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Model for Estimating the Threshold Mechanical Stability of Structural Cartilage Grafts Used in Rhinoplasty

Allison Zemek, BS, Rohit Garg, MD, and Brian J. F. Wong, MD, PhD

Department of Otolaryngology–Head and Neck Surgery (A.Z., R.G., B.J.F.W.); and Beckman Laser Institute and Medical Clinic (R.G., B.J.F.W.), and Department of Biomedical Engineering (A.Z., B.J.F.W.), Division of Facial Plastic Surgery, University of California Irvine, Irvine, California, U.S.A

Abstract

Objectives/Hypothesis—Characterizing the mechanical properties of structural cartilage grafts used in rhinoplasty is valuable because softer engineered tissues are more time- and cost-efficient to manufacture. The aim of this study is to quantitatively identify the threshold mechanical stability (e.g., Young's modulus) of columellar, L-strut, and alar cartilage replacement grafts.

Study Design—Descriptive, focus group survey.

Methods—Ten mechanical phantoms of identical size ($5 \times 20 \times 2.3$ mm) and varying stiffness (0.360 to 0.85 MPa in 0.05 MPa increments) were made from urethane. A focus group of experienced rhinoplasty surgeons ($n = 25$, 5 to 30 years in practice) were asked to arrange the phantoms in order of increasing stiffness. Then, they were asked to identify the minimum acceptable stiffness that would still result in favorable surgical outcomes for three clinical applications: columellar, L-strut, and lateral crural replacement grafts. Available surgeons were tested again after 1 week to evaluate intra-rater consistency.

Results—For each surgeon, the threshold stiffness for each clinical application differed from the threshold values derived by logistic regression by no more than 0.05 MPa (accuracy to within 10%). Specific thresholds were 0.56, 0.59, and 0.49 MPa for columellar, L-strut, and alar grafts, respectively. For comparison, human nasal septal cartilage is approximately 0.8 MPa.

Conclusions—There was little inter- and intra-rater variation of the identified threshold values for adequate graft stiffness. The identified threshold values will be useful for the design of tissue-engineered or semisynthetic cartilage grafts for use in structural nasal surgery.

Keywords

Rhinoplasty; mechanical properties; cartilage replacement grafts; allogeneic cartilage graft; engineered tissue

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Send correspondence to Brian J. F. Wong, MD, PhD, Beckman Laser Institute, University of California Irvine, 1002 Health Sciences Road, Irvine, CA 92612. bjwong@uci.edu.

Ms. Zemek is presently at the Stanford University School of Medicine.

Level of Evidence: 2c

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INTRODUCTION

In aesthetic and reconstructive facial surgery, surgeons often must harvest autologous cartilage from the nasal septum, ear, or rib.^{1,2} Although the use of autologous donor tissue is ideal for facial reconstruction, there are several limitations, including donor site morbidity, limited quantities of harvestable tissue, inhomogeneous or unpredictable stiffness of the cartilage, and potential for warping after placement in the recipient site.³ Due to these disadvantages, interest in the development of tissue-engineered cartilage grafts has received a great deal of attention. In theory, tissue-engineered cartilage grafts could be designed to have specific mechanical properties ideally suited for a given surgical procedure, and could provide a relatively unlimited source of tissue.

Cartilage grafts used in facial surgeries have a limited load-bearing role, unlike the grafts used in orthopedic surgery, which must maintain stability in the face of extreme physiologic forces and duty cycles.^{4,17} The production cost of engineered cartilage increases with the desired stiffness, as stiffer specimens require more time in a hermetic bioreactor; grafts needed to repair joints require significant time and attention to achieve clinically suitable structural stability and strength.^{3,5} Therefore, it is important to identify the minimum mechanical properties required for grafts used in the head and neck. Because facial cartilages do not undergo extreme cyclical loading, the performance criteria are potentially not as stringent as those for the joints. Instead, facial cartilages resist small static loads which act over prolonged time frames. However, the quantitative threshold for what defines “adequate stiffness” in facial cartilage is unknown, and little can be inferred from the analysis of man-made alloplasts, which typically have elastic moduli orders of magnitude higher than native cartilage tissue. An exhaustive electronic database search (PubMed, 1965 to present) did not identify any studies that examined the performance criteria needed for facial cartilage, though several studies examined the mechanical properties of native facial cartilage tissue and tissue-engineered specimens.⁶⁻¹⁵

Hence, the objective of this study was to identify the minimum stiffness required for cartilage grafts for use in rhinoplasty surgery. We focused on three cartilage grafts commonly used in rhinoplasty procedures: columellar struts, L-strut replacements, and lateral crural struts (alar struts). The columellar strut is used for both structural and cosmetic purposes to support of the tip of the nose and control projection. A cartilage graft used to support or replace the L-strut should require a higher stiffness relative to the other grafts, because it supports the dorsum and prevents collapse of the nasal vault. Alar struts require minimal stiffness because they are almost exclusively used for cosmetic modifications of alar shape. Mechanical cartilage phantoms of varying stiffness were evaluated by groups of surgeons who then identified the specific minimally acceptable threshold stiffness value for each of the three clinical applications.

MATERIALS AND METHODS

Although using human cartilage samples to determine the threshold stiffness of the three types of grafts we selected in this study would be ideal, human cartilage poses several problems in terms of long-term storage, geometric consistency, transportation, and limited supply. Furthermore, because the process of mechanical testing destroys the human cartilage graft, only unused conchal or septal samples obtained from rhinoplasties or other procedures can be tested. These remnant samples are mostly small and irregularly shaped, which makes mechanical testing inaccurate and difficult to perform, short of freezing specimens and performing mechanical analysis on ultra-thin specimens sectioned with a cryomicrotome. Also, human facial cartilages are anisotropic, so mechanical testing would have to be performed in three mutually orthogonal directions. This is extremely difficult because the

available human cartilage specimens are relatively thin, and presumably there is some degree of spatial variation in local tissue properties. Therefore, to avoid using human cartilage while maintaining an accurate evaluation of the required stiffness for replacement cartilage grafts, the study design relies on the experience and expertise of head and neck surgeons to distinguish between safe and inadequate stiffness for use in surgery. One advantage of this evaluation method is that surgeons can consider whether replacement cartilages softer than native cartilage are still safe for use.

Mechanical phantoms mimicking actual cartilage specimens with similar dimensions as those used in facial surgeries were cast from elastomers with varying elastic moduli. Ten distinct elastomer specimens were made with stiffnesses varying from 0.36 to 0.85 MPa in approximately 0.05 MPa increments (Fig. 1). Polyurethane prepolymer, polyol-plasticizer, and a white urethane dye (Smooth-On, Inc., Easton, PA) were combined and poured between two panes of glass 2.3 mm apart, and the mixture was allowed to set for 24 hours. The stiffness of the rubber was controlled by adding a phthalic acid, benzyl butyl ester softener (Smooth-On, Inc.), in different proportions with the liquid rubber mixture to interfere with cross-linking at varying degrees. The rubber sheets were then cut with a razor into 20 mm × 5 mm rectangles, so each specimen was nearly identical in color, sheen, and size (20 mm × 5 mm × 2.3 mm). The mass of each specimen was nearly identical.

It is important to emphasize that these elastomer specimens were only used as mechanical phantoms and were not used, nor intended to be used, as actual grafts in surgery. The elastic modulus of each urethane mechanical phantom was determined by unconfined compression with a mechanical testing platform (EnduraTEC ELF 3200; Bose, Eden Prairie, MN).

Unconfined compression testing was used rather than cantilever testing because the urethane elastomers are isotropic, which closely approximates anisotropic human cartilage over the stress and strain ranges we evaluated. The softest two (0.36 MPa) and hardest two (0.85 MPa) specimens had nearly identical elastic moduli, to act as controls. The base of each specimen was labeled with colored dots that were coded to allow identification of specimen stiffness while ensuring blind evaluation by test subjects (Fig. 2).

The study group for this experiment consisted of 25 head and neck surgeons surveyed at local, regional, and national professional meetings. Participants included residents, academic facial plastic surgeons, and facial plastic surgeons in private practice. The number of years in practice was recorded for each person. The participants could be segregated into different groups to allow for analysis based upon age, years of training, affiliation, and practice locale. Each study participant was tested individually and was blinded from all other participants. The surgeon was presented with all 10 specimens in a random order, and was asked to arrange the mechanical phantoms in order of increasing stiffness. The surgeon could examine the specimens in any manner short of mechanical destruction. In general, two types of mechanical deformation were used to test reaction force: simple concave flexure between the thumb and forefinger, and sigmoidal flexure between both hands.

After arranging the 10 phantoms in order of increasing stiffness, participants were then asked to select the mechanical phantom with the minimum acceptable stiffness for three distinct clinical applications: columellar, L-strut, and alar grafts. The surgeons were asked to consider whether the threshold grafts would result in positive surgical outcomes. This approach takes into account the surgeon's expertise in predicting long-term outcomes based on graft stiffness. Of the 25 surgeons tested, eight surgeons were available to be tested one week after their initial test, to evaluate intra-rater consistency.

The data collected from the surgeons were fit best with logistic equations of the form: $f(z) = 1/(1 + e^{-(a+bx)})$. The threshold stiffness values for columellar, L-strut, and alar grafts were

determined with a binary logistic regression between the mechanical acceptability and nonacceptability of each type of graft. The accuracy of the model was evaluated with the Hosmer-Lemeshow test; the resulting *P* values were .38, .39, and .43 for columellar, L-strut, and alar grafts, respectively. This indicated no statistical evidence for lack of fit; there was no statistical significance between the expected values calculated with model and the actual data collected. Because a binary logistic regression was used to model the data, the threshold values for the grafts were calculated at *P* = .5. Based on different ages, experience levels, and affiliations, the following respondent groups were tested for statistically significant biases in threshold selection: 1) surgical resident versus board-certified surgeon in practice; 2) practicing in California versus not practicing in California; 3) affiliated with University of California Irvine (UCI) versus not affiliated with UCI; 4) <20 years of experience versus >20 years of experience; 5) board certified by the American Board of Facial Plastic and Reconstructive Surgery (ABFPRS) versus not board certified.

RESULTS

The binary logistic regressions calculated for columellar, L-strut, and alar grafts were used to determine the threshold stiffness required for each type of graft. The threshold values were 0.56 MPa, 0.59 MPa, and 0.49 MPa for columellar, L-strut, and alar grafts, respectively (Fig. 3).

Rater accuracy was calculated with a 12-point scoring system. Two points were awarded for every graft placed in the correct order of stiffness, and up to three points were deducted for each pair of incorrectly ordered grafts, depending on the “distance” between the correct rank and the error. Rater consistency was also determined by using a similar 12-point scoring system. Two points were awarded for each graft placed in the same order as in the first round of testing, and points were deducted for incorrectly ranked cartilage grafts. The Hosmer-Lemeshow test was used to determine whether there is evidence for lack of fit between the data and the binary logistic regression (Table I).

Responses were also tested for statistically significant biases. Independent *t* tests were used to compare the threshold responses between different ages, experience levels, and affiliations. The Hosmer-Lemeshow test was also used to verify the accuracy of the *t* test results; the model used to fit all the data (*N* = 33) was used to fit the data of only the residents (*n* = 13), and only the data of the nonresidents (*n* = 20). The *P* values (columellar = .2, L-strut = .52, alar = .3) indicate that there is no evidence for lack of fit, confirming the *t* test results. A dependent *t* test was used to compare the consistency of the testers between the first test and a post-test 1 week later (Table II).

DISCUSSION

Tissue-engineered cartilage grafts will ultimately be available for use in aesthetic and reconstructive head and neck surgery because they can be designed to have homogenous material properties and specific stiffness values. However, production time and cost escalate with desired stiffness. A recent study indicated that it takes 7 months to culture bovine cartilage to have an equilibrium elastic modulus of 1.0 MPa.¹⁶ Therefore, it is important to determine minimum acceptable threshold values for each type of graft used in surgery. At present, surgeons qualitatively evaluate the stiffness of cartilage grafts, while actual data on acceptable stiffness values are unknown. To identify what defines adequacy, we attempted to assess the surgeons’ qualitative evaluation of cartilage and then identify quantitative threshold values using mock cartilage grafts made of polyurethane.

We determined that the threshold stiffnesses were 0.56 MPa, 0.59 MPa, and 0.49 MPa for columellar, L-strut, and alar grafts, respectively. Overall, the thresholds were fairly similar; the two structural applications (columellar and L-strut grafts) had very close values, whereas the cosmetic graft (alar graft) had a slightly lower mechanical threshold. These relatively low threshold values, compared with orthopedic cartilage grafts, suggest that engineering cartilage for facial surgery applications is feasible and cost-effective. A summary of the estimated cost of different orthopedic graft products is provided as a relative measure of potential costs (Table III). Furthermore, the threshold value of each graft is below the average stiffness for human nasal septal cartilage, which is approximately 0.8 MPa, but this is age-dependent and can range from 0.03 MPa to 1.5 MPa.^{9,11,15}

Although using human septal cartilage samples to determine the threshold stiffness of the three types of grafts would be ideal, human cartilage poses several problems in terms of storage, geometric consistency, transportation, and limited supply for studies of this nature, which were performed longitudinally at several meetings in the southwestern United States. The mechanical phantoms were used because large human nasal septal cartilage specimens are difficult to obtain, as they are usually scavenged from septoplasties and rhinoplasties. They are often fractured, inhomogeneous, and small. Finally, there are obvious biohazard issues for this type of testing. Careful consideration was invested to ensure the urethane struts' accurate mimicking of human cartilage in terms of being of similar stiffness to native cartilage tissue. The geometry of the samples also influences the qualitative evaluation of stiffness, so consistent geometry of the samples was especially important. The surgeons confirmed during testing that the stiffness range and mechanical behavior of the phantom grafts in response to large deformations were similar to human cartilage.

Concerning data analysis, a binary logistic regression was used to fit the data because it can determine a quantitative threshold between two variables, such as the unacceptable and acceptable stiffness for use in surgery. The Hosmer-Lemeshow test was used to determine if the binary logistic regression fit the data because it was an efficient method to test for evidence of lack of fit. Independent and dependent *t* tests were simple and effective to compare groups and thresholds to determine if there were statistically significant biases for threshold selection. Collectively, the *t* tests have indicated that there is no bias based on age, experience, type of training, or affiliation for selecting the mechanical threshold of the cartilage grafts.

CONCLUSION

This paper identified the threshold stiffness of columellar, L-strut, and alar grafts used by head and neck surgeons to be 0.56 MPa, 0.59 MPa, and 0.49 MPa, respectively. This data provides a guide to identify the minimum desirable stiffness that grafts must satisfy for use in rhinoplasty. This information will be valuable for bioengineering companies who are developing allogeneic cartilage grafts. With respect to further applications in cartilage research, this method of testing surgeons is also a potential way to identify and evaluate acceptable mechanical thresholds for structurally modified cartilage, which must still maintain this minimum threshold stiffness to support the shape of the nose.

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BIBLIOGRAPHY

1. Cardenas-Camarena L, Gomez RB, Guerrero MT, Solis M, Guerrero Santos J. Cartilaginous behavior in nasal surgery: a comparative observational study. *Ann Plast Surg*. 1998; 40:34–38. [PubMed: 9464693]
2. Glasgold MJ, Kato YP, Christiansen D, Hauge JA, Glasgold AI, Silver FH. Mechanical properties of septal cartilage homografts. *Otolaryngol Head Neck Surg*. 1988; 99:374–379. [PubMed: 3148886]
3. Ansari K, Asaria J, Hilger P, Adamson PA. Grafts and implants in rhinoplasty—techniques and long-term results. *Oper Tech Otolaryngol Head Neck Surg*. 2008; 19:42–58.
4. D’Lima DD, Chen PC, Colwell CW. Osteochondral grafting: effect of graft alignment, material properties, and articular geometry. *Open Orthop J*. 2009; 3:61–68. [PubMed: 19696917]
5. Wu W, Chen F, Feng X, Liu Y, Mao T. Engineering cartilage tissues with the shape of human nasal alar by using chondrocyte macroaggregate—experiment study in rabbit model. *J Biotechnol*. 2007; 130:75–84. [PubMed: 17434638]
6. Homicz MR, McGowan KB, Lottman LM, Beh G, Sah RL, Watson D. A compositional analysis of human nasal septal cartilage. *Arch Facial Plast Surg*. 2003; 5:53–58. [PubMed: 12533140]
7. Williams GM, Klisch SM, Sah RL. Bioengineering cartilage growth, maturation, and form. *Pediatr Res*. 2008; 63:527–534. [PubMed: 18427298]
8. Duda GN, Haisch A, Endres M, Gebert C, Schroeder D, Hoffman JE, Sittering M. Mechanical quality of tissue Engineered cartilage: results after 6 and 12 weeks in vivo. *J Biomed Mater Res*. 2000; 53:673–677. [PubMed: 11074426]
9. Grellmann W, Berghaus A, Haberland EJ, Jamali Y, Holweg K, Reincke K, Bierogel C. Determination of strength and deformation behavior of human cartilage for the definition of significant parameters. *J Biomed Mater Res A*. 2006; 78:168–174. [published correction appears in *J Biomed Mater Res A* 2006;79:758]. [PubMed: 16628548]
10. Haisch A, Duda GN, Schroeder D, Groger A, Gebert C, Leder K, Sittering M. The morphology and biomechanical characteristics of subcutaneously implanted tissue-engineered human septal cartilage. *Eur Arch Otorhinolaryngol*. 2005; 262:993–997. [PubMed: 16075238]
11. Rotter N, Tobias G, Lebl M, Roy AK, Hansen MC, Vacanti CA, Bonassar LJ. Age-related changes in the composition and mechanical properties of human nasal cartilage. *Arch Biochem Biophys*. 2002; 403:132–140. [PubMed: 12061810]
12. Park SS, Jin HR, Chi DH, Taylor RS. Characteristics of tissue-engineered cartilage from human auricular chondrocytes. *Biomaterials*. 2004; 25:2363–2369. [PubMed: 14741601]
13. Naumann A, Dennis JE, Aigner J, et al. Tissue engineering of autologous cartilage grafts in three-dimensional in vitro macroaggregate culture system. *Tissue Eng*. 2004; 10:1695–1706. [PubMed: 15684678]
14. Farhadi J, Fulco I, Miot S, et al. Precultivation of engineered human nasal cartilage enhances the mechanical properties relevant for use in facial reconstructive surgery. *Ann Surg*. 2006; 244:978–85. [PubMed: 17122623]
15. Rotter N, Bonassar LJ, Tobias G, Lebl M, Roy AK, Vacanti CA. Age dependence of biochemical and biomechanical properties of tissue-engineered human septal cartilage. *Biomaterials*. 2002; 23:3087–3094. [PubMed: 12102179]
16. Martin I, Obradovic B, Treppo S, et al. Modulation of the mechanical properties of tissue engineered cartilage. *Biorheology*. 2000; 37:141–147. [PubMed: 10912186]
17. Drobic M, Radosavljevic D, Ravnik D, Pavlovic V, Hribnik M. Comparison of four techniques for the fixation of a collagen scaffold in the human cadaveric knee. *Osteoarthritis Cartilage*. 2006; 14:337–344. [PubMed: 16406616]
18. Bursac P, York A, Kuznia P, Brown LM, Arnoczky SP. Influence of donor age on the biomechanical and biochemical properties of human meniscal allografts. *Am J Sports Med*. 2009; 37:884–889. [PubMed: 19336615]

Fig. 1.

Ten mock cartilage grafts were made to have varying stiffnesses, varying by increments of 0.05 MPa. Phantoms 1, 2 and 9, 10 had respectively equal stiffness to act as controls for rater accuracy.

Fig. 2.
The 10 mock cartilage urethane grafts were equal in size, shape, color, sheen, and mass. The correct order of the grafts was identified by colored dots to ensure blind testing.

Fig. 3.

The threshold values for columellar, L-strut, and alar grafts were determined with a binary logistic regression. The figures shown are integrated probability densities of stiffness acceptability, or the likelihood that a surgeon will consider the stiffness of the graft safe for use in surgical procedures. The stiffness (MPa) at $P = .5$ was calculated as the threshold value. At low stiffness, it is very unlikely for surgeons to evaluate the graft as adequate, whereas at higher stiffness, it is very likely that the graft will be deemed adequate for surgery.

TABLE I

Summary of the Threshold Values Calculated for Columellar, L-Strut, and Alar Grafts.

Graft	Threshold Value	Degrees of Freedom	χ^2	<i>P</i> Value*
Columellar	0.56 MPa	8	8.56	.38
L-strut	0.59 MPa	8	8.39	.39
Alar	0.49 MPa	8	8.02	.43

* By the Hosmer-Lemeshow test, high *P* values indicate that there is no evidence of lack of fit between the binary logistic regression and the actual data.

TABLE II

Statistical Analysis.

Comparison (No. of Surgeons), N = 33	<i>t</i> Value	<i>P</i> Value	Difference
Resident (13) vs. board-certified surgeon (20)*			
Alar	−0.51	.61	NS
Columellar	0.48	.64	NS
L-strut	0.15	.88	NS
Practicing in CA (25) vs. not practicing in CA (8)*			
Alar	1.17	.25	NS
Columellar	0.73	.47	NS
L-strut	−0.37	.71	NS
UCI affiliated (15) vs. non-UCI affiliated (18)*			
Alar	−0.01	.99	NS
Columellar	0.51	.62	NS
L-strut	−0.29	.77	NS
ABFPRS (11) vs. non-ABFPRS (22)*			
Alar	1.31	.20	NS
Columellar	0.14	.88	NS
L-strut	0.31	.76	NS
Initial test (8) vs. 1-wk post test (8)			
Alar	0.45	.66	NS
Columellar	−0.29	.77	NS
L-strut	−0.43	.67	NS
Alar (33) vs. columellar threshold (33) [†]	−2.93	.0051	SS
Alar (33) vs. L-strut threshold (33) [†]	−4.786	.0001	SS
L-strut (33) vs. columellar threshold (33) [†]	1.67	.09	NS

* Statistical analysis was performed to determine if there are threshold selection biases between different subgroups of surgeons.

[†] Independent *t* tests were done to determine if there is a statistically significant difference between the thresholds of the three types of grafts, and the consistency of the raters.

NS = not significant; UCI = University of California Irvine; ABFPRS = American Board of Facial Plastic and Reconstructive Surgery; SS = statistically significant.

TABLE III

Summarized Comparison of the Costs of Available Orthopedic Grafts.

Stiffness	Estimated Cost [*]	Product Type
Human septum, 0.03–1.5 MPa ¹⁶	\$100s	Animal chondrocyte cultures
	\$1,000s	Autologous cartilage regeneration system
	\$1,000s	Cell replacement technology
Human articular cartilage, 60–85 MPa ¹⁸	\$1,000s	Human cartilage explant cultures
	\$1,000s	Synthetic hydrogel
	\$1,000s	Synthetic cartilage plugs
	\$1,000s	Orthopedic replacements
	\$1,000s	Orthopedic plugs
	\$10,000s	Total knee replacement technology

* Price estimates were obtained from price listings, company websites, and catalogs from 13 companies.