Computational fluid dynamics simulation of changes in the morphology and airflow dynamics of the upper airways in OSAHS patients after treatment with oral appliances

Short title ：oral appliances and OSAHS

Song Baolong[1], Li Yibo[2], Sun Jianwei[1], Qi Yizhe[1], Li Peng[1], Li Yongming[1*], Gu Zexu[1*]

[1] State Key Laboratory of Military Stomatology &National Clinical Research Center for Oral Diseases& Shaanxi Clinical Research Center for Oral Diseases, Department of Orthodontics，School of Stomatology, The Fourth Military Medical University, Xi'an, P.R. China.

[2] Department of Orthodontics, Changsha Stomatological Hospital, Changsha, Hunan, P.R. China.

[*] Corresponding author:

Li Yongming, E-mail: liyongming@fmmu.edu.cn

Gu Zexu, E-mail: zeki99@163.com

Abstract

Objectives: To explore the changes of morphology and internal airflow in upper airways (UA) after the use of oral appliances (OAs) in patients with obstructive sleep apnea hypopnea syndrome (OSAHS), and investigate the mechanisms by which OAs function as a therapy for OSAHS.

Methods: Eight OSAHS patients (all male, aged 37-58, mean age 46.25) underwent CT scans before and after OA use. Then, computational fluid dynamics(CFD) models were built on the base of the CT scans using Mimics and ANSYS ICEM CFD software. The internal airflow of the upper airways was simulated using ANSYS-FLUENT and the results were analyzed using ANSYS-CFD-Post. The data were analyzed to identify the most important changes of biomechanical properties between patients with and without OA intervention. Upper airway morphology and the internal airflow changes were compared using *t*-tests and Spearman correlation coefficient analysis.

Results: The narrowest area of upper airways was found to be located in the lower bound of velopharynx, where the volume and pressure were statistically significantly increased ($P<0.05$) and the air velocity was statistically significantly decreased ($P<0.05$) in the presence of the OA($P<0.05$). After wearing OA, pharyngeal resistance was significantly decreased ($P<0.05$), from 290.63 to 186.25Pa/L, and the airflow resistance of the pharynx has reduced by 35.9%.

Conclusion: The enlargement of the upper airway after wearing the OA changed its airflow dynamics, which decreased the negative pressure and resistance in narrow areas of the upper airways. Thus, the collapsibility of the upper airways was reduced and patency was sustained.

Keywords Obstructive sleep apnea hypopnea syndrome; Computational fluid dynamics; Three-dimensional reconstruction; Upper airways; Oral appliance

Introduction

The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common respiratory sleep disorder that is characterized by repeated partial or complete obstruction of upper airway at the end-expiratory phase during sleep [1]. OSAHS is a highly prevalent disorder which can have serious effects on daily functioning, social life and general health and may even have potentially life-threatening consequences. Prevalence studies estimate that 24% of men and 9% of women in middle age are affected by OSAHS [2]. Furthermore, the prevalence of OSAHS increases with age and in older persons (≥ 65 years) there is a 2- to 3-fold higher prevalence compared with those in middle age (30–64 years) [3]. There is increasing evidence that untreated OSAHS is associated with ischemic heart disease, arterial hypertension stroke [4,5], hypertension [6], daytime sleepiness, and road traffic accidents [7]. Thus, it is now recognized that OSAHS is a serious public health problem.

Treatment modalities for OSAHS includes non-surgical treatments such as weight loss, nasal continuous positive airway pressure (CPAP) and oral appliance (OA) [8-10], as well as surgical treatments such as uvulopalatopharyngoplasty (UPPP), hyoid myotomy and suspension, mandibular osteotomy with genioglossus advancement, adenotonsillectomy and maxillomandibular surgery [11-12].Since Sullivan et al. first reported the use of CPAP therapy in OSAHS in1981[9], CPAP has been considered as an effective method for the treatment of OSAHS. However, its clinical effectiveness is limited by poor acceptance and tolerance, as well as suboptimal compliance of patients [13-14]. Disadvantages of UPPP surgery include the pain and expense of the procedure, but also a relatively poor long-term success rate [15]. Since Robin et al. first introduced an intraoral appliance to treat upper airway obstruction in 1934[10], OAs have

increasingly been used in the treatment of OSAHS as a viable alternative to CPAP. While the curative effect of OAs was affirmed by increasing numbers of studies [16], the recent research on the specific mechanism by which OAs affect OSAHS is mainly limited to morphological descriptions [17-19]. It is generally believed that after wearing an OA, the tissue surrounding the upper airways of OSAHS patients is pulled out, and the upper airways are expanded, so that local stenosis is released or entirely abrogated. Hence, the patient can breathe easily and have a higher blood oxygen saturation, a lower snoring sound or even no snoring. However, what happens to the flow dynamics of the upper airways after wearing the OA is still not clear. This study therefore probed the flow dynamics of the upper airways of patients with OSAHS in order to understand the relationship between the morphology of upper airways and their function. Ultimately, the data gathered here improves the understanding of the pathogenesis of OSAHS and the therapeutic mechanism of OA.

Materials and Methods

Participants

This study protocol was approved by the Ethics Review Committee at the College of Stomatology, Fourth Military Medical University. It conforms to relevant national and international guidelines. Written informed consent was obtained from each patient. In this study 8 Chinese adult OSAHS patients, aged 37 to 58 years (mean age 46.25 years), were selected. All OSAHS patients had an AHI index higher than 5 and lower than 40 per hour on standard polysomnography (PSG). Those who had active temporo-mandibular disfunction were excluded from the study as well as patients

93 suffering from untreated caries and periodontal disease, completely edentulous patients
94 and those having an insufficient number of remaining teeth.

95 Three-dimensional reconstruction of upper airways

96 All patients underwent a PSG detection and a CT scan before and three months
97 after wearing the OAs. CT scans from the lower rim of the epiglottis to the supraorbital
98 margin were performed with a spatial resolution of 512×512 pixels and zero space,
99 1.25mm thickness, to obtain DICOM (Digital Imaging and Communication in
100 Medicine) format images. Scanning was performed with the patients awake, in supine
101 and neutral position during one breath hold at the end of a normal inspiration. All
102 patients were scanned by the same radiology technicians in the Department of
103 Radiology, Fourth Military Medical University, Xi'an, China. The CT scans were used
104 to construct three-dimensional models for the analysis of fluid dynamics.

105 The DICOM image data of the patients was then loaded into Mimics 10.0
106 (Materialise NV, Leuven, Belgium). Subsequently, a segmentation of the upper airways
107 was done based on the Hounsfield unit (HU), a measure of the electron density of the
108 tissue, assigned to each pixel in the series of DICOM images. The HU had values from
109 1024 to 3071. For the upper airways, a range of HU between -1024 to -400 is regarded
110 as very good results [20]. The segmented region was successfully converted to a 3D
111 model, smoothed in Magics9.9 (Materialise, Leuven, Belgium), and finally exported
112 for further analysis (Fig 1).

113

Fig 1. Three-dimensional reconstruction of a patient's upper airways, without(a) and with (b) an oral appliance.

Three-dimensional mesh model building

To prepare the segmented upper airway model for CFD calculations, a computational grid was created using ICEM-CFD 14.0 (ANSYS, Canonsburg, PA, USA), in which both global and local mesh controls were used to improve mesh quality (Fig 2), followed by a mesh-independent test.

Fig 2. Three-dimensional mesh model of the upper airways.

Numerical simulation of the upper airways

The ANSYS 14.0-Fluid Dynamics-FLUENT 14.0 commercial code was used to solve the Reynolds averaged Navier–Stokes equations for the steady airflow simulation. The flow was assumed to be steady, homogeneous, incompressible, adiabatic and Newtonian. The density of air was set at 1.225 kg m^{-3}, and the viscosity was assumed to be 1.789 x10^{-5} kg m^{-1} s^{-1}. We applied the Reynolds averaged Navier-Stokes equation (RNG k-epsilon turbulence model) to simulate the airflow status. A second-order pressure discretization scheme was used for the pressure calculations, and a second-order upwind scheme was used for the momentum and turbulence transport equations. We used the SIMPLE algorithm to solve the pressure–velocity coupling. Atmospheric pressure was imposed at both nostrils, and a constant flow rate of 200 ml/s was applied at the planes in the pharynx. The upper airway wall was assumed to be no-slip (u=v=0).

To obtain a better initialization field and convergence acceleration, multigrid initialization was used to optimize the flow field.

The results obtained using Fluent were post-processed using CFD-Post (ANSYS, Canonsburg, PA, USA) to obtain the contours and vectors, and the function calculator was used to acquire values for the pressure gradient, pressure and velocity in cross-sectional planes at specified points in the upper airways.

Cross-sections selection of the CFD model

The magnitude of airflow velocity in the upper airways was calculated at the five different cross-sections shown in Fig 3. Section 1 constitutes the beginning of the nasopharynx, section 2 is located at the lower bound of the nasopharynx (upper bound of the palatopharynx), and section 3 at the lower bound of the palatopharynx (upper bound of the glossopharynx). Sections 4 and 5 are located the top and the base of the epiglottis, respectively.

Fig 3. Selected sections of the CFD model.

Statistical analyses

Statistical analysis was performed using SPSS 17.0 (IBM Corp., Armonk, NY, USA). The paired *t*-test was adopted to compare the changes of the cross-sectional area, volume, velocity, pressure and resistance before and three months after wearing the OAs. The association between AHI change, volume change and resistance change were analyzed using the coefficient of product moment correlation (Pearson's correlation

coefficient). For all analyses, a probability value of P <0.05 was considered to indicate differences that are statistically significant.

Results

Morphological changes in the upper airways after use of the OAs

As shown in Tables 1 and 2, the volume of the nasopharynx region of patients with and without OAs use showed no significant difference (P>0.05), while that of the palatopharynx, glossopharynx and hypopharynx increased significantly(P<0.05). Prominent changes occurred mainly in the palatopharynx (increased by 39.54%) and glossopharynx (increased by 44.48%). The narrowest region of the upper airway was located at section 3 (the lower bound of the palatopharynx). Notably, its cross-sectional area increased significantly by 129.06% with the OAs(P<0.05).

Table 1. Volumetric changes in the airways with and without the OAs (cm^3).

region	Without OAs	With OAs	*p*-value	Deformation rate
	Mean ± SD	Mean ± SD		
nasopharynx	2.3333±0.7377	2.3523±0.8019	0.542	0.81
palatopharynx	2.4482±0.8352	3.4161±0.5426	< 0.001**	39.54
glossopharynx	2.2759±0.3638	3.2882±0.6140	0.001**	44.48
hypopharynx	3.6281±0.8202	4.0505±0.6589	0.047*	11.64

total volume	10.6854±2.2740	13.1071±2.180	< 0.001**	22.67

* P<0.05; ** P<0.01

Table 2. Changes in the cross-sectional area of selected upper airway sections from patients with and without OAs (cm^2).

Section	Without OAs	With OAs	p-value	Deformation rate
	Mean ± SD	Mean ± SD		
A	3.1441±0.7028	3.1643±0.6017	0.283	0.64
B	2.1608±0.9456	2.3389±0.5536	0.058	8.24
C	0.2150±0.1032	0.4925±0.1018	0.001**	129.06
D	1.6430±0.6109	2.5817±0.5691	0.018*	57.13
E	2.3573±0.4370	2.6032±0.4092	0.035*	10.43

* P<0.05; ** P<0.01

Airflow velocity changes in the upper airways

The change tendencies of airflow velocity in the UAs of 8 patients were similar to those illustrated in Fig 4. Without the OA, the airflow velocity was turbulent, while it became smooth and steady after using OAs. The maximum airflow velocity in the narrowest part of the pharynx, i.e. the palatopharyngeal region, was determined both pre- and post-treatment. As can be seen in Table 3, there was no difference in the airflow velocity in the nasopharynx and epiglottis pre- and post-treatment (P>0.05), while that

of palatopharynx and glossopharynx decreased significantly($p<0.05$), from 11.55 m/s to 8.81 m/s post-treatment, representing a decline of 23.7%. The dif

ference was especially significant in the lower bound of palatopharynx ($p<0.01$).

Fig 4. Velocity vectors in the mid–sagittal plane of a patient's upper airways.

Table 3. Airflow velocity changes in different selected sections of the upper airways form patients with and without the OAs (m/s).

section	Without OAs	With OAs	p-value	Deformation rate
	Mean ± SD	Mean ± SD		
A	0.84±0.31	0.78±0.24	0.183	-7.14
B	1.24±0.43	1.03±0.55	0.048*	-16.94
C	11.55± 2.18	8.81±2.47	0.007**	-23.72
D	4.86±1.17	4.34±1.53	0.036*	-10.70
E	2.75±0.74	2.60±0.40	0.095	-5.45

Pressure changes in the upper airways of patients before and after using OAs

The pressure change trends in the UA of 8 subjects were similar to what was outlined in Fig 5. The pressure distribution in the UA became steady with OA. Both the initial and final minimum pressure was detected at the lower boundary of the palatopharynx, a narrow region in the UA. Moreover, the maximum flow rate was observed at this point, conforming with Bernoulli's equation. As shown in Table 4, after

195 wearing the OAs, no statistically significant difference of pressure was observed in the
196 nasopharynx and epiglottis ($P<0.05$), while pressure in the palatopharynx and
197 glossopharynx increased remarkably($P<0.05$), especially at the lower boundary of the
198 palatopharynx($P<0.01$), rising from 101240.25 to 101264.13Pa. The pressure in the
199 inlet of the nasal cavity was defined as the baseline (the practical atmospheric pressure
200 is 101325Pa), the pressure at the lower boundary of the palatopharynx without AOs
201 was calculated as -84.75Pa, and it transformed into -60.87Pa with the AOs, thus
202 denoting a pressure drop of 28.2% in the narrowest part of the UAs.

203

204 **Fig 5. Pressure contours in the mid–sagittal plane of a patient's upper airways.**

205 Table4. Pressure changes in different sections of the upper airways from patients with
206 and without OAs(Pa).

Section	Without OAs	With OAs	p-value
	Mean ± SD	Mean ± SD	
A	101303.61±18.37	101305.24±16.79	0.093
B	101308.52±8.46	101313.48±6.37	0.065
C	101240.25±16.24	101264.13±23.10	0.005**
D	101263.49±12.12	101272.34±13.47	0.039*
E	101255.58±20.66	101261.73±18.36	0.063

207

208 # Changes of resistance in the upper airways

209 Airflow resistance denotes the specific pressure needed to push a defined
210 volume of gas over a designated distance in a defined time. It can be described using
211 the formula: R=ΔP/Q, where ΔP indicates the pressure drop, Q indicate the gas flow,
212 which had a set value of 0.2L/s. As shown in Table 5, with the effect of the OAs, the
213 pharyngeal resistance decreased significantly($p<0.05$), from 290.63Pas/L to
214 186.25Pas/L, a decline of 35.9%.

215 Table 5. Changes of resistance in the pharynx of patients with and without OAs (Pas/L).

Patient	Without OAs		With OAs	
	ΔP	R	ΔP	R
1	50	250	29	145
2	42	210	35	175
3	85	425	32	160
4	58	290	56	280
5	82	410	53	265
6	36	180	33	165
7	43	215	31	155
8	69	345	29	145
Mean ± SD	-	290.63±93.63	-	186.25±54.30

216 Note: t=3.182 p=0.015

217 Correlations among AHI, pharyngeal volume and resistance
218 changes in the pharynx with and without OAs

219 The detailed data on AHI, pharyngeal volume and pharyngeal resistance
220 changes which was collected before and after the 8 patients used OAs is shown in Table

221 6. Fig 6 shows that there was a negative correlation between pharyngeal resistance
222 changes and pharyngeal volume changes (r= -0.786 p=0.0218, Fig 6-a) as well as
223 pharyngeal volume changes and AHI changes (r= -0.81 p=0.0158, Fig 6-b), while there
224 was a positive correlation between pharyngeal resistance changes and AHI changes
225 (r=0.976 p=0.0008, Fig 6-c).

226 Table 6. The changes of AHI, pharyngeal volume and pharyngeal resistance in OSAHS
227 Patients with and without OAs (cm^2).

patient	Without OAs	With OAs	Deformation rate of pharyngeal volume with OAs (%)	Deformation rate of pharyngeal resistance with OAs (%)
	AHI	AHI		
1	21.3	2.2	35.45	-42.00
2	23.2	5.1	28.08	-16.67
3	27.6	1.8	29.82	-62.35
4	16.1	16.0	13.73	-3.45
5	21.8	3.4	17.32	-35.37
6	14.3	12.1	10.31	-8.33
7	17.5	1.9	20.45	-27.9
8	24.2	1.4	34.46	-57.97

228

229

Fig 6. The correlation analysis between the pharyngeal volume changes and pharynx resistance changes(a); between AHI changes and pharyngeal volume changes (b); between AHI changes and pharyngeal resistance changes(c).

Discussion

airflow dynamics of the upper airways and OA

The nasopharyngeal airways almost remained unchanged after using OAs, while the cross-section of the glossopharyngeal and palatopharyngeal airways significantly increased, and that of the hypopharyngeal airway increased slightly. These results demonstrate that OAs mainly act on the glossopharyngeal and palatopharyngeal airways. In the narrow region behind the soft palate, the CSA increased obviously by 129.06% ($P<0.05$). Airway enlargement decreased the possibility of a collapse and obstruction of the UAs during the respiratory process, thus providing better flow conditions. This was confirmed by the analysis of velocity and pressure.

After wearing the appliance, the respiratory flow rate becomes more balanced, especially in the palatopharynx and glossopharynx, where it decreased from 11.55 m/s to 8.81 m/s, resulting in a reduced impact of the airflow on the pharyngeal cavity wall and thus preventing damage to the airway mucosa. The reduced impact will correspondingly reduce the patient's snoring which arises from high frequency vibrations of soft tissue under the conditions of violent airflow impact on the pharyngeal cavity wall. In the presence of the OA, negative pressure in the narrow area of the palatopharynx decreased significantly from -84.75Pa to -60.87Pa. Within the entire upper respiratory tract, only the palatopharyngeal region consists of soft tissue without bone support, and thus can collapse under the effect of negative pressure. Reducing the

253 negative pressure diminishes airway compliance, and therefore reduces the
254 collapsibility of airways and improves the patients' symptoms.

255 Air resistance in the upper respiratory tract is an important index for the
256 evaluation of the ventilation degree, and the resistance value determines the difficulty
257 of inspiration. High resistance indicates that it is difficult for gas to flow in the upper
258 airways, while the converse indicates that it is easy. Resistance in the pharynx decreased
259 significantly by 35.9% ($P<0.05$), which eased the air circulation in the UAs, further
260 reducing the probability of airway collapse.

261 By enlarging the upper airways, the OA altered the dynamic characteristics of
262 airflow in the upper respiratory tract, and bringing the morphology into correspondence
263 with function is the fundamental element for the success of OSAHS therapy. Therefore,
264 when devising an OA, one should consider how to achieve changes in airflow pressure
265 and resistance, not merely changes of morphology.

266 AHI, total volume and resistance of the pharynx

267 AHI, introduced in the 1980s, is widely applied as an important indicator in the
268 diagnosis, classification and efficiency evaluation of OSAHS, both in clinical and
269 academic settings. However, investigators found some deficiencies in using AHI to
270 assess efficiency. A study indicates that, after the use of OA, different patients obtained
271 the same AHI, but they suffered from different degrees of hypoxemia[21]. Similar studies
272 have also shown that although patients obtain the same AHI after the use of OA, the
273 probability of cardiovascular disease events was actually different[22]. Hence, we aimed
274 to identify auxiliary indicators to inspect OA efficacy. We conducted a correlation
275 analysis among the AHI, total volume and resistance of the pharynx before and after

the use of OA. There was a negative relationship between pharyngeal volume changes and AHI changes in patients with OA, as well as a positive relationship between pharyngeal resistance changes and AHI changes. Therefore, we extrapolated that the changes of pharyngeal volume and resistance may be auxiliary indicators to test the effect of OAs on OSAHS. Nevertheless, a multitude of clinical data still needs to be gathered and a thorough correlation analysis between these indicators and clinical outcomes needs to be conducted to verify this deduction.

limitations of the study

Nevertheless, some deficiencies of this study should also be considered. Firstly, the CT data was obtained with patients in the waking state, while respiratory collapse in OSAHS patients mainly occurs during sleep. Secondly, the study ignores the influence of soft tissues, such as muscle tension, which is vital for the stability of the respiratory tract during sleep, as well as changes and movement of the soft palate, tongue root and other soft tissues related to the respiratory tract may be important factors related to the pathophysiology of OSAHS. While in this study we failed to take the effect of soft tissue into consideration, the most likely site of collapse in the respiratory tract depends on respiratory compliance, a certain degree of muscularization, the so-called "tissue stress" and internal respiratory pressure. Therefore, high-resolution CT data and fluid-structure interaction (FSI) numerical simulation technology can be used to further support the present results. However, FSI technology is still in the early research phase and has been applied only to two-dimensional models [23]. To be applied in practical research on the oropharyngeal tract, FSI technology needs to overcome a major problem of data availability for particular material properties of tissues such as tongue and soft palate. In addition, the elastic modulus and Poisson's

ratio of tissues measured in vitro may not have a close correlation with tissue deformability in vivo. Therefore, recording CT images of patients in the sleeping state and attaining reliable soft tissue material properties for use in conjunction with Fluid-structure interaction technology(FSI) could enable the analysis of the impact coefficient of soft tissue surrounding the airways and air in the respiratory tract. The effects of these properties on respiratory stability will be the focus of our future research.

In spite of these limitations, our results show that analyzing the dynamic airflow changes in the upper airways in the presence of OAs by applying CFD technology helps us to recognize the mechanism by which OAs exert their effect in OSAHS treatment and the interactive relationship between structure and function of the upper airways, providing theoretical basis for clinical application of OA in OSAHS treatment.

Conclusions

In OSAHS that received OA treatment, changes in the morphology and flow dynamics of the upper airways were mainly observed in the palatopharyngeal and glossopharyngeal region. When wearing the OA, the upper airway was enlarged, dynamic airflow characters were changed, and negative pressure as well as resistance in the narrow area of the UAs was diminished, thus making the upper airways more resilient to collapse as well as maintaining their patency.

References

[1] Malhotra A, White DP. Obstructive sleep apnoea. Lancet. 2002;360(9328):237-245.

[2] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The Occurrence of Sleep-Disordered Breathing Among Middle-Aged Adults. New England Journal of Medicine. 1993;328(17):1230-1235.

[3] Bixler EO, Vgontzas AN, Ten-Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: I. Prevalence and severity. American Journal of Respiratory & Critical Care Medicine. 1998;157(1):144-148.

[4] Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, et al. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. Journal of the American Medical Association. 2012;307(20):2161-2168.

[5] Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005 Mar;365(9464):1046-1053.

[6] Peppard PE, Young T, Palta M, Skatrud J. Prospective Study of the Association between Sleep-Disordered Breathing and Hypertension. New England Journal of Medicine. 2000;342(19):1378-1384.

[7] Naegele B, Pepin JL, Levy P, Bonnet C, Pellat J, Feuerstein C. Cognitive executive dysfunction in patients with obstructive sleep apnea syndrome (OSAS) after CPAP treatment. Sleep. 1998;21(4):392-397.

[8] Awad KM, Malhotra A, Barnet JH, Quan SF, Peppard PE. Exercise Is Associated with a Reduced Incidence of Sleep-disordered Breathing. The American Journal of Medicine. 2012;125(5):485-490.

345 [9] Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep
346 apnoea by continuous positive airway pressure applied through the nares. Lancet.
347 1981;317(8225):862-865.
348 [10] Cartwright RD, Samelson CF. The effects of a nonsurgical treatment for
349 obstructive sleep apnea. The tongue-retaining device. The Journal of the American
350 Medical Association. 1982;248(6):705-709.
351 [11] Fujita S, Conway W, Zorick F, Roth T. Surgical Correction of anatomical
352 azbnormalities in obstructive sleep apnea syndrome: Uvulopalatopharyngoplasty.
353 Otolaryngol Head Neck Surg. 1981;89(6):923-934.
354 [12] Riley RW, Powell NB, Guilleminault C. Inferior sagittal osteotomy of the mandible
355 with hyoid myotomy-suspension: a new procedure for obstructive sleep apnea.
356 Otolaryngol Head Neck Surg. 1986;94(5):589-593.
357 [13] Engleman HM, Asgari-Jirhandeh N, Mcleod AL, Ramsay CF, Deary IJ, Douglas
358 NJ. Self-Reported Use of CPAP and Benefits of CPAP Therapy: A Patient Survey.
359 Chest. 1996;109(6):1470-1476.
360 [14] Weaver TE, Kribbs NB, Pack AI, Kline LR, Chugh DK, Maislin G, et al. Night-
361 to-night variability in CPAP use over first three months of treatment. Sleep.
362 1997;20(4):278-283.
363 [15] Larsson H, Carlsson-Nordlander B, Svanborg E. Long-time Follow-up after UPPP
364 for Obstructive Sleep Apnea Syndrome: Results of Sleep Apnea Recordings and
365 Subjective Evaluation 6 Months and 2 Years after Surgery. Acta Oto-
366 Laryngologica. 1991;111(3):582-590.
367 [16] Wilhelmsson B, Tegelberg A, Walker-Engström ML, Ringqvist M, Andersson L,
368 Krekmanov L, et al. A Prospective Randomized Study of a Dental Appliance

Compared with Uvulopalatopharyngoplasty in the Treatment of Obstructive Sleep Apnoea. Acta Oto-laryngologica. 1999;119(4):503-509.

[17] Haskell JA, McCrillis J, Haskell BS, Scheetz JP, Scarfe WC, Farman AG. Effects of Mandibular Advancement Device (MAD) on Airway Dimensions Assessed With Cone-Beam Computed Tomography. Seminars in Orthodontics. 2009;15(2):132-158.

[18] Kyung SH, Park YC, Pae EK. Obstructive sleep apnea patients with the oral appliance experience pharyngeal size and shape changes in three dimensions. Angle Orthod. 2005;75(1):15-22.

[19] Sam K, Lam B, Ooi CG, Cooke M, Ip MS. Effect of a non-adjustable oral appliance on upper airway morphology in obstructive sleep apnoea. Respir Med. 2006;100(5):897-902.

[20] Ferretti GR, Bricault I, Coulomb M. Virtual tools for imaging of the thorax. European Respiratory Journal. 2001 Aug;18(2):381-392.

[21] Series F, Marc I, Cormier Y, La Forge J. Utility of Nocturnal Home Oximetry for Case Finding in Patients with Suspected Sleep Apnea Hypopnea Syndrome. Ann Intern Med. 1993;119(6):449-453.

[22] Berman EJ, Dibenedetto RJ, Causey DE, Mims T, Conneff M, Goodman LS,et al. Right Ventricular Hypertrophy Detected by Echocardiography in Patients with Newly Diagnosed Obstructive Sleep Apnea. Chest. 1991;100(2):347-350.

[23] Malhotra A, Huang Y, Fogel RB, Pillar G, Edwards JK, Kikinis R, et al. The male predisposition to pharyngeal collapse: importance of airway length. Am J Respir Crit Care Med. 2002;166(10):1388-1395.

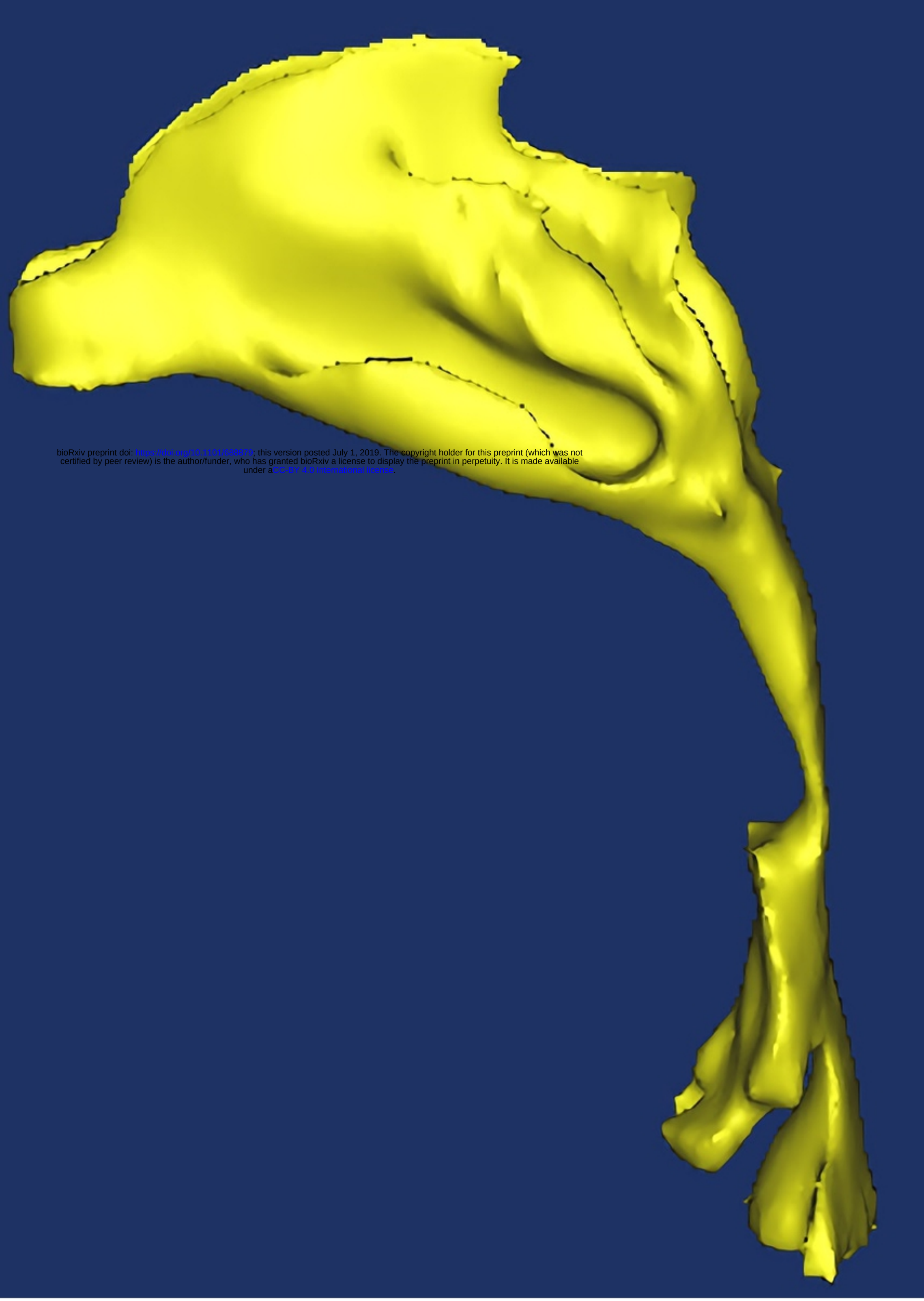

Figure 1-a

Figure 1-b

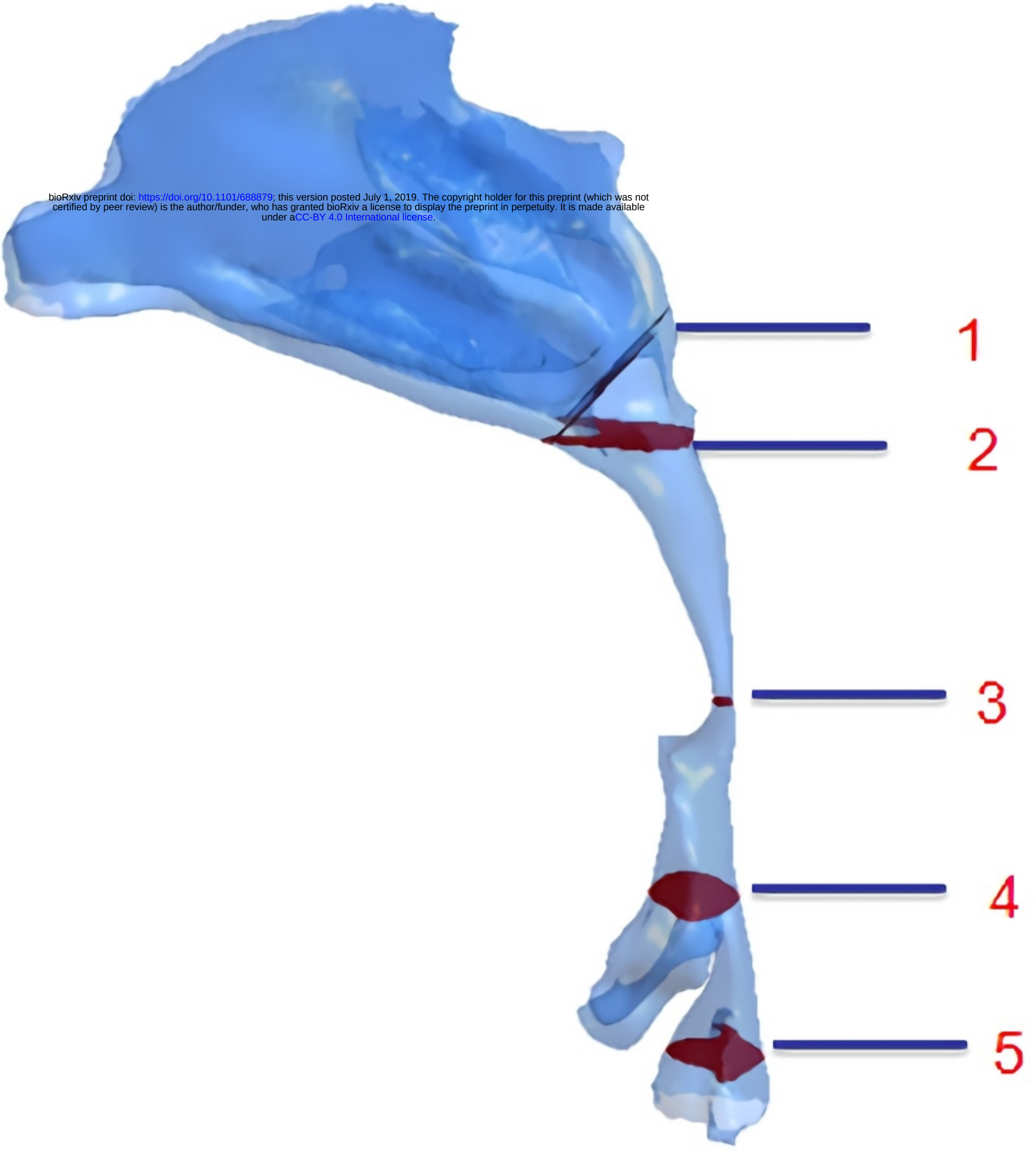

Figure 3

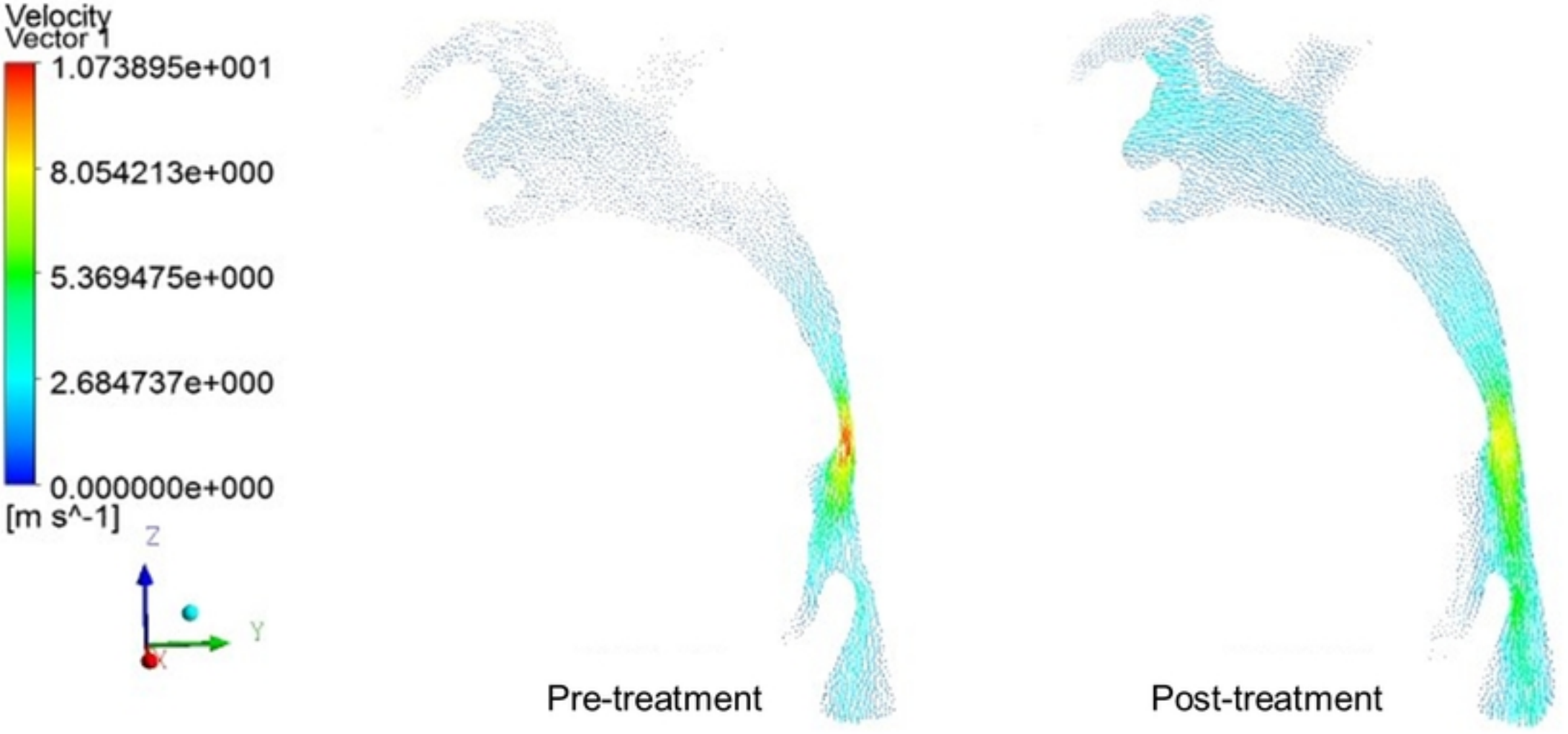
Velocity
Vector 1
1.073895e+001
8.054213e+000
5.369475e+000
2.684737e+000
0.000000e+000
[m s^-1]
Z
Y
X
Pre-treatment
Post-treatment

Figure 4

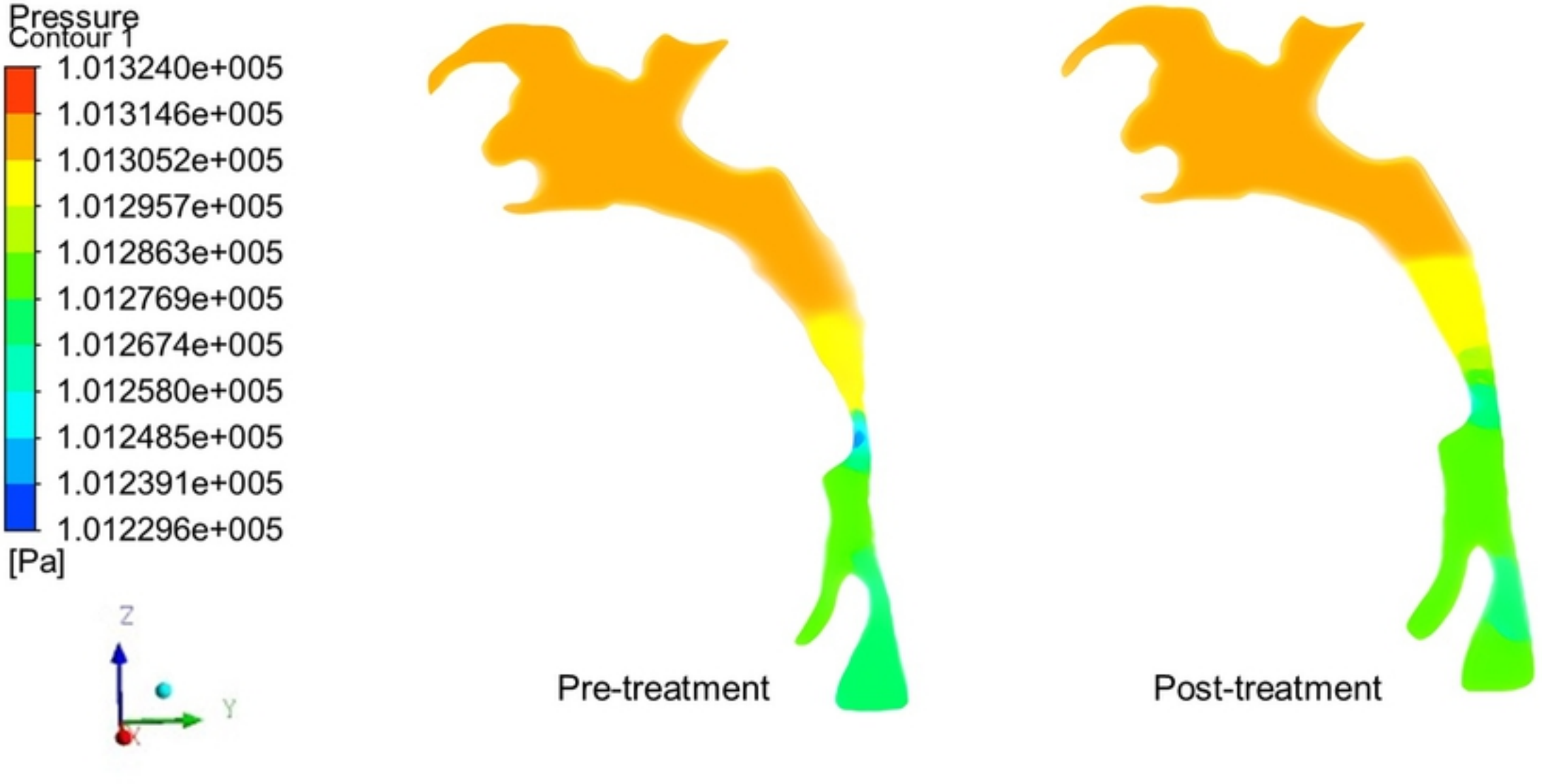
Pressure
Contour 1
1.013240e+005
1.013146e+005
1.013052e+005
1.012957e+005
1.012863e+005
1.012769e+005
1.012674e+005
1.012580e+005
1.012485e+005
1.012391e+005
1.012296e+005
[Pa]
Z
Y
X
Pre-treatment
Post-treatment

Figure 5

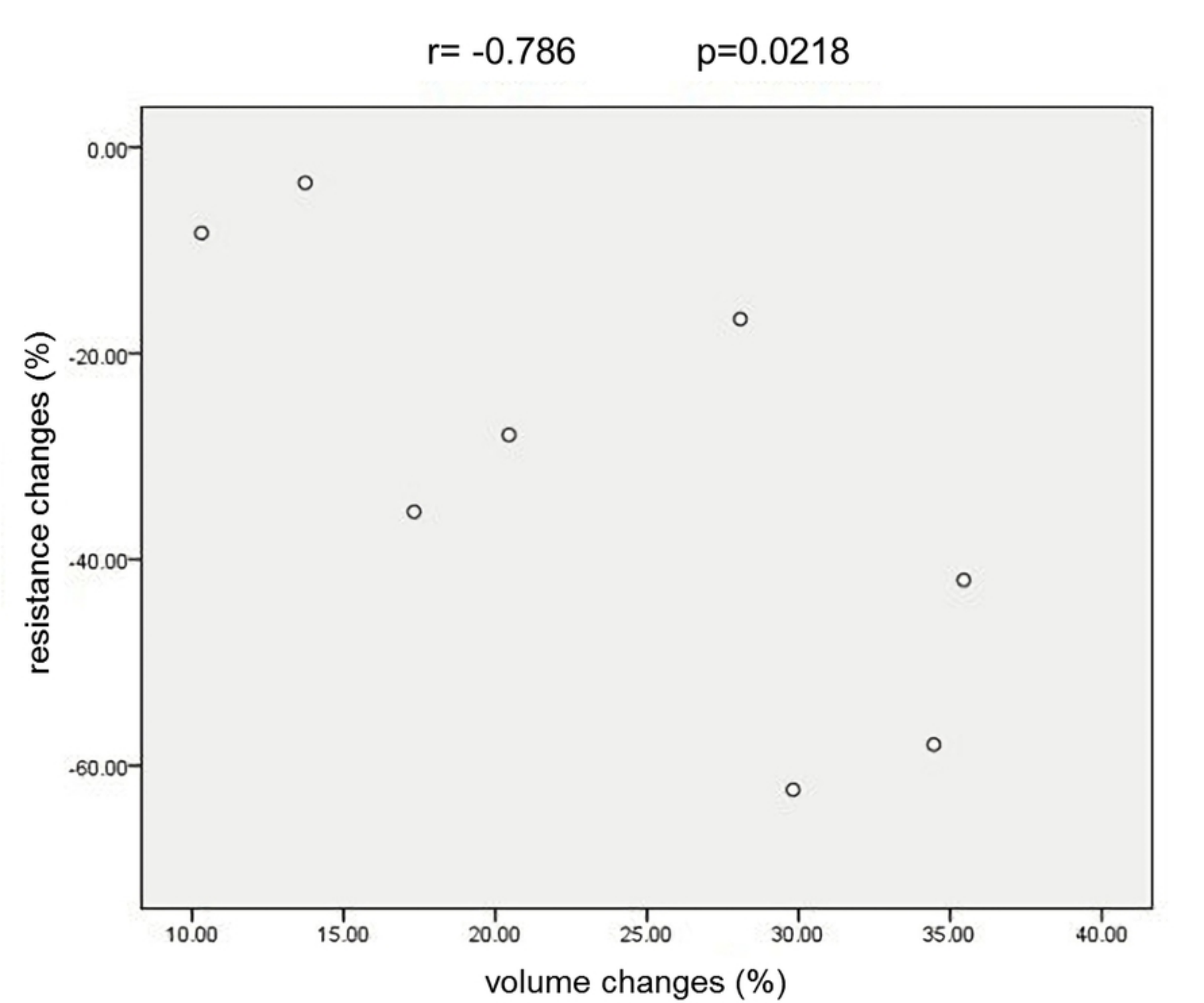
r= -0.786
p=0.0218
0.00
-20.00
-40.00
-60.00
resistance changes (%)
10.00
15.00
20.00
25.00
30.00
35.00
40.00
volume changes (%)

Figure 6-a

r= -0.81 p=0.0158

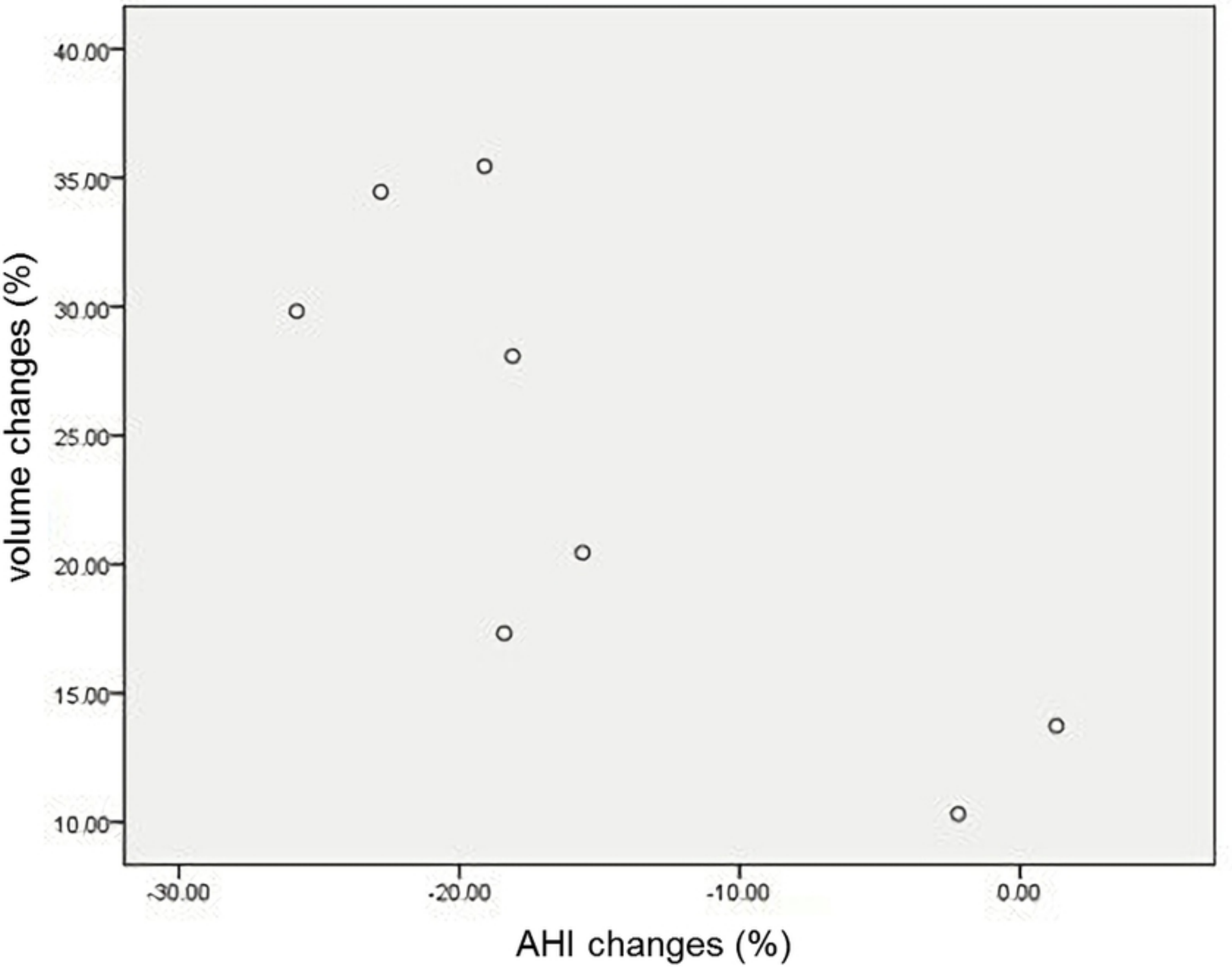

Figure 6-b

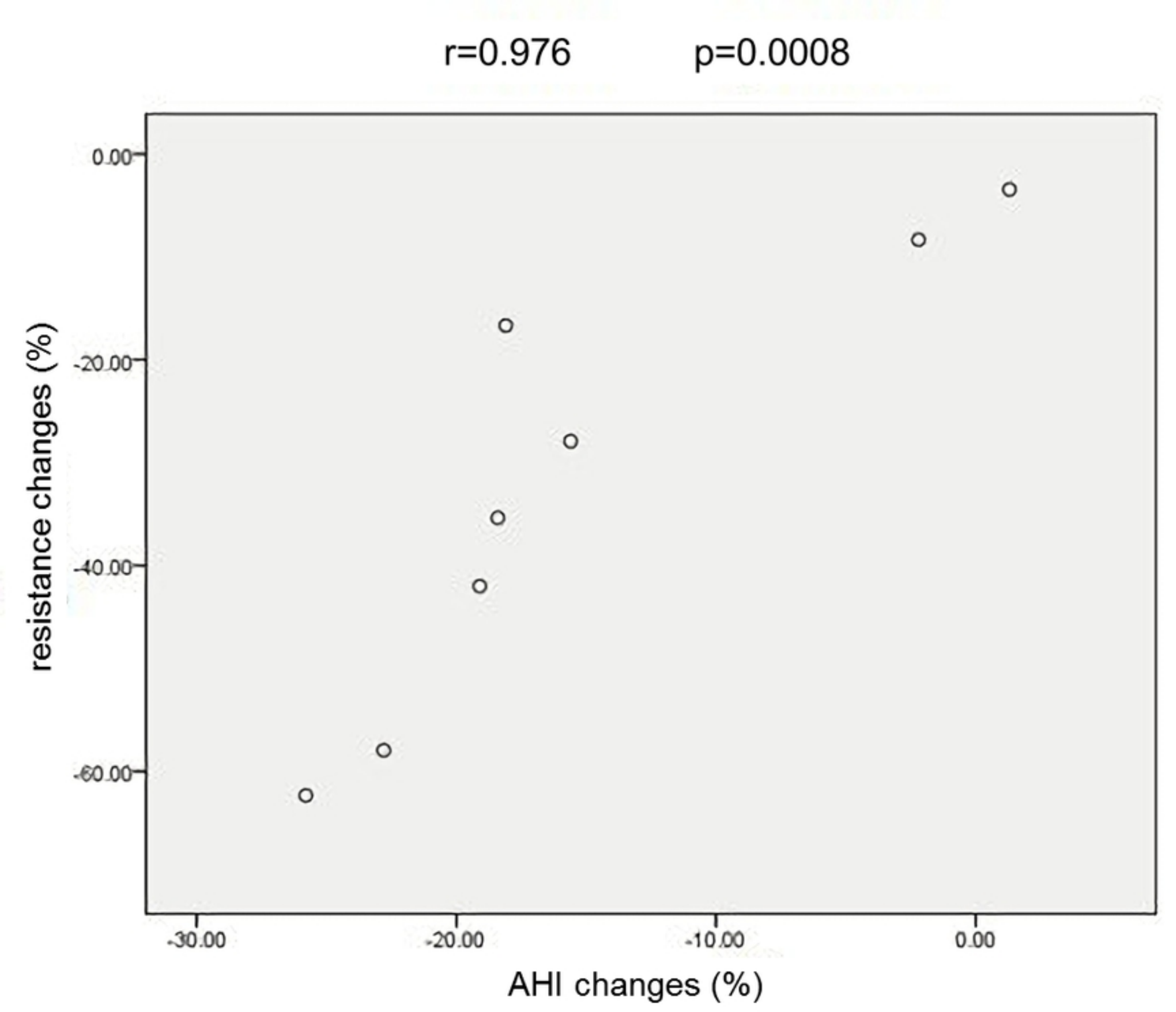
r=0.976
p=0.0008
0.00
-20.00
-40.00
-60.00
resistance changes (%)
-30.00
-20.00
-10.00
0.00
AHI changes (%)

Figure 6-c

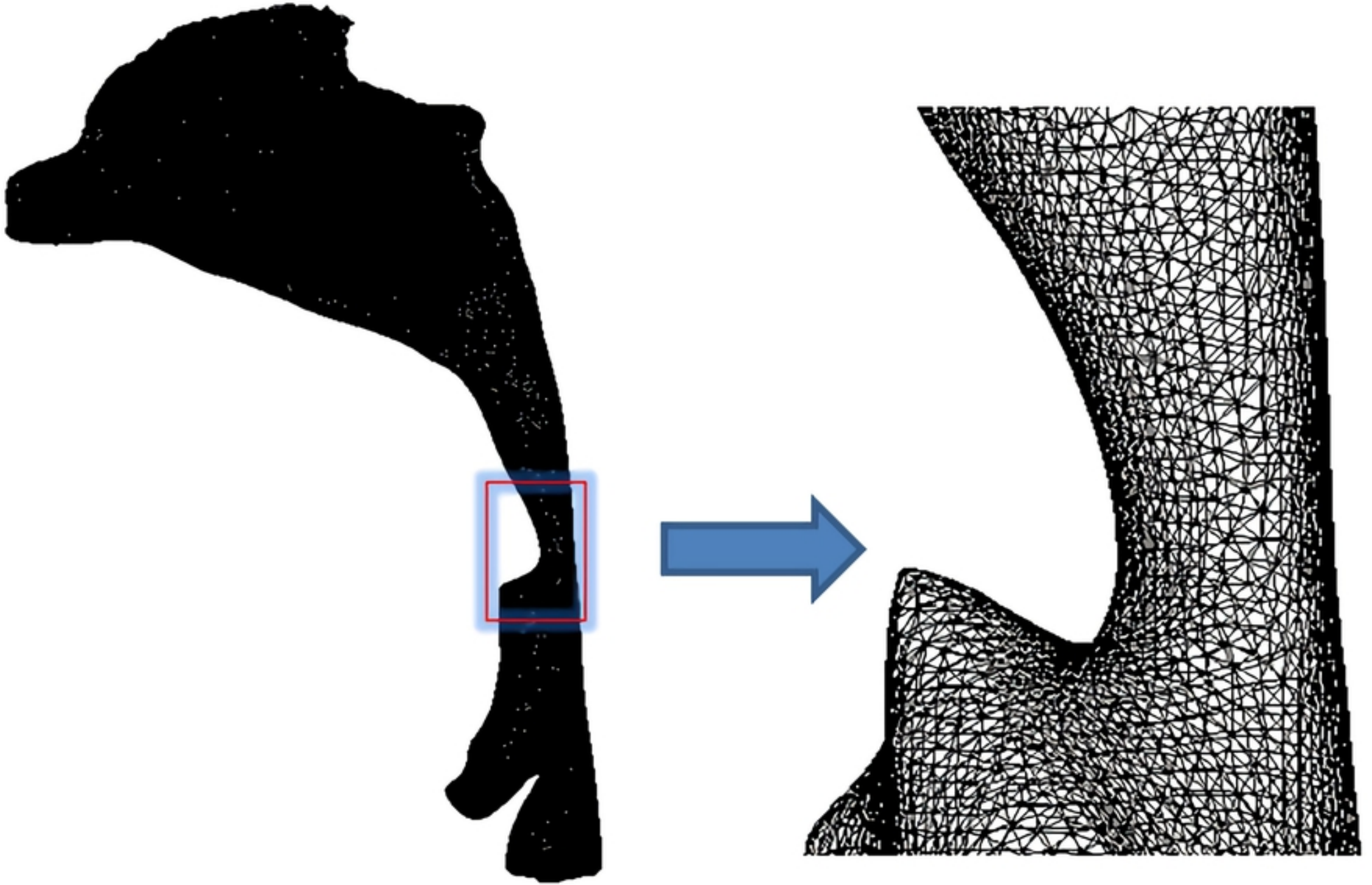

Figure 2