.

Figure 4: Analysis of the volume of the upper airways.

TABLE I

Table I: Summary of the measurements carried out with MIMICS.

Name	Age in years	Gender	Minimum sectional area in mm^2	Nasal cavity volume mm^3	Nasopharynx volume mm^3	Oropharyngeal volume mm^3	Angle between the nasal cavity / nasopharynx and the oropharynx	Distance between the minimum sectional area and the angle of the mandible in mm
GSAT	06	Female	34.88	9372.72	2034.14	9250.93	131,08º	+10,52
MPEL	08	Female	10.72	7285.96	1243.88	3338.18	133,04º	-5.73
JPRH	08	Male	44.8	6179.23	179.06	4926.45	107,65º	-6.17
ISR	09	Female	28.32	7672.71	2726.03	3988.73	149,17º	0
MCSF	9	Female	201.44	8482.87	2283.93	10256.86	153,56º	0
LFFM	10	Male	26.24	5360.68	2242.39	6133.53	147,12º	-11.25
GCS	10	Female	101.28	9820.90	2658.26	10184.22	147,71º	-6.83
JAV	10	Male	63.81	8720.57	3829.89	13417.71	138,69º	0
LFPB	12	Male	49.44	6205.85	1057.84	6646.87	152,17º	-6.34
GMR	14	Female	46.4	11730.44	3845.89	6823.64	122,48º	+5,18
LAD	15	Female	31.84	10948.88	703.92	6853.52	133,97º	-3,36
MRV	17	Male	46.88	10065.38	1994.78	5671.84	130,94º	-10.32
LMB	20	Male	77.76	13582.96	2554.26	14161.06	147,67º	-2,63
BAS	20	Female	93.92	11058.00	2484.50	20137.16	126,50º	-18.10

4 FINAL CONSIDERATIONS

4 FINAL CONSIDERATIONS

1. The minimum sectional area of the oropharynx is located in the retroglossal region in patients with Treacher-Collins syndrome.

2. Fluid dynamics simulations have demonstrated an increase in velocity and dynamic pressure in the most contracted areas of the oropharynx.

3. Fluid-dynamic simulations and three-dimensional analysis confirm the reduction in volume and obstruction of the nasal cavity/nasopharynx Nasal obstruction can induce oral breathing in the patient, and oral breathing can contribute to the collapse of the airways.

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ANNEXES

ANEXO 1 – Declaração de uso exclusivo de artigo a ser publicado em periódico de língua inglesa

DECLARATION OF EXCLUSIVE USE OF THE ARTICLE IN DISSERTATION/THESIS

We hereby declare that we are aware of the article (Treacher-Collins syndrome is often associated with upper airway obstruction and respiratory impairment.) will be included in Dissertation of the student RODRIGO BARBOZA NUNES were not used and may not be used in other works of Graduate Programs at the Bauru School of Dentistry, University of São Paulo.

Bauru, 24 de maio de 2021.

RODRIGO BARBOZA NUNES Author	Rodrigo Barboza Nunes **Signature**
VICTOR AUGUSTO DE OLIVEIRA COELHO Author	Victor Augusto de Oliveira Coelho **Signature**
RENATA MAYUMI KATO Author	Renata Mayumi Kato **Signature**
DANIELA GAMBA GARIB CARREIRA Author	**Signature**
ROSELI MARIA ZECHI-CEIDE Author	Roseli M. Zechi Ceide **Signature**
LEANDRO FRANCO DE SOUZA Author	**Signature**
NIVALDO ALONSO Author	nivaldo alonso **Signature**
CRISTIANO TONELLO Author	Tonello **Signature**

ANEXO 2 - Termo de Permissão para uso de registros para fins científicos (fotografias, radiografias, tomografias e respectivos laudos odontológicos e médicos, vídeo imagens, amostra de voz/fala, registros clínicos, imagens de órgãos e espécimes para pesquisa, fins didáticos e publicação de artigos científicos)

TERMO DE PERMISSÃO PARA USO DE REGISTROS PARA FINS CIENTÍFICOS

Identificação da pesquisa:

a) Título do Projeto: Análise tridimensional e simulação do fluxo de ar por meio de fluidodinâmica computacional das vias aéreas superiores na Síndrome de Treacher-Collins
b) Pesquisador Responsável: Rodrigo Barboza Nunes
c) Curso/Área/Instituição: Mestrado / Reabilitação / HRAC

Eu, _____, brasileir__, residente no endereço _____, na cidade de _____ - ___, RG nº_____, CPF nº _____ responsável legal pelo paciente _____ que o pesquisador acima utilize seus **registros clínicos em prontuário, laudos e imagens da endoscopia das via aéreas, laudos e imagens da polissonografia, laudos e imagens tomográficas, e registros de imagens fotográficas tradicionais e tridimensionais para fins científicos** especificamente relacionados ao projeto de pesquisa acima identificado. Estou ciente de que não receberei nenhum ressarcimento ou pagamento pelo uso de meus registros e que poderei ser reconhecido(a) por terceiros.

Este consentimento pode ser revogado, sem qualquer ônus ou prejuízo à minha pessoa, a meu pedido, desde que a revogação ocorra antes da publicação.

Estou ciente de que, caso não aceite assinar este termo, receberei dos profissionais citados acima a mesma qualidade de atendimento e tratamento.

_____, _____ de _____ de 20___.

Assinatura: _____

Nome do responsável:_____

O pesquisador se compromete a manter a confidencialidade sobre os dados coletados, bem como a privacidade de seus conteúdos, preservando integralmente o anonimato e resguardando o sigilo das informações pessoais do participante da pesquisa.

Assinatura do Pesquisador Responsável: _____

ANEXO 3

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: ANA¿LISE DAS VIAS AE¿REAS SUPERIORES NA SI¿NDROME DE TREACHER COLLINS E SEQUE¿NCIA DE ROBIN

Pesquisador: Cristiano Tonello **Área Temática:**

Versão: 1

CAAE: 35247120.0.0000.5441

Instituição Proponente: Hospital de Reabilitação de Anomalias Craniofaciais da USP

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.181.268

Apresentação do Projeto:

O projeto de pesquisa com o título:"ANALISE DAS VIAS AÉREAS SUPERIORES NA SÍNDROME DE TREACHER COLLINS E SEQUENCIA DE ROBIN" do pesquisador Lucas Antonio da Costa sob orientação do Prof.Dr.Cristiano Tonello é apresentado a este Comitê para ser avaliado em seus aspectos éticos. O pesquisador anexou o seguinte resumo:

"A Sindrome de Treacher Collins (STC) e a Sequencia de Robin (SR) compartilham a deficiência mandibular como um achado clinico similar e consequente obstrução da via aérea superior e insuficiência respiratória. Volumes de via aérea e informações sobre a dinâmica do fluxo aéreo de indivíduos com essas condições clinicas ainda não foram estudados e comparados com indivíduos com mandíbulas morfologicamente normais.

O objetivo deste estudo será comparar a morfologia, dimensões e volume da via aérea superior bem como a dinâmica do fluxo aéreo de indivíduos com STC e SR e indivíduos com mandíbula de morfologia normal. A amostra consisti de tomografias computadorizadas (TC) provenientes do arquivo

do Hospital de Reabilitação de Anomalias Craniofaciais da Universidade de São Paulo. O Grupo STC

será composto por 17 indivíduos com STC e apresenta idade media de 11,5 anos (7 do sexo masculino, 10 do sexo feminino). O Grupo SR foi pareado em número de participantes, por sexo e idade com o grupo STC bem como o GRUPO CONT (controle). Avaliações quantitativas serão realizadas em reconstruções tridimensionais da face e via aérea posterior utilizando o software Mimics Innovation Suite 17.0 (Materialize, Leuven, Belgium). A realização das mensurações de fluidodinamica computacional serão realizados no software Fluent (ANSYS).

A comparação intergrupos será realizada por meio do teste t independente/Mann-Whitney e do teste

ANOVA e Tukey para a analise bidimensional e tridimensional, respectivamente ($p<0.05$)."

Objetivo da Pesquisa:

O pesquisador descreve como objetivo:

"Objetivo Primário:

O objetivo deste estudo será comparar as dimensões e a morfologia das vias aéreas bem como os achados a fluidodinamica computacional de indivíduos com Síndrome de Treacher Collins (STC) e Sequencia de Pierri Robin (SPR) comparados a um grupo controle (CONT).

Objetivo Secundário:

Avaliação de imagens 3D de Tomografia computadorizada das vias aéreas superiores.

Avaliação Computacional da Dinâmica de Fluidos com pareamento das informações dos participantes por sexo e idade."

Avaliação dos Riscos e Benefícios:

O pesquisador anexou a seguinte informação:

"Riscos:

Não haverá risco direto aos participantes uma vez que serão avaliados prontuários e exames de diagnósticos por imagem os quais se encontram nos arquivos do HRAC-USP, porém há o risco de exposição de informações dos participantes, mas será de todas as formas preservadas de acordo com as normas vigentes.

Benefícios:

Não haverá benefício direto, contudo o melhor entendimento da dinâmica dos fluidos-fluxo de ar e nos indivíduos comprometidos e suas possíveis diferenças permitida melhor acompanhamento e tratamento clínico."

Comentários e Considerações sobre a Pesquisa:

O projeto de pesquisa apresenta mérito e encontra-se bem estruturado.

O pesquisador utilizará em sua amostra as tomografias do período de janeiro de 2005 a janeiro de 2020,que se encontram disponíveis nos arquivos da instituição.

Considerações sobre os Termos de apresentação obrigatória:

Foram anexados os seguintes termos:

- TERMO DE COMPROMISSO DE TORNAR PÚBLICOS OS RESULTADOS DA PESQUISA E DESTINAÇÃO DE MATERIAIS OU DADOS COLETADOS;
- TERMO DE COMPROMISSO DO PESQUISADOR RESPONSÁVEL;
- CADASTRO DOS PESQUISADORES;
- FOLHA DE ROSTO DO HRAC;
- CARTA DE ENCAMINHAMENTO;
- TERMO DE COMPROMISSO, CONFIDENCIALIDADE E AUTORIZAÇÃO DE UTILIZAÇÃO DE DADOS EM PROJETOS DE PESQUISA;
- SOLICITAÇÃO DE DISPENSA DO TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO.

Recomendações:

Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:

Uma vez que o referido projeto não apresenta envolvimento ético recomendo sua aprovação por esse colegiado.

Considerações Finais a critério do CEP:

O pesquisador deve atentar que o projeto de pesquisa aprovado por este CEP refere-se ao protocolo submetido para avaliação. Portanto, conforme a Resolução CNS 466/12, o pesquisador é responsável por "desenvolver o projeto conforme delineado", se caso houver alterações nesse projeto, este CEP deverá ser comunicado em emenda via Plataforma Brasil, para nova avaliação.

Cabe ao pesquisador notificar via Plataforma Brasil o relatório final para avaliação. Os Termos de Consentimento Livre e Esclarecidos e/ou outros Termos obrigatórios assinados pelos participantes da pesquisa deverão ser entregues ao CEP. Os relatórios semestrais devem ser notificados quando solicitados no parecer.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Outros	DISPENSA_v2.pdf	30/07/2020 00:00:40	Renata Paciello Yamashita	Aceito
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1584501.pdf	16/07/2020 19:19:00		Aceito
Outros	Termo_Tornar_publico.pdf	16/07/2020 19:17:23	Cristiano Tonello	Aceito
Outros	esclarecimentos_pendencias.pdf	15/07/2020 19:34:14	Cristiano Tonello	Aceito
Projeto Detalhado / Brochura Investigador	PROJETO_V2.pdf	15/07/2020 18:05:20	Cristiano Tonello	Aceito
Outros	TERMO_COMPROMISSO.pdf	15/07/2020 17:47:14	Cristiano Tonello	Aceito
Outros	CADASTRO_PESQUISADORES_HRAC.pdf	15/07/2020 17:43:03	Cristiano Tonello	Aceito
Folha de Rosto	folha_de_rosto.pdf	15/07/2020 17:41:28	Cristiano Tonello	Aceito
Outros	Carta_Encaminhamento_CEP.pdf	02/07/2020 11:01:23	Cristiano Tonello	Aceito
Declaração de Instituição e Infraestrutura	AUTORIZACAO_USO_DADOS.pdf	02/07/2020 10:52:18	Cristiano Tonello	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	DISPENSA.pdf	02/07/2020 10:46:11	Cristiano Tonello	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

BAURU, 30 de Julho de 2020

Assinado por:
Renata Paciello Yamashita
(Coordenadora)

Brasil, que o TCLE será obtido "(novos casos serão coletados somente após a assinatura do termo de consentimento livre e esclarecido)". PENDÊNCIA PARCIALMENTE ATENDIDA.
Os autores atenderam à solicitação com remoção da frase "novos casos serão coletados somente após a assinatura do termo de consentimento livre e esclarecido" do capitulo de metodologia na Plataforma Brasil. PENDÊNCIA TOTALMENTE ATENDIDA.

Considerações sobre os Termos de apresentação obrigatória:
Carta de encaminhamento dos pesquisadores aos CEP;
Formulário HRAC;
Folha de Rosto Plataforma Brasil;
Termo de Compromisso de Manuseio de Informações;
Termo de Permissão para uso de Registros para Fins Científicos;
Termo de Compromisso de Tornar Públicos os Resultados da Pesquisa e Destinação de Materiais ou Dados Coletados;
Termo de Compromisso do Pesquisador Responsável.

Recomendações:
Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:
Como a pendência foi resolvida sugiro a aprovação do projeto.

Considerações Finais a critério do CEP:
O pesquisador deve atentar que o projeto de pesquisa aprovado por este CEP refere-se ao protocolo submetido para avaliação. Portanto, conforme a Resolução CNS 466/12, o pesquisador é responsável por "desenvolver o projeto conforme delineado", se caso houver alterações nesse projeto, este CEP deverá ser comunicado em emenda via Plataforma Brasil, para nova avaliação.
Cabe ao pesquisador notificar via Plataforma Brasil o relatório final para avaliação. Os Termos de Consentimento Livre e Esclarecidos e/ou outros Termos obrigatórios assinados pelos participantes da pesquisa deverão ser entregues ao CEP. Os relatórios semestrais devem ser notificados quando solicitados no parecer.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Endereço: Rua Silvio Marchione, 3-20
Bairro: Vila Nova Cidade Universitária **CEP:** 17.012-900
UF: SP **Município:** BAURU
Telefone: (14)3235-8421 **Fax:** (14)3234-7818 **E-mail:** cephrac@usp.br

USP - HOSPITAL DE REABILITAÇÃO DE ANOMALIAS CRANIOFACIAIS

Continuação do Parecer: 1.938.354

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_827392.pdf	12/02/2017 19:08:14		Aceito
Outros	oficio_resposta2.docx	12/02/2017 18:47:44	Renata Mayumi Kato	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_apos_parecer2.docx	12/02/2017 18:44:42	Renata Mayumi Kato	Aceito
Outros	oficio_resposta.docx	20/12/2016 19:28:52	DANIELA GAMBA GARIB CARREIRA	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_apos_parecer.docx	20/12/2016 19:28:04	DANIELA GAMBA GARIB CARREIRA	Aceito
Outros	Checklist_Prot_Pesq_107_2016.pdf	01/12/2016 11:48:55	Rafael Mattos de Deus	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Term_Assentimento.pdf	30/11/2016 08:51:59	DANIELA GAMBA GARIB CARREIRA	Aceito
Projeto Detalhado / Brochura Investigador	projeto_uep.pdf	30/11/2016 08:51:44	DANIELA GAMBA GARIB CARREIRA	Aceito
Outros	Term_Comp_Tornar_Publico_Dest_Mat.pdf	29/11/2016 22:39:22	DANIELA GAMBA GARIB CARREIRA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	termo_consentimento.pdf	29/11/2016 22:33:17	DANIELA GAMBA GARIB CARREIRA	Aceito
Outros	termo_permissao_uso_registro_fins_cient.pdf	24/11/2016 23:53:08	Renata Mayumi Kato	Aceito
Outros	Daniela_Term_Comp_Pesq_Resp.pdf	24/11/2016 23:42:07	Renata Mayumi Kato	Aceito
Outros	Daniela_Term_Comp_Manuseio_Inform.pdf	24/11/2016 23:38:37	Renata Mayumi Kato	Aceito
Declaração de Instituição e Infraestrutura	Daniela_Form_Cadastro_HRAC.pdf	24/11/2016 23:23:28	Renata Mayumi Kato	Aceito
Outros	Daniela_Carta_Encaminham.pdf	24/11/2016 23:22:50	Renata Mayumi Kato	Aceito
Folha de Rosto	Daniela_Folha_Rosto.pdf	24/11/2016 23:13:42	Renata Mayumi Kato	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

Endereço: Rua Silvio Marchione, 3-20
Bairro: Vila Nova Cidade Universitária **CEP:** 17.012-900
UF: SP **Município:** BAURU
Telefone: (14)3235-8421 **Fax:** (14)3234-7818 **E-mail:** cephrac@usp.br

USP - HOSPITAL DE REABILITAÇÃO DE ANOMALIAS CRANIOFACIAIS

Continuação do Parecer: 1.938.354

BAURU, 22 de Fevereiro de 2017

Assinado por:
Renata Paciello Yamashita
(Coordenador)

Endereço: Rua Silvio Marchione, 3-20
Bairro: Vila Nova Cidade Universitária **CEP:** 17.012-900
UF: SP **Município:** BAURU
Telefone: (14)3235-8421 **Fax:** (14)3234-7818 **E-mail:** cephrac@usp.br