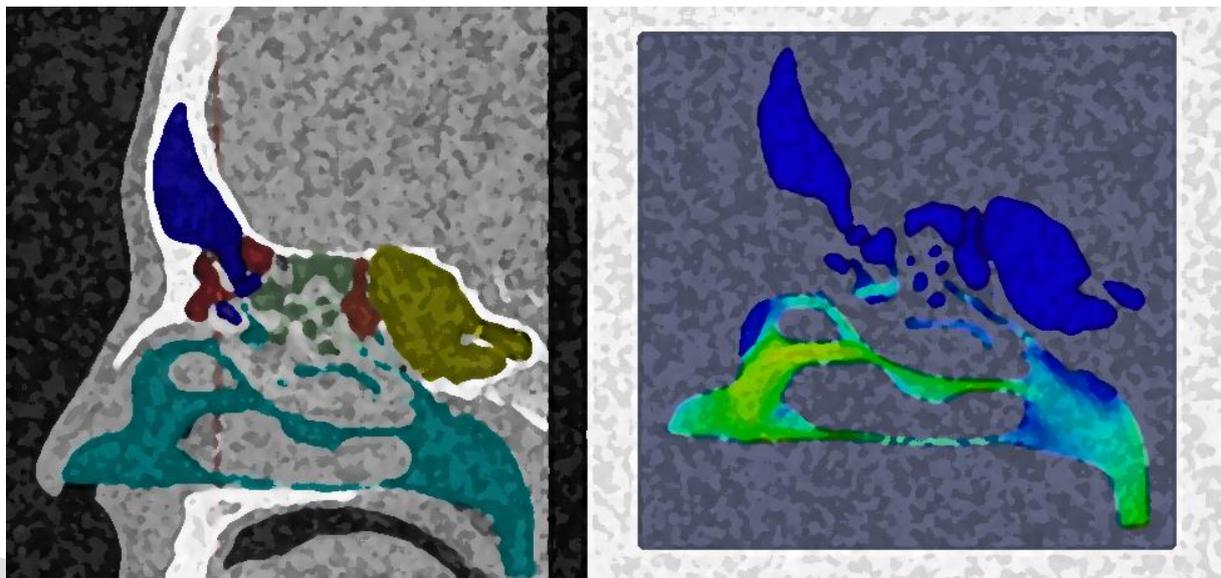


NOSE Pilot Study



Investigating the Practical Use of Computational Fluid Dynamics Simulation of Airflow in the Nasal Cavity and Paranasal Sinuses

NOSE

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***Investigating the Practical Use of Computational Fluid
Dynamics Simulation of Airflow in the Nasal Cavity and
Paranasal Sinuses***



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Abstract	<p>The NOSE Pilot study evaluated the technical and scientific environment required for establishing a service portfolio that includes CFD simulation and 3D visualization services for ENT specialists.</p> <p>For this purpose the state-of-the-art of these technologies and their use for upper airways diagnostics were analysed.</p>		
Keywords	Rhinology, Computational Fluid Dynamics, 3D Visualization, Clinical Pathways, Service Center, Knowledge Base		

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Preamble

Diseases, traumas or alterations of the nasal airways have one of the highest incidences within the world population, with a related enormous economic impact on health care expenses. About 11% of the European population suffer from an obstruction of nasal breathing or an inflammation of the nasal sinuses [1]. Nasal disorders strongly hinder the functionality of the entire airway and diagnosis and treatment of nasal diseases cover about 50% of the daily work of Ear-Nose-Throat (ENT) practitioners. Surgical corrections of the nasal airway – also in the framework of plastic surgery – are the second most frequent surgical interventions in otorhinolaryngology. ENT surgical planning is difficult even for experienced ENT surgeons, as the paranasal sinuses have complex three-dimensional geometries. Often it can only be guessed how the respiratory airflow in the nose and paranasal sinuses will improve after a surgery. Specifically, nowadays the understanding of nasal function and of the behaviour of air during the respiration cycle in the nasal area is still incomplete, which sparks controversy among ENT experts regarding physiology and pathophysiology. Thus, there isn't a widely accepted method to describe the airflow within the nasal sinuses for a given patient. Therefore, ENT surgeons lack a practical tool for CFD validation to help them in the decision-making. They have to rely on the interpretation of the patient's clinical history and the examination findings based on the ENT knowledge and experience which, of course, could lead to different assessments [2]. As a result, the success of surgeries of the nasal and paranasal sinuses is not always as good as expected and the rate of failed improvement of nasal breathing can be estimated to be as high as 40%. While the technical level of diagnostics for ear diseases is quite advanced, and the hearing aids on the market today are of much higher quality than those available just a few years ago, functional diagnostics in rhinology is still much less advanced.

The present study centred on a range of research topics related to the introduction of Computational Fluid Dynamics (CFD) simulation in the clinical pathway for ENT treatment and surgery. These topics included:

- Setting up a sample technical Infrastructure to provide CFD and Mesh services
- Developing a Workflow concept
- Investigating Mesh generation for the nasal cavities and paranasal sinuses
- Investigating CFD Simulation and Analysis for the nasal cavities and paranasal sinuses
- Initial Business Planning for a NOSE Service Center
- Developing a Knowledge base
- International Networking

The NOSE Pilot Study was partially funded by the Steirische Wirtschaftsförderungsgesellschaft mbH SFG and coordinated by AIT Angewandte Informationstechnik Forschungsgesellschaft mbH. Research and testing was carried out from September 2016 to August 2018 and involved a wide network of national and international medical ENT specialists, CFD and mathematical experts and 3D printing professionals.

Introduction

On the basis of computed tomographic images of the human nose and the paranasal sinuses three-dimensional surface models, so-called meshes can be created and the obtained surface information is then the basis for creating a 3D computer model. Using CFD simulations, the flow within the nose and paranasal sinuses can be calculated and then visualized.

This simulation method was developed at the beginning of the 21st century and has been described thoroughly in previous publications [3]. The objective of the method is to transfer quickly and efficiently real geometries from the computed tomography system into a mathematical model, in order to obtain a semi-automatic or fully automatic quantitative statement of the flow simulation in the nose and the paranasal sinuses. CFD simulations of nasal and paranasal sinus flow have already been successfully performed in numerous (clinical) projects since more than a decade. Nevertheless there is still no (standard) pathway that enables ENT specialists to easily obtain CFD simulations for their patients' pathologies and use them as additional decision aid for ENT treatment and surgery planning.

It is assumed that the nasal flow simulation could contribute to:

- the determination of the quality of nasal ventilation
- proposals for operational modifications
- the planning of nasal and sinus surgery
- preoperative surgical simulation
- the postoperative examination with simulation for quality assurance

Therefore, the present NOSE Pilot Study investigated the following research questions:

1. What is the **state of the art**? Will there soon (within the next 3 to 5 years) be solutions available in the problem area that can be used with reasonable effort in any medical practice: mesh generation, CFD simulation and validation of CFD simulations?
2. Could technical solutions be offered via a "**service center**"? What competencies must be available and how should the service center be conceived?
3. What would be the economic benefit and what **measures** (investment, education and training, marketing, etc.) are needed to introduce CFD simulations for surgery planning nationwide in medical practices and in the clinical field.

Chapters 1 to 3 will first introduce the research domain and the motivations for the pilot study. The results of the research effort and outlooks are described in chapter 4 to 6 of this document.

1 Diseases of the upper respiratory tract

1.1 Definition and pathologies

Nasal airway obstruction is a common disease with high prevalence and significant social and economic burden. Paranasal sinuses are a group of four paired hollow air pockets located in the bones of the face surrounding the nasal cavity. Each paranasal sinus takes its name from the bones that it belongs to; the frontal sinus is located above the eyes and lies within the frontal bone; the sphenoid sinus is located in the sphenoid bone; the ethmoidal (or ethmoid) consist of several air cavities located between the eyes and the nose within the ethmoid bone; the maxillary sinus is located under the eyes in the maxillary bone and is the biggest among the paranasal sinuses.

The wall of the paranasal sinuses are lined with a thin layer of tissues, which preserves the sinus healthy, lubricated and clean from germs by producing a small amount of mucus. In case of irritations and infections the layer of tissue surrounding the sinuses become swollen, which hinders the drainage of the mucus that accumulates in the sinuses. The persistence of this situation in time reveals a pathology named Chronic rhinosinusitis (CRS). Figure 1 shows the four paranasal sinuses and depicts a healthy sinus on the left side and an unhealthy one affected by sinusitis on the right side.

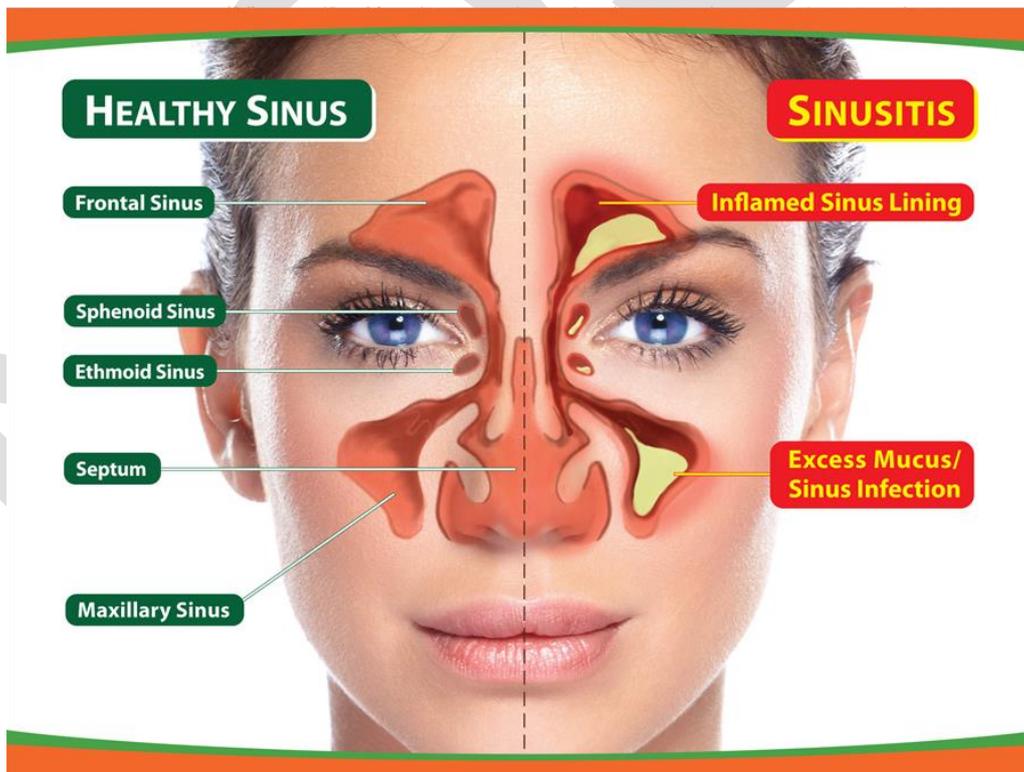


Figure 1 - Paranasal sinuses and comparison of healthy and unhealthy sinuses

CRS is a pathology associated to symptoms such as a pressure and pain in the face and nose area, congestion of the nasal cavity, an increased production of mucus and a general decreased sense of smell. Furthermore, the inflammation of the nasal airways could also lead to cases of rhinitis, an inflammation of the mucous membrane that lies within the periosteum (also known as perichondrium) in the nasal cavity. Symptomatically similar to CRS, acute rhinosinusitis is a pathology in which the infection of the paranasal sinuses is only temporary and is generally due to episodes of cold. However, acute rhinosinusitis is a situation less severe than CRS, which is persisting longer in time and, therefore, requires a proper supervised medical treatment.

CRS is often divided in different categories according to the existing features: CRS without nasal polyps, CRS with nasal polyps and CRS with allergic fungal. CRS without nasal polyps is the most common type of rhinosinusitis. In this case the swelling in the sinuses is generally caused by allergies and irritations due to substances in the air or infections. CRS can also be caused by nasal polyps, which are abnormal noncancerous growths that clog the paranasal sinuses when they occur in a large number or have increased size. Polyps can develop due to multiple reasons, including allergy, autonomic nervous system dysfunction and genetic predisposition [4]. Traditionally, polyps are removed through surgery operations or treated with medication in order to shrink their size. The third type of CRS is observed in patients allergic to airborne spores, a fungus presents in small amounts in the air and that can lead to a production of denser and thicker mucus. The density of the mucus rapidly fills the sinuses, leading to traditional CRS symptoms.

Usually, CRS is a creeping disease associated with a high impact on the quality of life, sleep, and everyday performance. Overall, CRS is a rather common pathology that can affect persons from every age group. In fact, it is calculated that approximately 11% of the European population suffers from a disability of nasal breathing or chronic inflammation of the paranasal sinuses, with 100.000 surgeries performed each year in Germany, Austria, and Switzerland alone. Furthermore, CRS is also one of the most widespread illnesses in the United States, with around 500.000 surgeries being carried out every year. Moreover, due to several precision shortfalls of the current diagnosis methods, which mostly rely on evaluation of the available static Compute Tomography (CT) [5] and Magnetic Resonance (MR) [6] images and on the personal experience of the doctors, the surgery error rate in case of CRS surgery ranges between 10% and 40%¹.

1.2 Treatment methods

Check-ups performed by ENT doctors or surgery specialists are a crucial step in order to make the adequate objective diagnosis for upper airways pathologies. In case of CRS in addition to a detailed history of the anamnesis, it is important to perform further examinations such as nose endoscopy and CT of the paranasal sinuses, preferably in an acute inflammation-free interval. The extent of shading in the CT of the paranasal sinuses and the anatomical relationships determine the degree of CRS [7]. However, the 2-dimensional images of the conventional CT examination of the paranasal sinuses merely give an idea of the ventilation of the sinuses.

¹ <http://www.sinuwave.com/sinusitis2/chronic-sinusitis/>, Accessed 2018-07-20

1.3 Costs

In Europe, the direct costs for a patient treated in a university hospital for severe chronic rhinosinusitis are about \$1861/year, in the US the total cost of treating a patient with CRS is even \$2609 per year. Health care spending in case of sinusitis is significantly greater than the expenses of other chronic diseases, such as ulcer, acute asthma and hay fever [8]. However, while septoplasty and turbinate surgeries are often successful in relieving nasal airway obstructions, between 10% - 40% of patients still suffer from persistent obstruction after surgery and the failure rate of further revision surgeries is about 23%².

1.4 Number of cases

1.4.1 D-A-CH area

In 2015, 145,085 patients were hospitalized in **Austrian** hospitals because of pathologies in the ear, nose, oral cavity, pharynx, face, facial skull, or neck (81,911 of which were male, 63,174 of which were female).³ In the same year, a total of 28,689 nose and paranasal sinus surgeries were performed in Austria (17,233 of them in male patients, 11,456 in female patients). The number of approximately 29,000 operations per year is consistent since 2009.³ The number of sinus surgeries in Austria amounts to approximately 10,000 per year, and is also consistent since 2009 with minor deviations.⁴ There are about 80 ENT specialists based in Styria and 700 in Austria.

It is estimated that nine million people in **Germany** suffer from chronic sinusitis (2008). Surgeries in this field are one of the most common interventions in German ENT clinics. The surgery costs about 4,000 euros and is paid by the statutory and private health insurance companies. In Germany, about 60,000 patients were hospitalized for chronic sinusitis in 2015. And in total, approximately 280,000 patients were hospitalized due to upper respiratory illnesses. Between 2006 and 2011, approximately 132,000 nose/sinus surgeries were performed each year. In 2016, there were approximately 6,273 ENT doctors working in Germany, 4,413 of them in the outpatient sector and 1,548 in the inpatient sector.

The Swiss hospital statistics show a total of 28,120 operations in the area of nose, mouth and pharynx surgery in 2015. Approximately 2,400 patients have visited a hospital because of chronic sinusitis. 8,400 patients were hospitalized for other diseases of the nose and sinuses. In 2016 the statistics of the FMH (Foederatio Medicorum Helveticorum), the professional association of Swiss physicians, lists 489 physicians in **Switzerland** working in the field of ORL (Oto-Rhino-Laryngology).

1.4.2 Europe and US

Overall, 6-15% of the population in **Europe** suffers from acute rhinosinusitis, the simultaneous inflammation of the nasal mucosa ("rhinitis") and inflammation of the mucous membrane of the

² <http://www.sinuwave.com/sinusitis2/chronic-sinusitis/>, Accessed 2018-07-20

³ Statistik Austria

⁴ Statistics Austria, Medical Services for Hospital Layouts



sinuses ("sinusitis"). Adults suffer 2-5 times a year, children 7-10 times a year. The GA²LEN study (2011) [9] conducted research in 19 medical centers in 12 European countries and found that approximately 11% of adults between the ages of 15 and 75 suffer from chronic rhinosinusitis. The total number of ENT doctors in Europe is estimated at about 27,000.

Recent studies show that almost 9.5 million people in the **US** visited their family doctor annually because of nose/sinus complaints. This situation generates considerable healthcare costs related to CRS pathologies, with the direct costs and indirect costs estimated to lie between \$6.9 to \$9.9 billion and \$13 billion 2014 USD per year, for an overall annual economic burden as high as \$22 billion USD. In addition, annual medication prior to surgery is estimated to cost the patients between \$1,547 and \$2,700 2014 USD [10]. In the US, approximately 340,000 operations were performed in 2012 due to chronic inflammation of the sinus mucosa. Between 10 - 40% of patients complain of persistent obstruction after surgery. A 2016 National Center for Health report shows that about 11% of adults in the US (26.9 million people) suffer from chronic sinusitis⁵. There are approximately 12,000 ENT doctors in the US (2016). It is noteworthy that in the period from 2000 to 2009 the number of frontal sinus surgeries in the US increased by 153%, and the number for surgeries of all 4 sinuses even by 200% [11].

⁵ <https://www.cdc.gov/nchs/fastats/sinuses.htm>, Accessed 2018-07-20

2 International Context

2.1 State of the art

Initial attempts to study the nasal airflow date back to the end of the nineteenth century, where analysis was conducted on cadavers and it was concluded that the nasal airflows are concentrated entirely within the upper nasal cavity [12,13]. However, successive studies disclaimed these initial results by observing, for example, that dust situated in the proximity of the nasal floor would spread through the central region as a consequence of an airflow [14,15]. Other successive works using cast models [16,17] reached conflicting results. After the middle of the twentieth century, an increasing number of works dealt with in vitro measurement of the airflow velocity [18,19] and later with numerical studies of the airflow. However, definite results were not possible due to the limited equipment [20], the application to an unrealistic situation (idealised geometry) [21] or the use of CT/MR images with a too wide spacing [22,23]. The discrepancies between the various studies and the limitations of these studies require a more rigorous, precise and detailed analysis of the nasal airflow in the paranasal sinuses.

Precise analysis of the paranasal sinuses is key to correctly diagnose the type of CRS pathology patients suffer from. An appropriate analysis should also evaluate the effectiveness of the treatment in relation to the patient-specific nasal functionalities and pathologies. However, today diagnostic quality is in general dependent on the quality of the training of the practicing physicians and their experience in the treatment of specific clinical pictures. Furthermore, the only aid generally available to doctors and ENT surgeons are static CT/MR images that provide details about the structure of the paranasal sinuses at a specific time. However, these images are not systematically interpretable and the doctors mostly rely on their previous experience when doing a diagnosis, planning treatments and surgeries. Moreover, CT/MR images only offer a 2-dimensional view of the nasal cavities and fail to portrait the intricate airflow ventilation within the sinuses. Besides, the gap in time between the day a CT/MR exam is performed and the day a patient undergoes an operation is crucial due to the evolving nature of paranasal sinuses that could alter the original medical situation.

The creation of 3D models and CFD simulations could help to improve the precision of airflow analyses in the nose and the paranasal sinuses, in order to provide valuable information for the findings of the examining doctor. Through inspection of high-quality CT/MR images, detailed CFD simulations and 3D models of the affected nasal areas, doctors and ENT surgeons get a better overview of the actual situation of the patient. Therefore, the combination of these tools becomes of vital importance not only for diagnostics of the pathology of a patient but also for improving the preparation of surgeries and, thus, plays a key role towards the complete recovery of patients [24].

Nowadays, the majority of CFD and mesh suppliers provide services for the development of technical products in specific fields (e.g. automotive or aeronautic industry). However, there are several providers specialized in the healthcare domain, with Siemens Healthineers, GE Health and

Philips Medical Systems being among the world's largest ones. At Siemens Healthineers the focus of IT-assisted diagnostics is on laboratory diagnostics and point-of-care, prenatal diagnostics and remote diagnostics. Philips Medical Systems develops and manufactures x-ray generator, tube and imaging components and specializes in digital, analogue, mobile and universal radiography. However, all of these suppliers do not currently offer standard IT solutions for CFD simulation, mesh generation or 3D printing specially intended for doctors, ENT surgeons and the general healthcare community.

Furthermore, previous developments in CFD simulations and 3D model creations have not been applied to practical real situations. Instead, these have been bound to experimental or demonstration in nature mostly [25]. Moreover, such developments have been limited to those (research) facilities and institutions that could afford the required High-Performance Computing (HPC) and had the necessary technical know-how for such experimentation (for example universities in Berlin⁶, Milan⁷, Ohio⁸). Unfortunately, such facilities tend to limit the use of their developed technologies to their internal structure and only seldom offer their results as a stable service to interested medical experts.

The setting up of an online platform providing the intended services to doctors and ENT surgeons has been hitherto difficult due to the interdisciplinary effort (medicine, physics, mathematics, computer science) required [26]. However, recent developments in computer technology, together with the standardization and stabilization of the methods in each disciplinary area, provide now the premises for the introduction of a future service platform that could serve different actors, such as physicians, doctors, surgeons and patients themselves.

⁶ http://ilp.charite.de/forschung/ag_biofluidmechanik/forschung/aerodynamik_der_nase/, Accessed 2016-04-28

⁷ <https://www.politesi.polimi.it/handle/10589/81309?locale=en>, Accessed 2016-04-28

⁸ <http://osuwmc.multimedianewsroom.tv/story.php?id=1116>, Accessed 2016-04-28

3 Pilot Study

3.1 Motivation for the Pilot Study

The NOSE Pilot Study examined the following assumptions: The integration of new simulation tools into the traditional workflow of rhinology treatment procedures should improve the effectiveness of the treatment. Additional information gained from CFD simulations and 3D models can optimize the decision-making process for ENT surgeons and doctors and shall lead to a more effective pre- and post-surgical assessment [27]. Current existing shortcomings of the state of the art surgery and treatment preparation could thus be overcome.

Besides this, the interaction between doctors/surgeons and patients could improve in a remarkable way thanks to these new simulation tools. For example, printed 3D models will aid doctors in providing detailed and vivid explanations of the individual pathology and planned manoeuvre. Thus, patients themselves will have a clearer understanding of the overall treatment. Furthermore, patients will feel more involved in the decision process, which in turn will increase their satisfaction during the counselling process. Moreover, printed 3D models obtained from real situations represent a highly valuable resource, as they could also be used in scholarly settings and hands-on surgery training.

The study brought together experts from various fields with the goal of improving the treatment of rhinology patients (by ENT doctors, surgeons, radiologists). A dedicated IT-infrastructure supporting testing and research was set-up.

Specifically, the pilot study dealt with the following:

1. Development of the necessary expertise in the field of CT/MR analysis, 3D model derivation and CFD simulation applied to the medical domain by direct experimentation with real case scenarios (CT/MR from patients as input);
2. Verification of the feasibility of the implementation of an infrastructure able to offer online services such as creation of 3D models and CFD simulation to the medical community (doctors and ENT surgeons in primis);
3. Outlining of goals, requirements and constraints for the proposed integration, highlighting of successive steps, business opportunities and future improvements (e.g. machine learning techniques applied to 3D models creation).

3.2 Research Method

The pilot study focused on the technical and scientific viability of a NOSE Service Centre. From 2016 to 2018 AIT, Angewandte Informationstechnik Forschungsgesellschaft, housed an internal incubator to test the viability of providing customized services for CFD simulation and 3D model creation and visualization to ENT specialists. To this end, various processes and CFD methodologies were tested. Simulation processes can be very time-consuming and in order to scale down the computing time needed for running CFD simulations and creating meshes based on patients' CT/MR

images, machine learning technologies were tested, as well. A Convolutional Neural Network (CNN) was implemented, which is now able to analyse the CT/MR images and automatize the otherwise manual segmentation process.

Given the wide scope of the project, AIT made a tremendous effort to join international research networks and to set up solid research collaborations in order to ensure access to top of the market technologies and state of the art knowledge in the multidisciplinary scope of this project. As a first result, in 2017 the "ERA-NET IraSME 19th Call for International Research Activities in SME" awarded a research grant for the project "Rhinodiagnost" to AIT and its technical research partners from Germany (Sutter Medizintechnik GmbH, Freiburg, Rheinisch-Westfälischen Technischen Hochschule (RWTH) Aachen, Forschungszentrum Jülich GmbH and Med Contact GmbH, Salmendingen). AIT and its partners are now cooperating in Rhinodiagnost.eu in order to further develop coordinated morphological and functional diagnostics for ENT surgeons and physicians.

On the medical side, AIT established a network of renowned local ENT specialists and radiologists, who provided their medical expertise and advice for the development of a NOSE service centre. The university hospital in Graz historically played a worldwide pioneering role in the ENT surgery scenario. In the 1970s, the Functional Endoscopic Sinus Surgery (FESS) [28,29] method was introduced by the medical experts Walter Messerklinger and Heinz Stammberger, both rhino surgeons that worked at the university hospital of Graz. Currently, the medical supervising team for the NOSE service centre includes surgeons from the Graz FESS School.

The local and international cooperative scientific networks of technical and medical experts provided the research backbone for the NOSE activities.

4 Results

The following paragraphs introduce to the various research topics of the NOSE Pilot study and describe the most important results that were obtained.

The project handbook issued at the start of the NOSE project clearly defined the tasks and activities that should be done in the pilot study. The overall work was divided into ten Work Packages (referred to as AP from the German word "Arbeitspaket") as depicted in Figure 2.

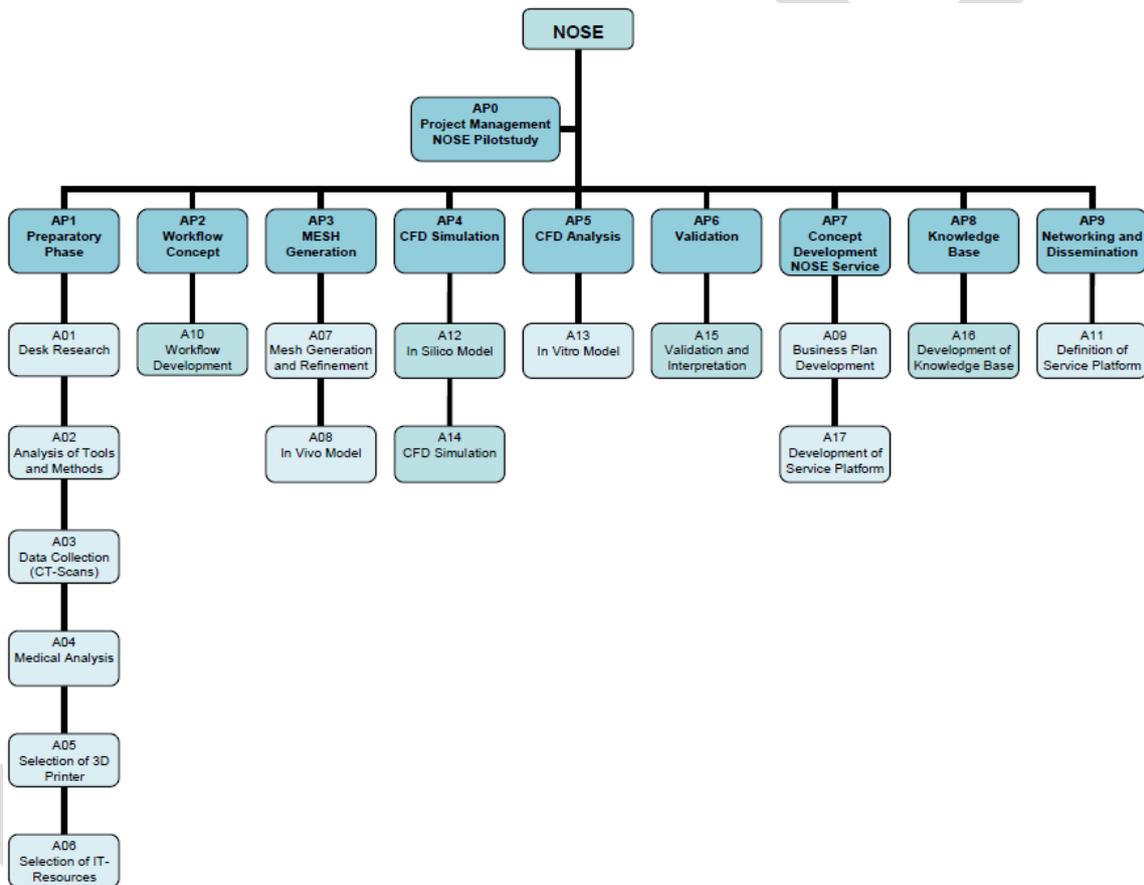


Figure 2 – NOSE project structure

Specifically, areas of investigation on the technical level were: reconstruction of nasal cavities (3D-modelling, chapter 4.2, AP3), execution of CFD simulation (chapter 4.3, AP4 and AP5) and interpretation of airflow simulation results (chapter 4.4, AP6). These essential activities have to be included into business processes that are to be optimized when offered as service to a global community of ENT specialists. The implementation of these processes is described in chapter 4.5 (AP2). To demonstrate the successful operations of a NOSE Service Centre, an NSC-business incubator was established at the premises of the pilot study contractor AIT (chapter 4.1, AP1). Staff was hired and trained. The necessary hardware and software components were installed to

perform on a day to day basis the three main technical activities mentioned above. The initial business planning activities for the NOSE service centre are described in chapter 4.6 (AP7). Besides, during the course of the pilot study, relevant literature and information resources were collected and indexed in a cataloguing system. This collection of current work in the field of CRS is made available online as the "NOSE knowledge base" (chapter 4.7, AP8). All performed activities have been guided by agile project management (AP0), and accompanied by continuous networking and dissemination activities (AP9). The ongoing cooperation that resulted from the active project networking endeavours, the current findings and future developments are outlined in chapter 5 and 6 of this document.

Figure 3 and Figure 4 represent the APs of the NOSE Pilot Study depicted as GANTT chart [30,31] and as Integrated Computer Aided Manufacturing DEFinition for Function Modeling (IDEFo) [32,33].

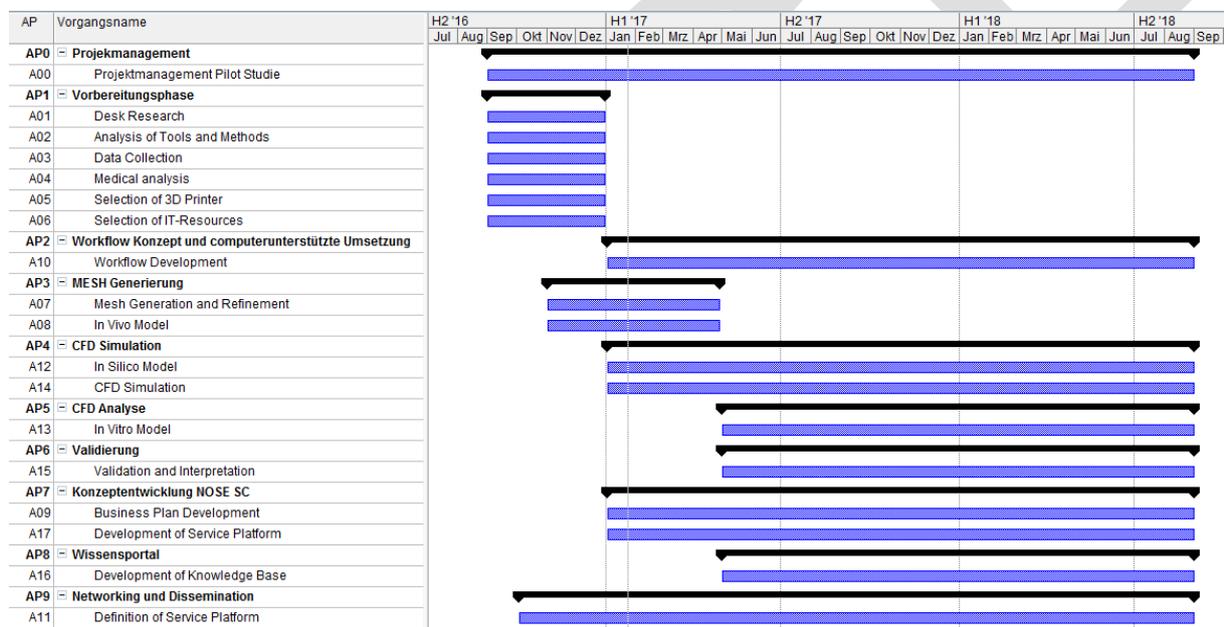


Figure 3 - GANTT Chart NOSE Pilot Study

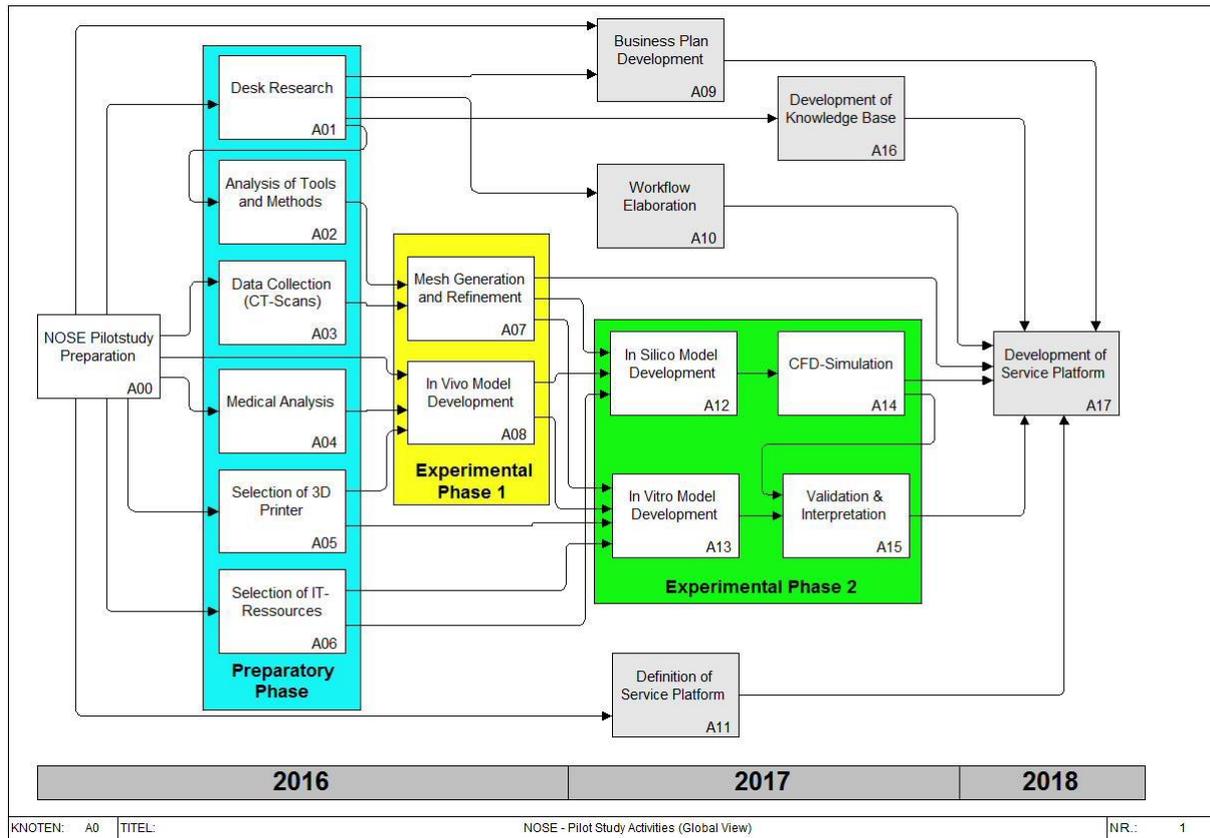


Figure 4 – IDEFo NOSE Pilot Study

4.1 Preparatory phase (AP1)

In this first activity, state of the art methods and researches in the field of CFD were analyzed with a particular attention to the physical airflow rules, CFD simulations and the DICOM standard used to manage CT/MR images. The required capabilities to correctly handle CFD simulations were set up, and the current limitations and problematics on how to overcome obstacles to CFD simulation were analyzed (more about the literature in chapter 4.7).

4.1.1 Desk Research

To proper approach the main objectives of this pilot study, one of the first tasks was the training of the NOSE team in a series of multidisciplinary fields. In particular, it was required to build up the necessary know-how to handle tasks such as CFD simulation. Notably, the investigated multidisciplinary area included physics (CFD), medical images (DICOM images and 3D model creation), machine learning (automatic segmentation) and medicine (CRS pathologies). Publications in these fields were collected and organized in an internal digital archive using the Zotero tool, also with the additional aim to make these later available through a web portal (see 4.8).

4.1.2 Analysis of Tools and Methods

The latest technologies and solutions were investigated. Focusing on the reviewed literature and on successful practice examples, several tools were analyzed to verify whether of use during the project hereinafter. In particular, we experimented with 3D Slicer, Meshmixer, Meshlab and Blender to visualize and modify CT/MR images and their segmentation; OpenFOAM and Fire2 to experiment with CFD simulations; Bonitasoft and Trisotech for the analysis and the development of the initial prototype of the NOSE Service Center.

4.1.3 Data Collection (CT Images)

The NOSE project team reached out to various local medical center, surgeons and doctors to support the collection of CT/MR images for the testing purposes of the project. Specifically, we collaborated closely with ENT surgeon Dr. med Schachenreiter (Privatklinik Graz Ragnitz), Univ.-Prof. Dr. Gerhard Ranner (CT/MR Zentrum Graz Geidorf) and ENT surgeon Dr. Jakse (Privatklinik der Kreuzschwestern Graz).

4.1.4 Medical Analysis

In this phase the NOSE project team defined in collaboration with medical experts the requirements and the desired outcomes that would be of use in the daily practice to treat patients suffering from CRS pathologies. Among the most interesting and desired outputs, are the possibility to evaluate the CT/MR images in the form of 3D models that could be also used for training purposes and the opportunity to simulate the respiration cycles through the use of CFD simulation in order to evaluate the benefits of surgery operations.

4.1.5 Selection of 3D Printer

The first experiments with 3D printing were done using a high-end 3D printer, namely XFAB from DWS Lab. This printer uses the laser stereolithography method (SLA) [34,35], which is a process where a photo-polymer resin in a vat is selectively cured by a light source, in this case, a point laser. In initial attempts, this appliance was used to validate the generated 3D model and to verify the stability and the characteristics of the printed object. First, the prints were done with invicta_915 ABS-like in white color, which is a high impact resistant material and suitable for functional prototypes, casings, snap-fit parts and assembly applications.

Figure 5 shows a print prototype, a model of a paranasal sinus before being removed from the printing device.

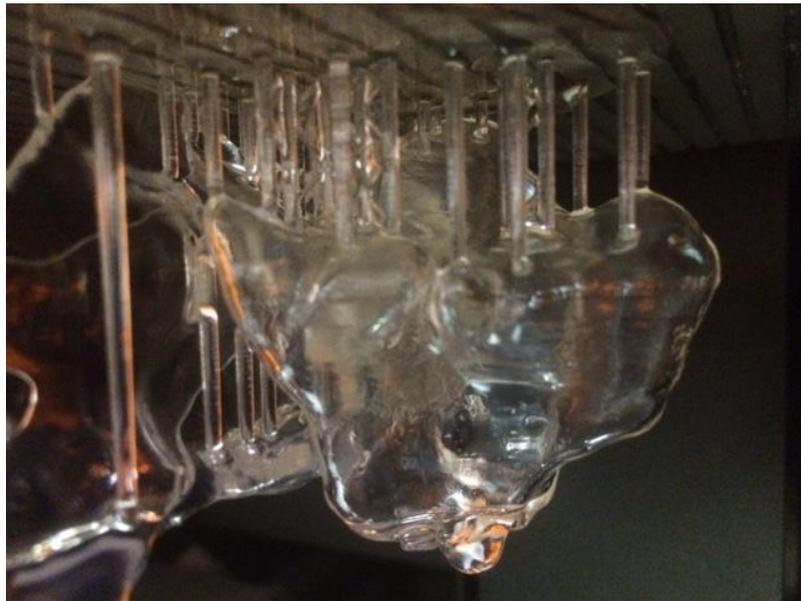


Figure 5 - Model of a paranasal sinus

The prototypes printed with XFAB were of great value and helped to verify the potentiality of 3D printing for the medical field. Advantages of the model printed with XFAB are the smooth surface, the high precision and the fine details obtained. However, the cost of the printing material and the software licenses are high and the printing time was too long for the NOSE project purposes. In addition, 3D models of the nasal cavities should resemble reality as close as possible and therefore, have different characteristics for each particular area. For example, the print-outs should distinguish soft tissues from hard ones. Specifically, while a hard material would be a good solution to print hard tissues such as bones, tooth enamel and dentin, a softer material could be used to print soft tissues such as tendons, skin, muscles, nerves and organs. That way, a more realistic representation could be obtained.

Because of these requirements additional experiments were done with the 3D Printer Prusa i3 Pro C from Geetech. This printer supports the printing with multiple types of filament with enhanced stability and reliability, and the cost of the material is lower than that for the XFAB. With the Prusa printer technology self-replicating machines can be created that can be used for rapid prototyping and manufacturing. It is a low-cost printer that provides the possibility of printing on different materials. Prusa printer is based on the concept of Material extrusion, more precisely Fused Deposition Modeling (FDM). During the 3D printing process a filament of solid thermoplastic material is pushed through a heated nozzle, melting it in the process. The printer deposits the material on a build platform along a predetermined path, where the filament cools and solidifies to form a solid object. With the Geetech printer selected regions of interest can be printed using different materials, and the materials can be optically differentiated by their various colors. Figure 6 depicts a set up consisting of a workstation and the Geetech printer. Figure 7 shows some of the printed 3d models.

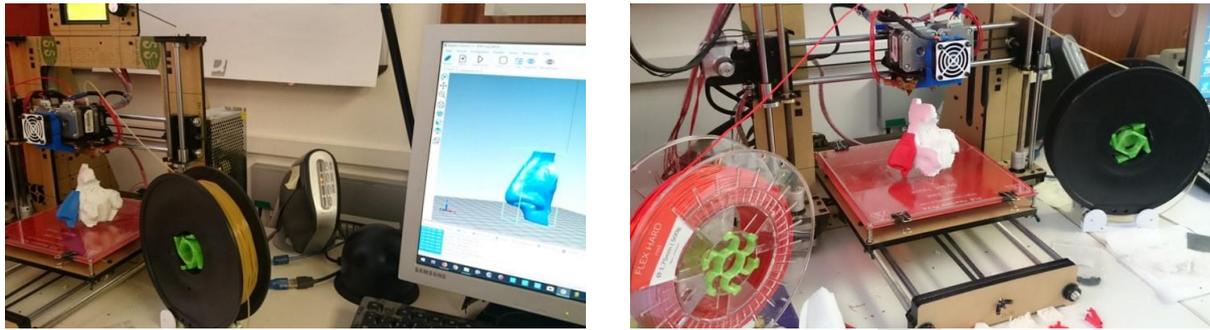


Figure 6 - Set up for the Geetech printer

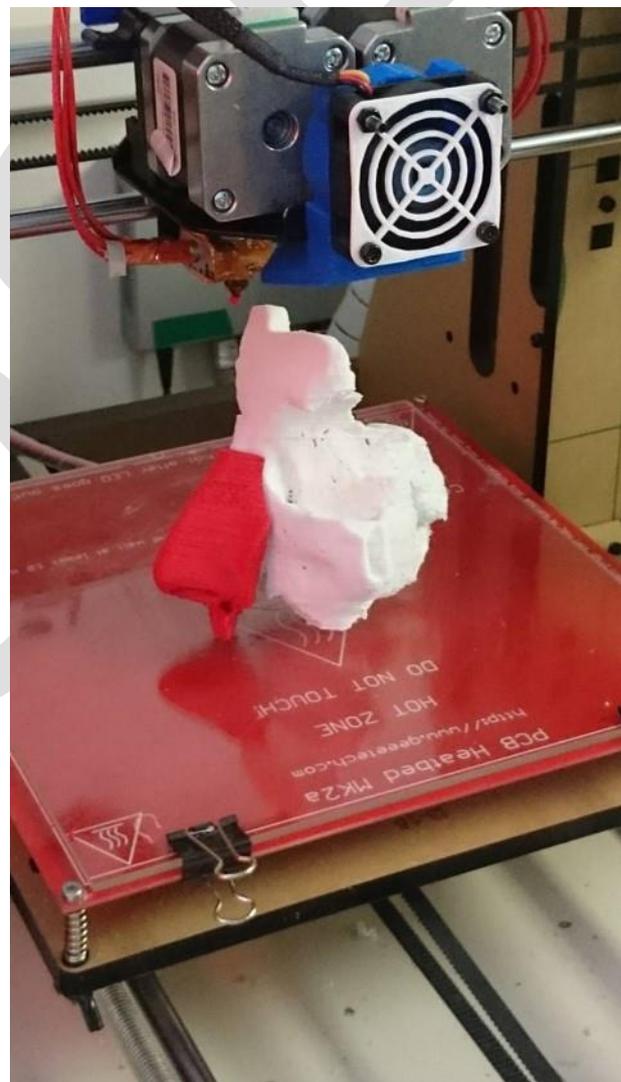


Figure 7 - Examples of printed models with the Geetech printer

4.1.6 Selection of IT-Resources

Based on these insights we defined the needed IT infrastructure for the NOSE project. The necessary software and hardware was set up and two different 3D printers to experiment with were purchased. An overview of the current IT infrastructure for the NOSE project is depicted in Figure 8.

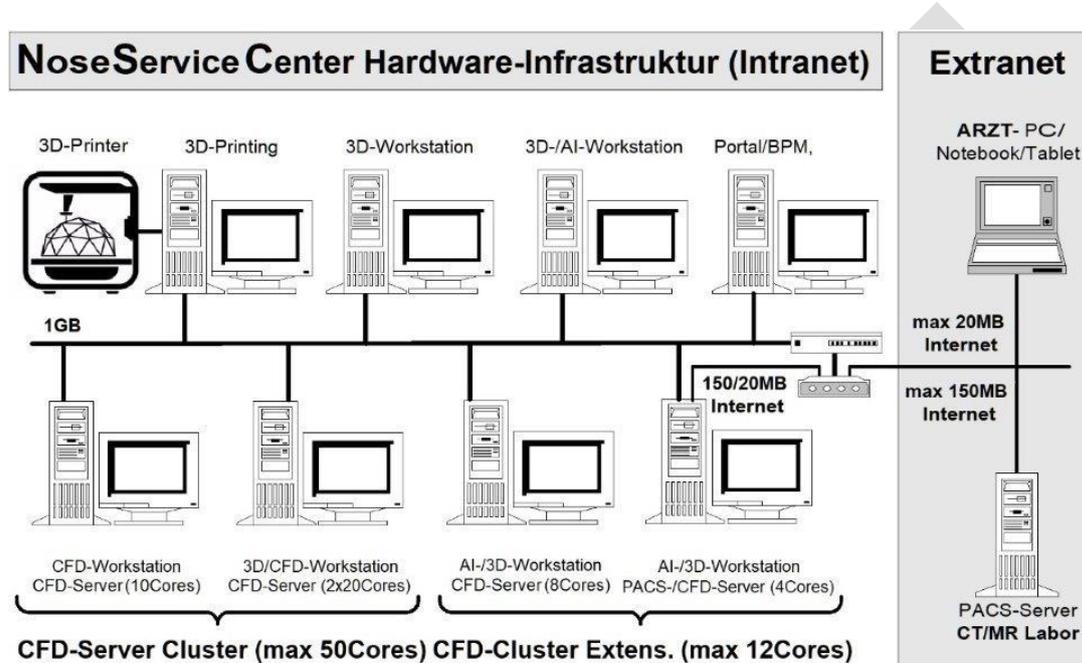


Figure 8 - Nose service centre infrastructure

3D Printers:

- FDM Printer + Desktopcomputer
- SLA Printer + Desktopcomputer

3D-Workstation

- 1 x 4 Core Intel CPU (Gen 6), 1x Nvidia GPU (Pascal)
- 1 x 8 Core Intel CPU (Gen 6), 2x Nvidia GPU (Pascal)
- 1 x 4 Core Intel CPU (Gen 4), 3x Nvidia GPU (Pascal)

Computer Workstation

- 1 x 10 Core Xeon (Gen 2)
- 2 x 10 Core Xeon (Gen2), 1x Nvidia GPU (Kepler)
- 2 x 10 Core Xeon (Gen2), 1x Nvidia GPU (Kepler)

The Computer Workstations are used to perform CFD Simulations with less computing-intensive methods. The NOSE team used them to run steady state (simpleFoam) and transient state (pisoFoam) solvers of the OpenFOAM CFD software suite. More computing-intensive simulations (RANS, DNS) which need a HPC Cluster are done by external partners to verify the results of the less computing-intensive simulations run on the NOSE workstations.

The 3D Workstations are used to train a machine learning algorithm to automate the segmentation of CT/MR images for the creation of 3D models. These segmentations are usually made manually. The machine learning mechanisms support this process by partially or fully automating a step in this process.

4.2 Workflow Concept (AP2)

Within the NOSE pilot study research on workflows and pathways concentrated on how to establish a Nose Service Center (NSC) as an interconnected network in which doctors, ENT surgeons, CT/MR centers and patients can request services and visualize the results in a transparent and homogeneous way. Some concept ideas for the future pathways were developed.

At the beginning a typical clinical pathway structure was drafted: *“Clinical pathways are used to reduce variations in practice and align decisions with evidence-based medicine, operational efficiency, and quality.”* [36]. A criteria for clinical pathways is to *“care for a specific clinical problem, procedure or episode of healthcare”*, a definition that puts emphasis towards their standardization [37]. The standardization of clinical procedures is also a main focus of the Object Management Group (OMG)⁹, which started in 2016 the “Health BPM Pilot”¹⁰ initiative, which is described in terms of the Healthcare Services Specification Project (HSSP) on Wikispaces¹¹. In October 2017, this initiative delivered a first version of the “Field Guide to Shareable Clinical Pathways” (downloadable from Wikispaces). This Field Guide recommends the use of OMG standards and recommendations, such as the Business Process Modelling and Notation (BPMN), the Decision Management and Notation (DMN) or the Case Management Model and Notation (CMMN). Notably, the use of DMN in a clinical environment was discussed already in 2015 based on a Breast Cancer use case [38]. Previous research and contributions, such as the presentation of “Clinical Algorithms” which can be found in a German ENT-related guideline [39], did not focus that much on standardisations and guidelines as the “Health BPM Pilot”.

4.2.1 Workflow Development

Complying with the OMG standard, the NOSE project elaborated a high level concept written in BPMN related to the preparation of a FESS, which describes the different actors, activities, communication and process flows. The integration of the NOSE model into a live system and the delivery of such an environment to the general public are planned as the final steps of implementation. Therefore, existing solutions to build up a Business Process Management (BPM) platform were investigated and experiments were carried out with two products: Bonitasoft¹² and Trisotech¹³. These two solutions are complementary: while Bonitasoft supports the creation and management of articulate business processes and their actors with a standardized approach, Trisotech allows for a deep domain analysis that can be used to refine the general process and domain constraints.

⁹ <https://www.omg.org/>, Accessed 2018-07-25

¹⁰ <https://hssp.wikispaces.com/bpm-pilot>, Accessed 2018-07-25

¹¹ <http://hssp.wikispaces.com/>, Accessed 2018-07-25

¹² <https://www.bonitasoft.com/>, Accessed 2018-07-25

¹³ <https://www.trisotech.com/>, Accessed 2018-07-25

4.2.1.1 Bonitasoft

Bonitasoft [40,41,42] is a platform that lets *"multi-disciplinary development teams create digital user experiences that connect personalized user interfaces with reliable back office operations"*. The platform supports the description of articulated business processes as compositions of smaller and self-contained sub-processes. Linking and synchronization between sub-processes, artifacts and involved actors are achieved by exploiting the Bonitasoft message functionality. With the use of the Bonitasoft environment some successful stories in the healthcare domain have already been developed, such as for Bristol-Myers Squibb¹⁴, the US Departments of Health & Human Services¹⁵ and Learning Health¹⁶. Therefore the NOSE project team decided to test the Bonitasoft platform.

In order to organize articulated business events, Bonitasoft recommends and suggests splitting up big processes into a set of smaller ones. The splitting promotes parallel work, makes testing and bug fixing easier and, renders the development process faster and more flexible. Sub-processes can have input and output variables and are linked within one another through messages. The sequences of actions within a particular sub-process are uncorrelated with the actions taking place in other sub-processes. Each sub-process can be developed in a stand-alone manner, using both a graphic component based on the BPMN notation and the apache groovy script as well. As a result, each sub-process can be modified independently, with input and output variables and synchronization messages assuring the consistency of the general business process. Moreover, Bonitasoft also offers the possibility to create connections between processes and databases (such as MySQL) to display, use, modify and save data stored in external databases. Besides, the User Interface (UI) portal allows to create and customize the widget and the look and feel of the page showed to the users.

Applying this paradigm within the NOSE pilot study, first, a high abstraction diagram was created, which describes the overall business process that should be developed. This first whole business process in form of BPMN diagram is reported in Figure 9.

¹⁴ <https://www.bonitasoft.com/customer-stories/bms/>, Accessed 2018-07-25

¹⁵ <https://www.bonitasoft.com/customer-stories/us-dept-health-human-services>, Accessed 2018-07-25

¹⁶ <https://www.bonitasoft.com/library/medical-best-practices-core-bpm-processes>, Accessed 2018-07-25

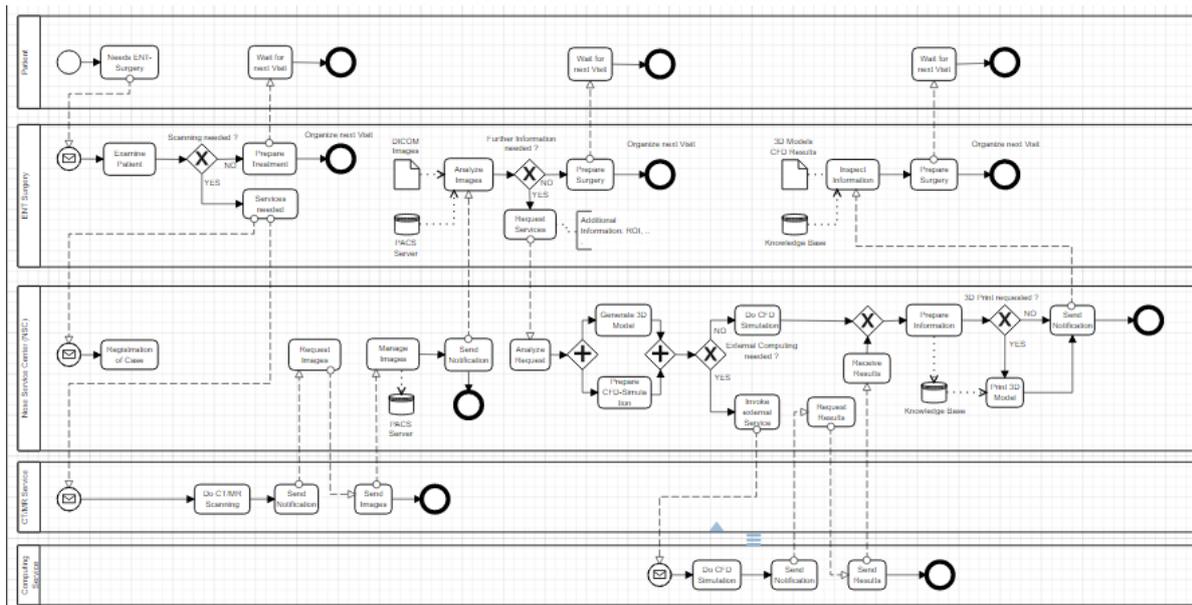


Figure 9 - Bonita BPMN Business Process for NSC

This diagram is an abstracted and low-detailed version of the overall process, but already includes certain decision points and events that have to be further detailed, such as “Patient going to a doctor appointment”, “Doctor requesting a CT/MR for a patient” and “Creation of a 3D Model based on the CT/MR of a patient”. A direct development of the whole process is not trivial. Thus, the first step was the identification of small sub-processes, which are the building blocks that when put together constitute the whole diagram. However, there is not a univocal way to split up the diagram into a set of small sub-processes. As a general rule, sub-processes should be designed as sets of actions and events completely self-contained and happening at the same location involving a well-defined subgroup of actors and artifacts. For example, it makes sense to split the process “Patient going to a doctor appointment” from the process “Patient going to a CT/MR center for an examination”. In fact, these two processes take place at two different locations (Doctor Studio and CT/MR center), they involve different sets of actors (Doctor’s Secretary, Doctor, Patient for the first process and CT/MR Center’s Secretary, CT/MR Operator and Patient for the second one) and use and produce different artifacts. Furthermore, there is a clear chronological order between the two processes and a condition that connects them: if the doctor suggests that a patient should undergo a CT/MR examination, then the patient will have to make an appointment for such examination. This logical and chronological separation makes it easier to identify the two processes as separated ones and connect them accordingly.

However, there are some “hidden” sub-processes that are missing from this initial big picture and will become clearer only while describing the process with finer granularity. For example, the sub-process “Patient goes to a CT/MR center for an examination”, itself includes a series of sub-tasks: the registration of the patient at the secretary, the patient waiting till the beginning of the examination, the examination itself and eventually a consultation between the patient and the doctor at the end of the examination. These sub-tasks are chronologically ordered and relate to

each other. Whether to create an extra sub-process for each of these or not, depends from case to case and relates to the complexity of each task and the interactions with the system (internal and external database) each sub-task might require. Automatized task updating SQL tables that are triggered by certain events are also not present in the above diagram. These should be defined separately for each sub-process when it is developed.

Beside the BPMN diagram, Bonitasoft also allows to define a specific UI for the various actors. Figure 10 depicts two sample screenshots of a data entry form to be filled in by the surgeon and her/his secretary.

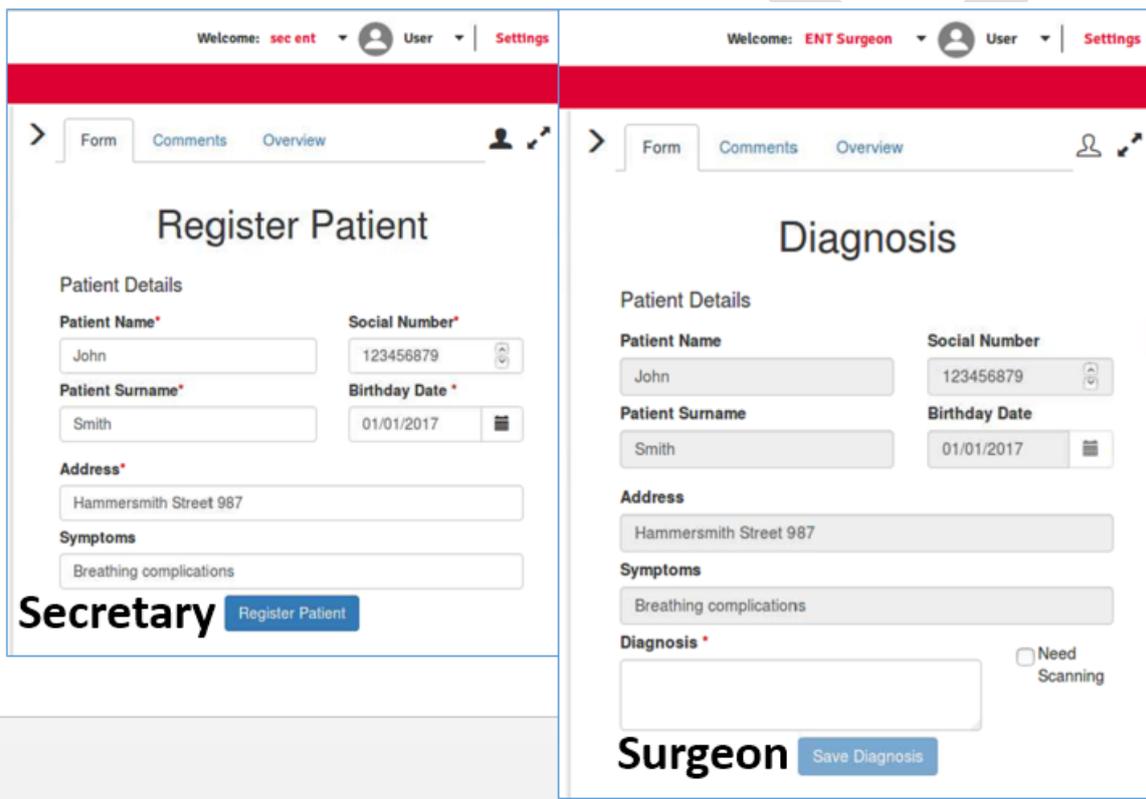


Figure 10 - Data entry forms

Using Bonitasoft, the communication between processes is assured by messages (or signals) that are sent between processes. At any point of its execution, a process can send messages to and receive messages from a defined set of target processes. After a message is sent, the target process execution is triggered and the target process' actions are executed accordingly. Notably, it is possible to have processes waiting for the completion of the target process before resuming their execution, as well as non-waiting processes that go on with their normal execution in parallel with the target process.

For this pilot study, the original diagram depicted above was split up into the following sub-processes:

- Patient Visit
- NSC Create Case
- CT-MR Schedule Appointment
- NSC Update Case
- CT-MR Exam
- CT-MR Results
- NSC Update Case CT-MR
- Schedule New Visit
- NSC CFD Simulation
- External CFD Simulation
- Schedule Next Visit
- Operation

Some of these sub-processes are automatized tasks that are executed without the need of human interactions because they simply update particular entries in an external MySQL database (for example the processes "NSC Update Case" and "NSC Update Case CT-MR"). Furthermore, some sub-processes are always executed while others take place if some particular conditions are met (conditional flow).

Based on the overall diagram the above listed sub-processes were defined. A graphical identification of these sub-processes is given in Figure 11.

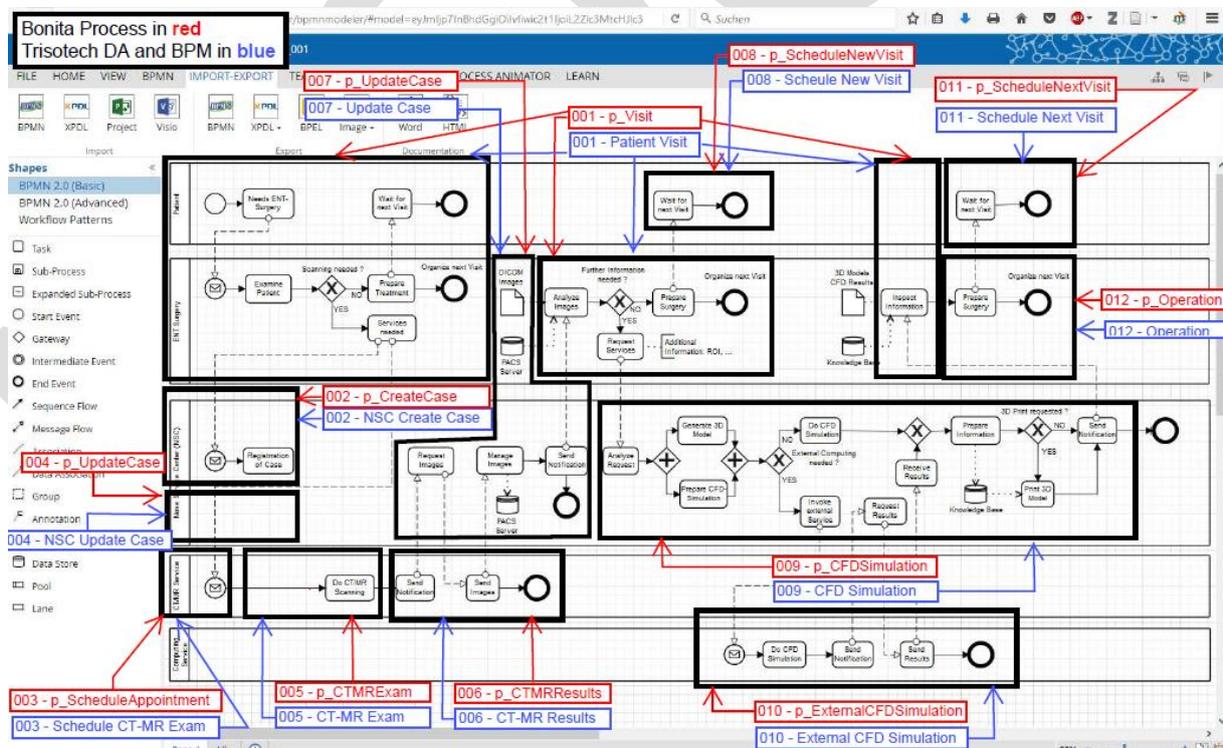


Figure 11 - Sub-processes derived from the original NSC diagram

In consequence, a detailed diagram for each sub-process and a UI for each actor in Bonitasoft were developed. Afterwards, the Trisotech tool was used to analyze each sub-process in greater detail. This procedure is explained in the next section.

4.2.1.2 Trisotech

Trisotech is a global leader in digital enterprise solutions, offering innovative and easy-to-use software tools that allow customers to discover, model, analyze and find insights into their digital enterprise. Trisotech offers a Digital Enterprise Suite, a “cloud-based software to Visualize, Innovate, Transform, and Improve your organization”. The Digital Enterprise Suite provides tools for non-technical business people to discover, model and analyze a digital enterprise, exposing insights into relationships between models. This suite aims at optimizing business processes by clearly identifying actors involved and their goals, activities and decisions that modify the flow of events and the artifacts that are needed. Overall, it helps to uncover every aspect of the business process in order to not miss any important point with the goal of an overall improvement in the shaping of the business process. Trisotech is also used by the “Health BPM Pilot” initiative of OMG.

The Digital Enterprise Suite consists of several parts with different focus and functionality (Discovery Accelerator, BPMN Modeler, CMMN Modeler, DMN Modeler and Insight Analyzer). Within the NOSE pilot study two of these components, the Discovery Accelerator and the BPMN Modeler, were evaluated.

Discovery Accelerator

The Discovery Accelerator is the part of the Digital Enterprise Suite that helps to understand and analyse the current business situation.

The Discovery Accelerator is used to:

- discover and document the structure and capabilities of an organization, and establish meaningful performance metrics;
- specify business goals and analyze how they relate to activities;
- analyze and assign responsibilities;
- capture and analyze time, cost, value and quality metrics for activities;
- export information for documentation, input to strategic planning or modelling activities

Particularly, the Discovery Accelerator allows describing processes in terms of a W5 board (Who, What, Where, When and Why):

- actors: **who** performs a particular task of a process;
- artefacts: **what** is needed in order for a task to be executed;
- events: **when** is a task triggered;
- systems: **where** does the task take place;
- goals: **why** is the task executed;

In Trisotech each of the 5W is referred to as a “collection”. An example of a W5 Board for the “Patient Visit” sub-process is depicted in Figure 12.

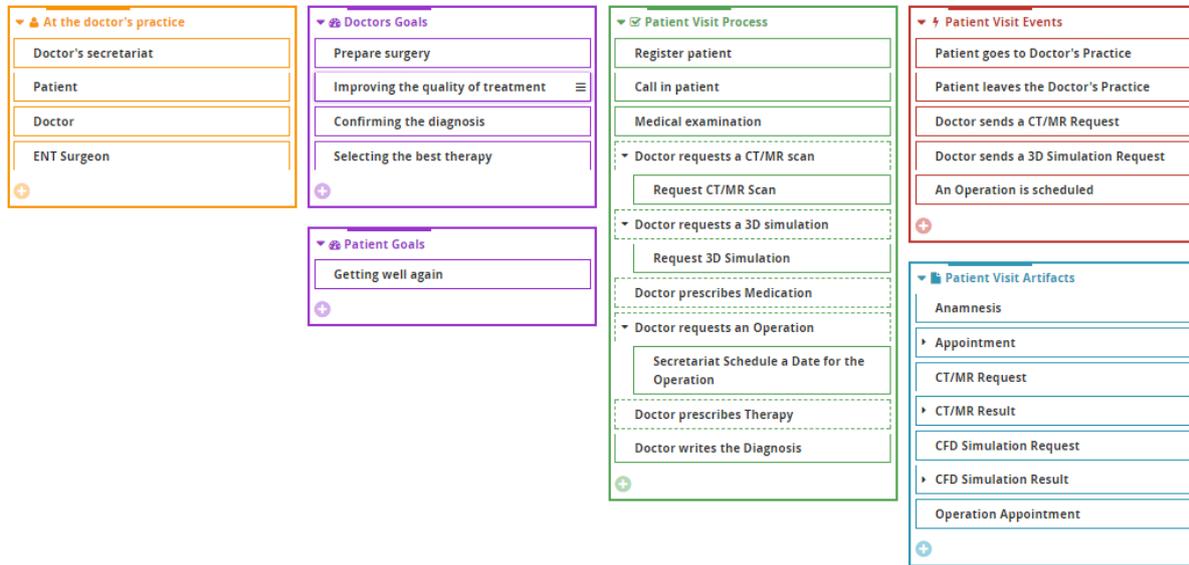


Figure 12 - Example of a W5 Board in Trisotech

Moreover, the Discovery Accelerator permits to define relations between collections to better describe the constraints and requirements of the process workflow. Overall, there are 4 different types of relations that could be defined, namely:

- RACI (Responsible, Accountable, Consulted, Informed) relations describing the way actors are involved in the tasks;
- Input/Output relations used to identify which artefacts a task receives as input and which artefacts are produced when the task is completed;
- Trigger/Results relations permitting to define the events that trigger a specific task and indicating which event is triggered once the task is completed;
- Achieve/Maintain relations describing the goals a task aims to achieve or indicating which goals should be preserved at the end of the task.

Figure 13 shows an example of a RACI relation between actors and activities.



Figure 13 - Example of RACI relations between actors and activities

Business Process Management

Another part of the Trisotech Digital Enterprise Suite is the BPMN Modeller. This tool is based on the BPMN, a standard published by the OMG. BPMN is used in Trisotech to document how things should be done. The BPMN Modeller helps to document business processes and drive process improvement initiatives. Furthermore, complete process models can be created and simulated for optimization, and can be exported to a Business Process Management System (BPMS) for process automation. Specifically, the Business Process Management (BPM) is used to

- create graphical business process models
- animate process models
- simulate process scenarios to predict outcomes
- accelerate model creation with standard workflow patterns
- bridge the gap between process modelling and implementation

An example of BPMN produced by Trisotech BPMN Modeller is depicted in Figure 14.

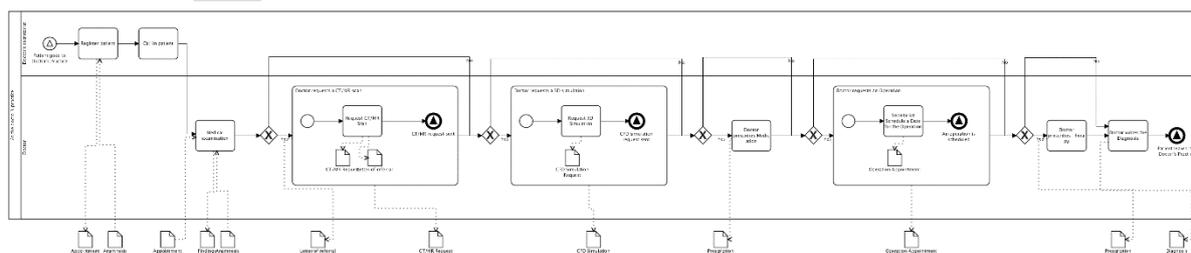


Figure 14 - BPMN produced for the Patient Visit process

4.3 Mesh Generation (AP3)

One of the aims of NOSE was to detail and analyze the intricate airflow ventilation in the nasal sinuses. To this end, the DICOM images from CT/MR served as input for creating a mesh of the nose and the paranasal sinuses (see Figure 15).



Figure 15 – Input DICOM images (0.5mm slice thickness)

Notably, it is best to work with DICOM images with a maximum slice thickness of about 0.5 mm, a thickness that allows for the successive creation of anatomically exact 3D digital models in a 1:1 scale. These 3D digital models can be visualized and examined on the PC or tablet and printed out using a 3D printer for haptical inspection.

Taking this approach, it is possible to analyze the obtained mesh from different perspectives and also cut digital slices along particular directions. As a result, the new findings are manifold under many aspects. In the first place, the highly complex anatomy of the paranasal sinuses and the pathology of each single patient can be represented in an intuitive and easy to explore way. Such representation improves the understanding of the individual anatomy of the paranasal sinuses and should be considered as an additional new standard for the practical diagnosis. Furthermore, the detailed mesh of the paranasal sinuses is a valuable additional aid for ENT surgeons and doctors towards the planning and the preparation of endoscopic surgery (like FESS). Moreover, the mesh and the 3D model could be used in scenarios of surgical education allowing students to use high precision virtual models to deepen their understanding and improve their training in FESS. In addition, this procedure offers the possibility to edit the meshes to reflect a hypothetical post-operation scenario on which CFD could be performed in order to assess whether a patient would benefit from a surgery or not (Virtual Nasal Surgery) [43, 44].

4.3.1 Mesh Generation and Refinement

Starting with the DICOM images of the patient as input, a mesh was produced as the basis to construct a 3D Model representing the region of interest (ROI). A 3D Model combines the information from the Axial, Sagittal and Coronal views of DICOM images into a 3D prototype, which can later be analyzed in simulation experiment and printed. The infrastructure capable of providing the necessary storage to save and manage CT/MR images (DICOM Images) can be offered by means of a Picture Archiving and Communication System (PACS) server [45,46], taken from open source domain (Orthanc [47]).

For the reconstruction of the nasal cavities the open source software 3D-Slicer [48,49] was chosen. This software enables a direct connection to PACS-Servers and was already used in various other research projects [50,51]. With the 3D Slicer software series of DICOM images can be loaded and displayed in the axial, sagittal and coronal views. One of the functionalities offered by 3D Slicer is the possibility to create a segmentation (also known as contouring), a set of organized segmented structures. Segmentation allows for delineating the structure of interest within the DICOM image as for example tissues and bones. Furthermore, 3D Slicer can put together the axial, sagittal and coronal view of a segmentation to compute the related 3D Model.

There are two ways to create the segmentation: Either to manually investigate and annotate the relevant parts in each DICOM image for each view or to make use of some of the tools 3D slicer offers. A manually generated segmentation is generally more precise as the annotation process is done by an expert who checks every single image. However, this process is not applicable in an everyday context when DICOM images from plenty of patients have to be segmented, because it is incredibly time-consuming (up to 24 hours). On the other hand, the various tools of 3D Slicer can be used to identify particular regions within seconds but they lack the accuracy of a manual inspection of the images. Specifically, 3D Slicer cannot fully automatically generate a (polygon) mesh.

For the NOSE pilot study a mixture of two approaches was chosen. First, automated filters from 3D Slicer were applied in order to obtain a coarse segmentation for a particular region of interest. Second, the automatically generated segmentations were inspected and corrections were manually applied if needed. Choosing this procedure the fast 3D Slicer filters capabilities were connected with the expert inspection of the created segmentation, serving as a correction and validation step. That way an accurate segmentation can be done in a reasonable time.

The NOSE services should include providing a complete set of information covering all properties of the nasal cavities (especially paranasal sinuses). To this end, it is important to separate the different sinuses in a 3D model. Therefore, some post processing steps have to be included to clean-up the obtained models. As a result an editor that can separate cavities that do not belong to the nasal cavity system was developed. This editor can separate paranasal sinuses from the (main) nasal cavity, it can generate covers to close cavities, combine different meshes (3D sub models) and add walls for enhance 3D printing. The model was enriched by working with open source products such as meshlab and meshmixer (which allow processing and editing 3D triangular

meshes). Figure 16 shows a 3D-Slicer screenshot of a 3D model combined with a 2D image in the coronal plane.

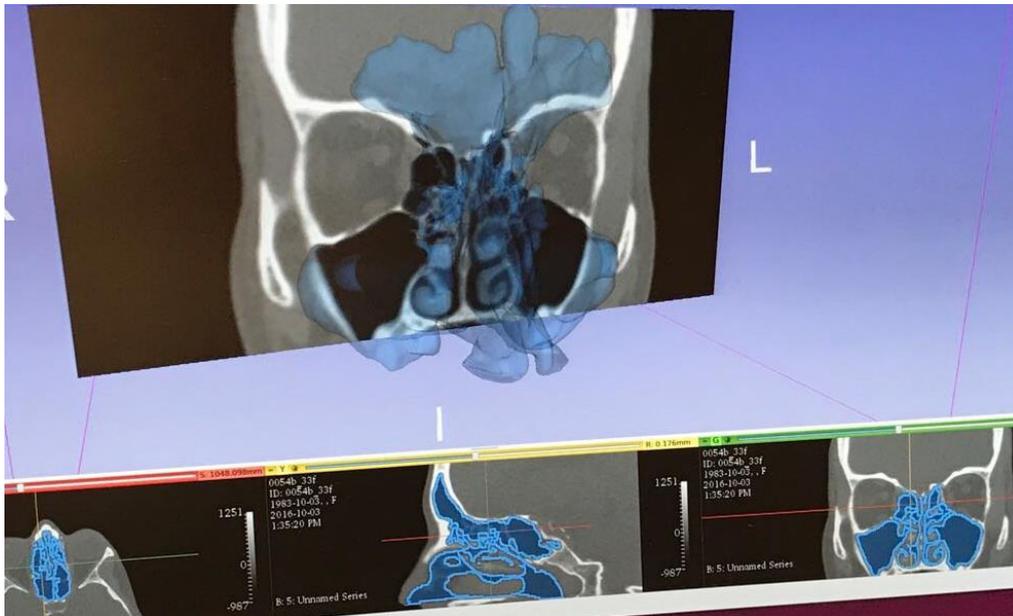


Figure 16 - 3D-Slicer screenshot of a 3D model combined with a 2D image

Additionally, the use of CNNs (Convolutional Neuronal Networks) in order to diminish the processing time was evaluated. The evaluation finally showed that CNNs can reduce the time of segmentation to a few minutes [52,53] and the use of CNNs shall increase the efficiency of creating segmentations and the relative 3D models tremendously.

3D Slicer filters

With the various effects (filters) offered by 3D Slicer segmentations are created for a set of DICOM images. The threshold effect fills segments based on the intensity range of the images. The value of the threshold can be modified and a preview of the resulting segmentation is shown in real time. Modifying the values of the threshold allows for selecting a particular segmentation that is later manually changeable. Figure 17 depicts the resulting segmentation (colored in green) in the sagittal view for two different values of the threshold.

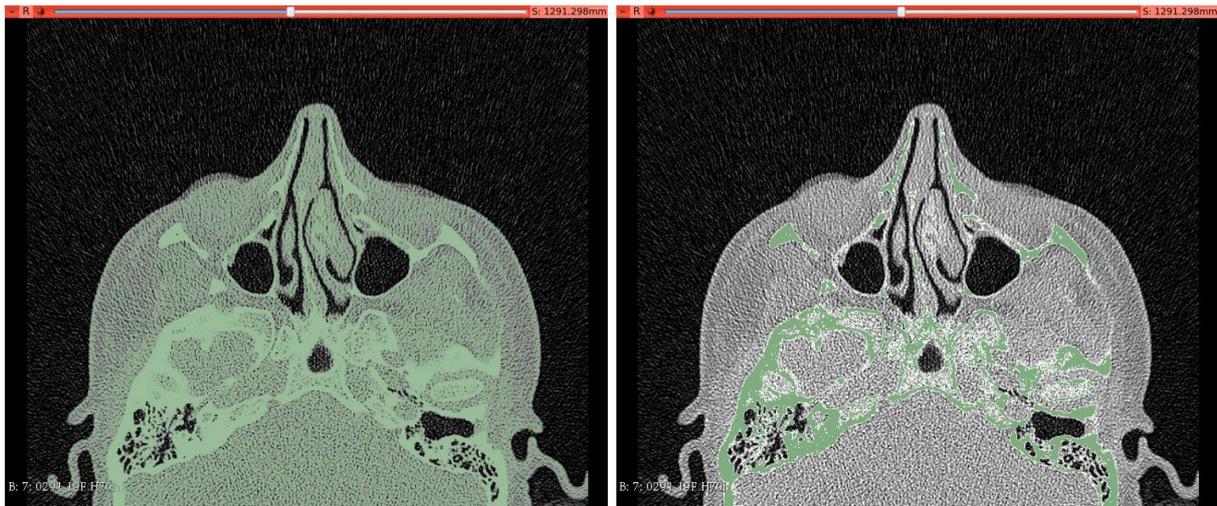


Figure 17 - Segmentation results for different threshold values (Sagittal view)

Smoothing is an effect that modifies the boundaries of the segmentation by removing extrusion or filling small holes. This effect offers various smoothing methods, such as opening (removes extrusions smaller than the specified kernel size), closing (fills sharp corners and holes smaller than the specified kernel size), Gaussian (smoothing of all contours) and median (removes small details while keeping smooth contours mostly unchanged). This effect includes the parameter kernel size that can be modified in order to increase or decrease the intensity of the modification applied by the filter.

Islands is a useful effect to edit a segmentation by altering its connected components (islands). Specifically, this effect allows various operations, such as keeping the largest component, removing small components and splitting components into segments. The last two operations also include a minimum size parameter to specify the dimension of the islands that will be modified. Despite these three effects that were heavily used, other automatic effects offered by 3D Slicer include Grow from seeds, Fill between slices, Margin and Logical operators.

Besides these automatic effects, 3D Slicer also provides three tools for manual segmentation: Paint and Draw to depict a segmentation on DICOM images using mouse clicks and Erase, for removing parts of a segmentation also by mouse clicks. In general, an automatic segmentation is first done by using the Threshold effect that can then be modified with the Islands and/or Smoothing effects. Then the obtained segmentation is optimized by manually editing the images if needed.

4.3.2 In Vivo Model

Within this pilot study, the focus was mostly on the creation of segmentation and the related 3D models, which constituted the input for CFD simulations. These in vitro and in silico experiments provided immense valuable insights and constitute the fundament for the in vivo experimentation. In vivo model and experiments are planned to be conducted as a future research steps in the ongoing project "Rhinodiagnost - Morphologische und funktionelle Präzisionsdiagnostik der Nase" (see chapter 6.2). In the context of this project, the use of a 4-Phase Rhinomanometer on real

patients suffering from CRS is planned. Moreover, also in-situ computational steering with real-time simulation is foreseen. Specifically, it will be possible to modify in real-time the computed segmentation/geometry with a direct feedback to the medical expert involved in the operation.

4.4 CFD Simulation (AP4)

Computational Fluid Dynamics (CFD) is an established methodology for the simulation of complex flows that can be used for simulating the airflow in nasal and paranasal sinuses. CFD solves the Navier-Stokes equations (momentum, mass, and energy conservation) with numerical methods (e.g. finite volume of Lattice-Boltzmann methods) and it has been discussed in many scientific papers during the last decades [54,55,56,57,58]. Computed tomography (CT) or magnetic resonance imaging (MRI) scans of the head serve as raw data for the mathematical CFD predications of the nasal airflow. However, the integration of CFD simulation into a day to day clinical treatment scenario has not yet been achieved due to the complexity and the multidisciplinary requirements of this approach.

4.4.1 In Silico Model

Once the segmentation is completed (see 4.3), 3D Slicer is used to create a 3D Model based on the segmentation from the three views (coronal, sagittal, axial). The "Show 3D" button available in the "Segment editor" module triggers the creation of the model. Figure 18 depicts the created 3D Model, together with the three different views.

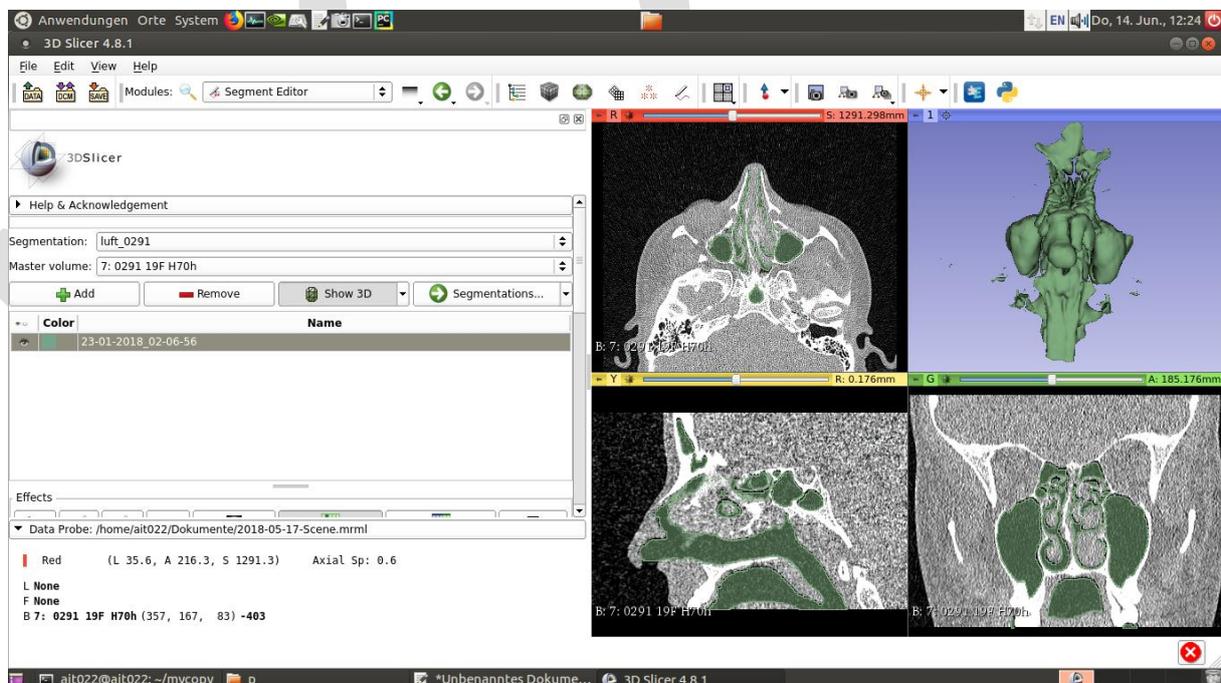


Figure 18 - Segmentation and the created 3D Model

At this point it is possible to save the generated segmentations and the related 3D Model, respectively as .nrrd and .stl files. The .stl file of the model can then be printed with the aid of a 3D printer or used in experimental simulations, as for example CFD simulation. Figure 19 depicts an example of a created 3D model.

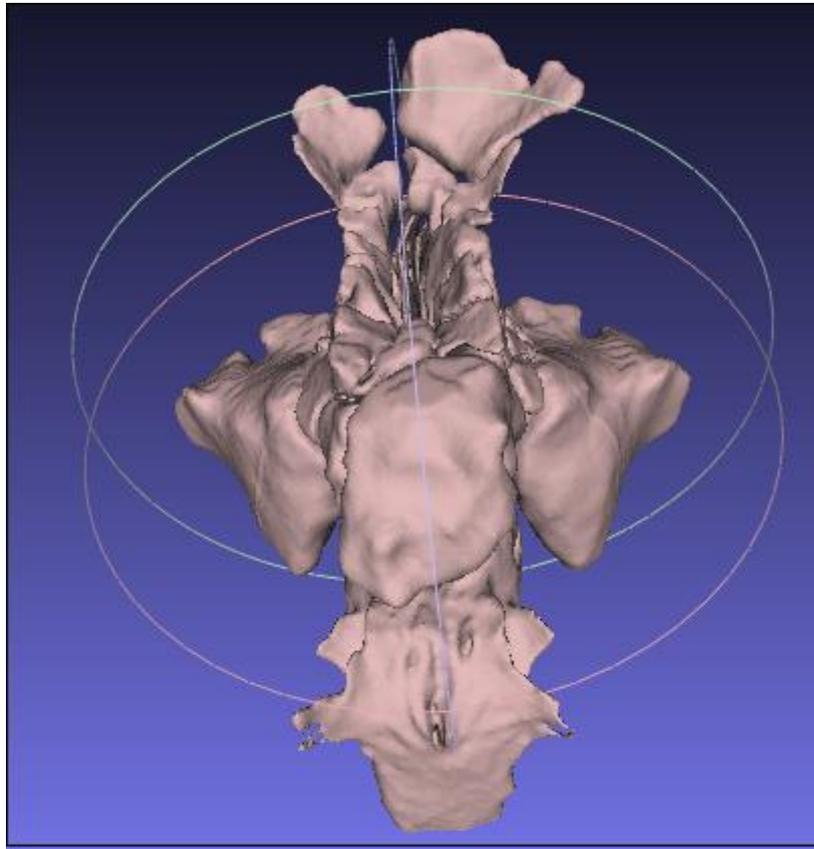


Figure 19 - Example of a created 3D Model

4.4.2 CFD Simulation

In the NOSE project upon completing the creation of the 3D model (a surface constructed on multiple meshes), a CFD simulation of the nose and of the paranasal sinuses [59,60] was performed. The first step in this process was the generation of a volume mesh for the region of interest, which is a polygonal representation of the interior volume of an object. For this task and the other CFD-related activities the OpenFOAM open source software was used, which supports CFD processing and simulation. Experiments were done under the hypothesis of incompressible flow; changes of pressure due to changes of the speed of the airflow are that small that the (small) changes of density do not alter the stream of the airflow. OpenFOAM's solvers were used to determine the Reynolds-averaged Navier–Stokes equations (RANS) for a $k-\omega$ -Menter's Shear Stress Transport ($k-\omega$ -SST) turbulent model. The RANS equations describe the motion of a turbulent flow (in our case an airflow) [61], while the $k-\omega$ -SST turbulent model consists of two eddy-viscosity turbulence model equations and it is a robust and widely used model for CFD

[62,63]. Two different k-epsilon turbulent solvers were tested for incompressible airflow: the steady-state simpleFoam and the transient (time-dependent) pisoFoam.

A steady-state solver, such as simpleFoam, tries to converge to a solution with a given number of iterations and a set of initial and boundary conditions. Alternatively, a transient solver as pisoFoam operates with timestamps and captures the evolution of the fluctuations and the dynamic formation of eddies. Thus, a transient solver computes the detailed evolution of the airflow but requires more computation time than a steady-state one. In this context, it was interesting to verify if the solutions that are obtained with different types of solvers are (on average) comparable with one another.

A CFD simulation on the whole nasal cavity area including paranasal sinuses with simpleFoam (steady-state) requires around 10 minutes of computing time on a cluster of two 2-processor (XEON 2690v2) engines with a total capacity of 40 cores. The tests revealed that applying a "domain decomposition" principle, in which different parts of the geometry are distributed to specific computing cores, ensures better performance. A total of 36 cores were used with a decomposition factor per coordinates: 3, 4, 3. Figure 20 shows three blocks (colored) of the whole geometry which are dedicated to 3 processor cores in different view.

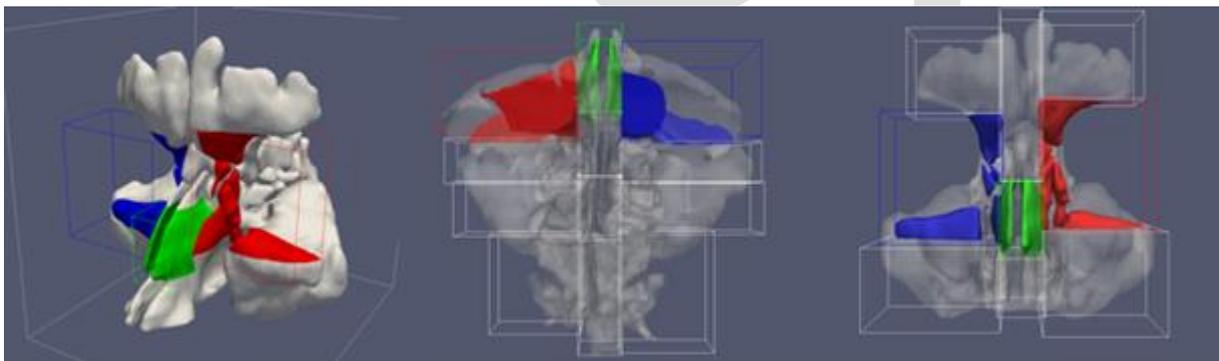


Figure 20 – Domain decomposition

The volume mesh consisted of 12 million cells and the pressure difference between the nostrils (the two channels of the nose) and the nasopharynx (the upper part of the throat behind the mount and the nasal cavity) was 130 Pascal. Figure 21 depicts the result of the simulation up to 1400 iterations. U_x , U_y and U_z are the velocity vector components in the three directions, p is the pressure, k is the turbulent kinematic energy and ω is the turbulent variable.

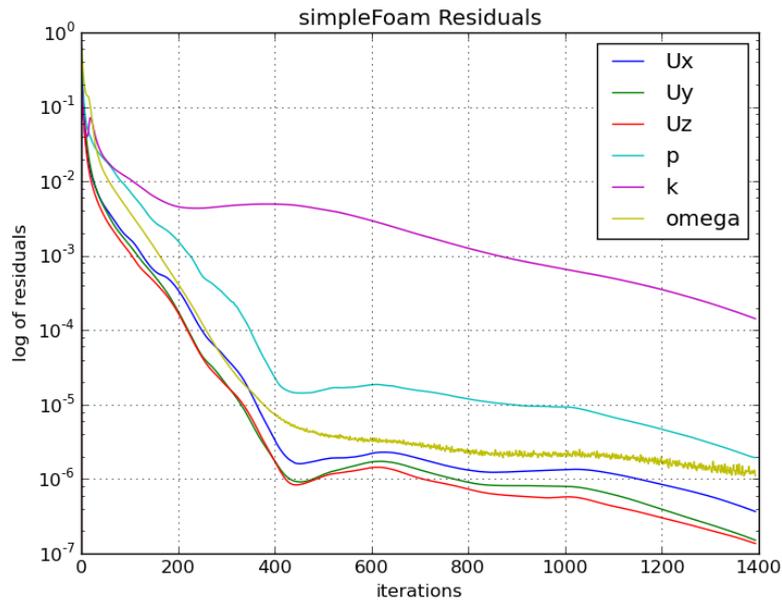


Figure 21 – Convergence of iterations

First, a steady-state CFD simulation at 20 time points of the respiration cycle was performed. And afterwards the simulation results were used to create a video to show the evolution of the airflow. Altogether, these simulations took less than 4 hours on the infrastructure set up at the NOSE incubator.

Furthermore, a CFD simulation was carried out with the transient pisoFOAM solver. In this case, with the same infrastructure as described before, the simulation took around 300 hours. A convergence (average Courant number less than 1) [64] was achieved by selecting a time step smaller than 10⁻⁴ seconds. Comparison of the outputs (videos) generated by both methods (simpleFoam at 20 selected points vs. pisoFoam) showed similar results. Figure 22 depicts the simulation result for both methods at second 0.92 of the respiration cycle.

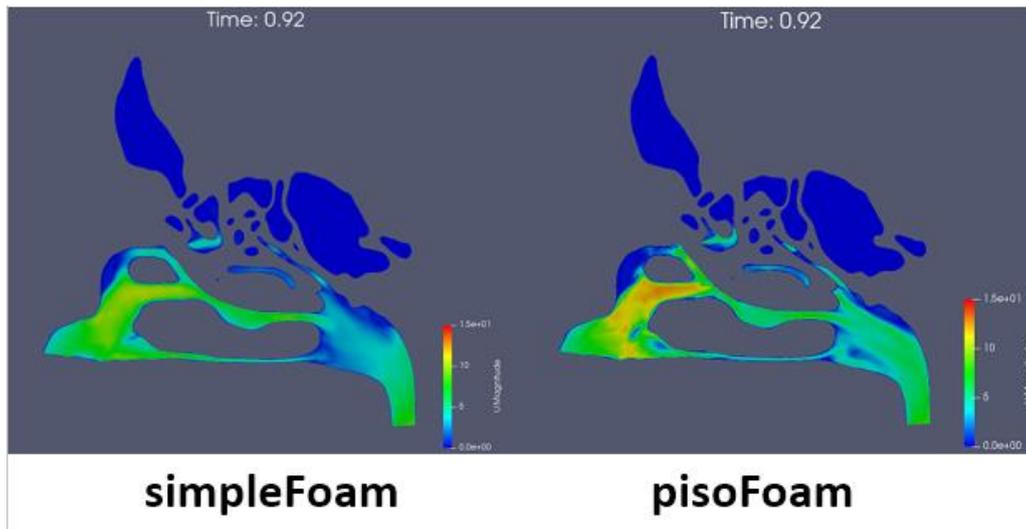


Figure 22 – Sec 0.92 of the respiration cycle

For this case a video, neglecting the paranasal sinuses, was created (available at <https://rhinodiagnost.eu/2017/09/26/video-stroemungssimulation/>). The whole 3D model is online available (<https://rhinodiagnost.eu/2017/09/26/3d-view/>).

By using these methods, the inner nose can be virtually traversed and the minimal airflow in the area of the paranasal sinuses, especially the very narrow passages [65,66] can be visualized. Radiologists and ENT experts can make use of this dynamic visualization of the ventilation in the nasal cavity and the paranasal sinuses to improve their understanding of the particular pathology the patient suffers from. Therefore, the enrichment of the static CT/MR images examination with the results of the CFD simulation helps to improve both sensitivity and specificity in the assessment of CRS pathologies. The results obtained and delivered within the scope of the OpenNOSE project [67] built the basis for future refinements in the fields of CFD.

4.5 CFD Analysis (AP5)

The computing time to complete CFD simulations for the whole nasal cavities is generally long, specifically in a transient setting with pisoFoam. However, the required time can be substantially reduced by discarding parts of the full 3D model and keeping only the paranasal sinuses and nasal cavities as regions of interest. Figure 23 shows a simulation which targets only the nasal cavities and the maxillary sinuses.

The open source software ParaView¹⁷, a multi-platform data analysis and visualization application, can be used for visualization. Other presentations of the airflow into the paranasal sinuses are given in Figure 24 and depict the airflow into three different paranasal sinuses: maxillary, sphenoidal and frontal sinus.

¹⁷ <https://www.paraview.org/>, Accessed 2018-07-25

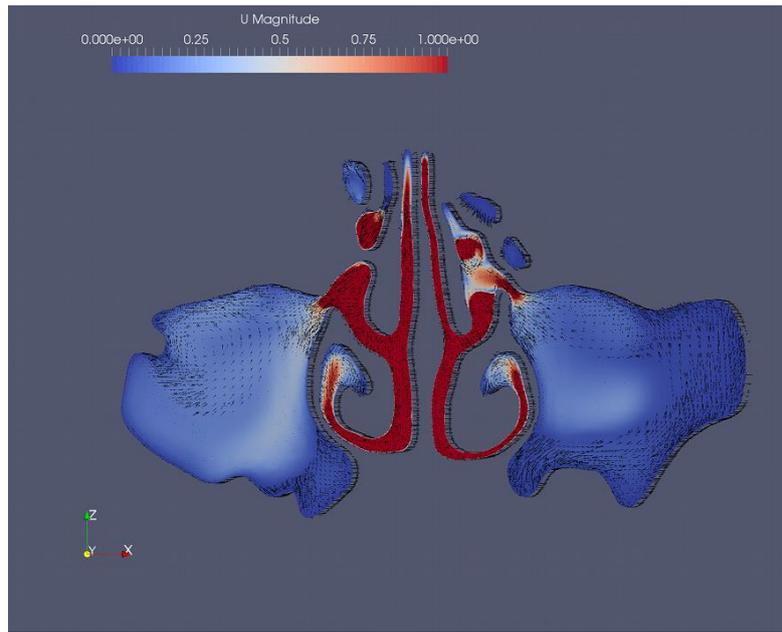


Figure 23 - Simulation of nasal cavity and maxillary sinuses

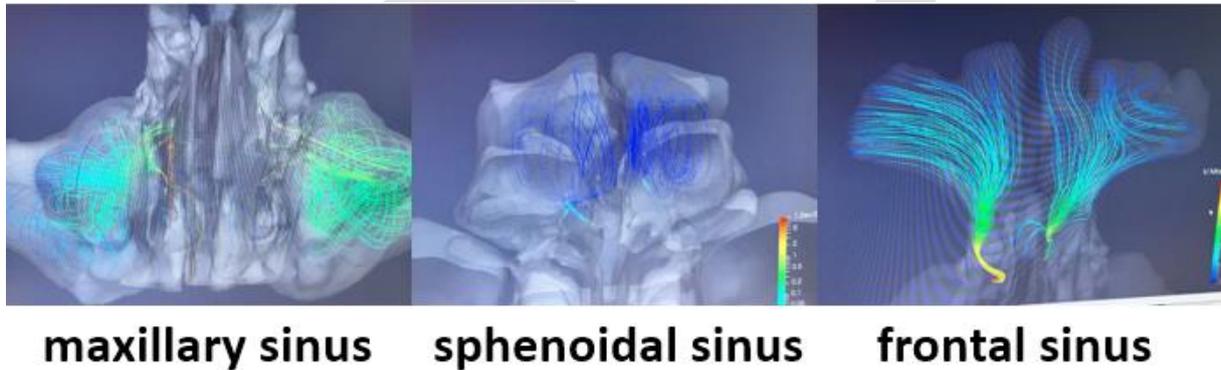


Figure 24 - Airflow into different paranasal sinuses

The CFD simulations based on the transient pisoFoam solver provide information about the exchange of air in a paranasal sinus during a respiration cycle. Preliminary calculations evidenced a quite small in and outgoing air volume in the paranasal sinuses. Further investigations of these initial results with an increasing number of considered cases (patients) will include a high number of CFD simulations on different geometries. The results obtained with such a considerable dataset shall deliver more insights into the actual volume of the airflow during a respiration cycle. The influence of the temperature of the airflow into a paranasal sinus was investigated with the aid of a different CFD system. Experiments were done with Fire2, a CFD simulation tool developed by the Austrian company Anstalt für Verbrennungskraftmaschinen List (AVL). The tool showed that airflow at 20 degrees Celsius at the nostrils warms up to around 38 degrees Celsius after passing the nasal concha and before reaching the frontal sinus.

Summing up, the result of the CFD simulations on the whole geometry of the nasal cavities showed that the airflow into the paranasal sinuses is very much smaller than the one in the main cavity. Moreover, the results obtained using a transient solver (pisoFoam) or a steady state one (simpleFoam) are quite similar: the difference in the volume of the airflow of the two solvers at selected points of the respiration cycle could be disregarded. Similarly, the influence of temperature on the airflow into and in a paranasal cavity can be neglected as well. Furthermore, provided that pressure or volume of the airflow at interesting points in the respiration cycle can be measured (e.g. by using a 4 phase rhinomanometer), CFD simulations can be simplified and require less computing power. Notably, in order to support ENT surgeons towards the preparation of surgeries in a paranasal sinus, it suffices to verify whether the airflow enters the paranasal sinus or not. Specifically, enriching the information within the DICOM images by providing additional information regarding the airflow in different views, improve the surgeons' confidence and increase the probability of surgery success. An example of airflows in relation to different DICOM images is given in Figure 25.

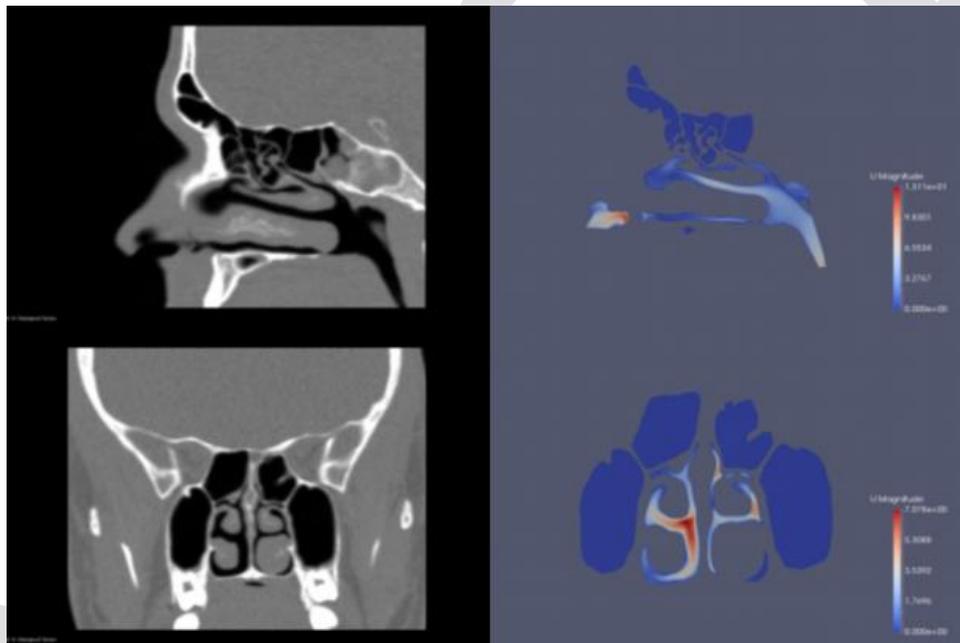


Figure 25 – DICOM images and documentation of airflows

4.5.1 In Vitro Model

A complete respiration cycle (inspiration and expiration) of 6 seconds was measured, using a 4-Phase Rhinomanometer [68,69,70]. Figure 26 shows this medical device.



Figure 26 - 4-Phase Rhinomanometer

The Rhinomanometer can measure the pressure and flow rate of air through each nostril separately. Figure 27 and Figure 28 show these measurements in function of the airflow rate and pressure over time respectively. These figures represent an average cycle obtained over a series of measurements. The breathing cycle has a duration of 6 seconds, right (blue) and left (orange) nostrils are recorded separately.

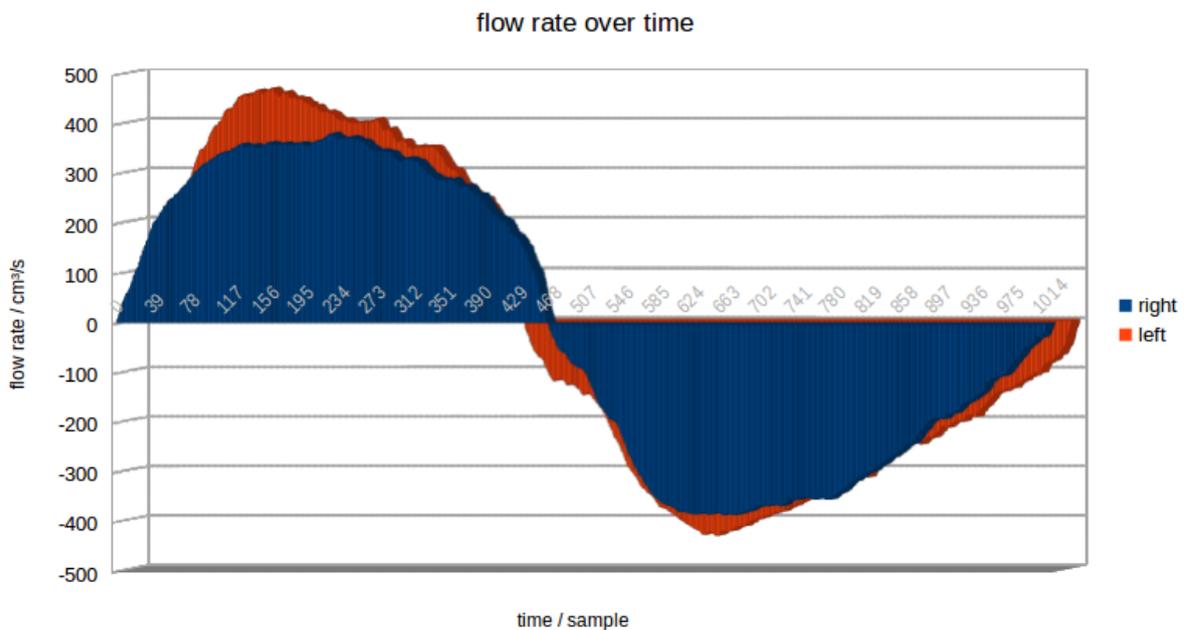


Figure 27 - Airflow rate over time measured by 4-Phase Rhinomanometer

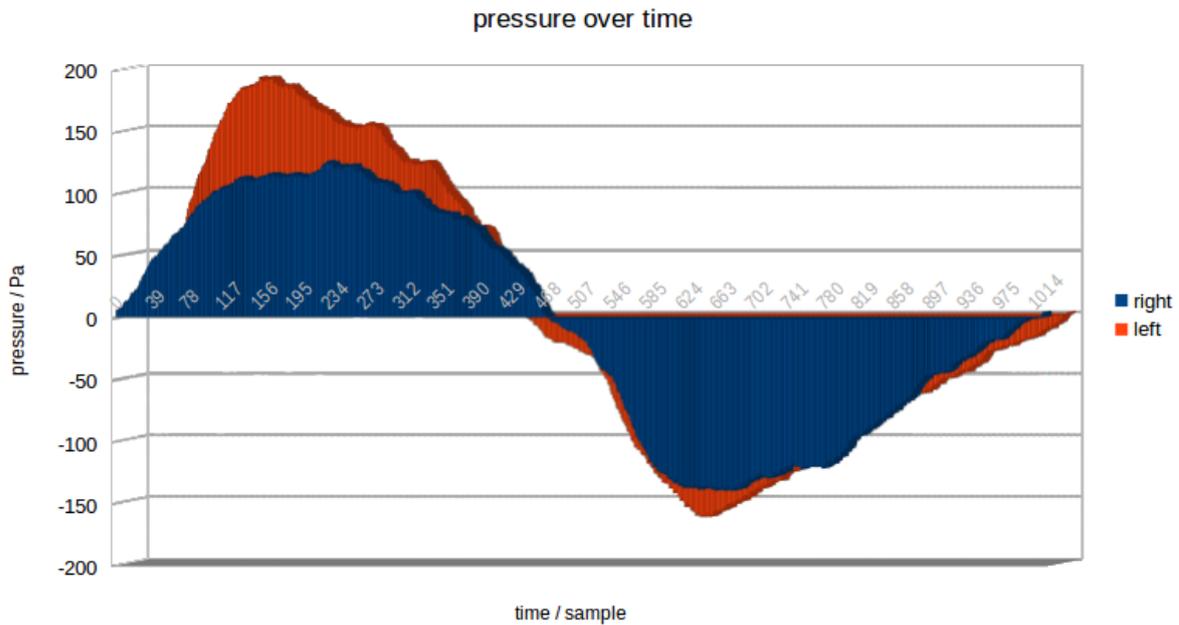


Figure 28 - Pressure over time measured by 4-Phase Rhinomanometer

4.6 Validation (AP6)

4.6.1 Validation and Interpretation

The validation and the interpretation of the results is the final planned activity of the Experimental Phase 2 as it requires the inputs from both CFD-Simulation and In Vitro Model Development tasks (see the GANTT chart in Figure 3). Due to time constraints, during this pilot study, it was not possible to perform a complete validation of the results obtained. Such analysis was mostly centered on a set of cases (patients) and focused on CFD simulations, in silico and in vitro models (see Sections 4.4 and 4.5). However, AIT will concentrate on this task in the ongoing project "Rhinodiagnost - Morphologische und funktionelle Präzisionsdiagnostik der Nase" (as detailed in Section 5.4) and possible future projects.

4.7 Concept Development NOSE Service (AP7)

CFD simulation and 3D visualization represent great innovations for ENT diagnostics that are currently not available for most of the established ENT specialists and surgeons. This results from the fact that these services require the involvement of highly experienced medical, fluid dynamic, as well as informatics experts – only to name a few – in combination with expensive High Performance Computing for visualization.

However, small scale IT-system including powerful software are currently entering the market [71] and could be used to provide the infrastructure for CFD simulation in public and private health centres in future. Therefore, the NOSE pilot study also investigated the setting up of an external

infrastructure and service concept for providing these services. The external infrastructure would be in charge of orchestrating the dialogue between the various actors; it would deliver on-demand services (e.g. computation of CFD simulation and creation of 3D models) and take care of the general IT tasks related to the services.

4.7.1 Business Plan Development

The NOSE Pilot Study examined the following assumption: The NOSE service center (NSC) would receive medical information (such as CT/MR images) and shall then provide to ENT surgeons and doctors large-scale high-fidelity CFD simulations, printable 3D models using modern computer-based technologies such as machine learning techniques. That way, the NOSE services should help to improve the treatment of nasal and paranasal pathologies and should allow planning nasal surgeries and therapies in a more effective and patient-specific way.

4.7.1.1 Prerequisites

The individual NOSE services will have to be integrated into an online platform (the NOSE platform) that hides unnecessary technicalities from the medical and physician experts, who will interact with the system via a web interface. All NOSE services have to be scalable and adaptable to the needs of users (general practitioners, clinical physicians, patients and so on). For example, doctors and ENT surgeons should be able to request specific details of an existing 3D model (e.g. a high-detailed 3D model of a peculiar area) or a particular CFD simulation in order to better prepare a surgical operation.

Delivering computational simulation services as easily accessible and affordable mass services for anyone working in the ENT domain should substantially improve diagnostics, therapy and surgery preparation. In the end, this will positively affect the quality of life of millions of patients suffering from CRS pathologies and will help to gain a better understanding of the functions of the nose for practitioners and experts. This is particularly needed as, due to epidemiological changes, there has been a strong prevalence of chronic diseases in the recent years. Therefore, in order to properly treat these pathologies, a fusion of care along the diagnostic and treatment process is required. And there is a need for increased and precise communication and coordination together with general process changes [72]. A comprehensive knowledge base for ENT specialists provided by NSC platform could contribute to this effort. If doctors, ENT specialists, and radiologist can communicate, and share results and diagnosis via the NOSE platform this will help to overcome known difficulties of collecting diagnosis and artefacts created by different doctors and medical centres.

Finally, the analysis of CFD simulations could provide valuable indications for the correct application of drugs [73,74]. Therefore, it is possible that NOSE services will in future serve clients from the pharmaceutical industry with CFD simulations and 3D models that help to validate the particle distribution in the nasal cavity to improve the application accuracy of medical drugs. Besides, the NOSE services could also be integrated as add-on services into existing clinical tools on the market, such as CT/MR scanners and 4-Phase Rhinomanometer (4PR).

4.7.1.2 Possible Markets

Research on industry data, competitors and additional interviews with potential customers showed that the design of an ENT-oriented NSC would constitute a significant innovation in the market and would meet the broad interest of the dedicated medical community. The main customer groups for the NSC would be doctors, ENT surgeons and clinics. However, in the future the infrastructure could be expanded to provide the services offered by the NSC to an extended set of customers, such as insurance companies, training institutions and pharmaceutical companies. Some preliminary market research for Austria, Germany and Switzerland showed also a strong interest for training facilities (virtual surgery training) together with an expressed willingness to join international cooperation projects. From these findings a good market potential for the proposed NSC infrastructure could be deducted.

Right from the start of the Pilot study the project team fostered cooperation with international experts and aimed at stimulating further scientific research via joint projects in the European Union research and innovation framework (eg. IraSME or Horizon2020). The NSC based in Graz could constitute in future the central node of an international network of partners that arrange NOSE service platforms at their own premises. The benefit of such a network of NSCs would be the stimulation and support of international cooperative research and the immediate distribution of research results among the medical partner community. The international network of cooperation partners will also play a key role in future marketing activities. Therefore, direct cooperation should be pursued with doctors and clinics that already expressed a strong interest in the services during the NOSE project lifetime.

A project similar to NOSE exists in Spain (nasalcom.es) and could also be a future cooperation partner. However, the fate of the Nasalcom project is rather unclear; the infrastructure is currently in a test phase and technical development seems to have stopped in 2015. Furthermore, to our best knowledge, nasalcom.es is not using machine learning technology for service optimization and mass service delivery, which is one of the most important and innovative aspects of the future NSC.

Summing up, digitization for healthcare offers a high market potential. In a study published in 2012 by Bitkom and Fraunhofer, the European e-health market is estimated at around 15 billion euros. For the whole of Europe, an annual growth rate of 2.9% is forecast. Globally speaking, digital medical technology sales and big data are growing at an average annual rate of 21%. Moreover, Manager Magazine forecasts a growth for the digital healthcare market of up to \$ 233 billion by the year 2020. A future NSC will most likely focus on the market segment that includes interdisciplinary IT services for diagnostic dedicated to ENT doctors.

4.7.1.3 Potential Target Customers

The initial group of customers consists of more than 700 **ENT doctors** based in Austria, 80 of which located in Styria, the region where the future NSC could have its main location (Graz). Additionally, there are around 800 **radiologists** located in Austria who are as well potential clients for the NSC services. Due to the web-based nature of the services offered by the NSC, the use of

the platform and of its services is in fact location-independent. It is planned to enhance the reach of the NSC by offering all services in English (translations into other languages will be discussed in the future).

Among the initial group of main customers are **patients**, who will have personal access to their 3D models and CFD simulations through the NSC. Patients shall be able to visualize their medical history, the produced results (including CT/MR images) and to download each of the previous digital artefacts.

Medical universities could make use of the NSC knowledge base of anonymized 3D models, CFD simulation and general visualization aids in ENT surgery training settings. A future option could be to enhance the platforms with a Virtual Endoscopic Sinus Surgery (VESS) tool [75].

Pharmaceutical companies are possible future client, as well. Notably, results of CFD simulations would provide valuable information on the optimal use of specific medications (e.g. nasal sprays, nose drops, irrigation, etc.) in the treatment of CRS.

Finally, analysis tools implemented upon the NSC platform will be helpful to collect and catalogue valuable information that could be used to shape dedicated **insurances** according to the patients' profiles.

4.7.2 *Development of Service Platform*

The to-be-developed future NSC platform will be an international cooperation task that will involve various partners of the NOSE project. On the technical side this effort will require the setup of a database and the integration of CFD simulations and 3D models in a homogeneous way to allow all customers (also non-medical users) to use the portal. Furthermore, a connection to external systems, such as CT/MR centers and archives and High Performance Computing Centers, will have to be established. To ease the administration and the use of the portal training material will need to be prepared (probably in online format using different solutions, like Moodle, Mediathread, or MOOC etc.) and the NSC collaborator will need to be trained accordingly. These tasks, together with the definition of the needed hardware, software and the dedicated technologies to be used, shall be outcomes of the ongoing project "Rhinodiagnost - Morphologische und funktionelle Präzisionsdiagnostik der Nase", which takes as inputs most of the results of this pilot study and further develops and enhances them (see chapter 6.2).

4.8 **Knowledge Base (AP8)**

During this pilot study, an extensive number of literature and publications from a multidisciplinary area of science was collected. Particularly, publications in the field of physics (CFD), medical images (DICOM images and 3D model creation), machine learning (automatic segmentation) and medicine (CTR pathologies) were analysed. Up-to-date researches (particularly) on CFD and 3D visualization for the upper airways was systematically collected, organized and made available to the project team.

4.8.1 Development of Knowledge Base

The tool Zotero¹⁸ was selected as cataloguing tool and with this tool a library of NOSE-related research literature was built. Zotero is a free and open-source reference management software to manage bibliographic data and related research materials (such as PDF files). This software allows saving different types of documents within the database, including scientific articles, books, theses, etc. Furthermore, Zotero can be integrated in a web browser, and allows the generation of in-text citations and of bibliographies among other features. Zotero shows an icon when a resource (book, article, thesis) is being viewed on many websites, such as library catalogues, PubMed, Google Scholar, Google Books, Amazon.com, Wikipedia, and publisher's websites. By clicking on this web icon, Zotero saves the full reference information into its internal library. Besides, Zotero can also save a copy of a webpage, or, in the case of academic articles, a copy of the full text as a PDF. Users can then add notes, tags, attachments, and their own metadata to a particular resource. All entries in a Zotero library can be exported as bibliographies into a csv file. Most important features include:

- Web browser integration
- Online syncing
- Generation of in-text citations
- Footnotes
- Bibliographies
- Integration with the word processors Microsoft Word, LibreOffice Writer, OpenOffice.org Writer and NeoOffice

At the moment of writing, the NOSE Knowledge Base (KB) includes more than 300 entries. Most of the items in the knowledge base are journal articles (more than 120), links to webpages (around 60), documents, presentations and books (around 30 items each), theses and conference papers (10 each). The collection is completed by reports, magazine articles and computer programs documentation. Notably, the majority of entries in the KB are written in English language, one journal article is Chinese and 14 books are published in German.

Datascheme

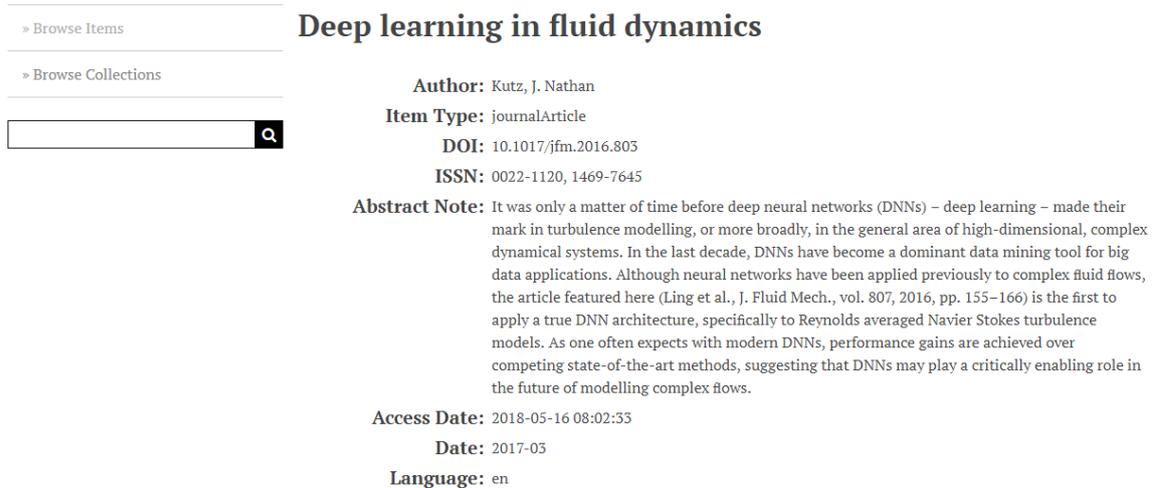
The Nose Knowledge Base portal (nose-kb) was published online using the web publishing platform Omeka¹⁹. Each item describes a publication, as for example a paper or journal. By default, Omeka items are described using the Dublin Core metadata schema (<http://dublincore.org/>). In order to describe each item in the KB in more detail, the Dublin Core metadata schema was enriched using the wider list of fields provided by the Zotero database schema. The Zotero fields were mapped to the Dublin Core metadata schema fields in order to maximize interoperability and ease of integration into Omeka (Zotero Import plugin). Each item consists of descriptive metadata and various attached files (e.g. pdf, presentations, online links, etc.). All the files are stored in a common folder on a server. Metadata as well as full text searches are possible (Invisible Schema plugin). Omeka supports the creation of new items and the import of other external collections (as

¹⁸ <http://www.zotero.org>, Accessed 2018-07-23

¹⁹ <http://omeka.org>, Accessed 2018-07-23

a list of items) saved as csv files. Each item is presented as a list of fields (bold) and their values. The field "Attachment URL" provides a list of links to the pdf or online versions of the particular item for the NOSE project team. The field "DOI" links to the official online site from where the publication is accessible. Figure 29 depicts a typical view of an item within our KB portal.

Nose knowlegde base



The screenshot shows the detail view of an item in the NOSE Knowledge Base. On the left, there are navigation links: "» Browse Items" and "» Browse Collections", and a search bar. The main content area displays the following information:

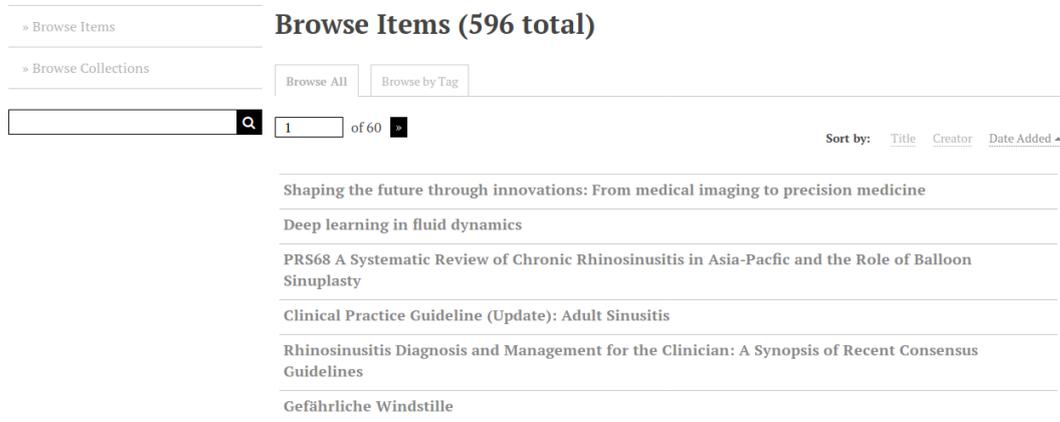
- Deep learning in fluid dynamics**
- Author:** Kutz, J. Nathan
- Item Type:** journalArticle
- DOI:** 10.1017/jfm.2016.805
- ISSN:** 0022-1120, 1469-7645
- Abstract Note:** It was only a matter of time before deep neural networks (DNNs) – deep learning – made their mark in turbulence modelling, or more broadly, in the general area of high-dimensional, complex dynamical systems. In the last decade, DNNs have become a dominant data mining tool for big data applications. Although neural networks have been applied previously to complex fluid flows, the article featured here (Ling et al., J. Fluid Mech., vol. 807, 2016, pp. 155–166) is the first to apply a true DNN architecture, specifically to Reynolds averaged Navier Stokes turbulence models. As one often expects with modern DNNs, performance gains are achieved over competing state-of-the-art methods, suggesting that DNNs may play a critically enabling role in the future of modelling complex flows.
- Access Date:** 2018-05-16 08:02:33
- Date:** 2017-03
- Language:** en

Figure 29 - NOSE Knowledge Base, Detail View

Publishing the Knowledge Base

As mentioned before the nose-kb is based on the web publishing platform Omeka. External collections of items can be easily imported into Omeka. Within the NOSE project a script was developed to construct a Omeka-ready csv file that can be imported using the Omeka CSV Import plugin. The import of Zotero collections into Omeka consists of three steps: the export of Zotero collections (resulting in a csv file), the adjustment of the obtained csv to Omeka settings (zotero2omeka script) and the upload of the csv file to the Omeka platform (CSV Import plugin). The public view of the nose-kb can be accessed via: <http://nose-kb.ait.co.at/> (see Figure 30)

Nose knowlegde base



» Browse Items
 » Browse Collections

Browse Items (596 total)

Browse All Browse by Tag

1 of 60

Sort by: [Title](#) [Creator](#) [Date Added](#) ▲

- Shaping the future through innovations: From medical imaging to precision medicine
- Deep learning in fluid dynamics
- PRS68 A Systematic Review of Chronic Rhinosinusitis in Asia-Pacific and the Role of Balloon Sinuplasty
- Clinical Practice Guideline (Update): Adult Sinusitis
- Rhinosinusitis Diagnosis and Management for the Clinician: A Synopsis of Recent Consensus Guidelines
- Gefährliche Windstille

Figure 30 - NOSE Knowledge Base

4.9 Networking and Dissemination (AP9)

Active networking is an indispensable success factor for modern research and development. To this end, the NOSE team reached out to a number of potential international partners in order to develop a strong network of cooperation. In addition, we collaborated with the following local medical centers and experts: ENT surgeon Dr. med Schachenreiter (Privatklinik Graz Ragnitz), Univ.-Prof. Dr. Gerhard Ranner (CT/MR Zentrum Graz Geidorf), ENT surgeon Dr. Jakse (Privatklinik der Kreuzschwestern Graz) and Ass. Prof. Dr. Wolfgang Köle (Medizinische Universität Graz). In regular meetings the existing problems and possible solutions were discussed. The cooperation with local medical experts provided invaluable input to achieve a profound understanding of the point of view of medical actors, their ideas, remarks and wishes.

4.9.1 Definition of Service Platform

Figure 31 shows an overview of the overall concept as developed within the NOSE Pilot study.

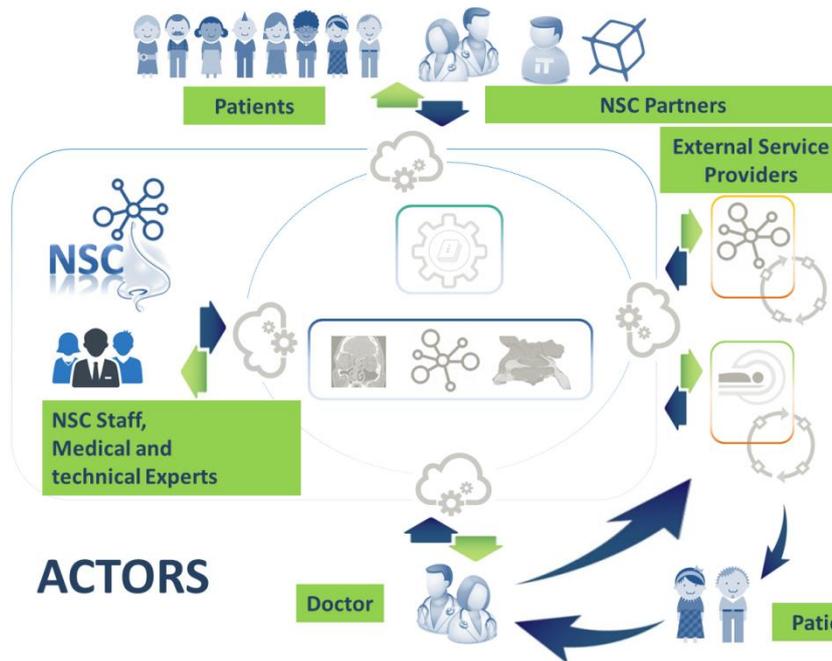


Figure 31 - NOSE Service concept

The NSC platform (in the middle of the figure) provides the central services:

- 3D Meshing
- 3D Visualization
- CFD Simulation
- Knowledge Base



The platform supports the exchange of information between all actors: the individual users, the service providers and the international experts and NSC partners.

The basic actors within a possible NSC start-up scenario are:

Doctors	An application interface provides flow simulation information and 3D views of the nasal and paranasal sinuses to doctors. These views, as well as the access to an international knowledge base, support the diagnosis and the surgical preparations.
Patients	Patients can query their examination data online.
NSC specialist staff	The NSC processes the CT/MR images , generates the mesh for 3D simulation and performs a flow analysis . The NSC also manages an extensive knowledge base that provides expertise for the evaluation of individual examinations. The

	<p>knowledge database will be constantly maintained and expanded in cooperation with international experts and should offer current literature and information from surgical experience. Based on the database, it should be possible to create statistics and contribute to research by indicating ideal treatment processes.</p>
<p>External service providers</p>	<p>The NSC receives CT/MR images from external service providers.</p> <p>In case that additional technical resources are needed (eg. computing power), the NSC will use the services of external infrastructure service providers.</p>
<p>NSC cooperation partners</p>	<p>The knowledge database and all other tools are available to other cooperation partners of the NSC via special service interfaces:</p> <p>3D service providers (eg. printing centres) can cooperate with the NSC and create printed models upon request.</p> <p>Scientific institutions (universities, research centres) can cooperate with the NSC in the scope of the knowledge base.</p> <p>The virtual services and tools of the NSC can be used for medical education.</p>

Table 1 - NOSE Actors

5 Summary

The NOSE Pilot study evaluated the technical and scientific environment required for establishing a service portfolio that includes CFD simulation and 3D visualization services for ENT specialists.

For this purpose the state-of-the-art of these technologies and their use for upper airways diagnostics were analysed. A sample technical infrastructure to provide CFD and Mesh services was set up at the premises of AIT Angewandte Informationstechnik Forschungsgesellschaft mbH. There the mesh generation and CFD simulation for the nasal cavities and paranasal sinuses were investigated. In addition a comprehensive international network of medical, CFD, 3D printing and other technical specialists was built and various supplementary research projects and proposals were initiated. All results gained contributed to an initial business planning for a NOSE Service Center.

The following chapters provide a concise overview of all results acquired and conclude with a proposal for services to be offered in future.

5.1 Workflow Concept (AP2)

Research on workflows and pathways concentrated on how to establish a NOSE Service Center (NSC) as an interconnected network in which doctors, ENT surgeons, CT/MR centers and patients can request services and visualize the results in a transparent and homogeneous way. For this purpose the NOSE project cooperated with the international Health BPM Pilot initiative of the Object Management Group. The NOSE project elaborated a high level concept for the preparation of a FESS. This sample pathway is written in the standard notation BPMN and describes the different actors, activities, communication and process flows. NOSE tested the two products Bonitasoft and Trisotech. The tools support creating and managing articulate business processes and their actors and enable a deep domain analyses that can be used to refine the general processes and domain constraints. Bonitasoft and Trisotech are two complementary solutions that can be used in parallel to help build up articulate business process by discovering hidden goals, constraints and requirements in a typical systems development life cycle manner. Both tools proved very valuable and apt to be used for developing clinical pathways and the final workflow-driven User Interface of the NOSE platform.

5.2 Mesh generation (AP3)

For preparing a mesh on the basis of CT/MR images it is best to work with DICOM images with a maximum slice thickness of about 0.5 mm, a thickness that allows for the successive creation of anatomically exact 3D digital models in a 1:1 scale. This allows for representing the highly complex anatomy of the paranasal sinuses and the pathology in an intuitive and easy to explore way. This representation improves the understanding of the individual anatomy of the paranasal sinuses and should be considered as an additional new standard for the practical diagnosis. Furthermore, the

detailed mesh of the paranasal sinuses is a valuable additional aid for ENT surgeons and doctors towards the planning and the preparation of endoscopic surgery (eg. FESS).

Within the NOSE pilot study first, automated filters from 3D Slicer were applied in order to obtain a coarse segmentation for a particular region of interest. Second, the automatically generated segmentations were inspected and corrections were manually applied if needed. Choosing this procedure the fast 3D Slicer filters capabilities were connected with the expert manual inspection of the created segmentation, serving as a correction and validation step. That way an accurate segmentation can be done in a reasonable time. Research further showed that the use of Machine Learning techniques, such as CNNs, will tremendously increase the efficiency of creating segmentations and the relative 3D models.

3D print-outs of the nasal cavities can be a valuable aid for displaying pathologies to patients, prepare for difficult surgeries or use the models as training sets for aspiring ENT surgeons. There are already low-cost printers, like the Geetech printer, on the market that support the printing with multiple types of filament that allow printing of hard and soft tissues in different color. Nevertheless, high quality and realistic printing of the nasal cavities is still an area where research is needed and done. The 3D printer market is very rapidly evolving and it is envisaged that printers and filaments are getting cheaper and more powerful in the coming years. A NOSE service center might then in future be able to provide 3D print-outs on demand at a reasonable price for individual doctors, surgeons or educators.

5.3 CFD Simulation and Analysis (AP4 and AP5)

A CFD simulation on the whole nasal cavity area including paranasal sinuses with simpleFoam (steady-state) requires around 10 minutes of computing time on a cluster of two 2-processor (XEON 2690v2) engines with a total capacity of 40 cores. The tests revealed that applying a "domain decomposition" principle, in which different parts of the geometry are distributed to specific computing cores, ensures a better performance. Then a steady-state CFD simulation at 20 time points of the respiration cycle was performed and the simulation results were used to create a video to show the evolution of the airflow. Altogether, these simulations took less than 4 hours on the infrastructure set up at the NOSE incubator.

Furthermore, a CFD simulation was carried out with the transient pisoFOAM solver. In this case, the simulation took around 300 hours. A convergence was achieved by selecting a time step smaller than 10^{-4} seconds. Comparison of the outputs (videos) generated by both methods (simpleFoam at 20 selected points vs. pisoFoam) showed similar results.

The computing time to complete CFD simulations for the whole nasal cavities is generally long, specifically in a transient setting with pisoFoam. However, the required time can be substantially reduced by discarding parts of the full 3D model and keeping only the paranasal sinuses and nasal cavities as regions of interest.

The CFD simulations on the whole geometry of the nasal cavities proved that the airflow in the paranasal sinuses is much smaller than the one in the main cavities. Moreover, the results obtained

using a transient solver (pisoFoam) and a steady state one (simpleFoam) are quite similar. Research further showed that the influence of temperature on the airflow into and in a paranasal cavity can be rather neglected. Furthermore, provided that pressure or volume of the airflow at interesting points in the respiration cycle can be measured (e.g. by using a 4 phase rhinomanometer), CFD simulations can be simplified and require less computing power.

Radiologists and ENT experts could use the dynamic visualization of the ventilation in the nasal cavity and the paranasal sinuses to improve their understanding of the particular pathology the patient suffers from. For the preparation of surgeries in the paranasal sinuses it possibly suffices to verify whether the airflow enters the paranasal sinus or not. The following figures show examples of future CFD information sheets for ENT specialists.

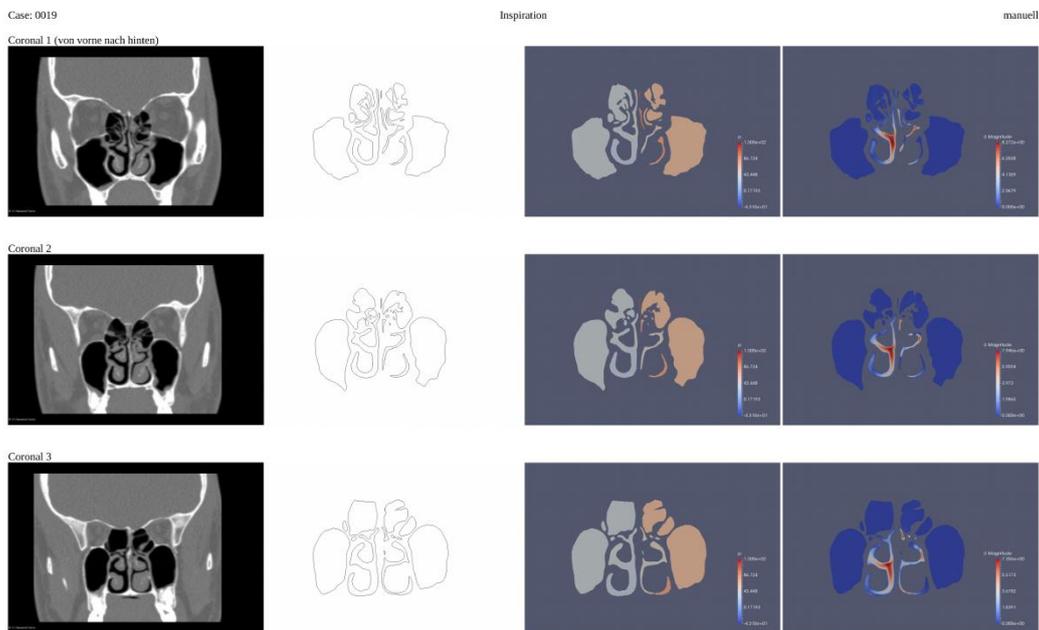


Figure 32 – CFD data sheet (inspiration in a coronal view)

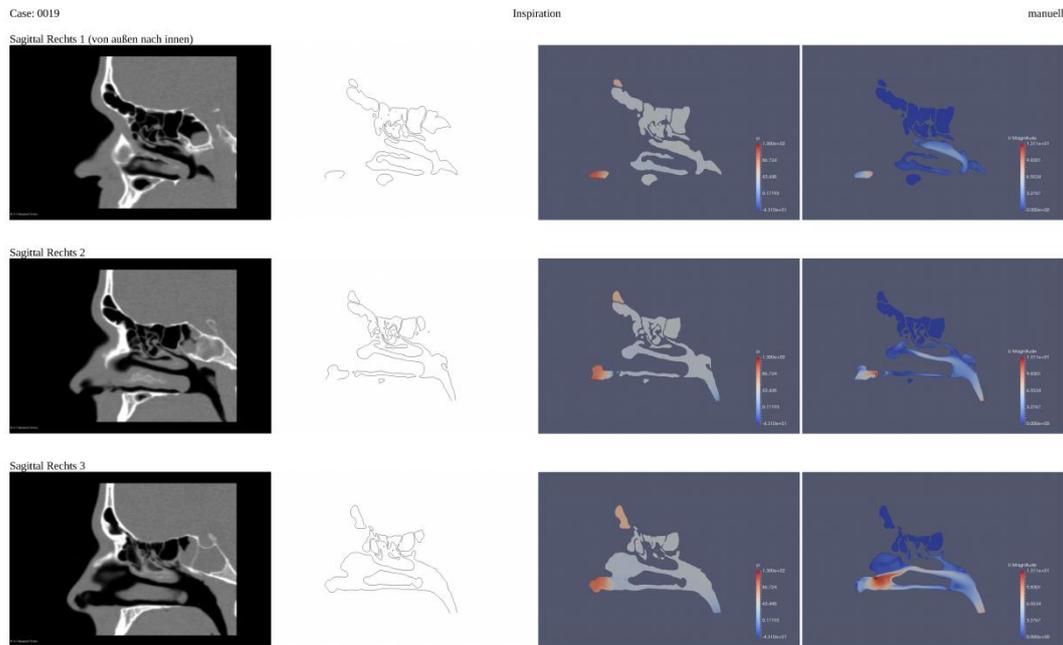


Figure 33 – CFD data sheet (inspiration in a sagittal view)

5.4 Validation (AP6)

The validation and interpretation of the outputs of this pilot study (segmentation, 3D models and CFD simulation) is a task of great importance. Due to the extensive amount of work that the other work areas required and to a restricted time, a complete validation of our results was only partially possible. However, AIT plans to complete this task in future projects. One project has already been established and set up. The “Rhinodiagnost - Morphologische und funktionelle Präzisionsdiagnostik der Nase” will further extend the work started within this pilot study and will put an emphasis on the validation, interpretation and use of the obtained results (see chapter 6.2).

In this sense, the aspects of development and validation of the methods and technology are complementary to one another, forming a feedback loop that should improve the overall procedure. Cross-validation activities that accurately compare different models and numerical methods are planned. First, different components will be tested and validated in an “environment of interested users”. Second, these results will be validated and evaluated in a real clinical environment. The output of these two testing tasks will be documented and will form the baseline for final business plans, sustainable use and deployment. Notably, the validation will be executed with the aid of medical partners via clinical testbeds.

The data collected from all the experiments will form a KB, which will be used not only for single parameter-space validation of the numerical methods, but also for further validation of simulations on realistic pathological cases. Moreover, study and understanding of a standard “healthy” nasal

airflow will constitute the base for future validations and research on nasal pathologies, particularly CRS ones.

Upon this extensive and adequate period of field-testing, a related web-based expert platform can be put into production.

5.5 Concept Development NOSE Service (AP7)

This chapter enlists possible NOSE services that have been identified in the pilot study.

Service	Description
 <p>Mesh Generation and 3D Visualization</p>	<p>The NOSE 3D visualization services should provide a complete set of information covering all properties of the nasal cavities (especially paranasal sinuses).</p> <p>Tool:</p> <p>A NOSE editor has been developed that can separate paranasal sinuses from the (main) nasal cavity, it can generate covers to close cavities, combine different meshes (3D sub models) and add walls for enhance 3D printing.</p>
 <p>3D printing</p>	<p>The NOSE 3D printing service should provide or act as an agent for delivering 3D print-outs of selected regions of interest. The models should include the printing of soft and hard tissues, and pathologies or regions of interest should be marked with different colors.</p> <p>Tool:</p> <p>A low-cost Prusa printer for simple print-outs</p> <p>Cooperation with specialized 3D printing centers for high-quality print-outs</p>
 <p>CFD Simulation</p>	<p>The NOSE CFD simulation results should be added to the DICOM images provided to radiologists and surgeons.</p> <p>Tool:</p> <p>CFD simulation on the whole nasal cavity area including paranasal sinuses with simpleFoam and output video.</p>
 <p>Workflow Management</p>	<p>The NOSE service center should offer workflow management know-how for developing standard clinical pathways for organizations involved in ENT treatment and surgery. Consulting activities should recognize international standards (such as BPMN, CMMN, DMN).</p>

Service	Description
	Tool: Bonitasoft BPM platform Trisotech Business Modelling Tool
 Knowledge Base	The NOSE knowledge base offers ENT research, simulation, visualization and treatment results. NOSE medical expert partners contribute to the knowledge base. Tool: Omeka web publishing platform

Table 2 – Identified NSC Services

5.6 Knowledge Base (AP8)

During the NOSE project up-to-date research information on CFD and 3D visualization for the upper airways was systematically collected, organized and made available to the project team. These information objects have been published in an online NOSE knowledge base that now can also be accessed by the public (Note: Access to paid literature is not supported.). The current version of the NOSE knowledge base presents a basic starting point to a future comprehensive information space for ENT specialists, researchers and trainee doctors that shall include research, simulation and treatment results.

5.7 Networking and Dissemination (AP9)

The NOSE team organized 3 meetings with international research partners, participated to 9 conferences in 6 different countries and attended 4 scientific workshops from autumn 2016 to summer 2018. A concise list of these activities is inserted in Annex II of this study. The networking activities led to the following results:

1. March 2017: Proposal Submission „INFA - Intelligent Nasal Flow Analyzer“
(Horizon 2020: H2020-SC1-2016-2017 Personalised Medicine)
2. March 2017: Proposal Submission “Rhinodiagnost - Morphologische und funktionelle Präzisionsdiagnostik der Nase“
(COIN – IraSME) – project awarded
3. April 2018: Proposal Submission „ PDVS - Platform for enhanced Diagnostics and Virtual medical Services“
(Horizon 2020: H2020-SC1-DTH-2018-2020 Digital transformation in Health and Care)



Furthermore the NOSE project has researched a list of research institutes dealing with the analysis of CFD in the upper respiratory tract. This list of involved entities and potential research partners is depicted in Annex I of this study.

NOSE

6 Discussion and Outlook

The results of the Pilot study indicate the importance of providing 3D models and CFD simulations for ENT treatment. In addition, future research needs to concentrate particularly on the validation of CFD results in order to develop a common criteria catalogue. The NOSE knowledge base is a first starting point for supporting scholarly activities by providing mass data (anonymized 3D models and CFD simulations) and documentation on nasal cavities. The integration of the different methodologies (3D models, CFD simulations) into a virtual surgery device for preparing ENT surgeries is also an interesting option that could be further investigated. And of course there is work left to fully integrate 3D modelling and CFD simulation into the standard ENT clinical pathways. The next chapters outline some immediate envisaged future activities.

6.1 Diagnostic Procedures

Within the NOSE pilot study 3D models were produced based of the CT/MR images obtained from cooperation partners. As a future extension of the work, these models could be made accessible to external entities that can request the creation of 3D models (digital and printed), a segmentation or a CFD analysis. In a first phase, access could be given to a selected group of test users. This test group could be continuously extended in cooperation with partner doctors, surgeons and radiologists. The final goal is to fine-tune the services and to increase the network of doctors, surgeons, CT/MR centers and patients that request services and visualize the results. During NOSE project lifetime private persons had already contacted us directly and offered to send their CT/MR images for further CFD analysis and visualization. Therefore, we already investigated the possibility to offer access to the service infrastructure for private persons.

Regarding the developing of a clinical pathway concept, NOSE experimented with the environment offered by Bonitasoft and Trisotech to shape, develop, analyze and better understand the requirements, constraints and needs of the business processes NOSE wants to implement for setting up the NOSE platform. The project team described the overall process (from the patient going to a medical appointment till the post operation handling) as a BPMN diagram using Bonitasoft and deconstructed the business process into smaller, self-contained sub-processes defined by specific actors and artifacts. In this context also the UI for some of the sub-processes was developed and the interactions among different actors was defined and successfully simulated. Using Trisotech tools an improved version of the initial model was developed by running a deep analysis of the domains, goals and constraints. In the future, the NSC will use Bonitasoft to further develop, refine and interconnect all of the sub-processes defined earlier. At the same time, NSC could employ the technology offered by Trisotech to assess the quality and the consistency of each sub-processes and of the overall business process.

However, research showed that additional effort may arise from the multidisciplinary of the NOSE domain. Specifically, every part of the business model has to be analyzed in orchestration with a set of experts such as ENT surgeon, IT specialist, physician, medical centers and patients. The

interoperability of the NSC is one of the most challenging tasks the NSC is confronted with, due to the facts that each actor has own needs, demands and concerns. The NSC will have to constantly communicate with Healthcare experts and physicists to assess the structure and collect feedback to better design the environment to meet the needs and demands. The NOSE project has already built a network of interested professionals (doctors, ENT surgeons, physician, CT/MR centers, etc.) that should constitute the future group of initial test users of the proposed platform. From a technical point of view, the NSC will have to structure a database schema adjusted to the needs of the project and of its actors. During project lifetime a MySQL test schema external to Bonitasoft was already developed and first interfaces to exchange data with the platform have been implemented.

The NSC will also have to define particular constraints and settings in relation to security and privacy. It has to be secured that personal information of the involved actors is made available only to the authorized actors. 3D models, segmentations and CFD simulations have to be carried out while preserving the anonymity of the patient if the data is contributed fe. to a joint knowledge base or to other European research infrastructures for Open Science²⁰.

6.2 Surgery Preparation

The testing of 3D models and CFD simulations mainly centered on different solvers, such as pisoFoam, simpleFoam. The influence of the temperature of the airflow was tested using a third CFD system called Fire2 (developed by AVL). Using this system proved, that an airflow entering the nostrils at 20 degrees Celsius, will warm up till around 38 degrees after passing the nasal concha and before reaching the frontal sinus. Within this area it is interesting to further investigate the influence of the temperature using OpenFOAM's solvers rhosimpleFoam and rhopimpleFoam.

A complete validation of the CFD simulation results is still to be finished due to the currently ongoing evolution of 3D printing devices and materials. The Rhinodiagnost²¹ project will carry out in vitro experiments as described in [76] by fabricating scaled mechanical airway models in a Stereo Lithography (STL) process using stereoscopic PIV for velocity measurements in the nasal cavities [77]. Notably, the project will employ SLA resin material for the airway wall, which should yield nearly uniform thickness. Moreover, within the scope of the Rhinodiagnost project, the results of the CFD simulation obtained by using simpleFoam and pisoFoam solvers will be checked against the CFD simulation results delivered by another system which used a different methodology [78].

Parts of these experiments are already developed by a Rhinodiagnost project partner. Specifically, a piston pump connected to a step motor and a motor controller which can be loaded with data delivered by a 4-phase Rhinomanometer. This device, originally intended to test the Rhinomanometer, will be connected to a transparently printed 3D model of selected nasal cavities and a nozzle, seeding tracer particles into the airflow. In a first phase, this system will be used only to visualize the airflow. In a second step, the project plans to combine this system with devices enabling particle image velocimetry.

²⁰ <https://eospilot.eu/>, Accessed 2018-07-25

²¹ <https://rhinodiagnost.eu/>, Accessed 2018-07-23

Additionally, Rhinodiagnost will experiment with pimpleFoam to investigate the laminar airflows only. Through comparison of these different methods, the most precise and suitable procedure and the optimal setting that requires the least computing time can be determined. Further on, the current model shall be tested with a considerable higher amount of anonymized CT/MR images.

With this experiment on a large collection of data, the results obtained shall help to achieve a more precise insight into the methodology and parameters that could lead to more accurate CFD simulations with regard to the paranasal sinuses. These indications shall constitute a new standard for future treatments and will be incorporated in the FESS clinical pathway.

Using radiopaque material it is possible to visualize more details of the source CT/MR images, like fe. the vessels (see upper right side of Figure 34). The resulting 3D meshes would deliver better input for ENT surgeons, especially when surgeries are difficult and critical.

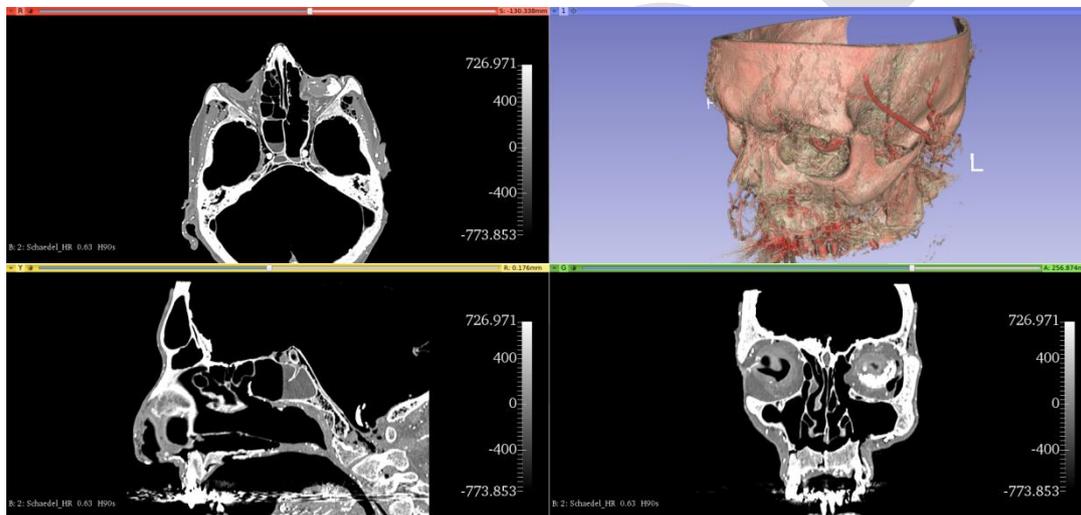


Figure 34 – 3D Visualization after radiopaque material

6.3 Training

The research results and methodologies delivered by the NOSE pilot study and the Rhinodiagnost project, will be very valuable for training future doctors, ENT surgeons and physicians. The combination of CT/MR images and their derived 3D models supply a complete overview of the condition of the nasal and paranasal sinuses of the patient at a specific time, which could be used by medical students to deepen their understanding of the morphology of the nasal cavities. Moreover, the printing of 3D models of particular regions, provide the possibility for haptical inspections of certain regions of interest. Furthermore, CFD simulations could help ENT surgeons to precisely assess the improvements in the airflow that an operation could bring.

Proper training on the methodologies could, for example, be achieved using a flipped classroom approach, a type of online blended learning that supports the transfer of knowledge in a student-mentor setting but also between different members of the same organization. Notably, in a flipped classroom the knowledge is generated collectively through interactions in the classroom or within teams of students [79,80] in a collaborative learning environment. In this context, the teacher takes over the role of a trainer or a coach and the self-organized interaction between the learners

become the source of knowledge transfer, acquired through activities such as questioning, observing and trying out (informal learning) [81,82]. The content of flipped classroom courses is generally organized in small lessons (micro learning compositions), which allow the students to consume the concepts fast and flexibly [83].

Given the nature of the content (3D models and CFD simulation) a platform for training should allow interaction with multimedia contents, along with traditional features of the flipped classroom, such as support for cooperation (discussion and feedback) and communication, collaborative problem solving with task assignments and the structuring of the course into micro learning units. Courses for ENT specialist could include topics such as visualization of nasal cavities (3D models), experimentation with CFD simulations and their interpretation. A first analysis of the possibilities and the requirements to set up a flipped classroom for ENT training on new diagnostic technologies will be done in the framework of the Rhinodiagnost project [84].

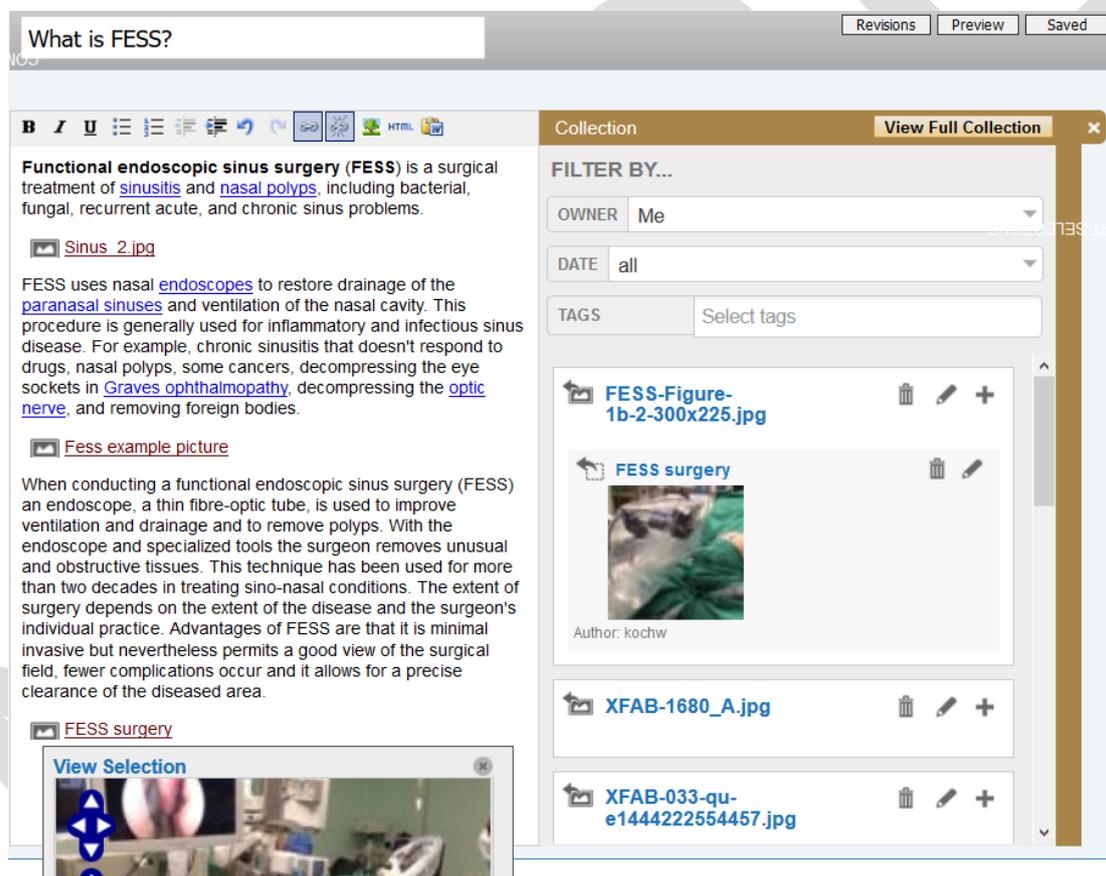


Figure 35 – Online lesson on FESS

Figure 35 shows a composition on FESS composed of texts and images, while Figure 36 depicts the integration of multimedia objects (3D models) within the content of a lesson.

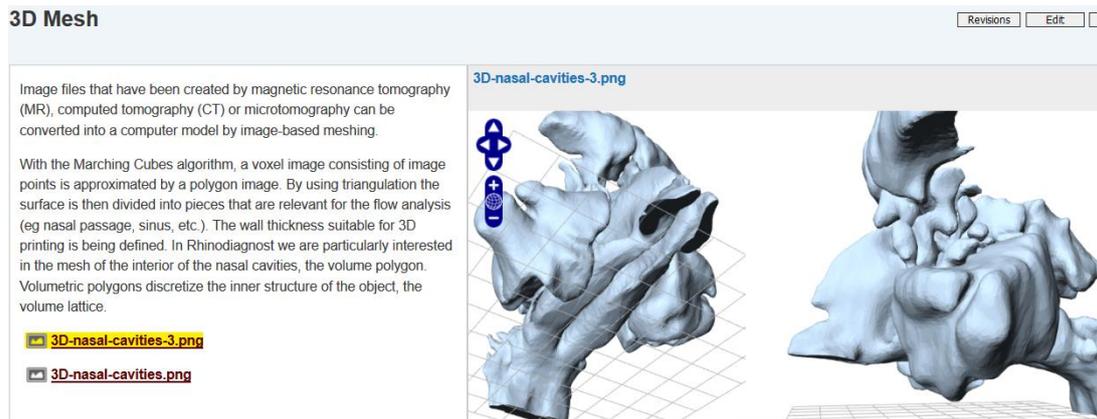


Figure 36 – Online lesson on multimedia (3D model) integration

6.4 Center of Excellence

The work carried out within the Networking and Dissemination area of the NOSE project clearly unveiled the importance of cooperating within a national and international expert network for setting up and maintaining the NOSE services. Therefore it is proposed to further evolve the NSC into a Center of Excellence with multiple players from different research fields as collaboration partners. A dedicated **NOSE Center of Excellence Graz** (CoE) could provide the necessary infrastructure and platform for the free exchange of ideas, methods and technologies between the scientists in the field of CFD and 3D visualization for ENT. Researchers would benefit from the state-of-the-art technologies and hardware that the NOSE CoE would supply in cooperation with High Performance Computing Centers, High Quality 3D printing specialists, Dedicated Software and other technical providers. Moreover, the hardware and service providers would benefit from the practical feedback received from users and scientists that will induce technical improvements, continuous optimization and technical development. Figure 37 shows the basic elements of the proposed NOSE CoE.



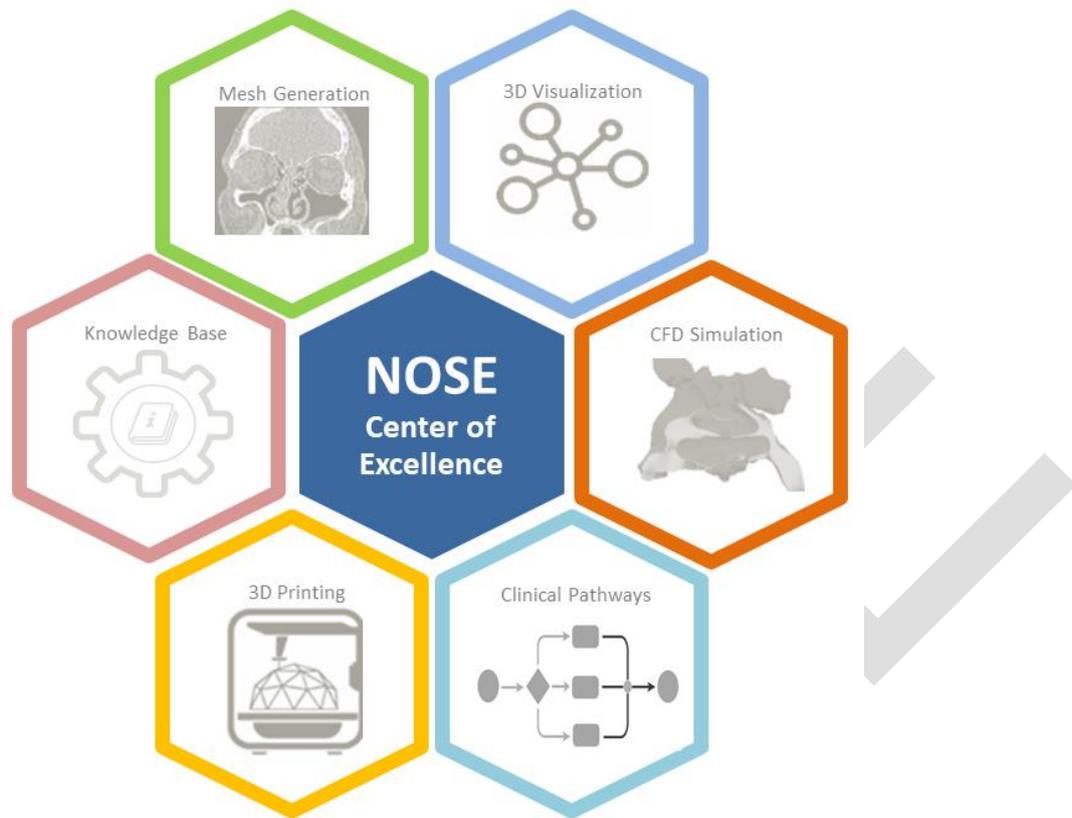


Figure 37 – Elements of the NOSE Center of Excellence

6.5 Legal Framework and Patentability

On 5 April 2017, 2 new Regulations on medical devices were adopted by the European Parliament, and they entered into force on 25 May 2017. These are the Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, and the Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices. The regulation on medical devices has to be incorporated in order to use the NSC Services for diagnostic purposes. During the project lifetime investigations started on patentability and international extension of intellectual property rights. The NSC innovative way of processing CT/MR images for CFD and 3D analysis and printing does not incorporate technology or represents an improved version of an invention that has been protected previously as a patent by another party. NOSE Service Center shall be based on a novel model for the automatic segmentation of CT/MR images (of nasal cavities and paranasal sinuses) using CNNs and is not using inventions for which third-party patents may hinder a commercial exploitation. Nevertheless there is further need to consult with patent experts and lawyers in due course of setting up the NOSE Service Center. But the most important achievement of the NSC is the delivery of the aforementioned simulation services as easy accessible and affordable mass services for anyone working in the ENT domain.



I. List of Entities doing Research on CFD in the Upper Respiration System

Country	Institution	Department
Australia	RMIT University, Melbourne	School of Aerospace, Mechanical and Manufacturing Engineering
Australia	The University of Sydney Westmead Clinical School	ENT Department
Austria	SimVis GmbH, Austria	-
Austria	Vienna University of Technology	Institute of Computer Graphics and Algorithms
Czech Republic	VŠB - Technical University of Ostrava	-
Germany	Asklepios Klinik Birkenwerder, Brandenburg	ChA der Sektion Rhinochirurgie, Abteilung für Plastische Chirurgie
Germany	CFX Berlin Software GmbH, Berlin	-
Germany	Charité Universitätsmedizin Berlin	Biofluid Mechanics Lab
Germany	European Laryngological Society, Gießen	-
Germany	German ENT society, Bonn	-
Germany	Jülich Aachen Research Alliance, Jülich	Simulation Laboratory "Highly Scalable Fluids & Solids Engineering" (SimLab FSE)
Germany	Ruperto-Carola University of Heidelberg	-
Germany	RWTH Aachen	Chair of Fluid Mechanics and Institute of Aerodynamics
Germany	RWTH Aachen	VR-Gruppe am Rechen- und Kommunikationszentrum
Germany	Städtisches Klinikum Karlsruhe	HNO-Klinik
Germany	Technische Universität Bergakademie Freiberg	-
Germany	Uniklinik Köln	Institut für Medizinische Statistik, Informatik und Epidemiologie
Germany	Uniklinik RWTH Aachen	Klinik für Diagnostische und Interventionelle Radiologie
Germany	Universität Ulm	Department of ORL, Head and Neck Surgery
Germany	Zuse-Institute Berlin (ZIB)	Visual Data Analysis
Iran	Shiraz University, Shiraz	School of Mechanical Engineering
Italy	Politecnico di Milano	School of Industrial and Information Engineering
Italy	Politecnico di Milano	Department of Aerospace Science and Technologies
Italy	San Paolo Hospital, Università degli Studi di Milano	Otorhinolaryngology Unit, Head and Neck Department



NOSE Pilot Study

Investigating the Practical Use of Computational Fluid Dynamics Simulation of Airflow in the Nasal Cavity and Paranasal Sinuses

Version 1.0

Country	Institution	Department
Italy	SuperComputing Applications and Innovation Department, CINECA, Casalecchio di Reno - Bologna	-
Japan	Teikyo University Chiba Medical Center	Department of Otolaryngology
Malaysia	Universiti Sains Malaysia, Malaysia	School of Aerospace Engineering
Malaysia	Universiti Sains Malaysia, Malaysia	School of Mechanical Engineering
Malaysia	Universiti Sains Malaysia, Malaysia	School of Medical Sciences, Health Campus
Malaysia	Universiti Sains Malaysia, Malaysia	Advanced Medical & Dental Institute
New Zealand	Fisher and Paykel Healthcare Limited, Auckland	-
New Zealand	The University of Auckland	Department of Engineering Science
New Zealand	University of Canterbury	Department Mechanical Engineering
Norway	Norwegian University of Science and Technology-NTNU, Trondheim	Department of Energy and Process Engineering
Norway	SINTEF Materials and Chemistry, Trondheim	-
Singapore	National University of Singapore	Department of Otolaryngology
South Korea	Konkuk University, Seoul	Department of Mechanical Engineering
South Korea	Korean Nuclear Society, Daejeon	-
South Korea	Sungkyunkwan University	-
South Korea	Sungkyunkwan University, School of Medicine, Seoul	Department of Otorhinolaryngology-Head and Neck Surgery, Samsung Medical Center
Spain	Hospital General Universitario Gregorio Marañón in Madrid	Department of Rhinology
Spain	Inspiralia, Madrid	-
Spain	Laboratorio Avanzado de Flujo Aéreo Nasal (N.A.S.A.L.) S.L, Madrid	-
Spain	Polytechnic University of Cartagena, Murcia	-
Spain	Technical University of Madrid	-
Spain	University of Malaga	Department of Mechanical, Thermal and Fluids Engineering
Thailand	King Mongkut's Institute of Technology Ladkrabang	Faculty of Engineering, Department of Electronics Engineering
The Netherlands	European rhinologic society, Amsterdam	-
UK	Imperial College Healthcare NHS Trust, London	-
UK	Imperial College London	Faculty of Engineering and Aeronautics
UK	Queens University, Belfast	-
UK	University of Exeter, Exeter	School of Engineering, Computer Science and Mathematics
UK	OpenCFD Limited (ESI Group)	-
USA	Marquette University and the Medical College of Wisconsin	Joint Department of Biomedical Engineering



NOSE Pilot Study

Investigating the Practical Use of Computational Fluid Dynamics Simulation of Airflow in the Nasal Cavity and Paranasal Sinuses

Version 1.0

Country	Institution	Department
USA	Medical College of Wisconsin, Milwaukee	Department of Otolaryngology and Communication Sciences
USA	Monell Chemical Senses Center, Philadelphia	-
USA	Pennsylvania State University	Computational Mechanics Division, Applied Research Laboratory
USA	Pennsylvania State University	Department of Mechanical and Nuclear Engineering, Gas Dynamics Laboratory
USA	School of Medicine, Stanford University, Stanford	Department of Otolaryngology
USA	The Ohio State University - Medical Center	Department of Otolaryngology-Head and Neck Surgery
USA	The Ohio State University - Medical Center	Department of Biomedical Engineering
USA	Thomas Jefferson University, Philadelphia	Department of Otolaryngology
USA	University of Cincinnati, Medical Center	Department of Otolaryngology-Head and Neck Surgery
USA	University of Cincinnati, Medical Center	Department of Aerospace Engineering and Engineering Mechanics
USA	University of North Carolina, Chapel Hill	Departments of Pharmacology
USA	University of North Carolina, Chapel Hill	Otolaryngology-Head and Neck Surgery
USA	University of Pennsylvania, Philadelphia	Bioengineering Department



II. Conference Participation and Presentations (2016-2018)

Meeting Type	Date	Title
Conference	30.10.-2.11.16, Riga (Latvia)	Consensus Conference on Function Tests of the Nasal Airway
Workshop	1.-3.12.16, Leipzig (Germany)	IRDC Kurs, Functional Rhinoplasty, Focus Breathe Implant
Workshop	13.-15.3.17, Basel (Switzerland)	Materialise Training Course
Conference	8.5.17, Vienna (Austria)	COMET Information Event
Conference and Workshop	23.-24.5.17, Vienna (Austria)	eHealth Summit 2017
Meeting	18.-19.9.17, Vienna (Austria)	KickOff Meeting RHINODIAGNOST Project
Workshop	14.-15.11.17, Vienna (Austria)	Workshop Artificial Intelligence
Meeting	5.-6.12.17, Milano (Italy)	NOSE Networking Meeting (Politecnico di Milano)
Conference	6.-7.12.17, Brussels (Belgium)	HealthBE2017
Meeting	9.-11.12.17, Berlin (Germany)	NOSE Networking Meeting (Park-Klinik Weißensee)
Conference	17.-21.12.17, Manipal (India)	ICCMEH 2017 International Conference on Computational Methods in Engineering and Health Sciences
Conference	21.-3.4.18, London (Great Britain)	SCONA 2018 World Congress on CFD (Computational Fluid Dynamics) of the Nose and Airway
Conference	8.-9.5.18, Vienna (Austria)	eHealth 2018
Conference	11.-16.6.18, New York (USA)	ICELW 2018 International Conference on E-Learning in the Workplace
Conference	21.-22.6.18, Krems (Austria)	14 th ENT Danube Symposium

III. Glossary

BPM **B**usiness **P**rocess **M**anagement (BPM) is a discipline in operations management that uses various methods to discover, model, analyze, measure, improve, optimize, and automate business processes. BPM focuses on improving corporate performance by managing business processes.
https://en.wikipedia.org/wiki/Business_process_modeling [Accessed: 2018-06-21]

BPMN **B**usiness **P**rocess **M**odel and **N**otation (BPMN) is a standard for business process modeling that provides a graphical notation for specifying business processes in a Business Process Diagram (BPD),[2] based on a flowcharting technique very similar to activity diagrams from Unified Modeling Language (UML).[3] The objective of BPMN is to support business process management, for both technical users and business users, by providing a notation that is intuitive to business users, yet able to represent complex process semantics.
https://en.wikipedia.org/wiki/Business_Process_Model_and_Notation [Accessed: 2018-06-21]

CFD **C**omputational **F**luid **D**ynamics (CFD) is a branch of fluid mechanics that uses numerical analysis and data structures to solve and analyze problems that involve fluid flows. Computers are used to perform the calculations required to simulate the interaction of liquids and gases with surfaces defined by boundary conditions. With high-speed supercomputers, better solutions can be achieved.
https://en.wikipedia.org/wiki/Computational_fluid_dynamics [Accessed: 2018-06-21]

CMMN **C**ase **M**anagement **M**odel and **N**otation (CMMN) is a graphical representation for graphically expressing a Case, as well as an interchange format for exchanging Case models among different tools.
<https://en.wikipedia.org/wiki/CMMN> [Accessed: 2018-06-21]

CNN In machine learning, a **C**onvolutional **N**eural **N**etwork (CNN, or ConvNet) is a class of deep, feed-forward artificial neural networks, most commonly applied to analyzing visual imagery.
https://en.wikipedia.org/wiki/Convolutional_neural_network [Accessed: 2018-06-21]

CRS **C**hronic **R**hinosinusitis
 Chronic sinusitis is a common condition in which the cavities around nasal passages (sinuses) become inflamed and swollen for at least 12 weeks, despite treatment attempts.

Also known as chronic rhinosinusitis, this condition interferes with drainage and causes mucus buildup. Breathing through your nose might be difficult. The area around your eyes and face might feel swollen, and you might have facial pain or tenderness.

Chronic sinusitis can be brought on by an infection, by growths in the sinuses (nasal polyps) or by a deviated nasal septum. The condition most commonly affects young and middle-aged adults, but it also can affect children.
<https://www.mayoclinic.org/diseases-conditions/chronic-sinusitis/symptoms-causes/syc-20351661> [Accessed: 2018-06-21]

CT **C**omputed **T**omography
 A CT scan, also known as computed tomography scan, makes use of computer-

processed combinations of many X-ray measurements taken from different angles to produce cross-sectional (tomographic) images (virtual "slices") of specific areas of a scanned object, allowing the user to see inside the object without cutting
https://en.wikipedia.org/wiki/CT_scan [Accessed: 2018-06-21]
<http://www.springer.com/de/book/9781852336172> [Accessed 20.03.2018]

DICOM **D**igital **I**maging and **C**ommunications in **M**edicine (DICOM) is the standard for the communication and management of medical imaging information and related data. DICOM is most commonly used for storing and transmitting medical images enabling the integration of medical imaging devices such as scanners, servers, workstations, printers, network hardware, and picture archiving and communication systems (PACS) from multiple manufacturers. It has been widely adopted by hospitals, and is making inroads into smaller applications like dentists' and doctors' offices.
<https://en.wikipedia.org/wiki/DICOM> [Accessed: 2018-06-21]
<https://www.dicomstandard.org/> [Accessed 2018-04-17]

DMN **D**ecision **M**odel and **N**otation (DMN) is a standard published by the Object Management Group.[1] It is a standard approach for describing and modeling repeatable decisions within organizations to ensure that decision models are interchangeable across organizations.
https://en.wikipedia.org/wiki/Decision_Model_and_Notation [Accessed: 2018-06-21]

ENT **E**ar-**N**ose-**T**hroat
 Otorhinolaryngology, (also called otolaryngology and otolaryngology-head and neck surgery) is a surgical subspecialty within medicine that deals with conditions of the ear, nose, and throat (ENT) and related structures of the head and neck
<https://en.wikipedia.org/wiki/Otorhinolaryngology> [Accessed: 2018-06-21]

FDM **F**used **D**eposition **M**odeling is an additive manufacturing (AM) technology commonly used for modeling, prototyping, and production applications as trademarked by Stratasys Inc.[6][7]. It is one of the techniques used for 3D printing. FDM works on an "additive" principle by laying down material in layers; a plastic filament or metal wire is unwound from a coil and supplies material to produce a part.
https://en.wikipedia.org/wiki/Fused_filament_fabrication#Fused_deposition_modeling
 [Accessed: 2018-07-09]

FESS **F**unctional **E**ndoscopic **S**inus **S**urgery (FESS) is a surgical treatment of sinusitis and nasal polyps, including bacterial, fungal, recurrent acute, and chronic sinus problems. FESS uses nasal endoscopes to restore drainage of the paranasal sinuses and ventilation of the nasal cavity.
https://en.wikipedia.org/wiki/Functional_endoscopic_sinus_surgery [Accessed: 2018-06-21]
<https://link.springer.com/article/10.1007/BF00183169> [Accessed: 2018-06-21]

Gantt chart A Gantt chart is a type of bar chart mostly used to illustrate project schedules. The tasks to be performed are listed on the vertical axis, and the time intervals on the horizontal axis, with the width of the horizontal bars showing the duration of each activity. Gantt charts also show the dependency relationships between activities.
https://en.wikipedia.org/wiki/Gantt_chart [Accessed: 2018-08-07]

HPC **H**igh **P**erformance **C**omputing most generally refers to the practice of aggregating computing power in a way that delivers much higher performance than one could get out of a typical desktop computer or workstation in order to solve large problems in science, engineering, or business.
<https://insidehpc.com> [Accessed: 2018-06-21]

HSSP	<p>The Healthcare Services Specification Project (HSSP) is a standards development effort to create health industry service-oriented architecture (SOA) standards supportive of the health care market sector. HSSP is a jointly sponsored activity operating within the Health Level Seven (HL7) and the Object Management Group (OMG) standards group.</p> <p>https://en.wikipedia.org/wiki/Healthcare_Services_Specification_Project [Accessed: 2018-06-21] http://hssp.wikispaces.com/ [Accessed: 2018-06-21]</p>
IDEFo	<p>IDEFo stands for Integrated Computer Aided Manufacturing DEfinition for Function Modeling. It is a function modeling methodology for describing manufacturing functions, which offers a functional modeling language for the analysis, development, reengineering, and integration of information systems; business processes; or software engineering analysis. It is part of the IDEF family of modeling languages in the field of software engineering, and is built on the functional modeling language Structured Analysis and Design Technique (SADT).</p> <p>https://en.wikipedia.org/wiki/IDEFO [Accessed: 2018-08-07] http://www.idef.com/idefo-function_modeling_method/ [Accessed: 2018-08-07]</p>
IPR	<p>Intellectual Property Rights include patents, copyright, industrial design rights, trademarks, plant variety rights, trade dress, geographical indications.</p> <p>https://en.wikipedia.org/wiki/Intellectual_property [Accessed: 2018-07-09]</p>
IT	<p>Information Technology (IT) is the use of computers to store, retrieve, transmit, and manipulate data,[1] or information, often in the context of a business or other enterprise</p> <p>https://en.wikipedia.org/wiki/Information_technology [Accessed: 2018-07-25]</p>
KB	<p>A Knowledge Base (KB) is a technology used to store complex structured and unstructured information used by a computer system. The initial use of the term was in connection with expert systems which were the first knowledge-based systems.</p> <p>https://en.wikipedia.org/wiki/Knowledge_base [Accessed: 2018-07-25]</p>
MR	<p>Magnetic Resonance Imaging (MRI) is a medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body in both health and disease. MRI scanners use strong magnetic fields, electric field gradients, and radio waves to generate images of the organs in the body.</p> <p>https://en.wikipedia.org/wiki/Magnetic_resonance_imaging [Accessed: 2018-06-21] http://www.cis.rit.edu/htbooks/mri/ [Accessed: 2018-06-21]</p>
OMG	<p>The Object Management Group (OMG) is an international, open membership, not-for-profit technology standards consortium. OMG Task Forces develop enterprise integration standards for a wide range of technologies and industries. OMG modeling standards enable visual design, execution and maintenance of software and other processes.</p> <p>https://en.wikipedia.org/wiki/Object_Management_Group [Accessed: 2018-06-21]</p>
OpenFOAM	<p>OpenFOAM (for "Open source Field Operation And Manipulation") is a C++ toolbox for the development of customized numerical solvers, and pre-/post-processing utilities for the solution of continuum mechanics problems, including computational fluid dynamics (CFD). The code is released as free and open-source software under the GNU General Public License.</p> <p>https://en.wikipedia.org/wiki/OpenFOAM [Accessed: 2018-07-09]</p>
PACS	<p>A Picture Archiving and Communication System (PACS) is a medical imaging technology which provides economical storage and convenient access to images from</p>

multiple modalities (source machine types).[1] Electronic images and reports are transmitted digitally via PACS; this eliminates the need to manually file, retrieve, or transport film jackets, the folders used to store and protect X-ray film
https://en.wikipedia.org/wiki/Picture_archiving_and_communication_system
 [Accessed: 2018-06-21]

PIV **Particle image velocimetry (PIV)** is an optical method of flow visualization used in education and research. It is used to obtain instantaneous velocity measurements and related properties in fluids.
https://en.wikipedia.org/wiki/Particle_image_velocimetry [Accessed: 2018-07-25]

RANS **Reynolds-averaged Navier-Stokes** equations re time-averaged equations of motion for fluid flow. The RANS equations are primarily used to describe turbulent flows.
https://en.wikipedia.org/wiki/Reynolds-averaged_Navier%E2%80%93Stokes_equations [Accessed: 2018-07-12]

ROI A **Region Of Interest (often abbreviated ROI)**, are samples within a data set identified for a particular purpose. For example, in medical imaging, the boundaries of pathological areas may be defined on an image or in a volume.
https://en.wikipedia.org/wiki/Region_of_interest [Accessed: 2018-08-28]

SLA or SL **Stereolithography** is a form of 3D printing technology used for creating models, prototypes, patterns, and production of parts in a layer by layer fashion using photopolymerization.
<https://en.wikipedia.org/wiki/Stereolithography> [Accessed: 2018-06-21]

STL **Standard Tessellation Language** (an abbreviation of "stereolithography") is a file format native to the stereolithography CAD software created by 3D Systems.
[https://en.wikipedia.org/wiki/STL_\(file_format\)](https://en.wikipedia.org/wiki/STL_(file_format)) [Accessed: 2018-07-12]

UI The **User Interface (UI)**, in the industrial design field of human-computer interaction, is the space where interactions between humans and machines occur. The goal of this interaction is to allow effective operation and control of the machine from the human end, whilst the machine simultaneously feeds back information that aids the operators' decision-making process.
https://en.wikipedia.org/wiki/User_interface [Accessed: 2018-06-21]

VESS **Virtual Endoscopic Sinus Surgery**
 A surgery simulator is computer technology developed to simulate surgical procedures for the purpose of training medical professionals, without the need of a patient, cadaver or animal.
https://en.wikipedia.org/wiki/Surgery_simulator [Accessed: 2018-07-25]

IV. Protection of Data Privacy

DICOM is an international standard to promote the transmission, storage, retrieval, printing, displaying and use of medical imaging information. It is a free standard that makes medical images interoperable. A DICOM image is described by a series of information about the examination, the device used and the patient. Each DICOM image includes the name, id, birthday date and the gender of the patient being examined. In this pilot study we did not make use of this information. Every DICOM received was anonymized in order to preserve the privacy of the patient. The age and the gender of the person were the only information left after anonymization.

In future, it might be of statistical value to analyze the segmentation and the 3D model created in relation to aspects such as gender and age of the patients. It could be interesting to investigate whether certain pathologies are more common in men than in women, or whether an age group is more prone to certain pathologies in the paranasal sinuses than another.



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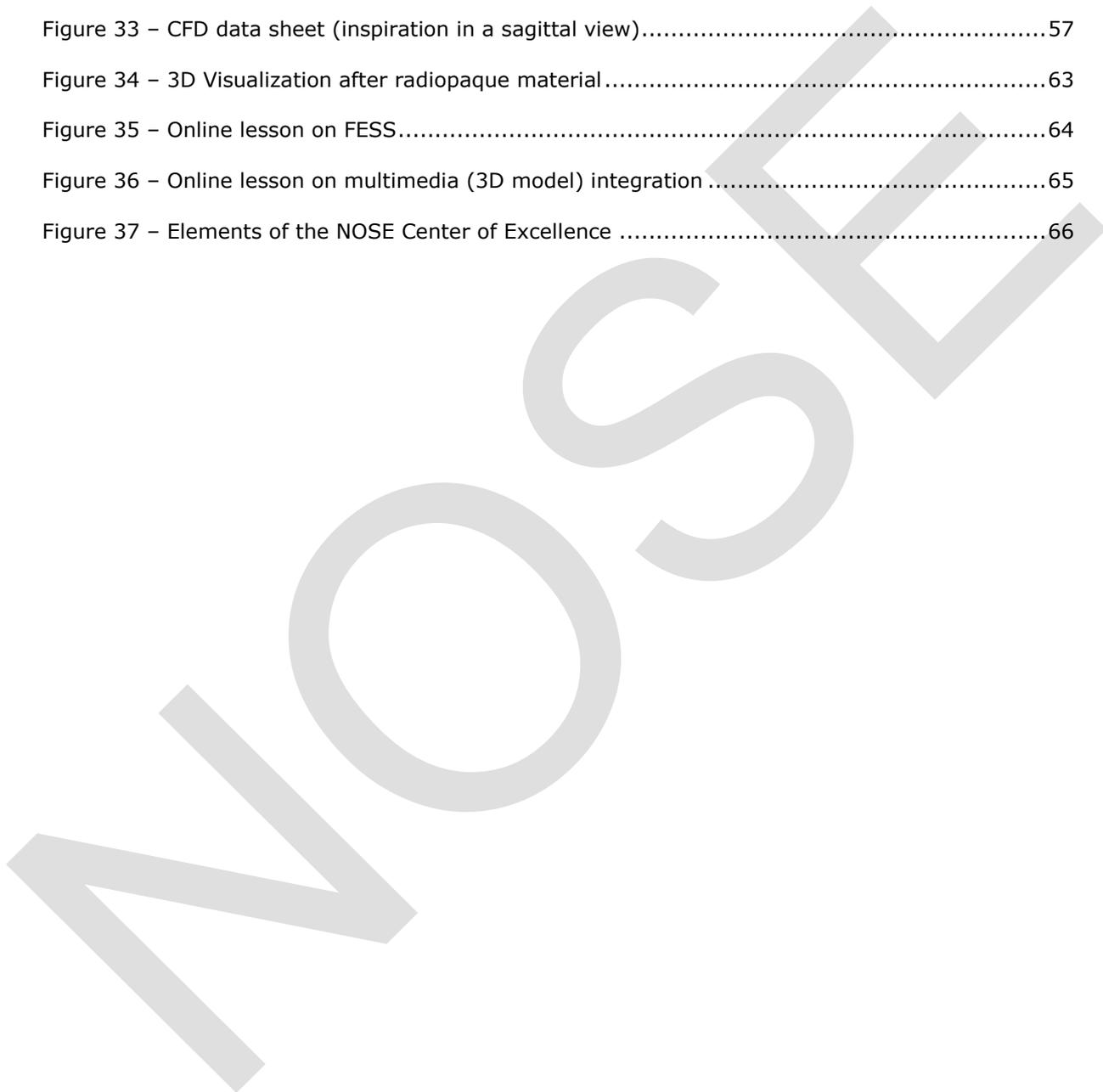
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