TITANIUM CRANIOFACIAL PROSTHESES: A DESIGN PROCEDURE FOR IDENTIFYING THE OPTIMAL FIXATION SYSTEM AND ITS APPLICATION TO A CASE STUDY

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ABSTRACT
Cranioplasty is a surgery in which a prosthesis must be anchored on skull bone to repair a defect. One of the most used materials is the titanium. However, titanium prostheses could be made using the incremental sheet forming (ISF). Since titanium and bone are characterized by different Young modules, a detailed design of anchoring system is required to avoid cranial rupture. Aim of this study was to present a design procedure in order to identify the optimal anchoring system in case of craniofacial prostheses made with ISF. In detail, an optimization process and a predictive model for bone stress were used, choosing the numerical outputs of different FEM analyses as input data. The results indicate that our predictive and optimization models are accurate and, so, that this procedure could be very helpful for the prosthesis design, as demonstrated by the application of the procedure to a real case study.

Keywords: titanium prosthesis, anchoring system, incremental sheet forming, design procedure

1. INTRODUCTION

Cranioplasty is a neuro-reconstructive surgery that repairs structural or morphological defects (Solaro et al. 2008) -created by congenital, developed or accidental causes-, using a prosthesis, which must be anchored to skull bone both for functional and aesthetic aspects (Toso et al. 2015).

Even if different bone substitutive materials are available (Neovius and Engstrand 2010), the most used ones are Titanium and its alloys because they are biocompatible, experimental and clinically tested (Calderoni et al. 2014), with excellent mechanical properties (Gepreel et al. 2013), and favor the osseointegration with the bone, that is to say the direct contact between implant and bone (Albrektsson et al. 1981).

Since the craniofacial implants have also an aesthetic function (Drstvensek et al. 2008), titanium customized prosthesis has been recently used in order to improve the aesthetics and obtain a normal appearance (Cho et al. 2015; Castelan et al. 2014).

Regarding the manufacturing process, craniofacial prostheses could be made using the incremental sheet forming (ISF), an innovative technology that presents significant vantages (Ambrogio et al. 2015; Castelan et al. 2014; Lu et al. 2014; Lu et al. 2015), such as the possibility to create both patient-specific and generic prostheses and low set-up cost. With this technique, the prosthesis has a greater area and, so, a larger perimeter in respect to the defect (Lu et al. 2015), but no information regarding the anchoring system is available, in terms of overlap length and diameter of screw shank.

Moreover, titanium and bone have different elastic modules (reported in Vosough et al. 2013 and Raul et al. 2006 respectively). So, the anchorage system must be correctly designed in order to avoid the skull bone rupture.

The aim of this study was to present a procedure for correctly designing the anchorage system in case of titanium prosthesis made using ISF.

2. DESIGN PROCEDURE

In order to identify the best anchoring configuration, in term of screw dimensions and overlap length between prosthesis and skull bone and for a specific damage area, considering the worst accidental load, an optimization process was carried out, using the response surface methodology - RSM - (Asiltürk et al. 2016).

First, a predictive model of the skull bone stress was identified considering five factors (damage area, screw shank, overlap length, load and its tilt angle) and just one response (skull bone stress). Moreover, the degree of this model was established comparing different polynomials by means of the analysis of variance (ANOVA) and choosing the best one through an optimization process.

Since the skull bone near the prosthesis and the anchorage system must resist to accidental loads, the maximum stress on bone due to loaded prosthesis was evaluated by means of FEM structural analyses. So the numerical results were used as input for the optimization process.

2.1. Design of experiment

As previously reported, the damage area, the screw shank, the overlap length, the load and its tilt angle are the factors. So, for each of them, the values range was defined, as reported in Table 1.

The number of simulation necessary to carry out this design could be calculated as

$$N = L^v \tag{1}$$

where L represents the levels number of factors and v represents the number of factors. So, since four factors have three levels (3^4) and one factor has two levels (2^1), the number of simulations is equal to 162.

Table 1: Design factors information

Factor	Name	Unit	Level	Values
A	Screw Shank	mm	3	1.5 - 2.0 - 2.5
B	Overlap Length	mm	3	7 - 10 - 13
C	Tilt Angle	Degree	3	0 - 45° - 90°
D	Load	N	3	100 - 300 - 500
E	Damage Area	mm^2	2	2,100 – 2,600

2.2. Structural FEM modeling

In order to create the dataset for the predictive modeling and for the optimization process, different structural FEM analyses were carried out.

2.2.1. Geometrical model

A 3D solid model of a healthy skull was reconstructed starting from CT images by means of the segmentation process, using the open source software Invesalius (de Moraes et al. 2011), and the reverse engineering (Maravelakis et al. 2008).

A circular defect was created in the fronto-parietal bone, considering the two values of the damage area (Figure 1A). According with these holes, different prostheses were modeled with each overlap length established in the design of experiment and with a thickness of 1.5 mm, as our titanium prototype made with ISF (Ambrogio et al. 2015).

Moreover, three micro-screws were inserted considering the same angle of 120°, to fix the prosthesis to the bone, placing the first one in correspondence of the sagittal plane (Figure 1B).

In order to reduce the computational cost and because of the axial-symmetry of the virtual model, a simplied model of 20° (Figure 1C) was used in the FEA analyses.

2.2.2. Material properties

Skull bone was approximated as a cortical one (Raul et al. 2006) and the Ti6Al4V (Vosough et al. 2013) was used for prosthesis and screw. Both materials were assumed to be homogeneous and isotropic (Raul et al. 2006), defined by linear elastic laws.

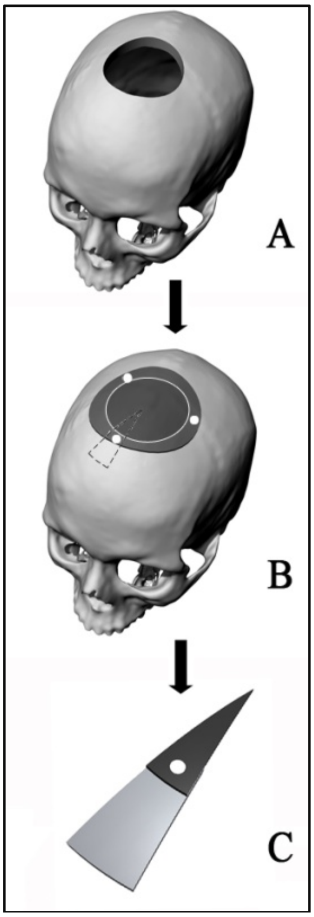

Figure 1: Geometric model of a skull with a circular fronto-parietal defect (A), of a skull repaired with prosthesis and three micro-screws (B) and of a simplified 20° model (C).

2.2.3. Boundary conditions

The bone was fixed in the bottom surface in order to model the remaining bone skull not considered in the geometrical model.

Moreover, a distributed compressive load was applied to the top surface of prosthesis to simulate accidental load. In details, the load has three intensities and three tilt angles, as specified in Table 1.

Furthermore, titanium is commonly used in cranioplasty because it favors the osseointegration, creating a perfect adherence between titanium components and bone, and, consequently, a permanent anchorage (Albrektsson et al. 1981). For this reason, a perfect osseointegration was implemented as boundary condition in this FEM modeling between bone and implant and bone and screw. Moreover, as the osseointegration was modeled, a rigid connection was assumed between prosthesis and screw.

Finally, a symmetry boundary condition was applied in the lateral faces of skull and prosthesis due to their axial-symmetry.

All boundary conditions are reported in Figure 2, in which each color represents a boundary condition: green represents symmetry, red represents fixation and black represents load. Also the symmetry axis is reported.

2.2.4. Simulation details

COMSOL 5.0 (COMSOL Inc, Stockholm, Sweden), a finite-element-based commercial software package, was used to perform all numerical simulations and for the post process. Furthermore, in all cases, a fine tetrahedral mesh was used, for a total of about 75,000 elements.
As the skull bone near the prosthesis and the anchorage system must resist to accidental loads, the maximum stress on bone due to loaded prosthesis was evaluated by means of the Von Mises criteria (Baggi et al. 2008).

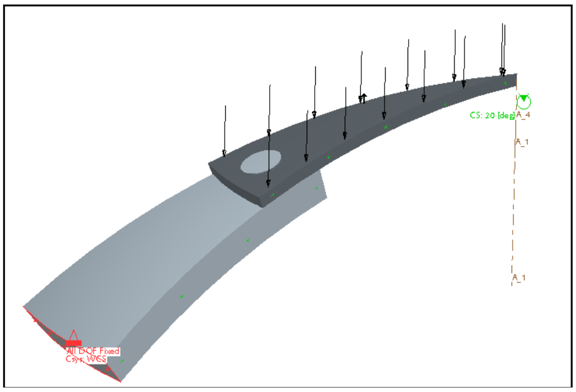

Figure 2: Boundary conditions.

2.3. Statistical analysis, predictive modeling and optimization process

As reported before, five factors were considered in the predictive modeling and their correlation with the bone stress (the only response) was statistically evaluated by means of the Design Expert Software (Stat-Ease, Inc., Minneapolis, USA - trial version).
Moreover, the optimal degree of the model was identified comparing 7 polynomial orders (linear, 2Factorial Interaction, quadratic, cubic, quartic, fifth and sixth) by means of ANOVA analysis. The best one was chosen considering a right compromise between complexity and reliability of the prediction, which can be expressed as number of polynomial terms and predicted residual sum of squares - PRESS - (Ho et al. 2002), respectively. Furthermore, a p_{value} threshold of 0.05 was adopted to select the statistically relevant parameters interactions.
The objective of the optimization process was to prevent the achievement of ultimate compression stress of skull bone (Raul et al. 2006) and, so, the rupture in case of accidental loads, in order to establish the optimal anchoring system for specific skull damage, in term of screw geometry and prosthesis overlap length, considering a worst unforeseen load.

3. RESULT AND DISCUSSION

As reported previously, the numerical results of skull bone stress obtained with the FEM structural simulations were used to create the dataset for the optimization process. Considering our 162 objects, the skull bone varies in the range [3, 300] MPa, with a mean value of 75.89 ± 73.00 MPa.

3.1. Statistical analysis and predictive modeling

The correlation value is -0.663 for tilt angle and 0.568 for load. So, the maximum stress occurs with the highest load (500 N) and the lowest tilt angle (0°). On the other hand, the correlation rate for shank and for overlap length is -0.008 and -0.181, respectively, indicating that skull stress decreases if screw shank and overlap length increase and that the last one is the most significant factor (0.181 compared with 0.008). Finally, the correlation rate for damage area is -0.078, so the stress increases with the decrease of damage area.
To establish the optimal degree of the polynomial for the predictive model, the PRESS value and the number of terms for all polynomials were calculated with the ANOVA and then were normalized in the range [0, 1]. The two waveforms are illustrated in Figure 3. The optimal result is obtained between the quadratic and cubic equations. So, the third degree model was chosen as the referenced one and it was reduced considering only the terms with p_{value}<0.05 (Lee at al. 2006).
Moreover, all R^2 variables are very high and almost equal to 1 (Table 2).
Using the reduced cubic polynomial, the stress in the skull bone could be predicted as:

$$\sigma_{bone} = c_1 \cdot A^2B + c_2 \cdot A^2C + c_3 \cdot A^2D + \cdots + c_{n-4} \cdot A + c_{n-3} \cdot B + c_{n-2} \cdot C + c_{n-1} \cdot D + c_n \cdot E \qquad (2)$$

in which c_1- c_n are the coefficients.
Furthermore, the normal plot of the residuals was employed to verify the normal distribution of data, that was confirmed (Figure 4).
To investigate the reliability of the prediction, the predicted versus actual values diagnostic plot was analyzed (Figure 5). All data were properly predicted, also around the ultimate compressive stress value (145 MPa).

3.2. Optimization process

Since statistical results have indicated that the worst compression tilt angle was 0° and that loads greater than 350 N always exceeded compression threshold of 145 MPa, the optimization process was carried out considering a maximum load of 350 N with 0° and a limit of 140 MPa. Moreover, the statistical analysis has highlighted that bone stress is negatively correlated both with screw shank and prosthesis overlap length. So, the optimization model was implemented minimizing the shank and the overlap length in order to identify the lower limit of these variables that generates the highest stress.
The results of this modeling, considering seven different damage areas, are illustrated in Table 3. Obviously, since stress value is less affected by shank geometry respect to the value of overlap length, all shank values of our initial range (1.5- 2.5 mm) can be used, whereas only high values of overlap length ensure stress less than 140 MPa.

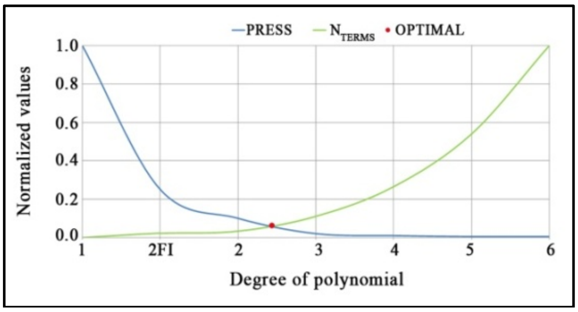

Figure 3: Identification of the best polynomial degree considering the normalized number of polynomial terms (N_{TERMS}) and the normalized PRESS value.

Table 2: ANOVA results of the reduced cubic model

Factor	Value	Factor	Value
Std. Dev	3.74	R-Squared	0.9979
Mean	75.89	Adj R-Squared	0.9974
C:V: %	4.92	Pred R-Squared	0.9963
PRESS	3,149.57	Adeq Precision	174.338

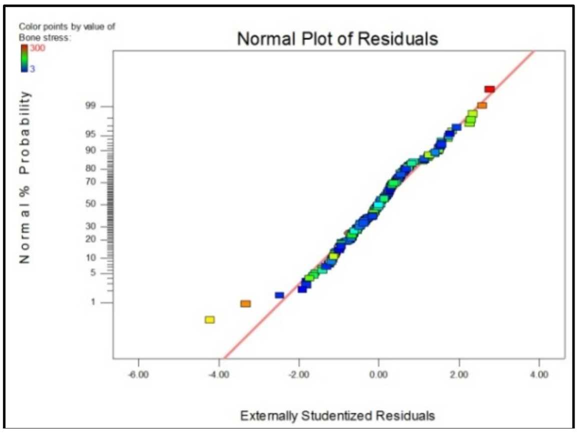

Figure 4: Normal plot of residuals for the reduced cubic model

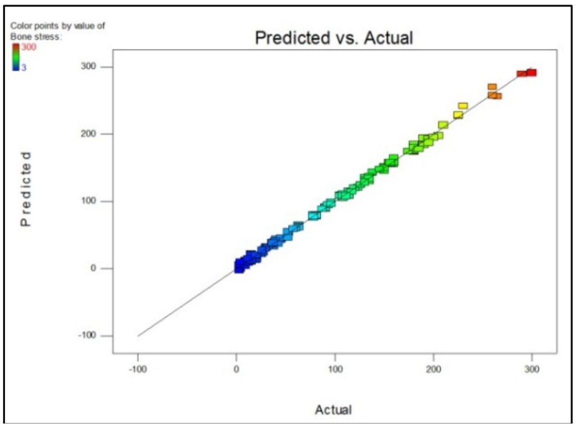

Figure 5: Predicted vs actual values for the reduced cubic model

3.3. Validation

To validate the design procedure three FEM analyses were carried out modeling different damage areas and anchorage systems (Table 4). Furthermore, an accidental load of 350 N with 0° was applied. As reported in Table 4, the error between the predicted stress and FEM skull bone stress is very low. So, our predicted model has a very high accuracy, generating a valid optimization process and a design procedure.

Moreover, these results indicated that bone stress overtakes the limit if low values of overlap length are considered. This means that our optimized model provides the best ranges, thanks to which the optimal anchoring system could be realized.

Table 3: Optimal screw shank and prosthesis overlap length ranges for specific damage area

Damage area [mm^2]	Range of Screw Shank [mm]	Range of Prosthesis Overlap Length [mm]
2,100	1.5 - 2.5	12 - 13
2,200	1.5 - 2.5	12 - 13
2,300	1.5 - 2.5	11 - 13
2,400	1.5 - 2.5	11 - 13
2,500	1.5 - 2.5	10 - 13
2,600	1.5 - 2.5	10 - 13
2,700	1.5 - 2.5	10 - 13

Table 4: Validation of the design procedure

	Model 1	Model 2	Model 3
Damage area [mm^2]	2,100	2,400	2,700
Screw Shank [mm]	2.5	2	1.5
Overlap Length [mm]	10	10	9
Predicted Skull Bone Stress [MPa]	148	148	147
FEM Skull Bone Stress [MPa]	147	141	141
Error [%]	0.68	3.55	4.26
Mean Error		2.83	

4. CASE STUDY

In order to test the presented procedure, it was applied to a real case study. The five steps illustrated in Figure 6 were followed in order to obtain the prosthesis.

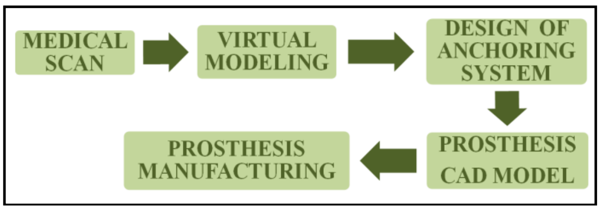

Figure 6: Realization steps of the case study

4.1. Medical scan

A series of in-vivo contrast-enhanced axial CT-scan 2D-images of a 65-year-old man, who presented a fronto-parietal defect, was acquired for clinical reasons. In details, 512 x 512 slices were obtained with a pixel spacing of 0.468.

4.2. Virtual modeling
Starting from the CT slices, a 3D virtual model of the skull and of the defect was reconstructed by means of the segmentation process that was performed by Invesalius. Since it produces an STL file, the model was subjected to the reverse engineering process in order to obtain a solid model (IGES or STL formats).

4.3. Design of anchoring system
As previously reported, the prostheses made with the ISF can be anchored to the skull bone creating an overlap between the prosthesis and the skull near the defect. So, to make the prosthesis with a greater area and, so, a larger perimeter in respect to the defect, the design procedure presented in the paragraph 2 was used, considering that the case study defect had an area of 2,680 mm^2.
The final anchoring system consisted of a prosthesis with an overlap length of 10 mm and three micro-screws with a shank of 2.0 mm.

4.4. Prosthesis CAD model
In order to manufacture the optimized prosthesis, the CAD model was modified to create the optimized overlap length (Figure 7).

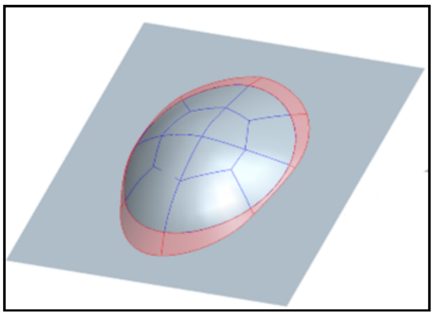
Figure 7: Craniofacial CAD prosthesis

4.5. Prosthesis manufacturing
Since the ISF is a CAD/CAM process, its code was created to describe the ISF operations on the CNC machine. This program was generated by means of the manufacturing module of Pro-Engieering.
The first step to manufacture the prosthesis was the right shape positioning on the sheet plane, done to respect the technological constraints. Moreover, a backing plate with a circular hole was positioned under the sheet in order to support it during the manufacturing. After that, the sheet was positioned on the CNC table and deformed using a hemispheric punch (diameter of 15 mm) with a continuous movement (constant tool depth step of 0.1 mm and a tool feed rate of about 2000 mm/min), following the trajectory generated by a CAD/CAM program (Figure 8).
The obtained prosthesis is reported in Figure 9.

5. CONCLUSION
During the cranioplasty, a prosthesis is anchored to the skull bone. So a detailed design is required. This study has presented a design procedure to identify the best fixation system for different damage areas.
In details, the method consists of a preliminary statistical analysis, the creation of a predictive model using the ANOVA analysis and finally the development of an optimization model based on the RSM.
The validation results have suggested that this methodology has a good accuracy, both in the prediction and in the optimization. Finally, the application of the methodology to a real case study has demonstrated that its use is very helpful in the manufacture of craniofacial prosthesis.

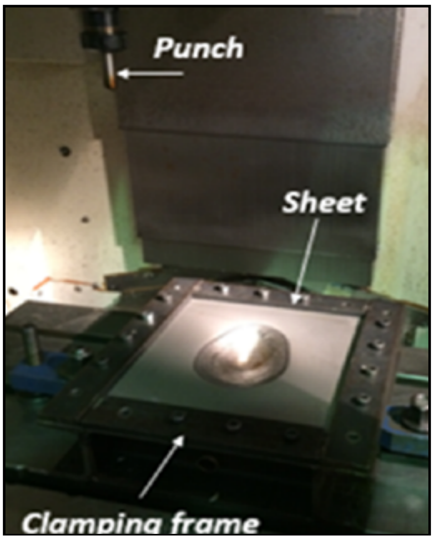

Figure 8: ISF machine

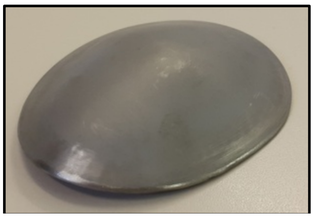
Figure 9: Craniofacial prosthesis made with ISF, applying the design procedure for the anchoring system.

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