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Biomechanical Properties of the Lip as an Approach for Tissue Engineered Lip

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Abstract

Background Tissue engineering is a rapidly progressing field of science that provided the surgery with better options for treatment; lip has unique anatomy, shape and functions. Large lip defect is one of the great challenges for plastic surgeons, the gold standard option is autologous tissue replacement with drawbacks of donor site morbidity and suboptimal outcomes, tissue engineering came up with new option for partial thickness defect to address the skin-vermilion loss as a composite graft but not the orbicularis oris muscle, before preceding for tissue engineered orbicularis oris muscle it is wise to study the biomechanical properties of the lip and then matching the measures with tissue engineered product as basic biomechanical properties affect the lip shape and functions.

Keywords Biomechanics, stiffness, tissue engineering, lip, orbicularis oris, vermilion reconstruction, perioral dynamics

Introduction

Reconstruction of large lips defect is one of the major challenges for plastic surgeons due to the complex lip anatomy and biomechanics. Improper reconstruction leads to poor aesthetic and functional outcomes in term of speech, facial animations, stiffness and oral continence which effects eating and drinking. Large lips defects could be attributed to iatrogenic causes after tumor excision, traumatic, burn, congenital anomalies and necrotizing soft tissue infections. The current available options for treatment are autologous tissue transfer whether it is local, regional or free tissue transfer; in addition to the donor site morbidities, they do not precisely mimic the original lost tissue in term of unique morphology and function. However, loss of more than 50% of the lip brings the face transplant as another option of treatment for functional concern but imposing the patient for life-long immune-suppression.

Tissue engineering and regenerative medicine came up with novel alternative option for lost tissue, tissue engineering is" An interdisciplinary field that applies the principles of engineering and the life sciences toward the development of biological substitutes that restore, maintain or improve tissue function”[1]. Different models now are available: skin [2], oral mucosa [3] and muscle [4].

Histology and Anatomy

Mechanical properties of the engineered tissue are effected by their components especially the scaffold for extracellular matrix, it is wise to be familial with lip histology which effects also the functional outcome also. Basically lip tissue engineering needs composite tissue from 3 types: skin, oral mucosa (for dry and wet vermillion) and muscle (orbicularis oris). Skin is composed from 3 layers: epidermis, dermis and hypodermis. Epidermis stratified squamous epithelium which contains five strata: Stratum Corneum (Cornified Layer), Lucidum, Granulosum, Spinosum, Germinativum (Basali). There are 3 types of cells encountered which are melanocytes, Langerhans cells and Merkel cells whereas dermis consists of connective tissue with structural elements of collegen and elastic fibers in addition to extracellular matrix. Skin appendages are involved mainly in the dermis as sebaceous glands, sweat glands, apocrine glands and hair follicles with papillary muscle. Blood vessels and nerve ending (Panician corpuscles) are located in the deep reticular layer of the dermis [(5)].

On the other hand, mucosa is composed also from 3 layers: surface epithelium, lamina properia and submucosa, there are few differences from skin histology table 1. Oral epithelium is keratinized stratified squamous which is either wet or dry depending on the amount of minor salivary glands, oral epithelium consists of 4 layers: the keratinized layer , granular layer, spinous layer and the basal layer. There are 3 types of cells as well which are melanocytes, Langerhans cells, and Merkel cells. The lamina properia is a connective tissue made by collagen and elastic fiber with extracellular matrix; mucosal appendages are minor salivary glands which are more abundant in the wet vermillion than dry vermillion. Fordcyte spot or granules are variant which can be found in the oral mucosa which correspond to sebum deposition from displaced sebaceous glands [(6)].

Table 1. Histology comparison between skin and lip mucosa

Skin	Oral mucosa
<u>3 layers</u>: epidermis, dermis, hypodermis	**<u>3 layers</u>**: surface epithelium, lamina properia, submucosa
<u>5 layers</u> of cells: Stratum Corneum (Cornified Layer), Lucidum, Granulosum, Spinosum, Germinativum	**<u>4 layers</u>** of cells: keratinized layer , granular layer, spinous layer, the basal layer
melanocytes, Langerhans cells, and Merkel cells	melanocytes, Langerhans cells, and Merkel cells
Skin appendages: sweat glands, sebaceous glands, apocrine glands, hair follicles	Salivary glands, Fordyce spots

Orbicularis oris muscle is complex striated muscle surround the oral fissure in form of spectrums of full ellipses as sphincter; there are four independent indentified quadrants (left, right, upper and lower) each quadrant consists from larger par peripheralis and smaller pars marginalis. So the lip has eight distinct anatomical segments. *Pars periphralis* attached to the modiolus through it stem fibers which are reinforced by buccinators, levator anguli oris, zygomaticus major and depressor anguli oris, then forms triangular muscular sheet which is thickest at skin-vermillion junction. *Pars marginalis*: is the part closely related to speech consists from fibers lodged within vermilion then meet with the other side fibers before attach to the dermis of vermilion, the anatomical and dynamic orientation between pars periphralis and pars marginalis is complex that maintains the unique lips' shape at both static and dynamic states (Fig. 1 A & B) [(7,8)].

The complexity of the lip action, in part, is related to the number of muscles attached, the upper lip is attached to 6 muscles at least: levator anguli oris, levator labii superioris, levator labii superioris alaeque nasi, zygomaticus major and depressor septi muscles, while the lower lip has attachments with 4 muscle:

depressor anguli oris, depressor labii inferioris, mentalis and orbicularis oris inferioris muscles [9], those direct labial tractors may act in group or individually to produce movement at the level of quadrants, pars or smaller portion.

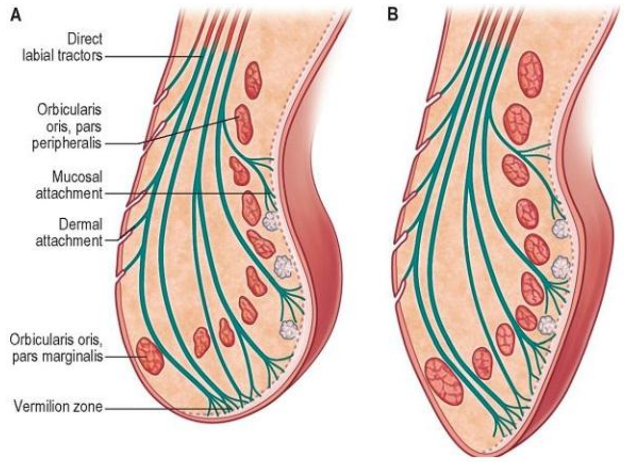

Fig. 1. Sagittal section of the upper lip in repose (A) Slightly contracted (B)

Lip protrusion is passive in its initial stages. It may be suppressed by powerful contraction of the whole of orbicularis oris or enhanced by selective activation of parts of the direct labial tractors However, the action of direct labial tractor will be modified by the oribularis and modiolar muscle, beyond a certain range of mouth opening the movement of the lips is almost dominated by the mandibular movement. Controlled three-dimensional mobility of the modioli enables them to integrate the activities of the cheeks, lips and oral fissure, the oral vestibule and the jaws [3].

Modiolar muscles themselves have anatomical variation that can be reflected on the movement's outcome e.g. risorius muscle found only in about 20% of Australians and 80% to 100% of Chinese and Malays [10], zygomaticus major muscle could be bifid with two distinct insertion points giving the appearance of dimple during smile [11].

Tissue engineering so far revolutionized a composite graft for lip reconstruction in form of muco-cutaneous junction (vermilion border) as continuous human oral mucosa-lip-skin construct, but they didn't address the orbicularis oris [12].

Stepping forward for full tissue engineered lip involving all three components (skin, mucosa and orbicularis oris) needs to know the biomechanical properties of the lip, as it is as intricate structure with different tissue compositions, attachment to different structures in variable directions and planes renders single movement of the lip quite complex in term of biomechanical parameters.

Basic of biomechanics

Biomechanics is the science concerned with the structure and movement of human, plants, organ and cells [13], there main potential parameters to be measured in biomaterials are biomechanical properties, strength (stress, strain and shear), modulus, elasticity, stiffness, viscoelasticity (creep, stress relaxation, and toughness and finally anisotropy, isotropy.

Strength: is ability of resistance of deformation before failure it can be expressed as a *stress* (when axial load is applied as compression force and expressed in pressure units) or *shear* (when the load is applied in multiple different directions and measured in pressure unit as well) or *strain* (when axial load is applied as tension force and it is quantified by division of length change over normal length so it is dimentionless), *Stiffness, elastic modulus or Young's modulus* is the ratio of stress to strain in the also can be calculated as the value of the force required divided by the degree of deformation, *elasticity:* is the ability of materials to return to its original shape after the load had been removed which is a basic requirement for lips, *toughness:* the amount of energy that absorbs by material then deforms before rupture *viscoelasticity:* is the response variability of stress and strain according to the rate of loading (time dependent) thus the lip is viscoelastic structure, *Creep* is the slow increase of the length (increasing strain) of a material over given period when imposed under a constant tensile stress, *Stress relaxation* is the decrease in stress over given period when a material is elongated to a set length, *Hysteresisis* the property of viscoelastic materials of having a different unloading response than its loading response, *anisotropy:* is the complex mechanical behavior in response to loading that differs according to the direction of the leading force so lips are anisotropic structure, while *isotropy* has similar behavior regardless the direction of the force due to uniform structural unit [14].

Application of those parameters could be in static or dynamic state, practical application is easier for tissue having uniform structural unit with implications in single plane like skin [15]. Lips have more complex measures due to 3D anisotropic structure which involves different consistency of tissues. Even though, through the last four decades, many scholars had studied the perioral biomechanics both passive and active forms.

Eric Muller, a pioneer of biomechanics revealed that the perioral muscular attachments are complex due to interdigitations which interacts with very low inertial load [16], hence, unlike limb muscle, represents a great challenge for biomechanical testing and sampling. The biomechanical properties of the passive perioral tissue like tension, torsion, stress and viscoelasticity have much greater influence on mechanical output comparing to limbs [17].

Muller developed the first device to study perioral stiffness; it was three-dimensional space-frame model to provide baseline biomarkers in order to compare them with disease cases effect the perioral performance [16]. Geometrical and mechanical baseline indices had been identified among children younger than 12 years age, upper lip curvature coefficient showed maximum values in those aged between 2-3 years whereas upper lip elasticity, like other indices, had no significant difference with age [18].

Both active and passive perioral movements had been analyzed in relation to the muscle length (interangle span) in both healthy and disease people, the results were that the active force increased 4 times during maximum voluntary contraction with the increment of length with dramatic increase in male more than female, whereas passive forces showed no significant difference in relation to muscle length [19].

Shadmehr defined the "postural module" when a group of muscles synergize together to achieve a class torque of functions at constant equilibrium position but the stiffness is variable at this stage as part of activation of that postural module [20].

Velocity of lips movement is substantial for voice production specifically the lips move in higher velocity when the oral closure occurs during consonant sound production, i.e. another potential importance is the coordination between upper and lower lip for closure of oral aperture in specific time [21].

The lip shape is highly affected by the orbicularis oris muscle anatomy which is clearly evident on the lip gestures and protrusion with a link to cultural differences, the same effect on the lip gestures and protrusion had been elicited by jaw posture using the 3D model study [22].

Lip stiffness is one of the major parameters had been thoroughly assessed due to its magnificent role in movement, it can been can quantified after exerting specific displacement on the tissue and calculating the ratio of the resultant force over the displacement distance this will be expressed as stiffness quotient [19, 23].

A 3D model with multilayer deformable mesh had been made to assess the facial biomechanics including the perioral tissues for both active and passive muscle state presenting the data by linear approximations and the main target parameters were mass and stiffness for different anatomical layers (epidermal, dermal fatty, fascial and muscular layer) [24]. Another 3D model (3D finite element face model) to study the elastic properties of the face identified the significant effect of muscle stiffness during activation on the lip shape in term of protrusion and rounding [25]. Lip stiffness is potential for proper sound production (especially fricative) throughout the articulation process [21,26].

Lip stiffness measurements can be obtained through automated non invasive technology with real time acquisition and analysis of data during non contraction phase, the nonlinear regression technique revealed significant relation between muscle stiffness and the provided displacement distance [27]. The same technique was used for both males and females proved no significant difference of gender on stiffness quotient [28].

Recently the (OroSTIFF) device provided measurements on non-participatory perioral stiffness; in addition to stiffness coefficient, the muscle activity pattern during active phase was also determined through the root-mean-square of both lips individually [29].

In conclusion, lips are intricate structure, mechanical properties had been studied because they affect the lip shape, gestures and functions in both static and active states, many properties are not related solely to the lip structure itself only but also to the attached surrounding tissues, also some measurements variations are attributed to the gender, age and race but baseline indices had been identified.

Limitations

Study of the tissue engineered product is usually done in vitro before application in vivo or clinical field, it is difficult to mimic the biomechanical environment with precise matching of tissue attachments and innervations, but, to some extent, is possible to identify some parameters in static or passive state and match accordingly. Another profound issue is the skeletal muscle tissue engineering, although the problem of vascularisation of tissue constructs had been resolved, the engineering of composite graft for 3 elements (skin, mucosa, muscle) simultaneously is still in challenge.

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