ANNOTATION

to dissertation work "Clinical possibilities virtual modeling of air flows in case of the nasal septum deformity", by Sagandykova Nazym Slyamovna, submitted for the degree of Doctor of Philosophy (PhD) in the specialty 6D110100 - "Medicine"

Relevance The dissertation research is devoted to the study of physical properties of nasal cavity air flow (NCAF) in patients with a nasal septum deviation (NSD). We have applied the method of nasal air flow virtual simulation (NAVS), which is based on the gases and liquids computational dynamics laws. This method allows to create dynamic three-dimensional models of NCAF and calculate the functional characteristics (flow velocity, flow temperature, partial flow pressure and wall shear stress). We studied the role of these characteristics in the nasal breathing disorders's diagnosis.

Nasal septum deviation is a widespread pathology throughout the world (T.W.Wang), which is a predictor of pathological conditions such as sleep apnea, nosebleeds, headaches, cardiovascular system complications, lower respiratory tract diseases, etc (Cappello ZJ).

Information on NSD prevalence varies from source to source. However, general data tend to suggest that the incidence of NSD in the population is quite high. Jamie et al published the results of their two-year study of 1095 computerized images of the nasal cavity and paranasal sinuses. 648 (65%) patients had a deviated septum; of these, 51% of the NSD were to the left, 49% to the right, and 2% had a bilateral deviation. Vainio Mattila found that 33% of adults had nasal breathing problems, of which 26% had a deviated septum. These data indicate a high incidence of NSD in the population (Sullivan).

This frequency of the NSD among the population explains the popularity of surgical interventions on the nose. Surgical correction of NSD is up to 40% of all surgeries in the otorhinolaryngology departments (Kryukov A.I.).

To assess the effectiveness of surgical treatment, in addition to improving the subjective sensations of patients, objective criteria for improving nasal breathing are needed, which characterize the respiratory function of the nasal cavity. Currently, there is no "gold" standard of examination that determines the surgeon's tactics in NSD (Clement PAR, "The International Standardization Committee on the Objective Assessment of the Nasal Airway in Riga"). Standard examinations of the nasal cavity include questioning patients for the presence of nasal congestion, anterior rhinoscopy, Cottle test, computed and magnetic resonance imaging of the nasal cavity. To assess the nasal respiratory function, active and passive rhinomanometry is used, which are based on measuring the mass flow rate and airflow resistance of the nasal cavity. However, there are some evidences of a low correlation of these data with patient's subjective feelings in the postoperative period (Hsu HC), which limits their use.

For an objective assessment of the nasal respiratory function, it is necessary to take into account the functional disorders of nasal breathing, and not just the anatomical features of the nasal cavity (Baumann H.). However, it is well known that changes in nasal cavity configurations bring aerodynamic disturbances (B. Guyuron). Therefore, we believe that the functional characteristics of NCAF pathology should be fully assessed. And parameters such as flow velocity, partial pressure, wall shear stress and flow temperature should be key in describing the functional state of the nose (Anderson KR).

Unfortunately, at present there are no clear criteria for assessing the functional state of the nasal airflow, which leads to relapses of nasal breathing disorders and postoperative complications (Garcia GJ).

Thus, according to a large 10-year prospective study in the United States, every second patient who underwent septoplasty experienced dissatisfaction with the results of the operation during this period (Tsang CLN). There are many works on the incidence of postoperative complications of septoplasty, mainly in English-language sources. According to various authors, the frequency of complications after septoplasty reaches 25% per year.

Dąbrowska-Bień et al. in a prospective study of 5639 patients after septoplasty noted a complication in 193 patients (3.42%).

Respiratory physiology and pathology are highly dependent on airflow within the nasal cavity. However, the nasal anatomy, characterized by complex airways and significant individual variation, is difficult to analyze. Thus, conventional diagnostic tools have had limited success. However, with the rapid development of computer resources, more sophisticated attempts have been made to correlate airflow characteristics in the human nasal airway with nasal symptoms and functions using computer fluid dynamics.

In this dissertation we studied the possibilities of NAVS for an objective assessment of nasal respiratory function, which are based on CFD modeling by nasal cavity CT scans and anterior active rhinomanometry data. CFD simulation, in comparison with existing tests, not only calculates the parameters of liquid / gas flows, but also fixes their trajectories with accuracy. Such computational potentials of the method are unique and are widely used in many areas of human life - architecture, shipbuilding, agriculture, etc. For clinical purposes, this technique is used in neurosurgery, vascular surgery to predict the possible outcome of surgical intervention on the vessels. The proposed method has been studied and modified by us into a virtual simulation of the NCAF using the initial air flow physical data.

The purpose of the research work: to study the possibilities of virtual airflow simulation of patient's NCAF with nasal septal deformity as an objective assessment tool.

In connection with this goal, the following tasks are solved:

1. To develop a technique for NAVS based on a three-dimensional model of the nasal cavity using the proposed boundary conditions.

2. Determine the velocity, temperature, partial pressure and wall shear stress in normal condition and deformed nasal septum using NAVS.

3. Determine the air flow characteristics of patients with different septum deviation locations and degrees of contact with opposite nasal cavity wall.

4. Conduct a comparative analysis of the NAVS before and after surgical treatment.

5. To determine the clinical and diagnostic possibilities of NAVS in an objective assessment of nasal breathing in comparison with standard methods.

Methodological base of the research:

1. Creation of the nasal cavity 3D models: software MIMICS MEDICAL 22.0 (Leuven, Belgium)

2. Evaluation of patient's subjective sensation: a standardized questionnaire NOSE (Nasal Obstruction Symptoms Evaluation)

3. Assessment of mass flow rate and nasal cavity resistance during inspiration: active anterior rhinomanometry (Otopront RHINO-SYS, Germany)

4. Clinical methods.

5. Computer modeling: 3D/CFD modeling using standard and personal data using 3-matic Medical 14.0 (Leuven, Belguim, 2019), ANSYS Fluent 19.2 (ANSYS Inc., Canonsburg, PA) programs.

6. Evaluation of the results of numerical simulation: ANSYS Fluent 19.1 program in the viewing mode.

7. Cytological examination: microscopic examination of a smear from the nasal mucosa (rhinocytogram)

8. Functional tests: saccharin test – determination the rate of mucociliary transport.

9. Instrumental: video endoscopic equipment (Medstar UE-3000, Medstar Co. Ltd (South Korea)).

10. Statistical: All statistical calculations were performed using the SPSS program (version 25.0, IBM SPSS Inc., Chicago, USA), p value <0.05 was considered statistically significant. All data were summarized using descriptive statistics methods. All parameters were visually checked and also tested using the Shapiro-Wilk test. All parametric data were compared using Student's t-test for normal distribution, as well as using the Mann-Whitney test for parameters with non-normal distribution. Pearson's correlation coefficient assessed any bivariate associations of variables. The mean (SD±) was applied for continuous variation, and the median Me and interquartile range with an upper limit (Q1) and a lower limit (Q4) were used. When describing qualitative data, the percentage ratio and proportions of observations of the entire sample were used. Results with $p \leq 0.05$ were considered significant; Spearman's rank correlation method was used to determine the direction and strength of the correlation between two features;

Object of study: patients with the nasal septum deviation

Subject of study: aerodynamic characteristics of the nasal cavity

Inclusion criteria: presence of nasal septum deviation of any shape and localization, positive informed consent of the patient to the study, age 18 years and older, the patient has not previously underwent the surgical treatment on nasal cavity, the presence of computed tomography of the nasal cavity with a slice step of no more than 0, 6 mm on electronic media (on flash media, in a virtual cloud).

Exclusion criteria: refusal to participate in the study, lack of informed consent from the patient, age under 18 years, pregnancy, presence of the nasal valve pathology, emergency patients, history of nasal surgery, neoplastic process of the nasal cavity, patients with inflammation of the nasal mucosa and paranasal sinuses to exclude swelling; unsuitability of electronic files for modeling (low quality, thick sections, etc., etc.)

Research stages

The study consisted of two blocks: 1. Experimental; 2. Clinical

1. Experimental block

The study was conducted in the technical laboratory of Nazarbayev University, Kazakhstan and the biomedical laboratory of Munjal University, India. The experimental part of the dissertation compared the results of nasal airflow modeling of 60 patients with deviated septum and 21 healthy participants. To obtain a virtual model, nasal cavity computed tomography scans and data on the volumetric air flow during inspiration were used.

Three-dimensional virtual models of nasal airflow were made from computer images on the software MIMICS MEDICAL 22.0 (Leuven, Belgium), 3-matic Medical 14.0 (Leuven, Belguim, 2019), ANSYS Fluent 19.2 (ANSYS Inc., Canonsburg, PA). The airflow simulation was carried out under two input data conditions: the first, with the standard mass flow rate data, which is equal to 250 cm3/s. To fulfill the second condition, we used personal data on the volumetric flow rate of each patient by active anterior rhinomanometry.

A joint work was carried out by an engineer and a clinician to evaluate the results obtained using the visual add-ons of the ANSYS Fluent 19 program. Specialists evaluated the functional characteristics of air flows (velocity, partial pressure, temperature, and wall shear stress in each nasal halfes) in 4 coronary planes: 1. The entrance of the right and left nasal cavities; 2. Anterior end of the inferior turbinate; 3. Median line of the middle turbinate; 4. Nasopharynx.

The nasal airflow virtual simulation stages:

1. Creation of the nasal cavity 3D model

A 3D model of the nasal cavity surface was generated from the CT scan data and further processed to create a 3D solid model using Ansys Space Claim.

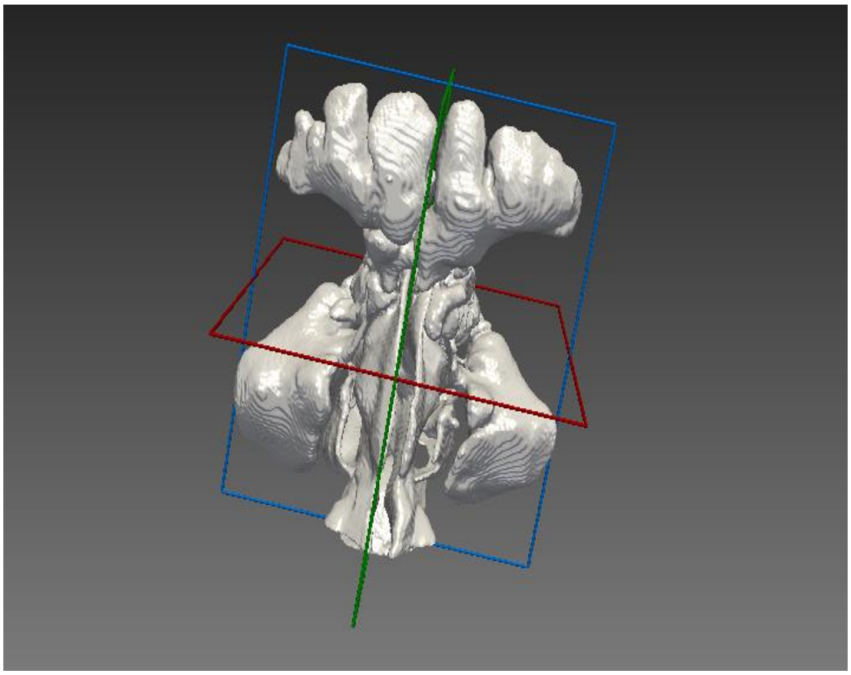


Figure 1- 3D model of the nasal cavity

2. Mesh generation

The 3D solid model was discretized using a tetrahedral quadratic grid (Tet10). The division of the grid depends on the change in flow in different areas. To discretize the model, a very fine mesh of 4,894,368 elements was created.

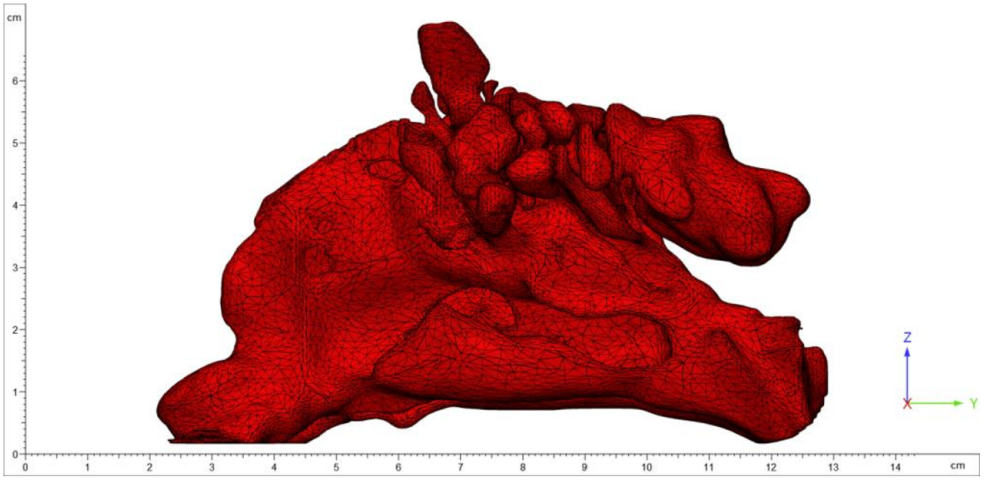


Figure 2 - three-dimensional model of the nasal cavity in the sagittal projection, grids are installed on the surface

3. Setting Boundary Conditions

To simulate the air flow close to the real breathing process, boundary conditions are required that provide initial data of the airflow out and in the nasal cavity.

The lower part of the three-dimensional model of the nasal cavity has two openings (nasal vestibules-inlet, nasopharynx-outlet) with the boundary condition

of the mass flow rate (by active anterior rhinomanometry). The inlet is defined as a pressure inlet at atmospheric pressure (gauge pressure 0 Pa). The rest of the nasal cavity is defined as a non-stick wall. The type of air flow is turbulent with a transition to laminar.

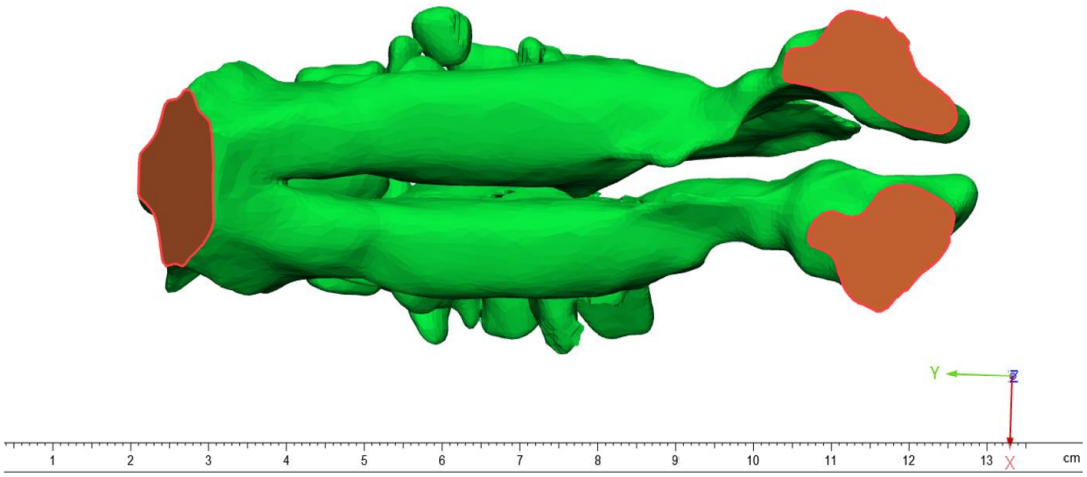


Figure 3 - three-dimensional model of the nose, ventral view, the nasal vestibule and nasopharynx are colored orange

3. Virtual Simulation of Nasal Airflow (CFD Simulation)

The Navier-Stokes flow solver was used to calculate the quasi-stationary air flow (SST model, k-Ω). Atmospheric air was used as a continuous source.

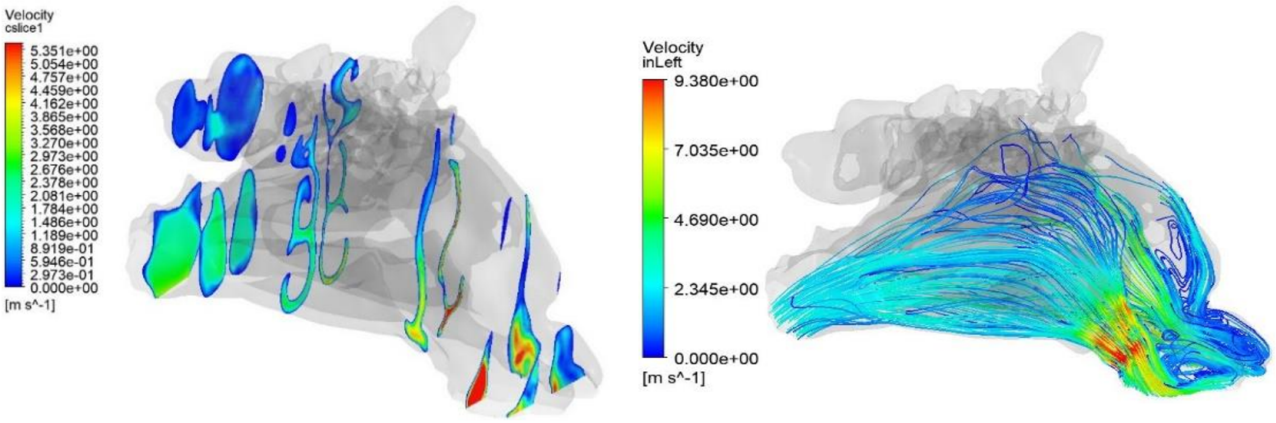
For the simultaneous numerical solution of the equations, an equation scheme was implemented, including a solver related to pressure and velocity.

The airflow in four planes (A) of the cross section perpendicular to the nasal cavity floor were analyzed by examining

flow direction (B), flow velocity (C) and partial pressure (D) of the air flow in each half of the nose in the coronal projection and their longitudinal distribution (E, F). Simulation results are analyzed in Ansys Fluent 19.0 software.

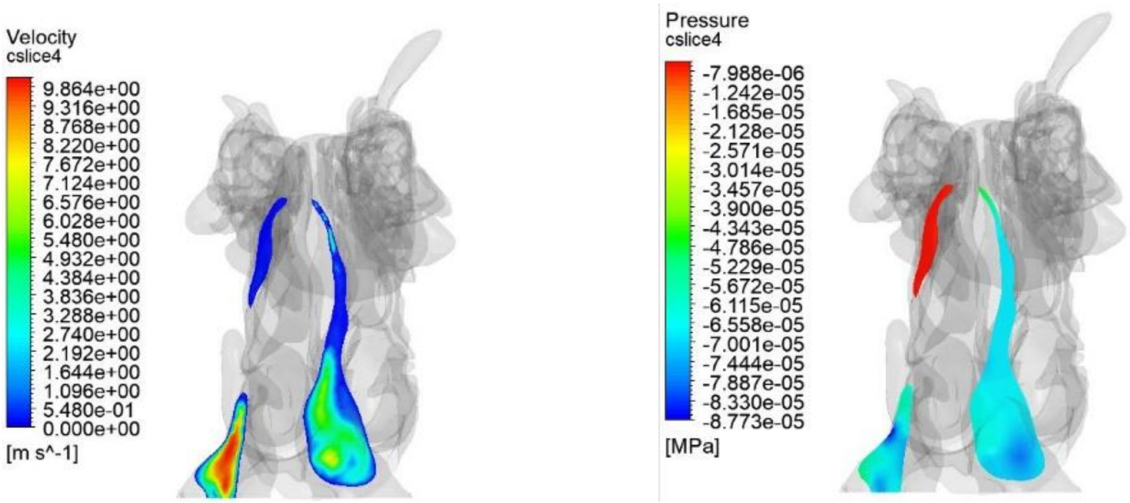
To obtain data on the temperature and pressure on the walls of the nose, we used Workbench add-ons in version 19 of the Ansys Fluent software.

Data visualization:



A B

Figure 4 - virtual models of the NCAF, cross-section in four planes (A), flow path (B)



C D

Figure 5 - Velocity and partial pressure of the flow in the coronal projection (C, D) and sagittal projection (E, F)

The obtained characteristics of the NCAF are used to form the concept of normal and pathological violation of the nasal air flow. The resulting criteria may be key in assessing the dysfunction of the nasal flow.

Clinical block

The study in the clinical part was carried out in accordance with the ethical principles of conducting clinical trials, regulated by the Declaration of Helsinki of the World Medical Association, adopted at the 18th WMA General Assembly, Helsinki, Finland, June 1964.

The results of surgical treatment of 60 patients who were admitted in a planned manner to the "City Hospital No. 5", Almaty from January 2019 to December 2019 were evaluated.

After obtaining informed consent, a plan of general and special procedures for prevention, diagnosis and treatment was carried out in accordance with the treatment protocols of the Ministry of Health of the Republic of Kazakhstan, as well as the objectives of the study.

These patients underwent a comprehensive otorhinolaryngological examination based on the protocol of the Ministry of Health (dated June 23, 2016, protocol No. 5) "Deviated septum".

A comparative analysis of the results of standardized methods for assessing nasal breathing (NOSE questionnaire, anterior active rhinomanometry) and the results of NAVS before and after 90 days of surgical treatment was carried out. To identify the clinical and diagnostic significance of the virtual simulation method, the correlation (according to Spearman) between nasal flow characteristics and the scores of the patient questionnaire was assessed.

Provisions for defense:

1. The NAVS method is an objective tool in assessing nasal breathing.
2. The characteristics of normal and pathological NCAF in the case of NSD were determined.
3. The role of NCAF functional characteristics in assessing the surgical treatment effectiveness for patients with NSD has been established and proven.

Scientific novelty

1. A method has been developed for optimizing surgical treatment in patients with nasal breathing disorders (RoK Patent, No. 34705 dated November 20, 2020) by using computer technologies.
2. A new approach has been applied for objective assessment of NSD surgical treatment effectiveness, based on changes of the NCAF functional characteristics.
3. It's determined the NCAF functional characteristics in normal and NSD.
4. The clinical significance of the division NSD by degree of contact to the opposite nasal wall was determined.

Theoretical significance of the study results

The results obtained during the dissertation research are important for the development of theoretical and methodological foundations for the study of the biophysical processes of NCAF in normal and pathological conditions. In the course of the study, new knowledge was obtained about the temperature regime and other characteristics of NCAF with a NSD, and about the influence of deviation location in nasal cavity on the various airflow parameters. The results of the dissertation research can become the basis for setting new research tasks: the development of the CFD method for modeling air flows in various pathologies of the nasal cavity.

Practical value of the research results

1. The results obtained during the dissertation research are important from the point of view of formation a new approach in the objective assessment of nasal breathing.

2. The proposed NAVS method is recommended for evaluation the surgical treatment results of patients with NSD, and is recommended for otorhinolaryngologists at the outpatient and inpatient levels.

3. The obtained NCAF parameters in normal and pathological conditions can become the main criterion for selecting patients in the preoperative period.

4. The developed algorithm can be used by engineers of related specialties as the basis for modeling a human organ.

5. Conclusions, suggestions and scientific and practical recommendations can be taken into account and used in the implementation, development and improvement of strategies, programs, concepts and development plans of the Ministry of Health in relation to the tactics of managing patients with nasal breathing disorders at the outpatient and inpatient levels.

6. The materials contained in the dissertation work can be used in the educational process in the training of specialists in the following specialties: otorhinolaryngology, radiology, public health.

The author's personal contribution

The presented work is the author's work of Nazym Slyamovna Sagandykova, where she independently planned all stages of the study, design, and also carried out a thorough literary analysis. The author carried out preparation for the study, data collection, data analysis, design.

As a result of the work, the author developed a NAVS method for an objective assessment of nasal breathing quality, which is confirmed by protective documents (Patent for invention No. 34705 dated November 20, 2020 "Method for optimizing surgical treatment in patients with impaired nasal breathing").

The proposed method for an objective assessment of nasal breathing and the algorithm of work have been introduced into the clinical activities of the specialized clinic "City Hospital No. 5" in Almaty (Act of implementation "Optimization of surgical treatment in patients with nasal breathing disorders using computer simulation" dated 13.06.22).

Conclusions

1. The developed NAVS method makes it possible to evaluate the functional characteristics and trajectory of nasal airflow based on three-dimensional modeling and using initial physical data of air stream.

2. Indicators of NCAF flow velocity of 1.50-1.89 m/s, partial pressure of 2.70-3.70 Pa, flow temperature of 21.20-23.01 C, wall shear stress of 0.60-1 .00 Pa detected were detected in healthy participants; flow velocity 1.90-8.66 m/s, partial pressure -0.01- (-82.65) Pa, flow temperature 23.02-33.60 C, wall shear stress 1.02-6, 10 Pa were detected in patients with NSD.

3. NCAF characteristics in patients with anterior NSD not differ from those with posterior NSD ($p>0.05$). A statistically significant difference ($p < 0.05$) in the velocity, wall shear stress and partial pressure between patients with reached and not reached the opposite site by septum deviation was determined.

4. After septoplasty velocity, temperature, partial pressure and wall shear stress changed to the healthy participants values ($p < 0.0001$).

5. A high positive correlation (r=0.98) between the questionnaire scores and NCAF velocity, temperature, partial pressure, wall shear stress was determined in comparison with standard methods for an objective assessment of nasal breathing (r=0.19-0.25) .

Approbation of the dissertation

The main provisions of the dissertation were discussed at scientific and practical seminars and meetings of Otorhinolaryngology Department, KazMUNO and the Department of Aerospace Engineering, Nazarbayev University.

The results and conclusions of the dissertation research were reported and presented on the following platforms:

IX International Scientific and Practical Conference "Medicine Pressing Questions" (May 6-8, 2020, Baku, Azerbaijan)

III All-Russian Congress of the National Medical Association of Otorhinolaryngologists of Russia (November 20–22, 2019, Nizhny Novgorod, Russia)

at the International Conference of Young Scientists and Students "Apsatarov Readings: "New Vectors in Science of the 21st Century: Questions, Hypotheses, Answers"", May 15, 2020, Almaty, Kazakhstan

at the II International Congress "Continuing Education in the Republic of Kazakhstan" "Emergency Medicine: Education, Science and Clinical Practice" (October 24-25, 2019, Almaty, Kazakhstan)

Publications

totally 11 printed works have been published:

1. 1 publication in a journal indexed by the Scopus database –«Computer Methods in Biomechanics and Biomedical Engineering Imaging & Visualization», ISSN:2168-1163E-ISSN:2168-117, Cite score- 3.4, percentile-68, «Patient-specific CFD simulation of aerodynamics for nasal pathology: a combined computational and experimental study»;
2. In journals recommended by the Committee for Control in the Field of Education and Science of the Ministry of Science and Higher Education (3 articles);
3. In the materials of 5 international and republican scientific and practical conferences;
4. Patent to invention No. 34705 of 20.11.2020 "Method for optimizing surgical treatment in patients with nasal breathing disorders";
5. Act of implementation "Optimization of surgical treatment in patients with impaired nasal breathing using computer modeling" dated 13.06.22. in the clinical work at the City Hospital No. 5;

Scope and structure of the dissertation

The dissertation is presented on 110 typewritten pages and consists of normative references, definitions, a list of abbreviations and designations, an introduction, a literature review, a description of materials and methods, the results of own research, a conclusion, including conclusions, practical recommendations and a list of references. The work is illustrated with 34 figures and 21 tables. The bibliographic index includes 165 sources.