Skull base reconstruction after endoscopic endonasal surgery: new strategies for raising the dam

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***Abstract* — In the last decades a variety of innovative craniofacial approaches has been adopted to entire skull base. The endonasal endoscopic route has emerged as a suitable methodology for several skull base lesions. An effective watertight closure is essential to isolate the intracranial cavity in order to restore the natural intra and extradural compartment division, necessary to prevent postoperative cerebrospinal fluid (CSF) leakage and complications such as meningitis, brain herniation, and tension pneumocephalus. The reconstruction can be performed using different materials, both autologous (autologous grafts) and non-autologous, individually or combined in a multilayer fashion. The harvesting a nasoseptal flap is one of the most effective techniques: it reinforces the skull base closure granting isolation of the surgical field. The current study was focused on the development of new advanced devices and techniques, aiding in reducing postoperative CSF leak, which is one of the most feared complication of this surgical procedure. Additive manufacturing allows to design devices with tailored structural and functional features, in order to satisfy all the requirements. On the other hand, the development of injectable semi-IPNs and composites clearly benefits from specific mechanical/rheological and injectability studies. Accordingly, starting from some basic concepts, innovative principles and strategies were also proposed towards the design of additively manufactured and injectable devices.**

Keywords: endoscopic endonasal surgery, skull base reconstruction, CSF leakage, reverse engineering, additive manufacturing, design of injectable systems.

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I. INTRODUCTION

The skull base is one of the most fascinating and complex areas of the human body, from both an anatomical and surgical perspective. It is located in a peculiar position, between the brain and the extracranial compartment, and composed of many different anatomical structures.

A wide variety of lesions, either neoplastic or not, may primarily arise from this area or subsequently involve it. Their surgical management can be extremely difficult, above all for deep seated lesions, despite a variety of innovative craniofacial approaches that have been adopted to access the entire skull base in the last decades [1-9].

Furthermore, these access routes are often characterized by tissue disruption and neurovascular manipulation, causing an increase of perioperative morbidity and/or mortality rates.

The continuous technological innovations and surgical advances, together with the progress in diagnostic imaging techniques and the intraoperative neuronavigation systems, have led to a progressive reduction of the invasiveness of skull base approaches.

In particular, they allowed the development of a trans-sphenoidal technique for the treatment of lesions previously amenable only to a transcranial route. In fact, during the last decades, the endonasal endoscopic route has emerged as a viable corridor to access first the sellar region and then the surrounding areas, representing today a suitable route of approach for several skull base lesions [10-12].

These technological advancements and surgical refinements have been paired with an increasing comprehension of the region's anatomy leading to this revolution of skull base surgery [13].

In more detail, the main advantage of skull base surgery performed through the nose, with the aid of an endoscope, is the possibility of achieving a direct visualization of neurovascular structures of different areas of the skull base while minimizing brain displacement and manipulation.

The endoscope also allows for a wider and multiangled close-up view of the surgical field. Consequently, patients treated with this approach may benefit of reduced

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postoperative morbidity, early discharge and faster return to work [14].

On the other hand, the main issue of this approach resides in the reconstruction, due to a higher risk of postoperative cerebrospinal fluid (CSF) leak when compared to the conventional transcranial technique [15].

Skull base lesion removal via the endonasal corridor requires a wider osteo-dural opening and, above all, extensive opening of arachnoid cisterns and/or sometimes third ventricle. As a result, a large communication between a sterile intradural compartment and a septic cavity (i.e. the sinonasal tract) is created.

An effective watertight closure is mandatory to isolate the intracranial cavity in order to restore the natural intra and extradural compartment division, essential to prevent postoperative CSF leakage. Failure to obtain adequate reconstruction may lead to life-threatening complications, such as meningitis, brain herniation, and tension pneumocephalus tool [16].

An optimal skull base reconstruction after extended endoscopic endonasal surgery should meet some crucial points, such as obliteration of dead spaces, isolation of the intradural compartment from the sinonasal tract, water and airtight closure, promotion of the healing process, preservation of function and cosmesis, management of risk factors of increased intracranial pressure (i.e. obesity) [15, 17,18]. Accordingly, the reconstruction can be performed using different materials, both autologous and non-autologous, individually or combined in a multilayer fashion.

The recent trend is pushing toward the adoption of autologous materials [19-21]. Autologous grafts interact with the surrounding structures of the osteo-dural skull base defect, promoting the migration of fibroblasts and favoring complete recovery. Each component plays its peculiar role, with the bone and cartilage offering support and the mucosa providing the matrix for the new vascularization of the tissues.

The harvesting a nasoseptal flap is one of the most effective techniques: it bolsters the skull base closure granting isolation of the surgical field and has shown a strong impact in reducing CSF leak rate after endoscopic skull base surgery [22]. However, it may cause nasal morbidity, so it should be harvested only when performing reconstruction of wide skull base defects [19, 23].

The availability of reliable reconstructive materials goes hand-to-hand with the development of new closure techniques, aiding in reducing one of the most feared complication of this kind of surgery: postoperative CSF leak [22,24,25].

In this scenario, further efforts are required in the attempt to develop new strategies and devices, capable of lowering CSF leak rates after endoscopic skull base surgery, thus reducing post-operative patient discomfort and morbidity.

II. STRATEGIES TOWARDS AN ADVANCED DESIGN OF ADDITIVELY MANUFACTURED AND INJECTABLE DEVICES

Over the past years, many efforts have been devoted to the use of natural and synthetic polymers for different kinds of biomedical applications.

In particular, the attention has been focused on the design of materials and devices with improved mechanical and functional properties, possessing appropriate strength, flexibility and structural integrity at the same time [26-28].

3D devices with enhanced and tailored properties may be designed and fabricated by processing polymer-based materials.

In this context, advanced structures may be developed in the form of solid or injectable devices, according to the specific application and the selected surgical procedure.

With regard to skull base reconstruction after endoscopic endonasal surgery, challenging strategies would involve advances in the design of injectable semi-interpenetrating polymer networks (semi-IPNs) and composites, CAD-FE modelling and 3D additively manufactured structures with tailored architectural features and mechanical properties [26-38].

The approach related to the development of injectable semi-IPNs and composites with tunable properties clearly benefits from specific mechanical/rheological and injectability analyses.

Injectable systems were also fabricated combining conventional methods and additive manufacturing eventually combined with electrospray-based technique.

In particular, semi-IPNs were obtained by promoting the polymer network formation using both synthetic and natural (i.e., collagen) polymers, which were also properly modified.

The system components were selected trying to promote a clinical translation of the injectable tools as dura mater substitutes and sealant systems to reduce the risk of CSF leakage.

The viscoelastic properties were assessed at 37°C by a rheometer (Bohlin Gemini; Malvern Instruments, Malvern, UK) equipped with parallel-plate geometry.

To determine the linear viscoelastic region, strain sweep tests were performed at a fixed oscillation frequency.

Small amplitude oscillatory shear tests were carried with a frequency ranging from 0.01 Hz to 2 Hz.

The storage modulus (G') and the loss modulus (G") were evaluated as follows:

$$G' = \frac{\tau_0}{\gamma_0} \cos \delta$$

$$G'' = \frac{\tau_0}{\gamma_0}\, sen\, \delta$$

where δ is the phase shift between the input and output signals; $\tau 0$ and $\gamma 0$ are the stress and strain amplitudes, respectively.

The developed semi-IPNs showed G' values which were always higher than G" in the frequency range investigated (Figure 1).

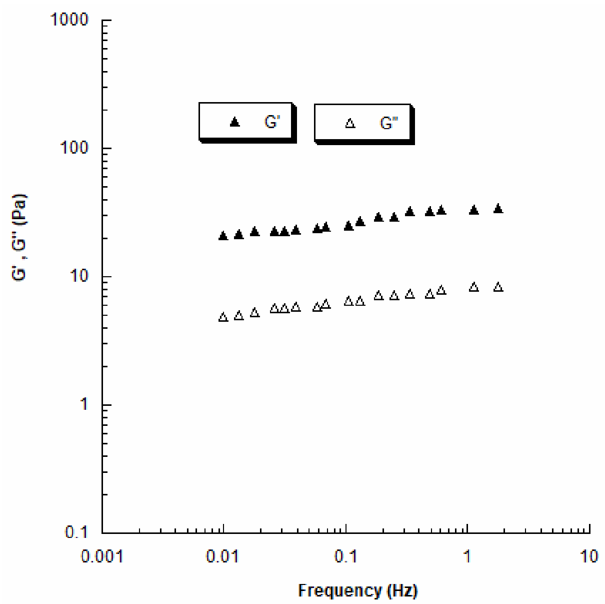

Figure 1: Typical results from small amplitude oscillatory tests on the developed semi-IPNs. Storage modulus (G') and loss modulus (G'') as function of frequency.

In addition, the inclusion of micro/nanoparticles also provided interesting results in improving both viscoelastic moduli, until a threshold limit value was reached for the particle concentration.

Viscosity as a function of shear rate was assessed at 37°C by steady shear measurements, in a wide range of shear rate (0.01 - 10 s-1) (Figure 2).

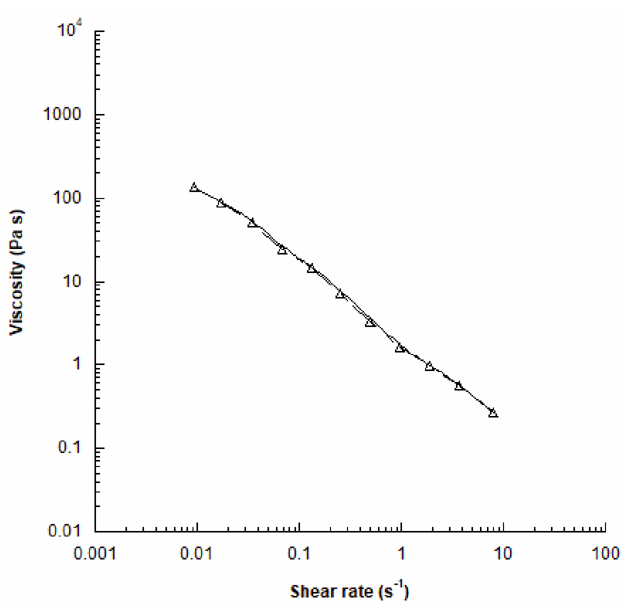

Figure 2: Typical results from steady shear tests on the developed semi-IPNs. Viscosity as function of shear rate.

The viscosity decreased as the shear rate increased (shear thinning behavior), also suggesting the possibility to inject the materials.

The effect of the injection through different clinical needles on the viscoelastic properties plays an important role in the design of functional devices, and the injectability analysis allows to simulate clinical practice.

Results from injectability tests on several semi-IPNs showed load-displacement curves characterized by a linear region at low displacements, until the load reached a maximum value. Then, it sharply dropped to a plateau value while increasing the displacement. At the end of the plateau-like region the material was fully injected. According to the different material compositions and clinical needles, the measured values of maximum and plateau loads were in the range of 6.3 – 3.5 N and 2.2 – 0.8 N, respectively.

On the other hand, the introduction of additive manufacturing has led to the possibility to develop multifunctional, complex and customized devices.

Additively manufactured devices with different architectures can be fabricated by Fused Deposition Modeling (FDM)/3D fiber deposition technique.

3D virtual models of skull base defects were generated through image capture and analysis techniques, starting from medical scans (i.e., magnetic resonance imaging – MRI, computed tomography - CT).

Successively, 3D customized devices were manufactured by FDM/3D fiber deposition.

Specifically, 3D reconstruction of skull base defects was performed starting from a CT (Figure 3).

Then, a 3D virtual model was created (Figure 4).

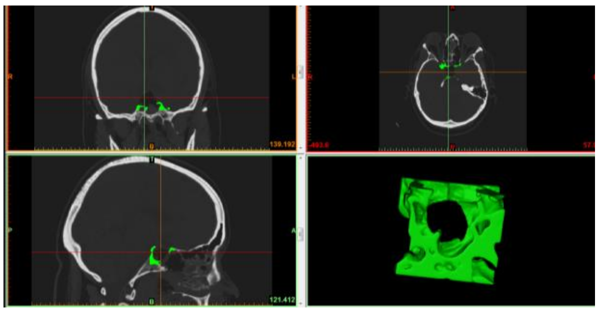

Figure 3: Results from image capture and analysis. 3D reconstruction of skull base defects.

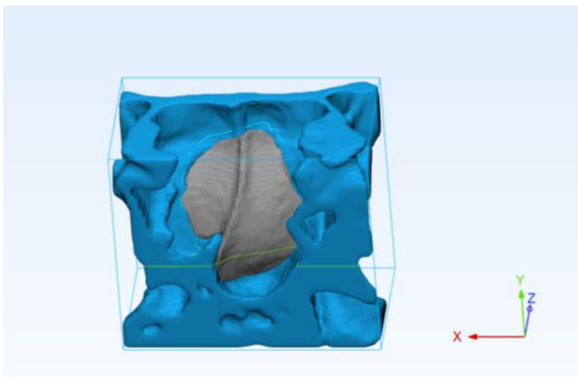

Figure 4: An example of 3D virtual model for a skull base defect.

If compared to conventional fabrication techniques, additive manufacturing allows for a higher control of the structural features and, hence, of the functional properties of the devices, in order to satisfy all the requirements.

For this reason, additive manufacturing techniques (i.e., FDM/3D fiber deposition) was considered to design 3D customized devices with complex geometry.

Polymeric or micro/nanocomposite pellets were placed in a syringe and then heated using the cartridge unit placed on the mobile arm of a 3D plotter.

The material was injected/extruded through a nozzle and properly deposited. Thus, the devices were built layer-by-layer [26-28].

Images of customized devices developed for skull base defects were reported in Figures 5 and 6.

Figure 5: A customized system obtained at different steps of the design/fabrication process.

Figure 6: A customized system with specific geometry and morphology according to the skull base defect.

The customized devices were properly designed to provide high flexibility and relatively high strength, according to the considered application.

However, in the case of structures and geometries normally required for complex defects, 3D additively manufactured hybrid devices, based on the combination/integration of "solid" systems and injectable materials, were also fabricated.

III. CONCLUSIONS

The reported design strategies and experimental results provided an insight into the development of advanced devices for skull base defects by integrating image capture and analysis techniques, CAD-based approach, additive manufacturing and materials science.

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