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REVERSE ENGINEERING AND PROTOTYPING OF A NASAL CAVITY MODEL FOR ODORANT DETECTION EXPERIMENTS

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ABSTRACT

Reverse engineering (RE) is an evolving discipline in information science that offers computer-based reproductions of components, products, or even anatomical structures. Focusing on the human nose, various approaches, including basic 3D scanning, silicone rubber impressions, or medical imaging techniques, have been used for acquisition. Among these, just imaging techniques such as CT and MRI allow us to completely visualize the internal anatomy of the nose, also enabling three-dimensional reconstructions.

Based on these considerations, this work aims to create an accurate 3D reconstruction of the nose, with a special focus on the nasal cavity, starting from a preoperative CT scan dataset. A thresholding-based segmentation approach was chosen to derive the inner volume occupied by the air. From this, a constant-thickness wall was generated with a hollowing operation. After further design modifications and improvements, the assembly was 3D printed with a stereolithography machine.

The obtained model was then integrated into an experimental setup, including an odor sensor and a vacuum pump to generate airflow. Preliminary tests were run to evaluate the effectiveness of the proposed solution in guaranteeing signal detection.

As a preliminary output, this study showed the feasibility of an experimental workbench to replicate human sniff. This was successfully tested with odorant molecules and an odor sensor. Now, more extensive tests will have to be conducted, even comparing results with those from numerical simulation.

Keywords: Nasal cavity, segmentation, medical 3D printing, odor sensor

1. INTRODUCTION

Sensory impairments significantly affect individuals' daily functioning. While prostheses and implants for hearing impairments have been developed, efforts are underway to create similar solutions for impairments affecting other senses. The sense of smell is probably the least investigated among them, despite the COVID-19 pandemic raising attention in this direction. The total or partial loss of smell affects up to 24% of the global population [1]. Although erroneously considered a "minor" impairment, it profoundly impacts the quality of life [1]. Despite this, there hasn't been progress in developing devices to restore the sense of smell due to insufficient scientific understanding of connecting artificial systems with human olfaction. The ROSE project, funded under the Horizon 2020 FET-Open program, aims to address this gap by generating new scientific insights that will culminate in creating the Digital Olfaction Module (DOM). This breakthrough technology will allow individuals with olfactory loss to perceive their olfactory surroundings, enhancing their overall sensory experience.

To achieve this result, the ROSE project combines interdisciplinary competencies and skills related to the study of the human olfaction system, such as neurosurgery, clinical olfaction, neuroscience, and cognitive psychology, with other technological competencies (nanotechnology, microtechnology, biotechnology, and mechanical design), to develop a proof of concept combining miniaturized odor sensors and stimulation arrays that will be evaluated in patients with smell disorders. It is clear how the detection part of the DOM plays a crucial role in conveying the correct stimulation to the patients, depending on the odor detected in the environment.

To this end, the research has focused on different approaches to detecting and discriminating odors. The electronic nose (e-nose) encompasses a broad spectrum of technologies designed for artificial scent detection. These systems detect the makeup of volatile substances in the air that carry odor, often focusing on volatile organic compounds [2]. In contrast to techniques like gas chromatography or mass spectrometry, which identify the specific chemical makeup of a sample, e-noses aim to capture the overall scent profile. In other words, e-noses assess the collective odor profile of a sample rather than breaking it down into its chemical constituents. However, these technologies have been mostly investigated as desktop applications and, as per the knowledge of the authors, no study has been conducted on the possibility of using them as wearable devices, backing up the real nose of people affected by odor impairments.

In this context, testing odor detection sensors with real people is challenging because of the inherent variability of human-in-the-loop testing protocols and the lack of knowledge about the fluidics related to the sensors themselves. For these reasons, it is desirable to have a test bench replicating, as much as possible, the real scenario where the odor sensor would be placed close to the human nostrils. Unlike the situation where humans are involved, the testbench allows the sensor to be tested in an environment where all the relevant variables are kept under control.

This paper aims to present the design of such testbench to be used in the design of bespoke miniaturized artificial noses. A fundamental part of the research activity is the acquisition and modelling of the nasal cavity of subjects to better replicate the real scenario. Specifically, the 3D reconstruction of the nasal cavity and the derived 3D printed replica is beneficial for two main reasons:

- perform experimental activities to test the sensor's effectiveness in detecting smells during natural breathing;
- define the shape of the miniaturized odor sensors and adequately place them according to the morphology of the subject's nasal cavity.

After a review of the potential reverse engineering (RE) approach for nasal acquisition, this work aims to investigate an appropriate RE approach to capture the human nose's external and internal shape. This will allow us to create a physical prototype through 3D printing. The obtained prototype will be then integrated into an experimental setup for odorant detection tests.

2. STATE OF THE ART

In the industrial engineering domain, the process of RE is generally intended as the process of generating a 3D digital representation of a physical object. More generally, RE is an affirmed discipline in the domain of information science, which can provide a computer-based reproduction of a component, a product or even an anatomical structure. Over time, RE technology has become more and more accessible, allowing the possibility to choose among a multitude of technical solutions. A general classification of them can be found in [3], as provided in Fig. 1.

Because of their noninvasiveness, methods that do not necessitate physical contact with the original object are of significant interest in medicine. These contact-free methods can be further classified into transmission-based and reflection-based methods [3]. Laser or structured light-based 3D scanners are adopted in many medical applications, from personalized orthoses production [4] to dental field treatment planning [5], but have the limitation of not being able to acquire anatomies "inside" the body. For this purpose, the most efficient non-contact devices are based on the transmission principle, including medical computed tomography (CT) and medical resonance imaging (MRI).

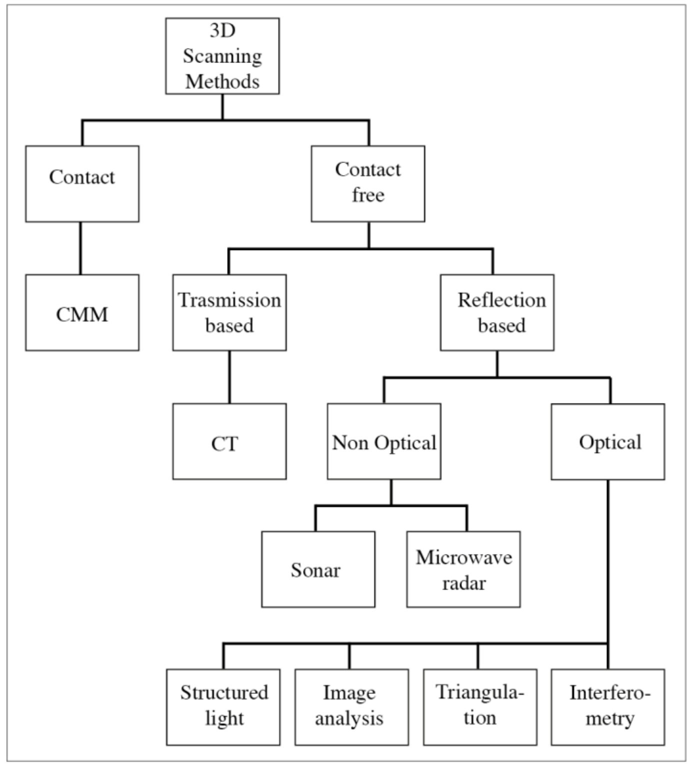

FIGURE 1: A CLASSIFICATION OF 3D SCANNING OPTIONS. ADAPTED FROM [3]

In the literature, there are several examples of medical uses of RE. Focusing on the nose, Ritschl et al. [6] compared and determined the applicability of three different 3D scanning systems in clinical practice: one was based on structured-light technology, another one on stereophotogrammetry, and the last one relied on a mobile application. Even with differences in accuracy and cost, they concluded all of them were suitable for nose imaging in clinical applications. Another study used a 3D laser scanner for the objective evaluation of the nasal shape before and following rhino surgery [7]. The goal was to have an objective assessment of the procedure in a fast, easily accessible, and reliable way. Eventually, in [8], white-light 3D scanning was used to create a database and study the growth and development of children's nasolabial units. The authors stated the approach is suitable for gaining 3D imaging of nasolabial soft tissue to build a normal morphology database. All the aforementioned techniques are limited in the acquisition of the external shape and the initial portion of the nasal cavity.

An alternative pursued strategy to derive the inner shape of the nose is based on the use of impressions, as reported in [9]. There, silicone rubber impression material was mixed and injected into the nasal cavity. A few minutes later, after solidification of the material, the silicone rubber impression was removed (Fig. 2). This was then acquired with a high-precision 3D scanner and used for the design and printing of personalized nasal stents for cleft lip.

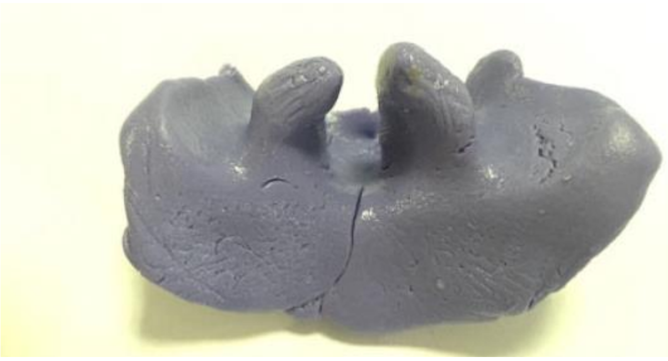

FIGURE 2: SILICONE RUBBER IMPRESSION TO DERIVE THE INNER NASAL SHAPE. REPRINTED FROM [9]

However, this approach is time-consuming and can be uncomfortable for the patient. Due to operative and safety concerns, it is suitable for acquiring just a limited portion of the nasal cavity.

Imaging techniques such as CT and MRI allow the internal anatomy to be completely visualized. CT is nowadays the gold standard in diagnostics of nasal cavity diseases; thus, it can be applied successfully as a tool for assessing anatomical structures [10]. CT scans provide detailed information relating to the radio densities of different cross-sectional volumes (slices). Additionally, the data obtained from CT scans can be utilized to create accurate, three-dimensional models. These digital models, properly post-processed, can be then exploited to realize physical replicas, through 3D printing [11], or to run fluid dynamics simulations [12]. CT images are also sometimes used to produce nasal cast models, for *in vitro* evaluation of nasal drug delivery [13].

From this overview, it emerged that the only valid techniques for the complete and accurate acquisition and reconstruction of both the exterior and the interior of the nose are those based on medical images. As already hinted, the CT represents the gold standard and so can be effectively employed even for reconstructions of 3D models.

3. METHODS

3.1 Nasal cavity prototyping

To create the nasal 3D printed model, a standardized workflow widely reported in the literature for medical disciplines was followed [14, 15]. A dataset of anonymized CT scans of a 59-year-old male patient was chosen. Images were imported into Mimics software (Leuven, Belgium). The stack consisted of 192 slices in the axial plane, with a resolution of 512 × 512 pixels and a slice thickness equal to 1 mm (Fig. 3).

FIGURE 3: CT DATASET USED AS INPUT FOR THE SEGMENTATION

The nasal cavity was first isolated through a greyscale thresholding algorithm, to get a preliminary mask. What was derived here is the inner region filled with air, corresponding to the lowest values of Hounsfield Unit. Paranasal sinuses were not required for our purposes, so they were neglected. From this mask, the 3D model corresponding to the nasal cavity was derived: the result is shown in Fig. 4.

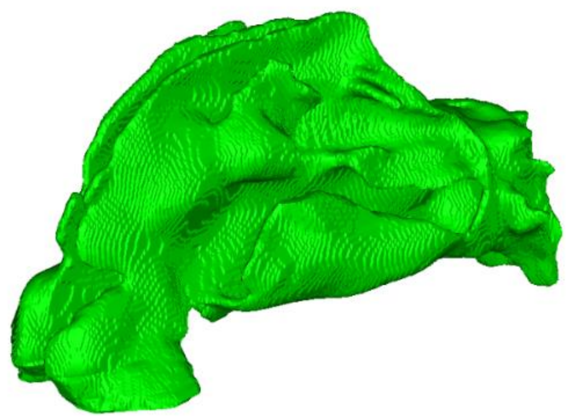

FIGURE 4: NASAL CAVITY MODEL (AIR POOL)

Together with the nasal cavity, other structures were segmented, including a portion of the skull and the outer skin. To derive the region in between, including nasal cartilage, Boolean operators were exploited. Then, to get a more regular polygonal model and ensure watertightness, all the 3D models were post-processed by wrapping, smoothing, and remeshing operations performed in the 3-Matic software (Leuven, Belgium). The obtained nasal cavity was hollowed outwards, with a constant thickness of 2 mm, and inlets and outlet were “opened”. This to guarantee the possibility of 3D printing the model, letting air flow inside for experiments. The results are presented in Fig. 5, wherein the nasal cavity walls are delineated in red, the soft tissues in yellow, the skin in pink, and the skull in grey.

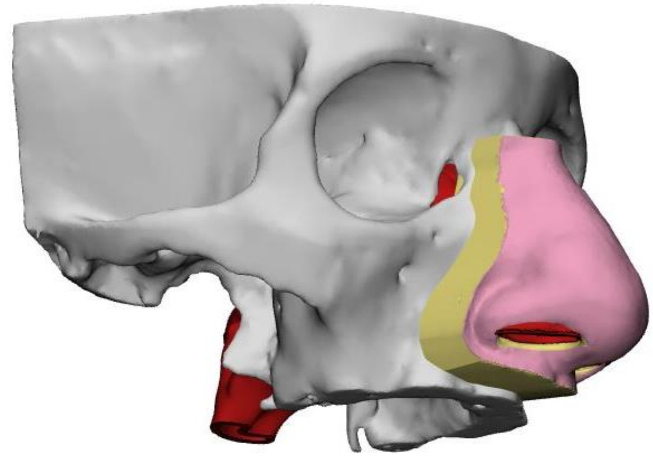

FIGURE 5: STL ASSEMBLY AFTER POST-PROCESSING

For the 3D printing process, other design modifications were performed. To have the possibility of removing internal supports, the model was split transversally into three parts, that could be separately cleaned without difficulties. The connection between them was guaranteed by flanges and bolts. A small cylinder (6 mm as external diameter) was added at the outlet of the cavity model to allow the pump mimicking the breath to be connected. The result is shown in Fig. 6.

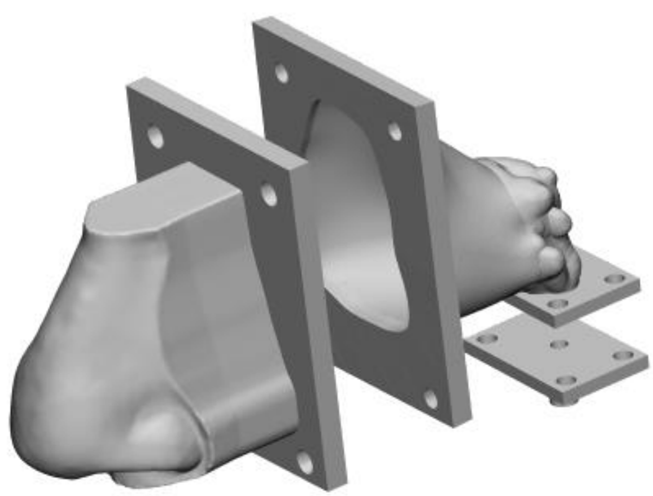

FIGURE 6: NASAL CAVITY MODEL AFTER DESIGN MODIFICATIONS

For the printing phase, a Formlabs 3B (Somerville, USA) was employed. It implements the stereolithography technology, with a resolution of the building layer up to 25 µm.

In Preform environment by Formlabs, the position and orientation of the model parts on the printing platform were properly set. The commercially available White resin V4 was chosen. After print, supports were removed and parts were washed in isopropyl alcohol, to remove uncured resin. This was followed by post-curing in a UV oven. The obtained 3D printed assembled model is shown in Fig 7.

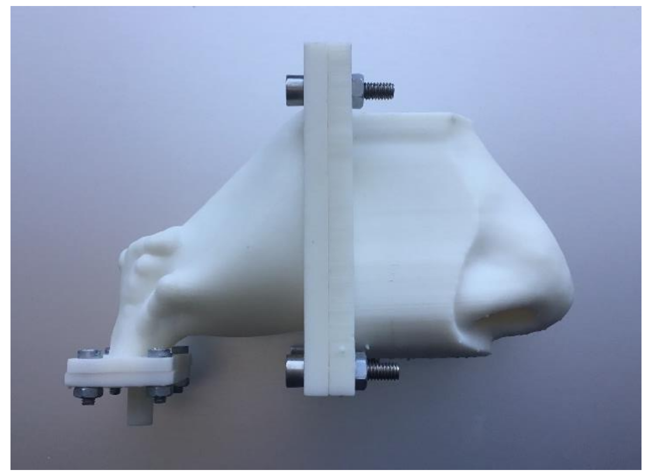

FIGURE 7: 3D PRINTED RESULT AFTER SUPPORTS REMOVAL AND ASSEMBLY

3.2 Test bench integration

The printed model was then integrated into a properly designed testbench for odorant detection. The key component is a smell sensor patented by Aryballe (Grénoble, France). It is based on a technology called functionalized silicon photonics. It consists of a silica chip with an array of Mach-Zehnder Interferometers (MZI) printed on it [16]. Each MZI is then functionalized with a peptide that is chemically grafted. Using a laser to inject light on the chip and a camera to collect the intensity at the output of the chip, it is possible to catch a phase shift (in radians) between the reference arm and the functionalized arm on the 64 channels simultaneously. The diversity of peptides that can be grafted on the chip is the key innovation that can lead to the discrimination of odors [15].

The usual working configuration of this sensor (i.e. the one it has been designed for) is represented on the left of Fig. 8. The active layer, i.e. the sensory part the air carrying the odor molecules should hit, is covered by a fluidic cap. In the current configuration, the air is taken from the environment thanks to a pump that pushes the air through the sensor. For the intended application, the airflow hitting the active layer of the sensor should be driven by the natural breath of a human being. To mimic this situation, a commercial membrane vacuum pump (N86 Laboport, KNF Group, Freiburg im Breisgau, Germany) was connected to the prototype using PTFE tubing, as shown on the right of Fig. 8.

Fig. 9 shows the setup of the testbench. The 3D printed prototype, connected to the vacuum pump, has been mounted on a frame made of standard aluminum profiles. A 6 degrees of freedom arm, mounted on the same frame, has been used to hold the sensor. This configuration allows the position and orientation of the sensor with respect to the nostril to be finely adjusted.

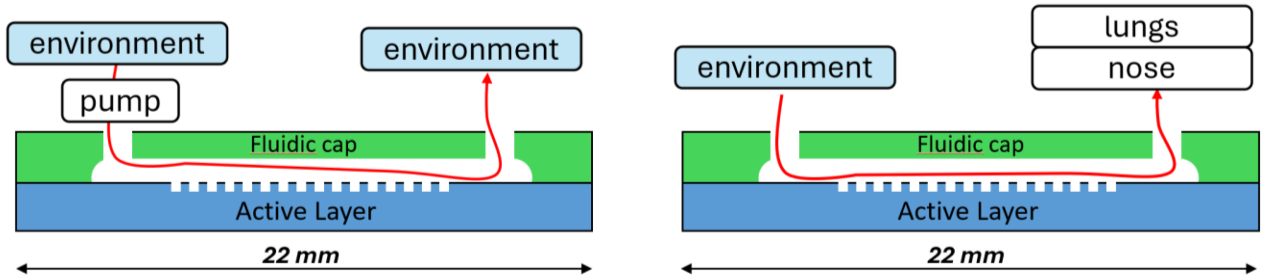

FIGURE 8: SENSOR WORKING CONFIGURATIONS. ON THE LEFT, THE USUAL WORKING CONFIGURATION. ON THE RIGHT, THE CONFIGURATION FOR THE EXPERIMENTAL SETUP.

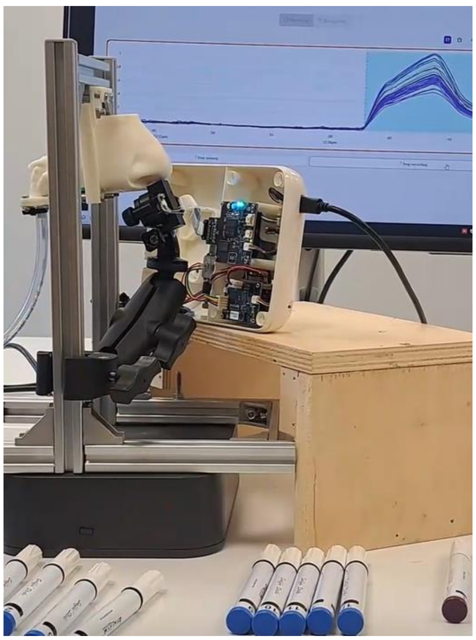

FIGURE 9: WORKBENCH TO TEST THE SMELL SENSOR, INCLUDING 3D PRINTED NOSE, SENSOR, 6 DOF ARM AND CONNECTED LAPTOP RUNNING THE SOFTWARE DEVELOPED BY ARYBALLE

This testbench configuration wants to realistically replicate human sniff, particularly the airflow which develops inside and near the nasal cavity, which is crucial for the mechanism of odorant perception. In this way, it is possible to properly characterize the odor sensor.

4. RESULTS AND DISCUSSION

Some qualitative tests of the overall setup have been conducted. The sensor was placed in proximity to the 3D-printed nose, close to the nostrils. Indeed, due to its current dimensions, we are still way far from the possibility of putting it inside the nostrils, which is, anyway the ultimate goal. Sniffin Sticks (Burghardt, Wedel, Germany) [15] were exploited as an odor source: they are pen-like odor dispensing devices. In particular, the smelly cap of the Sniffin Stick was used, which was manually held close to the sensor. The flow was ensured by the pump sucking air through the nose prototype. Up to 12 Sniffing Sticks caps were tested and all of them provided good qualitative signals, from 1 to 3 radians. In Fig. 10, showing signals recorded by the sensor, Sniffin Stick number 6 from the blue series was evaluated. The chart shows 32 curves, each one being the signal of an MZI grafted with a peptide. When the cap is presented to the setup, the gas is driven to the sensor and each MZI records an immediate phase shift increase. Then, a stabilization phase is obtained in less than 15 seconds, before the cap is removed and the gas is correctly flushed from the sensor. This shows the dynamic of the sensor in order of seconds, which is potentially

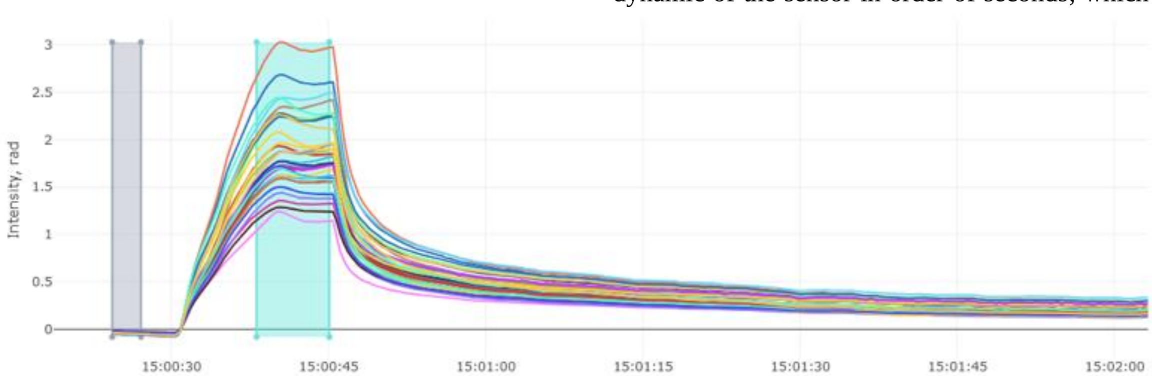

FIGURE 10: SIGNALS RECORDED BY THE SENSOR, FOR SNIFFIN STICK NUMBER 6 (BLUE SERIES)

compatible with daily use if packaged in a technology for anosmic people. This level of signal is sufficient to extract the signature of the smell in a very classical way for e-noses [17] and to do classification tasks where the output of the test is a label ("fruity" or "spicy", for example) rather than a collection of digital signals.

These experiments were successfully completed. Technically, it was possible to obtain a signal from the sensor when the smell was presented to the complex fluidic setup using a simulated sniff.

5. CONCLUSION

Despite the significant impact of impairments affecting the sense of smell, difficulties in developing effective solutions persist. The ROSE Project aims to address this gap by creating the Digital Olfaction Module (DOM), which wants to restore the sense of smell for individuals with olfactory limitations. The ROSE Project focuses on detecting and discriminating odors, utilizing technologies like e-noses to assess the odor profile of a sample. However, e-noses have been mostly investigated as desktop applications, with limited exploration as wearable devices. Testing odor detection sensors with real people is challenging due to variability and fluidic complexities. Thus, in this work, a test bench was designed to replicate real scenarios where odor sensors would be placed close to human nostrils. This involved acquiring and modelling the subject's nasal cavity to create a 3D-printed replica for testing sensor effectiveness and placement through the creation of a physical prototype integrated into an experimental setup for odorant detection tests. Preliminary feasibility tests were successfully run, and now a more extensive experimental campaign is needed.

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REFERENCES

[1] Lee, L., Luke, L., Boak, D., Philpott, C.: Impact of olfactory disorders on personal safety and well-being: a cross-sectional observational study. European Archives of Oto-Rhino-Laryngology. (2024).

[2] Barbosa, A.J.M., Oliveira, A.R., Roque, A.C.A.: Protein- and Peptide-Based Biosensors in Artificial Olfaction. 36, 1244–1258 (2018).

[3] Galantucci, L.M., Percoco, G., Angelelli, G., Lopez, C., Introna, F., Liuzzi, C., De Donno, A.: Reverse engineering techniques applied to a human skull, for CAD 3D reconstruction and physical replication by rapid prototyping. J Med Eng Technol. 30, 102–111 (2006).

[4] Redaelli, D.F., Gonizzi Barsanti, S., Fraschini, P., Biffi, E., Colombo, G.: Low-cost 3D devices and laser scanners comparison for the application in orthopedic centres. In: International Archives of the Photogrammetry, Remote Sensing and Spatial Information Sciences - ISPRS Archives. pp. 953–960. International Society for Photogrammetry and Remote Sensing (2018).

[5] Racasan, R., Popescu, D., Neamtu, C., Dragomir, M.: Integrating the concept of reverse engineering in medical applications. In: 2010 IEEE International Conference on Automation, Quality and Testing, Robotics, AQTR 2010 - Proceedings. pp. 352–356 (2010).

[6] Ritschl, L.M., Classen, C., Kilbertus, P., Eufinger, J., Storck, K., Fichter, A.M., Wolff, K.D., Grill, F.D.: Comparison of three-dimensional imaging of the nose using three different 3D-photography systems: an observational study. Head Face Med. 20, (2024).

[7] Largo, R.D., Wettstein, R., Fulco, I., Tremp, M., Schaefer, D.J., Gubisch, W., Haug, M.D.: Three-dimensional laser surface scanning in rhinosurgery. Facial Plastic Surgery. 29, 116–120 (2013).

[8] Zhang, S., Zhang, S., Fang, C., Lan, D., Dong, C.: Application of 3-Dimensional White-Light Scanning to Observe the Lip and Nose Morphology of Chinese Children. Journal of Craniofacial Surgery. 34, (2023).

[9] Luo, D., Li, T., Wang, H., Chen, Y.: Three-Dimensional Printing of Personalized Nasal Stents for Patients With Cleft Lip. Cleft Palate-Craniofacial Journal. 56, 521–524 (2019).

[10] Likus, W., Bajor, G., Gruszczyńska, K., Baron, J., Markowski, J.: Nasal region dimensions in children: A CT study and clinical implications. Biomed Res Int. 2014, (2014).

[11] Valtonen, O., Ormiskangas, J., Kivekäs, I., Rantanen, V., Dean, M., Poe, D., Järnstedt, J., Lekkala, J., Saarenrinne, P., Rautiainen, M.: Three-Dimensional Printing of the Nasal Cavities for Clinical Experiments. Sci Rep. 10, (2020).

[12] Tretiakow, D., Tesch, K., Meyer-Szary, J., Markiet, K., Skorek, A.: Three-dimensional modeling and automatic analysis of the human nasal cavity and paranasal sinuses using the computational fluid dynamics method. European Archives of Oto-Rhino-Laryngology. 278, 1443–1453 (2021).

[13] Djupesland, P.G., Messina, J.C., Mahmoud, R.A.: Role of nasal casts for in vitro evaluation of nasal drug delivery and quantitative evaluation of various nasal casts. In: Therapeutic Delivery. pp. 485–495. Newlands Press Ltd (2020).

[14] Bertolini, M., Rossoni, M., Colombo, G.: Operative workflow from ct to 3d printing of the heart: Opportunities and challenges. Bioengineering. 8, (2021).

[15] Osti, F., Santi, G.M., Neri, M., Liverani, A., Frizziero, L., Stilli, S., Maredi, E., Zarantonello, P., Gallone, G., Stallone, S., Trisolino, G.: CT conversion workflow for intraoperative usage of bony models: From DICOM data to 3D printed models. Applied Sciences (Switzerland). 9, (2019).

[16] Laplatine, L., Fournier, M., Gaignebet, N., Hou, Y., Mathey, R., Herrier, C., Liu, J., Descloux, D., Gautheron, B., Livache, T.: Silicon photonic olfactory sensor based on an array of 64 biofunctionalized Mach-Zehnder interferometers. Opt Express. 30, 33955 (2022).
[17] Brenet, S., John-Herpin, A., Gallat, F.X., Musnier, B., Buhot, A., Herrier, C., Rousselle, T., Livache, T., Hou, Y.: Highly-Selective Optoelectronic Nose Based on Surface Plasmon Resonance Imaging for Sensing Volatile Organic Compounds. Anal Chem. 90, 9879–9887 (2018).