Topological optimization for designing patient-specific large craniofacial segmental bone replacements

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Restoring normal function and appearance after massive facial injuries with bone loss is an important unsolved problem in surgery. An important limitation of the current methods is heuristic ad hoc design of bone replacements by the operating surgeon at the time of surgery. This problem might be addressed by incorporating a computational method known as topological optimization into routine surgical planning. We tested the feasibility of using a multiresolution three-dimensional topological optimization to design replacements for massive midface injuries with bone loss. The final solution to meet functional requirements may be shaped differently than the natural human bone but be optimized for functional needs sufficient to support full restoration using a combination of soft tissue repair and synthetic prosthetics. Topological optimization for designing facial bone tissue replacements might improve current clinical methods and provide essential enabling technology to translate generic bone tissue engineering methods into specific solutions for individual patients.

bone tissue engineering | craniofacial reconstruction | midface reconstruction | segmental bone defects | massive facial injury

Restoring normal function and appearance after massive facial injuries is an important unsolved problem in surgery. Inadequate reconstructive techniques result in long-term disfigurement with devastating physical, psychological, social, and economic consequences for the suffering individual. The importance of the problem and inadequacy of current treatments are reflected by the establishment in 2008 of the Armed Forces Institute of Regenerative Medicine, a cooperative effort between academic biomedical research institutions and the US Department of Defense that has craniofacial reconstruction as a major area of focus (1).

The most severe facial injuries destroy portions of the facial skeleton. Reconstruction requires facial bone replacement. This is an extremely challenging problem. Facial bones are small, delicate, and located near areas highly contaminated with bacteria. Proper function depends not only on load bearing but also on permanently maintaining a specific three-dimensional shape. They support soft tissue structures and specialized organs essential for many basic life functions—breathing, speaking, chewing, and swallowing. They form the basis for the unique physical appearance of every human being.

The most reliable current techniques for replacing facial bones involve surgical manipulation of autologous tissue (i.e., tissue obtained elsewhere on the same patient) (Fig. 1 A–C). Synthetic bone substitutes exist, but for major facial bone replacement they are not reliable because of a tendency to mechanical failure, soft tissue erosion, and infection. The surgeon must obtain mature formed bone from an uninjured location such as the cranial vault (2), scapula (3), radius (4), iliac crest (5), or fibula (6) and transfer it to the face. The amount of bone removed from the donor site must be limited to prevent skeletal instability and other complications (7). Fig. 1D represents a clinical scenario with gun shot injury, and Fig. 1 E and F show standard radical and partial maxillectomy surgical defects. The surgeon reshapes the bone to simulate the missing skeleton and fixes it into position using metal plates and screws. For massive defects, the bone must be transferred with a blood supply that is independent from the surrounding damaged tissues. The bone is isolated based on a single artery and vein that are surgically reattached to other uninjured blood vessels in the nearby face or neck. These vessels are typically 2–3 mm in diameter and require microscopic vascular surgery to restore blood flow. The surgery is highly technical and takes many hours to complete. The results are never perfect because there are no analogies to facial bones elsewhere in the human skeleton. Tissue for reconstruction must be obtained from bones that are quite dissimilar from those of the face. The surgeon must fashion tissue to simulate the facial bones using heuristic design and manual reshaping. The final outcome depends upon the severity of the original injury and the skills of the individual surgeon. Patient may be improved but still suffer from significant deformity. The ideal solution for facial bone replacement would be custom tissue fabrication. This may be possible using tissue engineering methods to guide bone formation into specific shapes. This is demonstrated by animal studies and limited clinical experience (8, 9).

An essential enabling technology for clinical application of bone tissue engineering is computer assisted design to translate generic bone tissue fabrication methods into specific solutions for individual patients. The process would involve imaging of the bone defects, analysis of functional consequences, and determination of patient-specific bone replacement needs. The final solution to meet functional requirements might be shaped differently than the natural human bone, but be optimized for functional needs sufficient to support full restoration using a combination of soft tissue repair and synthetic prosthetics (e.g., ocular prosthesis, dental prosthesis, etc.). This type of problem is well-suited for the computational approach known as topological optimization.

Topological optimization is a powerful computational technique that provides optimal solutions for a given design domain based on a set of considerations such as expected loads and boundary/initial conditions. Although mechanical loading is emphasized in this work, other types of problems or constraints can also be considered (10). Thus topology optimization is an attractive method for design of topology, shape, and the material for continuum and discrete structural systems (11). It is applicable to a broad range of problems, including stress constraints, compliant mechanisms, material design, micro-electro mechanical systems design, and more (10, 12). In fact, microstructural topological optimization has been used to generate periodic microstructures in scaffolds to achieve specific material properties at desired fixed porosity (13).
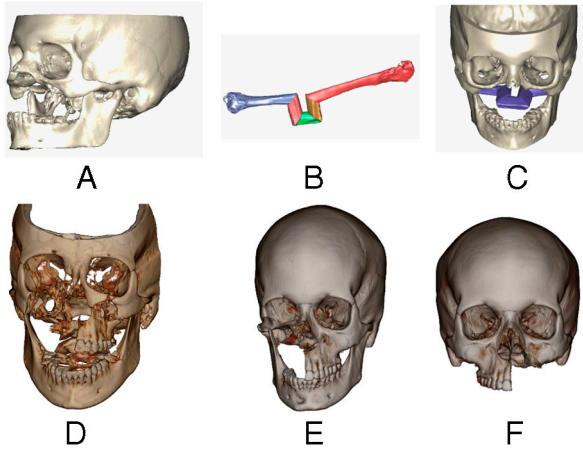
Fig. 1. (*A*) Craniofacial skeleton of the patient with severe midface deformity. (*B*) Ad hoc shaping of a bone graft (fibula) to create the bone replacement. (*C*) Insertion of the bone graft on the defect location. (*D*) A patient's skull with severe craniofacial deformity due to gun shot injury. (*E*) Craniofacial defect with total maxillectomy. (*F*) Craniofacial defect with partial maxillectomy.

The primary aim of this paper is to demonstrate the potential utility of topological optimization to design bone replacements to meet specific criteria within the constraints of a given design space as defined by a massive facial injury with bone loss. We focus on developing feasible bone replacement forms for large segmental defects that not only can meet requirements for load-bearing, but also position tissue elements in the proper locations in space to support soft tissues and prosthetic appliances. These forms would ultimately be intended to serve as design templates for custom bone segments fabricated using principles of tissue engineering.

Topological Optimization

Topology optimization is a structural optimization method that combines a numerical solution method (e.g., the finite element method) with an optimization algorithm to find the optimal material distribution inside a given domain. It determines which portions will have material and which will have voids. This technique has the potential to guide and clarify in which places skeletal materials are necessary to withstand the expected loads (e.g., for mastication) and support soft tissue structures, specialized organs (e.g., orbital contents), and prosthetic devices. The purpose is to find the most optimized macrostructure to replace the missing bone that contains the minimum amount of tissue positioned appropriately in three-dimensional space and supported upon remaining uninjured portions of the facial skeleton. The quantitative analysis of such cases may require consideration of (*i*) mechanical variables such as structural integrity during load bearing, (*ii*) biological considerations such as vascularization for healing, and (*iii*) functional considerations such as creating passageways for respiratory airflow and transit of food and liquid from the mouth to the pharynx. Each of these must be accomplished while preserving normal human appearance. Such variables can be included in a multiscale topology optimization framework, which seeks the optimal layout of the reconstructed craniofacial region.

Basic Framework. In designing the topology of a structure, which points of space should be material and which points should be void (i.e., no material) are determined. This is the basic setup of a topology optimization problem. The problem is specified mathematically hereafter. In continuum structures, topology optimization aims to optimize the material densities that are considered design variables in a specific domain. In this study, minimum compliance is considered to maximize the stiffness of the structure while satisfying a volume constraint. The basic problem statement is expressed as follows

$$\min_{\boldsymbol{\rho}} \ C(\boldsymbol{\rho},\mathbf{u}) = \mathbf{f}^T\mathbf{u} \qquad s.t.\text{: } \mathbf{K}(\boldsymbol{\rho})\mathbf{u} = \mathbf{f} \qquad V(\boldsymbol{\rho}) = \int_{\Omega} \boldsymbol{\rho}\mathrm{d}V \le V_s,$$

$$[1]$$

where $\boldsymbol{\rho}$ is the density vector, $\mathbf{f}$ and $\mathbf{u}$ are the global load and displacement vectors, respectively, $\mathbf{K}$ is the global stiffness matrix, and V_s is the prescribed volume. The desirable solution specifies if the density at any point in the domain is either 0 (void) or 1 (solid). In a relaxed problem, the density can assume values between 0 and 1 (composite materials). For example, in the popular model named Solid Isotropic Material with Penalization (SIMP) (14), Young's modulus is parameterized as follows

$$E(x) = \rho(x)^p E^0,$$

$$[2]$$

where E^0 is the original Young's modulus of the material in the solid phase, corresponding to the density $\rho = 1$, and p is the penalization parameter which, in general, evolves following a continuation technique (15). To prevent singularity of the stiffness matrix, a small positive lower bound (e.g., $\rho_{\min} = 10^{-3}$) is placed on the density. Using the penalization parameter $p > 1$, the intermediate density approaches either 0 (void) or 1 (solid),

$$0 < \rho_{\min} \le \rho(x) \le 1.$$

$$[3]$$

In the element-based approach, the density of each element is represented by one value ρ_e and the global stiffness matrix $\mathbf{K}(\boldsymbol{\rho})$ in Eq. **1** is expressed as

$$\mathbf{K}(\boldsymbol{\rho}) = \sum_{e=1}^{N_{el}} \mathbf{K}_e(\rho_e) = \sum_{e=1}^{N_{el}} \int_{\Omega_e} \mathbf{B}^T \mathbf{D}(\rho_e)\mathbf{B}\mathrm{d}\Omega$$

$$[4]$$

where $\mathbf{K}_e(\rho_e)$ is the stiffness matrix of the element e, $\mathbf{B}$ is the strain-displacement matrix of shape function derivatives, and $\mathbf{D}(\rho_e)$ is the constitutive matrix that depends on the material density. The solution of the gradient-based optimization problem, Eq. **1**, requires the computation of sensitivities of the objective function and the constraint. In the element-based approach, element density ρ_e is used as the design variable; therefore, these sensitivities can be obtained as follows

$$\frac{\partial C}{\partial \rho_e} = -\mathbf{u}_e^T \frac{\partial \mathbf{K}_e}{\partial \rho_e} \mathbf{u}_e = -p\rho_e^{p-1}\mathbf{u}_e^T \mathbf{K}_e^0 \mathbf{u}_e \qquad \frac{\partial V}{\partial \rho_e} = \int_{\Omega_e} \mathrm{d}V, \quad [5]$$

where $\mathbf{K}_e^0$ is the element stiffness matrix of the solid material.

In its simplest configuration, the basic scheme of topology optimization is described in Fig. 2. First, the geometry and the loading are set up, and the density distribution ρ is initialized. Then, we start the optimization loop. We need a linear solver for the equilibrium equations $\mathbf{Ku} = \mathbf{f}$ in the finite element analysis. In the sensitivity analysis, we compute the derivatives of the objective function and the constraint. After this, we can apply an optional low-pass filter to remedy the checkerboard problem (16). The next step is the kernel of the optimization. There are various optimization algorithms that can be used for topology optimization. For instance, the method of moving asymptotes, which is a mathematical programming algorithm, is adopted in this work.

Multiresolution Scheme in Topology Optimization. To get higher fidelity resolution the multiresolution scheme by Nguyen et al. (15) is used. For example, in the element-based approach, a uniform density of each displacement element is considered as a design variable. Different meshes are employed for the topology optimization problem: the displacement mesh to perform the analysis, the design variable mesh to perform the optimization,
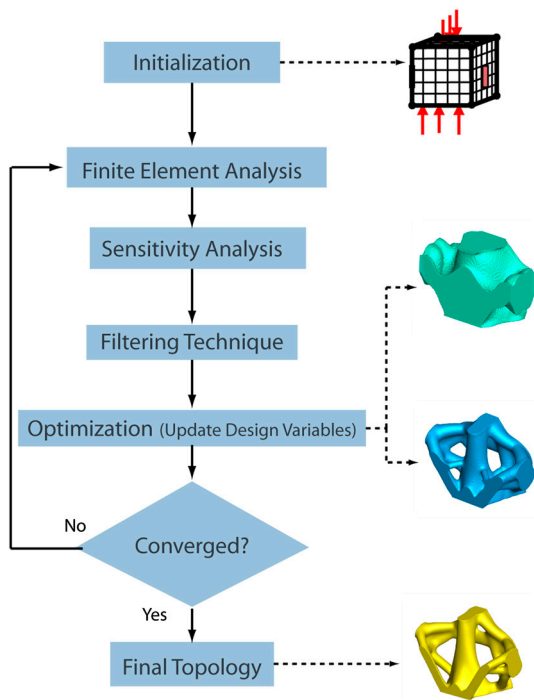
Fig. 2. The general flow of computations for topology design.

and the density mesh to represent material distribution and compute the stiffness matrices. Design variables are defined as the material densities at the center of the density elements. The design variable mesh can be different from the finite element mesh. In this scheme, the element densities are computed from the design variables by projection functions. The topology optimization problem definition Eq. **1** is then rewritten by including one more expression

$$\rho = f(\mathbf{d}), \qquad [6]$$

where **d** is the vector of design variables and $f(.)$ is the projection function. A finer density mesh than the displacement mesh is employed to obtain high resolution design. Within each density element, the material density is assumed to be uniform. Furthermore, a scheme to integrate the stiffness matrix, in which the displacement element consists of a number of different density elements, is introduced. Fig. 3 shows a displacement brick element of 8 nodes (B8), together with the density mesh with 125 density elements (also 125 design variables) per B8 displacement element. The sensitivity of the compliance requires the computation of the sensitivity of the stiffness matrix with respect to the design variable, which can be calculated as

$$\frac{\partial \mathbf{K}_e}{\partial d_n} = \frac{\partial \mathbf{K}_e}{\partial \rho_i}\frac{\partial \rho_i}{\partial d_n} = \frac{\partial \sum_{j=1}^{N_n}(\rho_j)^p\mathbf{I}_j}{\partial \rho_i}\frac{\partial \rho_i}{\partial d_n} = p(\rho_i)^{p-1}\mathbf{I}_i\frac{\partial \rho_i}{\partial d_n} \qquad [7]$$

where

$$\mathbf{I}_i = (\mathbf{B}^T\mathbf{D}^0\mathbf{B})|_i A_i, \qquad [8]$$

and d_n and ρ_i are the design variable and element density, respectively. The sensitivity of the constraint by the chain rule is as follows

$$\frac{\partial V}{\partial d_n} = \frac{\partial V}{\partial \rho_i}\frac{\partial \rho_i}{\partial d_n}. \qquad [9]$$
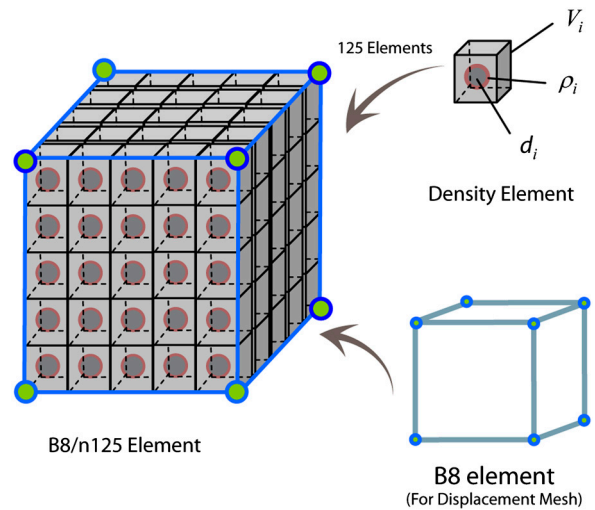
Fig. 3. Multi level topological optimization (MTOP). B8/n125 element showing embedded displacement mesh and design variable mesh.

Results

The type of defect that occurs clinically following a blast injury to the central face or with surgical resection of a paranasal sinus tumor possesses a region of major loss of bone in the midface. First, we perform a two-dimensional topological optimization of the cross-section on a vertical plane through the first molar to motivate the potential of using the topological optimization for this type of reconstruction. The design domain is a rectangular region in the midface as shown in Fig. 4A. The load is applied in the upward direction from the teeth to simulate masticatory forces, two fixed supports are provided on the two sides, two holes to mimic sinus cavities are embedded, an opening for the hard palate is provided in the lower region, and finally another set of load is applied at the top to emulate trauma forces that may be transferred from the upper region as shown in Fig. 4A. The simulation is performed in the elastic range. The domain was discretized using displacement Q4/U quad elements (15)

Fig. 4. (A) Design domain with loads, boundary condition, and cavity constraints. (B) Plot of density distribution to depict the optimized solution. (C) A section of the skull from a normal skull to compare the optimized topology.

(4 nodes and 1 density elements per element) with a mesh size of 384×192. The volume fraction constraint of 35%, and the penalization parameter $p = 4$ are employed. The topological optimization solution is represented by a density distribution plot on the domain. The result from the topological optimization simulation is shown in Fig. 4B. The topologically optimized solution has good similarity to a slice taken from a MRI normal skull data at the same location as shown in Fig. 4C. Our aim is not to mimic that, however, this gives a good confidence that this technique has good promise for the purpose.

Topological optimization method yields structural form optimized for a set of loading and constraints. Additional cases with different loading conditions, boundary constraints, and hole/cavity orientations are provided in *SI Text* (Fig. S1).

For the second example, a real patient defect following a gun shot injury is selected (Fig. 1 *E* and *F*). The design domain was selected from the craniofacial skeleton as shown in Fig. 5A. The rectangular prism simulates a region of major loss of bone in the midface consisting of the maxillary bones bilaterally. Due to excessive fragmentation due to the injury, (following surgical guidelines) bilateral radical maxillectomy is necessary and the bone replacement needs to be designed. Forces in amount and distribution as might occur with mastication (chewing) were applied on the lower plane of the dom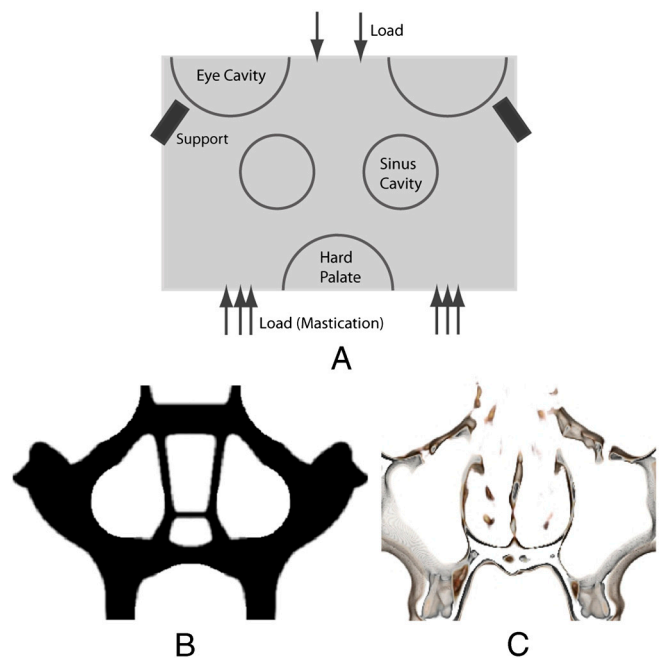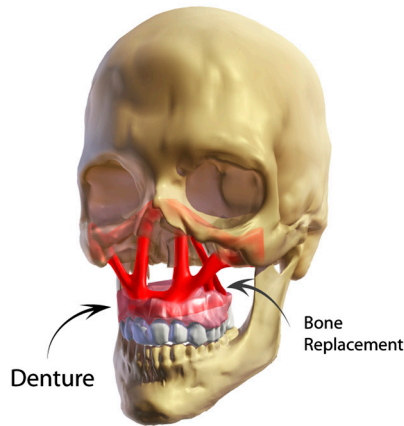ain (denoted by F2 in Fig. 5A). The lateral and superior surfaces are in contact with the uninjured portions of the facial skeleton. Supports (S) are provided on the lateral surfaces and support S1 in the superior plane. Alternatively for the case, when an additional applied force is considered being transmitted from the top of the superior surface, a force (F1) is applied instead of the support (S1) in the superior plane. For functional purposes, eye cavity, nasal cavity, and oral cavity constraints are introduced. These constraints help to simulate the natural anatomy of the roof of the oral cavity, which is essential for normal speech and swallowing (17). The support on the lateral surfaces will ensure material is included at points of contact with the bone present at the margins of the defect. These points are necessary for conduction of mechanical forces from the construct to the uninjured portions of the facial skeleton and for integration of the construct by the bone healing process. Additional load (F3) can also be applied in the domain. Based on these loading, boundary and cavity conditions, four cases were generated for simulation. The domain was discretized using a mesh size of $15 \times 32 \times 22$ using 10560 B8/n125 elements. The penalization parameter $p = 4$ is employed.

Case 1. In the first case, the loadings are F1 and F2, supports are S. Volume fraction constraint is 15%. The oral and nasal cavities are embedded; eye cavities are not embedded. (See Fig. 5B.)

Case 2. In the second case, F1 is replaced by the support S1 and additional load F3. Volume fraction constraint is 12.5%. The load F2 and support S are active. Nasal and eye cavities are not embedded but oral cavity constraint is embedded. (See Fig. 5C.)

Case 3. In the third case, the load and boundary conditions are similar to Case 1. Volume fraction constraint is 12.5%. Nasal cavity and constraints for oral cavity are embedded but eye cavities are not included. (See Fig. 5D.)

Case 4. In the fourth case, the loading and boundary conditions are similar to Case 2. Volume fraction constraint is 17.5%. Nasal cavity, eye cavities, and constraints for oral cavity are introduced. (See Fig. 5E).

For two-dimensional problems, density distribution is plotted to represent the topologically optimized solution (Fig. 4B). However in three-dimensions, isosurfaces of the density distribution are plotted to illustrate the topologically optimized solution. The isosurfaces of the density distribution of the solution obtained herein for the four cases are shown in Fig. 5 *B–E*.

The simulated optimal bone topology of the second example (Case 3) was inserted into the skull to confirm the practical feasibility of the final configuration (Fig. 6). We tested the robustness of the method by simulating a case of unilateral radical maxillectomy (Fig. 1E) and partial maxillectomy (Fig. 1F). The optimized topologies for these cases are shown in Fig. 7.

Additional simulations with different load ratios, boundary conditions, volume fraction variations are presented in *SI Text* (see Fig. S2). A movie (Movie S1) showing the evolution of the optimized topology during the numerical simulation is included in *SI Text*, as well as another movie (Movie S2) depicting a rendition of the design and insertion of the topological optimization method for the craniofacial reconstruction.

Discussion

Massive facial injuries can occur for a variety of reasons but are most often associated with cancer surgery or major force application such as in war-related injuries. Defects from cancer surgery are created under controlled circumstances and can be more predictable if the location and size of the tumor permits using standardized technique for removing portions of the facial skeleton (Fig. 1). Traumatic injuries cause a pattern of bone loss that is less predictable and lead to a wide range of deformities. Regardless of the cause, massive injuries have two distinguishing characteristics: (*i*) severe disruption of normal anatomy and (*ii*) tissue loss. Reconstruction involves returning salvageable tissue elements to their normal relationships and replacing unsalvageable tissues. Because of the highly specialized nature of some elements of the face (e.g., eyes, eyelids, nose, lips, teeth, and ears), complete

Fig. 5. (*A*) Selection of the design domain from the skull MRI data. Design domain showing details of loads, boundary conditions, and different cavity constraints. (*B*)–(*E*) Isosurfaces of the density distribution to depict the optimized solution (density value for the isosurface is 0.25).

Fig. 6. Illustration showing the solution of the simulated topologically optimized segmental bone (case 3) as it is inserted into the craniofacial skeletal region. Denture is included.

restoration of normal function and appearance likely requires a complementary use of prosthetic appliances and autologous tissue for the foreseeable future. Bone replacement is essential because both soft tissues and prosthetics need a stable foundation for proper function.

The clinical goals of reconstruction for massive injuries are (*i*) to achieve primary wound healing, (*ii*) to provide durable protection of vital structures, (*iii*) to restore normal form, and (*iv*) to provide a stable platform if prosthetics are needed (18). It is particularly important that facial bones permanently maintain a specific three-dimensional shape. Current methods rely primarily on obtaining autologous bone from the calvarium, iliac crest, fibula, scapula, radius, ulna, or ribs (19). For large defects with impaired soft tissue, bone is often transferred as vascularized units using microvascular surgery techniques to provide a blood supply independent of the adjacent compromised tissues. This provides one of the incentives to develop tissue engineering methods to custom fabricate living bone replacements in optimum shapes and amounts as part of the reconstructive approach.

The midface consists anatomically of the paired maxillary bones and the nasal bones. Each maxillary bone presents four
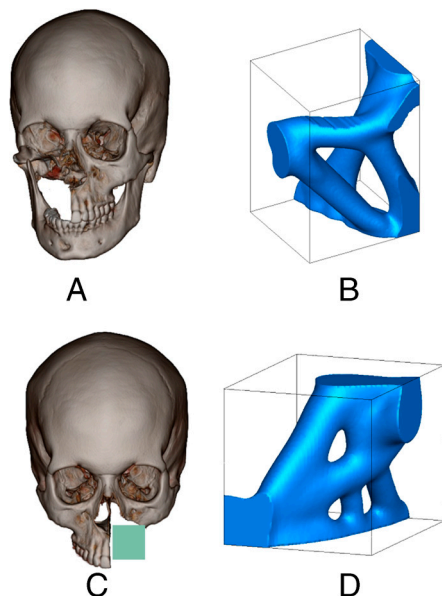
surfaces: the malar, orbital, palatine, and the lateral nasal walls. Although all facial bones must occasionally sustain external impact loads, under physiologic conditions the highest loads are repetitive forces applied by the muscles of mastication. The force generated during routine mastication of food like carrots or meat is about 70–150N. The maximum biting force is around 500–700N (19). Much lower forces are applied by muscles for facial expression, speech, and deglutition (swallowing), but these still require a stable foundation for proper function (17). The nasal bones serve primarily to define the contours of the nose and support internal structures to maintain patent airways. Midface bones and soft tissue are responsible to a large extent for facial contour. Midface reconstruction is complicated. In the midface these forces are born primarily by the maxillary bones. By interpreting patterns of facial fractures to determine the flow of forces, Manson et al. (20) described supporting columns of bone referred to as facial pillars or buttresses that conduct forces away from the midface. The midfacial supporting structure consists of three principal maxillary buttresses, the zygomaticomaxillary (ZMB), pterygomaxillary (PMB), and naso-maxillary buttresses (NMB) (see Fig. 8). These hold the position of the midface bones with respect to the cranial base. They maintain the vertical height, horizontal width, and anterior projection of the midface. The facial buttresses have been compared to the supporting pillars of the roof of a building (21). Hilloowala and Kanth (22) studied the stress distribution and the deformation using two-dimensional finite element model to draw a similarity between the load transfer mechanism of the masticatory force to the base of the skull to the transmission of load from the cathedral roof to the ground. They described three main mechanical functions: (*i*) transmit vertical forces, (*ii*) resist lateral shear, and (*iii*) achieve maximum function with minimum material. These principles guide selection of design constraints for topological optimization.

The bone replacement structures that have been obtained in the numerical examples using the current topological optimization technique fullfils all the three main mechanical functions. The maxilla is often described as a hexahedron; i.e., a geometric structure with six wall (17, 23). The roof of the maxilla is the floor of the orbit, the floor of the maxilla is the hard palate, whereas the anterior, posterior, medial, and the lateral walls are the vertical buttresses. The current practice of repairing these defects are mostly guided by the reconstruction of the maxillary buttresses (17, 24). The deficiency of the current available methods that typically result in unusual shape and size, is obvious (24). The first example (two-dimensional problem) shows good resemblance with a real section of a skull in the same location. For the next example, if we trace the maxillary buttresses on our optimized structures (represented by isosurfaces), they present similar pathways as the buttresses as shown in Fig. 8. The current practice is heuristic ad hoc design by the operating surgeon without any quantified planning of developing a stable structure with appropriate load transfer mechanisms. Until now researchers have hypothesised the buttresses system in the midface, our research fills the gap by showing the topology of optimized
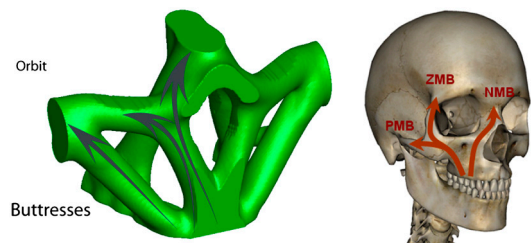

Fig. 7. (*A*) A skull (from MRI data) with radical maxillectomy defect. (*B*) Optimized topology solution (isosurface of density value = 0.25). (*C*) A skull (from MRI data) with partial maxillectomy. (*D*) Optimized topology solution (isosurface of density value = 0.25).

Fig. 8. Illustration showing the location of the buttresses in the topologically optimized solution and comparing them with the buttress system in a generic skull.

midface structure required to resist anticipated load and to support orbital components.

We have addressed the structural design problem of midface bone replacement by using the topological optimization technique to obtain an optimum topology to withstand the applied loads and satisfy imposed constraints. These techniques have been applied to microstructure for design of tissue conducting scaffolds but not to the macrostructural problem of whole bone replacement. The simulation results show promise to develop a patient-specific modeling solution to design bone replacements for large segmental defects. Other challenges must be overcome before clinical application of bone tissue engineering methods for facial bone reconstruction can be realized. For example, once formed, bones must permanently maintain the desired three-dimensional shape. A variety of strategies can be envisioned to achieve this, such as permanent incorporation of a form-stable scaffold within the bone. Nevertheless, the computational approach presented in this paper represents the type of enabling technology needed to plan custom fabrication of living bone replacements.

Concluding Remarks

The present results should be considered a "proof of concept." The current optimization algorithm is based on compliance only. There are extensions and refinements that we are currently

exploring such as the behavior of the midface due to external impact loading configurations (e.g., traumatic applications of external impact force) and different combinations of soft tissue and prosthetic designs. Other important variables such as biological variables (e.g., risk of contamination) and aesthetics may be added. Another important biological variable that may be embedded into the optimization algorithm is the oxygen level in the replacement bone, and associated surgical flaps (25).

As advances are made in devising bone tissue engineering methods, additional constraints can be added, including cost. This type of computational approach is likely to be an essential aspect of clinical tissue engineered bone replacements. The bone tissue engineering strategy incorporating this approach may present a unique paradigm in reconstructive surgery based on its potential in patient-specific surgical planning.

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