THE EFFECTIVENESS OF HYALURONIC FILLER IN THE GUMMY SMILE TREATMENT

THAZIN THET TIN

MASTER OF SCIENCE
IN
DERMATOLOGY

SCHOOL OF ANTI-AGING AND REGENERATIVE MEDICINE
MAE FAH LUANG UNIVERSITY

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EXAMINATION COMMITTEE

.....CHAIRPERSON
(Prof. Thamthiwat Nararatwanchai, Ph. D.)

.....ADVISOR
(Rassapoom Sumaetheiwit, M. D.)

.....EXTERNAL EXAMINER
(Assoc. Prof. Wongdyan Pandii, Dr. P. H.)

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Thazin Thet Tin

Thesis Title	The Effectiveness of Hyaluronic Filler in the Gummy Smile Treatment
Author	Thazin Thet Tin
Degree	Master of Science (Dermatology)
Advisor	Rassapoom Sumaetheiwit, M. D.

ABSTRACT

Background : A perfect smile is balanced with 3 parameters, teeth, gum and lips. Gummy smile can be a cause of esthetic embarrassment for many patients, so affecting their psychological behavior. With different causes of gummy smile, treatment could be facial surgery, oral surgery, laser or botox.

Objective: To study the effect of HA filler in the gummy smile treatment and to know the HA filler imporves or not.

Material and method: quasi-experimental study of injecting HA filler in the gummy smile correction, total 10 patients of gummy smile average 4.5cm exposure is collected and gave the treatment. 0.3ml of hyaluronic filler is injected into canine fossa/ upper part of nasolabial fold of both sides, total 0.6ml of hyaluronic filler, close to the bone (intramuscular) injection. Then measure the gummy smile exposure immediately.

Result: gummy smile exposure average 4.5mm is reduced to 1.5mm, average 3mm of gummy smile is reduced immediately.

Conclusion: So it is effective in treating gummy smile by using filler in the canine fossa (upper part of nasolabial fold). The gingival display is reduced immediately and improves up to 15th day and still effective up to 90th day

Keywords: Hyaluronic Filler Injection, Gummy Smile

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CHAPTER 1

INTRODUCTION

1.1 Introduction

A smile is everything that people want to see on our face. It is important for our daily life, because smiling can relieve our stress, enhance our immune system, elevate our mood, increase our productivity, make us a more positive person and look younger, the last thing is building the trust. So we need to smile everyday for that reasons and it is better if we smile perfectly.

The concept of a perfect smile is based on the balance among 3 parameters – the teeth (white) , the gum (pink) and the lips together while smiling, how the smile is harmony with the entire face. [1] An ideal smile, the upper lip sits just above the top of the teeth usually 0 to 2 mm above the teeth to be exact. Excessive gingival display (>2 mm) while smiling is known as “gummy smile” [2] which becomes a cause for esthetic embarrassment.

Correcting the gummy smile is a patient’s choice. When we smile and we feel our gum is too much exposed and it can haunt us and let us feel that is our single biggest source of self - consciousness and sometimes as well as make you embarrassed to smile or laugh in your whole life. So they will feel insecure while they smile. A lot of people will understand that feeling. Because everyone has something that they are really conscious about it. Do not feel alone and shameful. Because gummy smile can be corrected if you want.

Because gummy smile is very limited and rare conditions in which that can be medical concerned. It means there is no functional concern with gummy smile. If a person has gummy smile and he is happy with aesthetics, there is usually no need to fix it.

However, nowadays, people are more concerned about their smile as society gives an increasing importance currently. There are many treatments for gummy smile surgical or nonsurgical methods according to its etiology. For surgery, it includes lip reposition surgery and crown lengthening surgery. For non-surgical treatment, botox injection and lip filler injection can be done.

For me, I have asymmetrical gummy smile when I laugh intensely. Although it was not that obvious, I felt insecure about it. So I have been spending my time researching more about this topic. Then I noticed that botox is really a gold standard treatment for the treatment of gummy smile due to hyperactive lip muscle, even though the effect is temporary. But when I keep searching about it, HA fillers work on gummy smile too. It has their own case studies according to their clinical experiences. And this is the research of the effectiveness of HA filler in gummy smile treatment.

1.2 Research Question

Does injection of HA filler can improve in the treatment of gummy smile reduction?

1.3 Objectives

1.3.1 To evaluate that the hyaluronic acid filler injection really works in the treatment of gummy smile

1.3.2 To assess the onset and duration of action of HA filler in the treatment of gummy smile.

1.3.3 To evaluate the patient satisfaction after treatment with hyaluronic acid filler for the treatment of gummy smile.

1.4 Hypothesis

The injection of HA filler injection at canine fossa (3 mm lateral to the lateral alar cartilage) deep injection, 20 mg/ml is effective in the treatment of gummy smile due to muscular problems.

1.5 Conceptual Framework

For gummy smile patients, the etiology is due to (1) Excessive gum tissue covering the teeth, (2) The lip rises higher than it should, hyperactive lip muscle and short upper tip and (3) The upper jaw maxilla is taller than ideal, vertical maxilla excess. It has four types, anterior, posterior, mixed and asymmetrical type. Botox is widely used in the treatment of gummy smile especially on the hyperactive lip muscles. There are many papers of gummy smile treated with botox. For the filler injection to treat the gummy smile, the injection site is mostly upper lip to volumize it and release the gummy smile. Filler has the filling capacity, pushing and pulling effect so that it makes the lengthening of the upper lip and it releases the gummy smile. Here what I want to know about is injecting filler at the canine fossa near the nostril is safe and effective to have better result in the gummy smile correction due to muscular problems.

1.6 The Scope of the Research

This study is to evaluate the effectiveness of filler injection in gummy smile. The sample size, total 10 patients with the age of 20 to 40 years old patients were selected for this study, who are having gummy smile more than 2mm, using inclusion and exclusion criteria. They are injected with HA filler 0.3ml (ultraplus XC) single point deep injection at the canine fossa, for the reduction of excessive gingival display. Before and after treatment result are kept by measuring dental digital caliper: vertical distance from the zenith of gingiva of the upper right central incisor to the inferior border of the upper lip. Gummy smile volunteers who complaint about it were

explained thoroughly about the filler and injection technique and took consent forms. Satisfactory score and adverse factors or events were observed and recorded throughout the study.

1.7 Operational Definition

1.7.1 Effectiveness of Injection

Effectiveness is the capability of producing a desired result or the ability to produce desired output (the gummy smile length is reduced comparing baseline result) by using injection method.

1.7.2 Canine Fossa

A bony depression lateral to the incisive fossa which is larger, deeper and separated from it by the vertical ridge called canine eminence, corresponding to the canine tooth. (Grey Anatomy 20th edition)

1.7.3 Single Point Deep Injection, Up to the Supraperiosteal Level

Small amount of materials into the skin up to the bony level of canine fossa (3 mm lateral to the lateral alar cartilage). This injection technique is used for augmentation of the facial appearance, the volume restoration of the face and can be injected between the needle and skin is about 45-90 degrees in angle and up to the bony level.

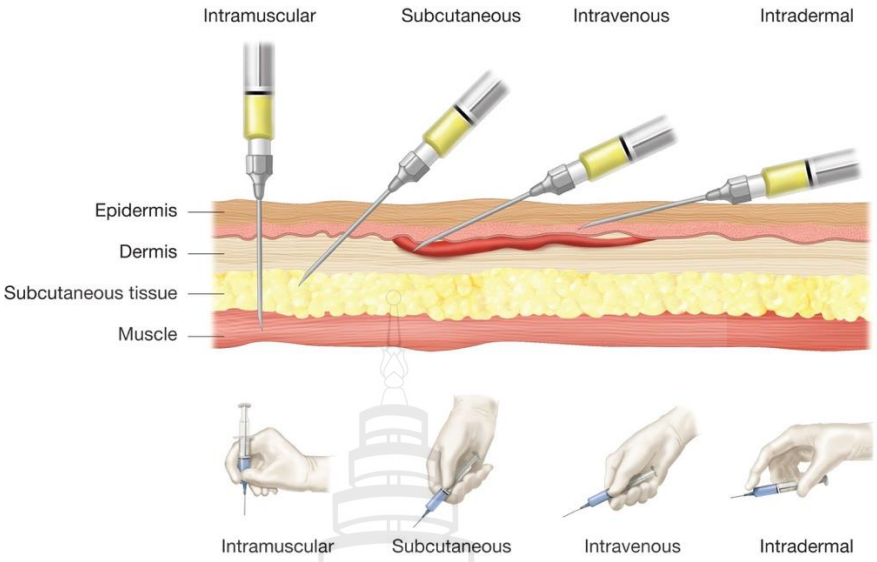


Figure 1.1 Singe point injection technique

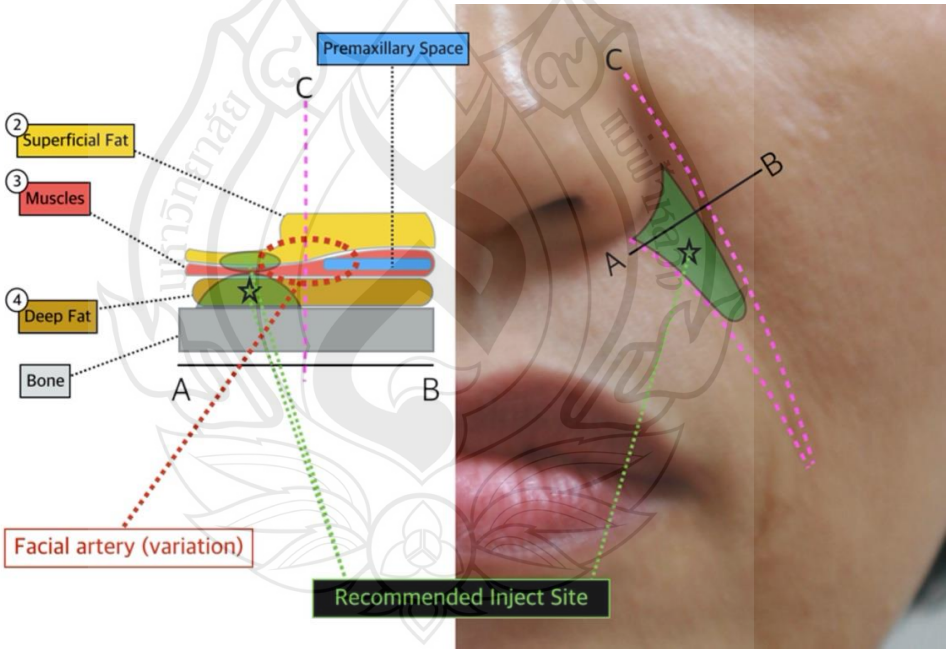


Figure 1.2 Injection point site

1.7.4 Hyaluronic Acid

Hyaluronic acid is usually found in skin and connective tissue. Polymers of hyaluronic acid can absorb water, forming gel like substance that assists in hydration and turgor. It also has the filling effect and can enhance the facial appearance such as volume restoration and augmentation of the face. So these days, HA is widely used for facial rejuvenation and augmentation for facial contouring.

The crosslinked hyaluronic acid filler, Juvederm Ultra plus XC: is a high quality product from the ALLERGAN French laboratory

1. Manufacturer : ALLERGAN
2. Innovative, patented technology, hylacross® technology, high cohesive
3. Hyaluronic acid concentration : 24 mg/mL
4. Volume per syringe : 1 ml , 27G needle

Figure 1.3 Juvederm ultra plus XC

CHAPTER 2

LITERATURES REVIEWS

2.1 Smile and Esthetics

The perfect smile depends on the three parameters – gum, lips and teeth.

In the esthetic of smiling, the gum plays an important factor; harmony is bound up with multiple criteria including gingival health, the alignment and shape of the tooth neck, an esthetically pleasing and harmonious smile line.

The teeth also takes part in enhancing your smile based on not only on their size, shape and color, but also on arcade symmetry, which is an aspect of overall intra and inter-arcade relations.

The lips, being the third important aspect and having great influence on an excellent smile, as they define the esthetic area. The figure of teeth and gum presented during smiling is considerably estimated by their inter-relation and length.

The smile line is primordial and it consists of three fundamental types. [3-4]
A high smile line which reveals the entire coronary height and a continuous band of gum is termed as the gummy smile.

A medium line, with 75-100% of anterior maxillary coronary height and the interproximal gum.

A low smile line, which shows less than 75% of anterior maxillary coronary height: males are more prominent in this type.

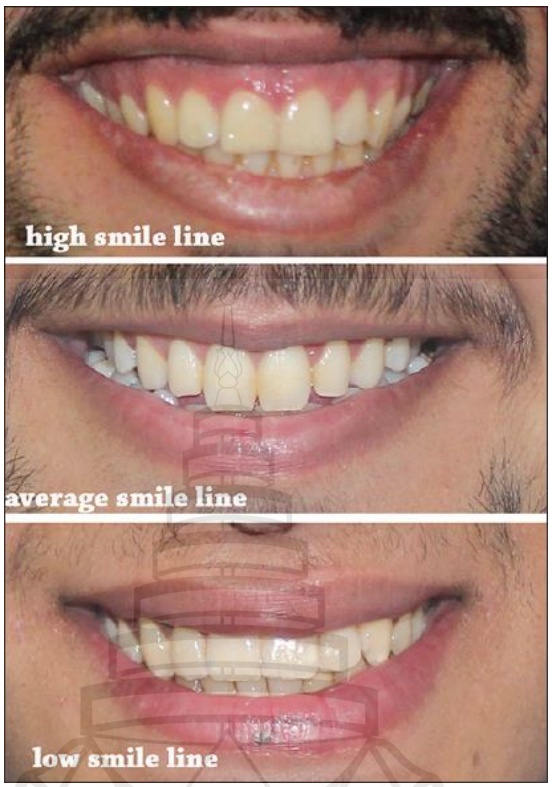
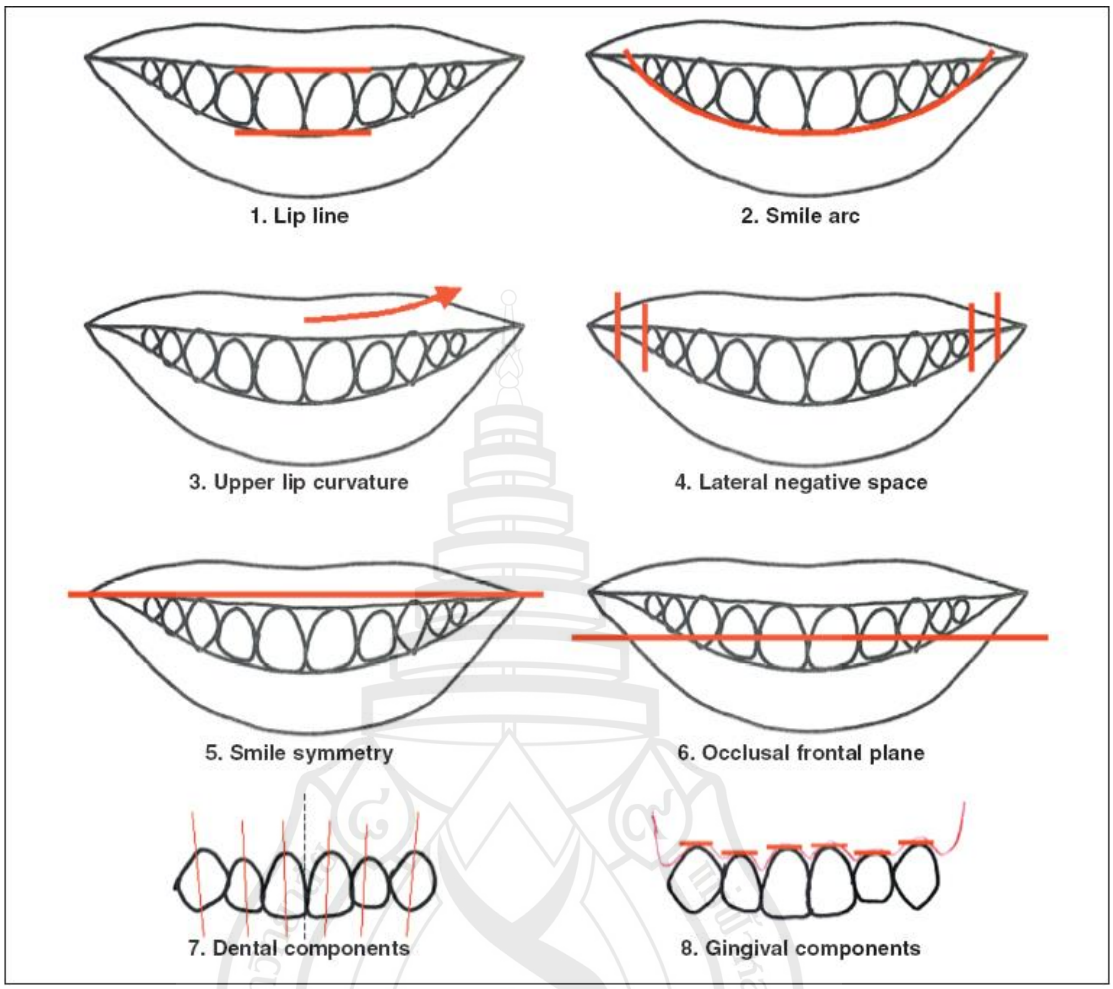


Figure 2.1 Different smile line

According to the Miller, the beautiful smile is described as follow [5]. The marginal gum along the maxillary teeth should be in harmony with the upper lip, and the incisor edge of the anterior teeth with the lower lip.

The left and right marginal gum should be mirror image to one another. The central incisors and canines should be about 13 mm in length and the lateral incisor should be 11-12 mm. The marginal gum line of the central incisors should be covered by the upper lip line. The incisor edge of the 6anterior maxillary teeth should be in accordance with the lower lip line. The size and shape of teeth are also critical in the perfect smile.



Source [6]

Figure 2.2 Components of balanced smile

So, an optimal smile is characterized by an upper lip that reaches the gingival margins, with an upward or straight curvature between the philtrum and commissures; an upper incisal line coincident with the border of the lower lip; minimal or no lateral negative space; a commissural line and occlusal frontal plane parallel to the pupillary line; and harmoniously integrated dental and gingival components.

2.2 Gummy Smile

A condition characterized by excessive exposure of maxillary gingiva during smiling ,more than 2 or 3 mm of the gum , it is called gummy smile, high smile line or gingival smile line. And it is confirmed by forced smiling. It has no functional defect. So it is up to the patient choice to correct it or not. It can be easily diagnosed, but determining the causes is complicated.

Figure 2.3 Gummy smile

2.2.1 Causes of Gummy Smile [1]

Having the knowledge of what causes a gummy smile is also necessary in order to maximize the effects of a treatment. There are three main causes – they can be combined in some cases.

Cutaneo-mucosal origin - short upper lip length, hyperactive lip muscle

Dento-periodontal origin - abnormal maxillary incisor size with short crowns, gum hypertrophy and hyperplasia, impaired passive eruption (dental development is delayed)

Alveolo-skeletal origin - vertical maxillary excess (longer lower third of the face in relation with the upper and middle thirds of the face), greater display of maxillary incisors at rest.

Prevalance of gummy smile 7% of male, 14% of female

Diagnosis of gummy smile [7] it is descriptive term, rather than a diagnosis. It has numerous factors and interplay of several etiologies.

To know the cause, we have to check the facial examination first. It is important to check the facial symmetry and proportion.

Secondly, we should measure the upper lip length. The upper lip length is measured in the sense that from the subnasale to lower border of upper lip at rest. Normal length in young adult female is 20-22 mm and in young adult male is 22-24 mm. The one less than 20 mm of the upper lip shows short upper lip length. The third one is to check the display of maxillary central incisors at rest. That can be seen in young women as 3-4 mm and in young men as 2 mm.The extent of exposure from the maxillary central incisor to lower border of upper lip should be 1 to 2 mm normally. And take a look for smile line. The elevation of the lip for the posed smile stopped at the gingival margin (<1-2 mm) is an average smile line.The last one is gingival margin outline, central incisors at the midline should be in symmetry while more lateral teeth are permitted to be asymmetry to a certain amount.

For the intraoral examination, we can check the occlusal plane which should closely coincide with the imaginary line connecting the commissures of the lip and two- thirds the height of retromolar pad. So during the smile, there is mild exposure of the tip of the mandibular canines and premolars. Anatomy, proportion, color of the teeth is checked to know the short clinical crown. The teeth should fit the rule of "Golden Proportion" 1:0.618 maxillary anterior teeth with the adjacent to it.

For the periodontal examination, the width and thickness of attached gingiva must be checked. There are 3 main biotypes 1thin and scalloped, 2 normal, 3 thick and flat. Surgical treatment is mainly determined by the above types.

2.2.2 Types of Gummy Smile

There are 4 types of gummy smile according to the area of the gum exposed. They are anterior type, posterior type, mixed type and asymmetry type. [8] Muscles that involve in gummy smile are lip elevators which are Levator labii superioris alaeque Nasi (LLSAN), Levator labii superioris (LLS), Zygomatic minor, Zygomatic major and Depressor septi nasi. [9] Anterior type is mainly cause by LLSAN Posterior type is due to Zygomatic major and Zygomatic minor Mixed type is because

of LLSAN, Zygomatic major and Zygomatic minor Asymmetrical type has one side only (LLSAN and /or Z major/minor ipsilateral)

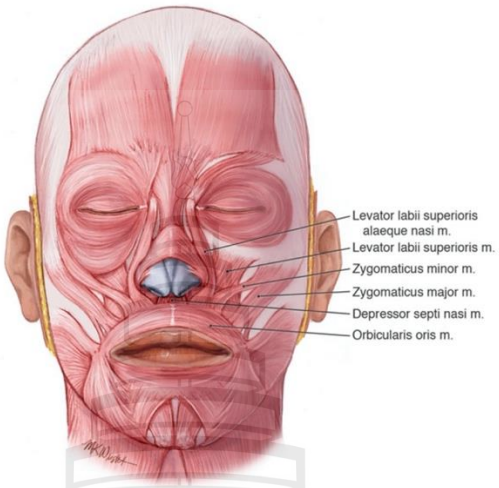


Figure 2.4 Different muscle involved in gummy smile

2.2.3 Treatment for Gummy Smile According to its Causes [10]

Table 2.1 Treatment for gummy smile according to its causes

Main Cause	Concern explained	Treatment methods
Excess gum tissue, short clinical crown	An overgrowth of tissue that covers too much of the teeth,	Gingivectomy, Crown lengthening by laser excision done by periodontist
Hyperactive lip muscle	The muscle that controls the lip raises too far, which exposes more of the gum	Botox injection treatment
Short upper lip	It cannot cover gingiva and their upper teeth	lip reposition surgery or orthognathic surgery
Vertical maxillary excess (VME)	A predominantly vertical facial growth (tall face)	Orthognathic surgery

2.3 Hyaluronic Acid

2.3.1 Discovery of Hyaluronic Acid

Hyaluronic acid is naturally found in living things, from microorganisms to higher life forms including human beings. It is a polysaccharide with a linear, non-branched structure, with a repetitive consequence of two elements, N-acetylglucosamine and glucuronic acid.

HA filler was first discovered by Karl Meyer and John Palmer, scientists at Columbia university, New York in 1934. The name hyaluronic is derived from hyalos (the Greek word for glass), it is isolated from a cow's eyes and the uronic sugar found in the substance. [11]

In 1960, researchers Balazs and Denlinger identified strong concentration of the molecule in other tissues, thus implying its main function in the body and setting the course into its medical purposes. It was then hyaluronic acid "modern era" commenced.

In order for the treatment of skin lesions, hyaluronic acid-based preparations were created in the early 1960s. In the 1980s, hyaluronic acid plan to heavily utilized during certain eye surgery procedures, such as cataract extraction was initiated.

The prime of Hyaluronic acid joint injections was portrayed by the 1980s. Then later into the 1990s, hyaluronic acid paved its way into the field of cosmetic industry, which is now the most recognized and in popular demand [12]

High concentrations of hyaluronic acid takes place in particular body areas in the dermis - both the deep underlying dermis, as well as the visible top layers of the epidermis and in the connective tissue; in the joint cartilage and the synovial fluid that fills the joint cavity; in the tendons and ligaments; in the vitreous body of the eye, where it was originally identified.

Hyaluronic acid is metabolized with astounding speed, and is replaced daily in the skin and joint fluid, therefore an appropriate correspondence between synthesis and degradation is crucial in order to maintain hyaluronic acid homeostasis in the body. The level of hyaluronic acid incorporating in a body lowers with age. As a consequent, loss of elasticity and volume in the skin leading to increased wrinkling

and joint problems, including osteoarthritis will begin to appear as a sign of ageing. And also it is used as new injectable material for skin augmentation that promises to be an ideal material. [11]

2.3.2 The Effect of HA Filler

Injectable HA is a type of temporary dermal filler. Injection of Hyaluronic acid into the skin causes water to be lured which in turn supports the skin to be more hydrated. The fat, muscle, bone and skin in our face starts to slim down as we grow older. As a result of deprivation of volume, sagging appearance of the face, fine line, wrinkles, folds and thin lips are inflicted. Injectable HA is then applied to diminish the appearance of fine line, wrinkles and folds and to build structure, framework and volume to the face and lips. The results can be witnessed instantly [13]

As we age (or due to disease), there will be volume loss and in order to counteract that hyaluronic filler is injected to provide the facial contour and maintain a youthful look. Hyaluronic filler differ depending on the concentration, cross linking density, particle site, duration and presence of lidocaine. High density, larger particle ones are used for deep dermal injection and low density for superficial cases. HA fillers are becoming to be high in demand due to its lower incidence of hypersensitivity, ease of usage, speedy recovery and quick impact. They are the most accomplished procedure in dermatological practice [14]

2.3.3 Clinical Uses of HA Filler Injection

Dermal fillers are gel-like substances that are injected into the skin to increase facial volume and enhance facial contours. It can also be used for the purposes of smoothing out lines around the facial features, rebuilding volume to sunken cheeks, plumping slender lips, improving facial feature symmetry and acne scar treatment. It is mainly used for facial rejuvenation and contouring of the face [15]

2.3.4 The Depth Level of HA Placement

2.3.4.1 Superficial dermis : fine line

2.3.4.2 Mid dermis : moderate wrinkle

2.3.4.3 Reticular dermis : Fold, groove, enhancement

2.3.4.4 Subcutaneous, periosteal : Augmentation

There are many types of dermal fillers available depending on the substance they contain. Only an skilled physician should perform the FDA approved branded dermal fillers to a patient.

2.3.5 Hyaluronic Filler

The main differentiation between HA fillers are

2.3.5.1 Source of HA

2.3.5.2 Concentration of HA

2.3.5.3 Type of cross-linking agent

2.3.5.4 Monophasic or biphasic

2.3.5.5 Presence of anesthesia

There are two main sources. The first is avian, predominantly in rooster combs. The second one is found in bacteria, which is a result of fermentation from Staphylococcus equinebacterium. The bacteria-sourced HA are now more sought after due to its relatively lower allergic reaction, purity and can be synthetically made.

Higher HA concentration is significantly used in deeper tissues which results in a longer period of effect and the lower concentration ones are used for superficial cases. The standard concentration of HA is now 20 mg/ml.

Earlier HA has single cross-link and used topically. However, more recent products are now either double or multiple cross-link and effectively last longer with the main use being in injection.

Concentration of HA, cost, cross linking- degree, quantity and type of technology used, G'elatic modulus, hydration,presence of lidocaine, needle size for injection ,sizing technology are factors to be considered in choosing hyaluronic acid filler. [16]

2.3.6 Hyaluronic Acid Filler

It is Monophasic and resorbable implant, highly cross-linked.

The HA concentration is 18-25mg/ml and has 2-3 millions Dalton molecular weight. It contains low protein concentration and low nendotoxin level <0.25 UE/gm. HA has uniform density and equal consistency. It is non-animal origin and highly purified for perfect biocompatibility.

Low viscosity for skin rejuvenation and high viscosity for augmentation

2.3.7 Side Effects of Hyaluronic Ecid [17]

2.3.7.1 Common side effect

1. Pain sensation
2. Odema or erythema around the injection site
3. Ecchymosis lasting 3 to 10days
4. Lump under the skin lasting 2days
5. Tenderness at injection point

2.3.7.2 Rare and peculiar side effects

Numbness and paranesthesia, Dizziness or syncope

2.3.7.3 Severe side effects

1. vascular compromised - swelling, dull aching pain, ischemia, blindness
2. Reaction of foreign body material, granulomatous formation
3. Infection, biofilm infection

2.3.8 Immediate Hypersensitivity Reaction

Rash, pruritus, allergic rhinitis, watery eyes, hay fever Dyspnea, wheezing, acute exacerbation of asthma, angioedema, anaphylaxis, shock

2.3.9 Contraindications of Hyaluronic Acid

2.3.9.1 Previously known allergy to Hyaluronic acid.

2.3.9.2 Hypersensitivity to gram positive bacteria protein.

2.3.9.3 Bleeding disorder

2.3.9.4 Injection into sites other than the labeling recommended sites.

2.3.9.5 The usage of Hyaluronic acid in pregnancy and lactating females and pediatric population have not been well established to be safe and effective.

2.3.10 Toxicity of Hyaluronic Acid

Hyaluronidase, an enzyme that can break down the hyaluronic acid. It can be used in overcorrection or superficial HA implantation. Inflammatory nodule or non-inflammatory nodule. Local or remote vascular occlusions. If an injection is administered intravascularly, the following procedure must be performed effectively. [18]

2.3.10.1 Stop the injection immediately.

2.3.10.2 Inject hyaluronidase under the dermis of the affected area; 100 units or more may be required.

2.3.10.3 Administer 1 tablet of aspirin.

2.3.10.4 Massage and apply warm compress.

2.3.10.5 Sildenafil (Viagra) and nitropaste should be considered if not effective.

2.3.10.6 Reassess every 1 hour and inject more hyaluronidase if needed.

2.3.10.7 If there is a high risk of tissue loss, hyperbaric oxygen referral should be carried out.

2.3.10.8 If vision field is compromised, notify the ophthalmologist and perform a retrobulbar hyaluronidase injection within an hour.

2.3.10.9 Antibiotics or steroids are not recommended.

2.3.11 The Usage of HA Filler Injection in Gummy Smile

Gummy smile is an excessive gum exposure (>2 to 3 mm) above the upper teeth during smiling and it may considered as unattractive, many people who having it will find the way to improve this condition.

It has different etiologies such as hyperactivity of the perioral muscle, length of lip and crown, excessive vertical growth of the maxilla bone, over-eruption of the maxillary anterior.

Gummy smile is treated by surgery but it is a slow and expensive procedure with a high rate of morbidity. Botox is gold standard treatment for the hyperactive lip muscle, having several reports in its efficacy. By using 2 or 3 units of botox injected through to 1 to 2 sites per side, hyperactive muscles can be treated.

24 mg/ml, high cohesive vycross hyaluronic acid is injected into or superficial muscle fibers and they can produce a small amount of reduction in muscle contraction, resulting in the decrease of gum exposure. In this way, we use Hyaluronic acid to treat the gummy smile.

2.3.12 Injection Site and procedure [19]

Evaluation	*Muscular Involvement*	*Injection Pt.*	*Dosage (mL)*	*Delivery*	*Depth*
Anterior (central)	Depressor septi nasi	Ant. nasal spine	0.2–0.4 mL	27-G needle	Deep (on bone) or intramuscular
	LLSAN	Canine fossa	0.2–0.3 mL/side		
Posterior (lateral)	Zygomaticus major and zygomaticus minor, and levator labii superioris	Canine fossa & Lower cheek	0.2–0.4 mL/side	Cannula	Deep subcutaneous to muscular layer
Mixed (full) type	Multiple	Lower cheek	0.4–0.5 mL/side	Cannula	Deep subcutaneous to muscular layer
Asymetric	One side of muscle involvement	Varies by case	Treat one side only	Varies by case	Varies by case

LLSAN, levator labii superior alaeque nasi.

Figure 2.5 Mummery of gummy smile type and hyaluronic acid filler injection methods

2.3.13 Facial Anatomy of Canine Fossa / Upper Part of Nasolabial Fold

A bony depression lateral to the incisive fossa which is larger, deeper and separated from it by the vertical ridge called canine eminence, corresponding to the canine tooth. (Grey Anatomy 20th edition)

2.3.14 How to Minimize the Vascular Complication by Injection

Through the canine fossa, the facial artery goes in the superficial muscular aponeurotic system (SMAS) layer or deep subcutaneous layer. The injection procedure should be done deep beneath the (SMAS) layer preferably nearer to the bone in order to prevent occlusion-related complications. Before injecting the filler, aspiration should be performed first and observe the patient for any signs of discomfort. [19]

2.3.15 Mechanism of Hyaluronic Acid Filler Deep Injection in That Area

To support the mechanism of action in this anatomical field, publish data are not currently available. It may be probably due to the muscle physiology, general property. As the muscle is compressed by the filler, the smaller bridges between the muscles are stretched and it decreases the partial contractile force of the muscle. [20]

CHAPTER 3

MATERIAL AND METHOD

3.1 Research Design

This study is quasi experimental study.

3.2 Subjects

Healthy volunteers of both female and male subjects, age between 20 to 40 years old, having gummy smile 2 mm above, but not more than 8mm who want to improve it due to muscular problems.

3.3 Sample Size

I took the result of previous study related to the use of botox for treating gummy smile because the paper using hyaluronic acid filler with gummy smile doesn't provide with statistic data.

The sample size was calculated by using 2 means dependent from the previous study of gummy smile treatment by botox. (Efficacy of botulinum toxin for treating gummy smile, Ahmeet Fatih Cengiz)

Previous study for 14patients having gummy smile treated

Before treatment, gummy smile is 4.96 mm +/- 1.82

After treatment, gummy smile is 2.48 mm+/- 1.85

$$n = (Z_{\alpha/2}+Z_{\beta})^2 \sigma^2 / d^2$$

whereas

d = 4.96-2.48 = 2.48

σ = 1.835

$Z_{\alpha/2}$ = 1.96

Z_{β} = 0.84

N = 9

For the drop out 10%, n = 10

3.4 Inclusion Criteria

3.4.1 Male and female healthy volunteers of age 20 to 40 years

3.4.2 Having chief complaint of mild and moderate gummy smile due to muscular problems above 2mm less than 8mm

3.4.3 All volunteers follow the research guideline, rules and can come to evaluate the clinical response every appointment.

3.4.4 All volunteers are required to sign an informed consent after being well explained.

3.5 Exclusion Criteria

3.5.1 Having too much exposed gummy smile more than 8mm due to severe dental and bony causes

3.5.2 Allergy to hyaluronic acid

3.5.3 Allergy to lidocaine

3.5.4 Current taking of anticoagulant

3.5.5 Diagnosis of any cutaneous pathology of infectious, inflammatory, autoimmune and diabetes and wound healing problems

3.6 Discontinuation Criteria

3.6.1 Volunteers could be withdrawn if any exclusion criteria becomes apparent or voluntary discontinuation.

3.6.2 If serious health disease occurs.

3.7 Intervention

The volunteers are treated with HA filler 24-mg/mL, high- cohesive Vycross hyaluronic acid (Juvederm ultra plus xc). Fillers can be injected into or superficial to muscle fibers, and their presence can create a partial decrease in muscular function, which can be used to treat the gummy smile.

3.8 Hyaluronic Filler (Ultra Plus XC)

The crosslinked hyaluronic acid filler, Juvederm Ultra plus XC: is a high quality product from the ALLERGAN French laboratory

1. Manufacturer : ALLERGAN
2. Innovative, patented technology, hylacross® technology, high cohesive
3. Hyaluronic acid concentration : 24 mg/mL
4. Volume per syringe : 1 ml, 27G needle

Figure 3.1 The crosslinked hyaluronic acid filler, Juvederm Ultra plus XC

3.9 Variable in the Study

3.9.1 Independent Variables

Hyaluronic acid filler

3.9.2 Dependent Variable

Measurement of the gummy smile line by using the dental caliper

Patient's satisfaction score

3.10 Study Procedure

3.10.1 Preparation of Research Subjects

3.10.1.1 By using inclusion and exclusion criteria, all volunteers are selected for the procedure.

3.10.1.2 All volunteers are explained well in all parts of the research including aim of study, method, benefits of research, goal and possible side effects before the treatment.

3.10.1.3 After the informative explanation of the research, all volunteers need to sign at informed consent sheets for participation in this study.

3.10.1.4 All volunteers' profile data are recorded.

3.10.2 Measurement of Gummy Smile

A the distance from subnasale to upper border of the upper lip

B the distance from the subnasle to the whole upper lip.

C the distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile (gingival display)

Measure A, B, C length by using Electronic Digital Caliper Orthodontic Tip Dental Caliper, before treatment.

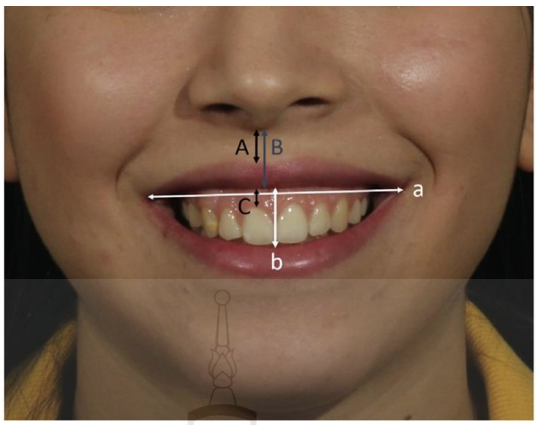


Figure 3.2 Measurement of gummy smile

Standardized pretreatment photographs of patients while smile are obtained. During the photo taking, the following are set:

1. Automatic focus
2. 12 megapixel solution
3. Take the photo during smiling from 30 centimeter apart
4. Good lightening and exposure

3.10.3 Treatment Procedure

Prior to the treatment, the volunteer's face is washed with mild soap. The sterile ice pack bag is used to minimize pain and swelling in the treatment area. Then, 0.3 ml of 20 mg/ml, high G hyaluronic filler is injected into canine fossa which is upper part of nasolabial fold,using 27G needle, deep injection, up to the bony level. Then inject into another side of the face. So total two injection points (0.6ml of high G hyaluronic filler) and reevaulate for the immediate effect of the treatment (the length of gingival display). Injection is done by well expereicend doctor by Arjan Rassapoom Sumaetheiwit.

Injection site

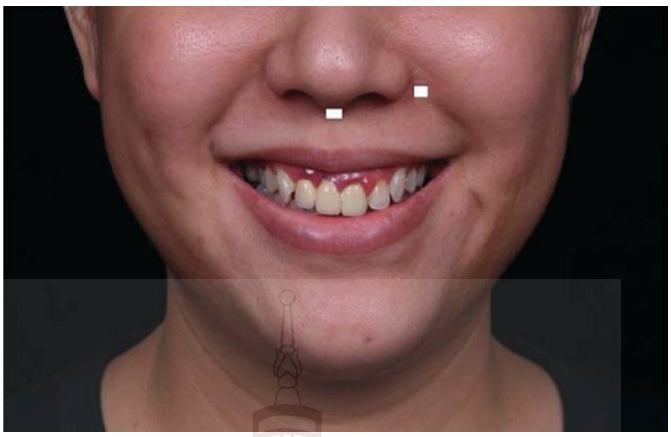


Figure 3.3 Immediately after the treatment

3.10.4 Follow Up

Immediately after the treatment, all subjects are taken photographs again to evaluate the immediate gummy smile improvement by using the dental clipper and taking standarized photographs.

All volunteers need to visit follow up at 0, 15^{th}, 90^{th} days after the treatment.

The researcher evaluated the subjects' side effect such as pain, redness, skin rash, itchniess, bruising, ischemia.

The researcher advised post treatment care to the subjects.

Their gummy smile photographs are recorded during the follow up. The researcher evaluatd side effects and treatment satisfaction at each follow up visit.

3.11 Outcome Measurement and Data Collection

Efficacy Evaluation

3.11.1 Investigator's Assessment

The investigator measured the gummy smile length (A, B, C) by dental clipper for in each follow up visit up to 90 days,

A the distance from subnasale to upper border of the upper lip

B the distance from the subnasle to the whole upper lip.

C the distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile.

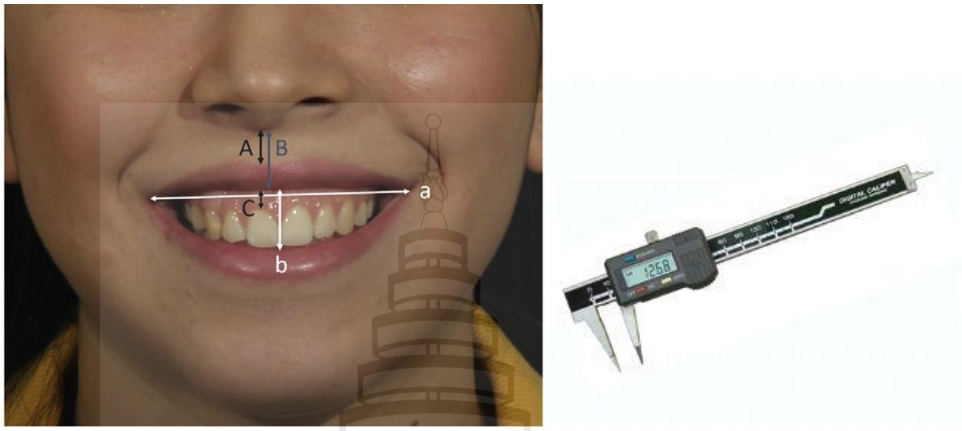


Figure 3.4 Site of Measurement by using Electronic Digital Caliper Orthodontic Tip Dental Caliper

3.11.2 Subject's Assessment

Satisfaction questionnaire about the treatment of filler in their gummy smile is asked and rated as 0 to 4 (0 = no satisfaction, 1 = little satisfaction, 2 = average satisfaction, 3 = more satisfaction, 4 = most satisfaction)

3.11.3 Side Effect Assessment

All subjects are asked about any side effects after injection like pain, redness, skin rash, itchniess, bruising, ischemia or other discomfort symptoms.

3.12 Statistic Used for Data Analysis

Significance levels for all analyses were set up P value <0.05. All these measurements during smile (A, B, C length) are done at baseline, immediately after filler injection and at each visit. Descriptive analysis was performed and calculated for mean length of A, B, C length at each time .Compare the result of the measurement A, B, C at baseline, after, 15 th, 90 th day by using repeated measure

ANOVA test if normal distribution and paired t test to compare between the pair such as immediate and baseline, baseline versus day 15. In case of non-normal distribution, use non-parametric, repeated measure, Friedman test and paired sign-rank test to compare the paired visit. Subjects' research profile data were analyzed by using descriptive statistical analysis to provide descriptive information such as percentages, means, modes, medians, ranges and standard deviations. Onset and Duration of action of injecting filler in the treatment of gummy smile was analysed from the data from each visit. Side effects, and subject's satisfaction after filler for gummy smile treatment were accessed by asking questionnaires.

3.13 Ethical Consideration

We have to follow the international ethical and scientific quality standard for designing, conducting, recording and reporting of the study under the good clincal practice (GCP) guidelines which involve the participation of human subjects, provided by international confrence on Harmoniation (ICH). The researcher respected the volunteer's rights.

1. Research was reviewed and approved by an ethic committee
2. The research protocol were clearly described
3. All participants are clearly understood about the research purpose, methodology, benefits and potential risks with signed in informed consent.
4. This study is conducted with appropriate risk managemtn by qualified researchers in an appropriate setting.
5. The researcher had to protect the privacy of volunteers an confidentiality of their information.
6. This study was done in accordance with Thai law and reguations as well as international norms and standards wth all qualifed drugs by Thailand Food and Drug Administration.

CHAPTER 4

RESULT

4.1 General Characteristic of the Sample

General demographic data of 10 participants were record and analyzed with descriptive statistics in the following table 4.1.

Table 4.1 Participants' demographic characteristic

Demographic	n = 10
Sex, n (%)	
Male	3
Female	7
Age (years)	
Mean ± SD	27.60±3.27
Min - Max	20 - 32
Occupations, n (%) (n = 9)	
Doctor	6
Officer	1
Housewife	1
Student	1
History of following treatment before this study	
No	10
Yes	0

According to collected demographic data of the participants, most of subjects were female (n=7) and male (n=3), respectively. The mean age of the subject was 27.60±3.27 years, and there were 6 Doctor, 2 students, 1 Officer and 1 Housewife. All subjects hadn't history of following treatment before this study.

4.2 Measurement of Gummy Smile

4.2.1 The Distance from Subnasale to Upper Border of the Upper Lip

Table 4.2 Statistical analysis of distance from subnasale to upper border of the upper lip on baseline, immediately, 15th, and 90th day (n=10)

	Distance (mm.) mean±SD	P-value
Baseline	11.31±1.74	<0.001*
Immediately	12.09±1.81	
Follow-up 15th day	12.13±1.75	
Follow-up 90th day	11.87±1.76	

Note P-value determine by Repeated measure ANOVA

* Statistically significant at the 0.05 level

According to the statistical analysis results from table 4.2, mean of distance from subnasale to upper border of the upper lip at baseline 11.31±1.74 mm., immediately 12.09±1.81 mm., follow-up 15th day 12.13±1.75 mm. and follow-up 90th day 11.87±1.76 mm. The mean of distance from subnasale to upper border of the upper lip was a statistically significant changed at the 0.05 level ($p<0.001$). Therefore, the multiple comparison test was performed as shown in figure 4.1.

Baseline	Follow-up 90th day	Immediately	Follow-up 15th day
(11.31)	(11.87)	(12.09)	(12.13)

Figure 4.1 The comparison of mean of distance from subnasale to upper border of the upper lip (measurement A) at baseline, follow-up 90th day, immediately and follow-up 15th day by line joining variables

The Unjoining line denotes that the pairs are significantly different. According to the comparison, follow-up 15th day has the most significant changes.

According to the Joining line comparisons results from figure 4.1, the distance from subnasale to upper border of the upper lip were statistically significant different between baseline versus immediately (change 0.780 mm., $p<0.001$), and follow-up 90th day (change 0.560 mm., $p=0.007$). However, the distance from subnasale to upper border of the upper lip were not statistically significant between immediately versus follow-up 15th day and follow-up 90th day ($p=1.000$ and $p=0.600$, respectively).

4.2.2 The Distance From the Subnasale to the Whole Upper Lip

Table 4.3 Statistical analysis of distance from the subnasale to the whole upper lip on baseline, immediately, 15th, and 90th day (n=10)

	Distance (mm.) mean±SD	**P-value**
Baseline	18.30±2.09	<0.001*
Immediately	19.10±2.19	
Follow-up 15th day	19.20±2.16	
Follow-up 90th day	18.99±2.23	

Note P-value determine by Repeated measure ANOVA

* Statistically significant at the 0.05 level

According to the statistical analysis results from table 4.4, mean of distance from the subnasale to the whole upper lip at baseline 18.30±2.09 mm., immediately 19.10±2.19 mm., follow-up 15th day 19.20±2.16 mm. and follow-up 90th day 18.99±2.23 mm. The mean of distance from the subnasale to the whole upper lip was a statistically significant changed at the 0.05 level ($p<0.001$). Therefore, the multiple comparison test was performed as shown in figure 4.2.

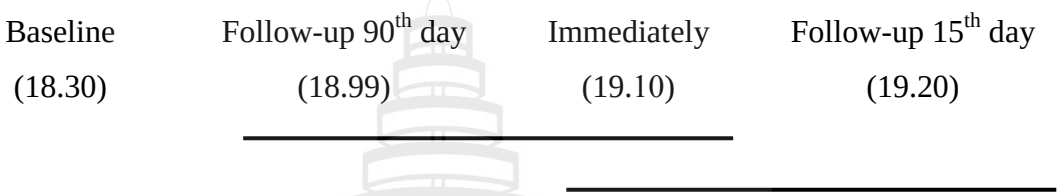


Figure 4.2 The comparison of mean of distance from the subnasale to the whole upper lip (Measurement B) at baseline, 90th, immediately and 15th day by line joining variables

The unjoining line denotes that the pairs are significantly different. According to the comparison, Follow-up 15th day has the most significant changes.

According to the joining line comparisons results from figure 4.2, the distance from the subnasale to the whole upper lip were statistically significant different between baseline versus immediately (change 0.800 mm., $p<0.001$), follow-up 15th day (change 0.900 mm., $p<0.001$) and follow-up 90th day (change 0.690 mm., $p=0.001$). However, the distance from the subnasale to the whole upper lip were not statistically significant between immediately versus follow-up 15th day and follow-up 90th day ($p=0.192$ and $p=1.000$, respectively).

4.2.3 The Distance Between the Gingival Margin of the Upper Central Incisor and Lower Marginal Line of the Upper Lip on Full Smile

Table 4.4 Statistical analysis of distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile on baseline, immediately, 15th, and 90th day (n=10)

	Distance (mm.) mean±SD	P-value
Baseline	4.50±0.97	<0.001*
Immediately	1.50±0.85	
Follow-up 15th day	1.50±0.85	
Follow-up 90th day	2.10±1.20	

Note P-value determine by Repeated measure ANOVA

* Statistically significant at the 0.05 level

According to the statistical analysis results from table 4.6, mean of distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile at baseline 4.50±0.97 mm., immediately 1.50±0.85 mm., follow-up 15th day 1.50±0.85 mm. and follow-up 90th day 2.10±1.20 mm. The mean of distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile was a statistically significant changed at the 0.05 level ($p<0.001$). Therefore, the multiple comparison test was performed as shown in figure 4.3.

Baseline	Follow-up 90th day	Immediately	Follow-up 15th day
(4.50)	(2.10)	(1.50)	(1.50)

Figure 4.3 The comparison of mean of distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile (Measurement C) at baseline, 90th, immediately and 90th day by line joining variables

The unjoining line denotes that the pairs are significantly different. According to the comparison, Immediately and Follow-up 15th day has the significant changes

According to the Multiple comparisons results from figure 4.3, the distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile were statistically significant different between baseline versus immediately (change -3.000 mm., p<0.001), follow-up 15th day (change -3.000 mm., p<0.001) and follow-up 90th day (change -2.400 mm., p<0.001), immediately versus follow-up 90th day (change 0.600 mm., p=0.031).

However, the distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile were not statistically significant between immediately versus follow-up 15th day (p=1.000).

4.3 Subject's Satisfaction Score

Table 4.5 Subject's satisfaction on follow-up 90th day

Satisfaction level	n = 10
Average satisfaction (2)	4
More satisfaction (4)	6

According to above table 4.5 showed subject's satisfaction on follow-up 90th day, most of subjects 6people rated as more satisfaction and 4 people rated as average satisfaction respectively.

4.4 Side Effects

The side effect found that in Hyaluronic acid filler injection in the treatment of gummy smile was pain in one subject.

CHAPTER 5

DISCUSSION, CONCLUSION AND SUGGESTION

5.1 Discussion

By injecting hyaluronic filler near the nasolabial fold (canine fossa) deep to the bone, can improve the gummy smile immediately and people are very satisfied. Here, the author wants to know it really works or it is effective. So 10 people with gummy smile average 4.5 mm exposure is taken and given the treatment. With immediate effect, gummy smile exposure average 4.5 mm to 1.5 mm, average 3 mm of gummy smile is reduced. With the statistic method, we can observe, the immediately gummy smile exposure average distance is significantly different than the original. We define filler treatment is effective immediately and it is still effective the same, until 15^{th} day. At 90^{th} days, it increased to gummy smile average 2.1 mm exposure. It means it does not go back to normal exposure and it is still working and effective. It is because when filler is injected into the canine fossa, the filler has partial decrease in lip muscle contraction, reducing the gummy smile exposure. Patient satisfaction is good (6 people gives more satisfaction and 4 people give average satisfaction). Pain is found as side effect in one subject during the procedure.

5.2 Conclusion

In conclusion, injecting hyaluronic filler near the nasolabial fold (canine fossa) deep to the bone is effective for the gummy smile treatment. The gingival display is reduced immediately and improves up to 15^{th} days and still effective up to 90 days.

5.3 Suggestion

For gummy smile correction, in order to get better result, Hyaluronic filler should be injected again after 90 days of duration or when the gum exposure turns back to preinjection state. It is not necessary to wait on the drug action as required when botox injections are performed.

For gummy smile correction, hyaluronic filler injection in the canine fossa can be used. In my opinion, it is better to use two or more injection sites together with adjacent muscles (zygomatic major and zygomatic minor) to have better result for much gummy smile exposure. Because here the author used only deep injection in the canine fossa and the effect was good.

Figure 5.1 Injecting hyaluronic filler near the nasolabial fold for gummy smile correction

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APPENDICES

APPENDIX A

RESEARCH ETHICS CERTIFICATE

The Mae Fah Luang University Ethics Committee on Human Research
333 Moo 1, Thasud, Muang, ChiangRai 57100
Tel: 053-917-170 to 71 Fax: 053-917-170 E-mail: rec.human@mfu.ac.th

หนังสือรับรองด้านจริยธรรมการวิจัย

COA: 081/2021

รหัสโครงการวิจัย: EC 20249-20

ชื่อโครงการวิจัย : ประสิทธิภาพของการฉีดฟิลเลอร์กรดไฮยาลูโรนิกในการรักษาการยิ้มเห็นเหงือก

ชื่อผู้วิจัยหลัก: แพทย์หญิงทาชิน แทด ทิน

สำนักวิชา: เวชศาสตร์ชะลอวัยและฟื้นฟูสุขภาพ

ผู้สนับสนุนทุนวิจัย: -

การรับรอง :

(1) โครงร่างการวิจัย	ฉบับที่ 3 วันที่ 18 เมษายน 2564
(2) เอกสารชี้แจงข้อมูลแก่ผู้เข้าร่วมโครงการวิจัย	ฉบับที่ 2 วันที่ 28 กุมภาพันธ์ 2564
(3) แบบแสดงเจตนายินยอม	ฉบับที่ 1 วันที่ 24 ธันวาคม 2563
(4) แบบบันทึกข้อมูล และ แบบประเมิน	ฉบับที่ 1 วันที่ 24 ธันวาคม 2563
(5) ข้อมูลประชาสัมพันธ์รับสมัครผู้เข้าร่วมโครงการวิจัย	ฉบับที่ 2 วันที่ 28 กุมภาพันธ์ 2564
(6) ผู้วิจัย และผู้วิจัยร่วม - แพทย์หญิงทาชิน แทด ทิน	

ขอรับรองว่าโครงการดังกล่าวข้างต้นได้ผ่านการพิจารณารับรองจากคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง ว่าสอดคล้องกับแนวทางจริยธรรมสากล ได้แก่ ปฏิญญาเฮลซิงกิ (Declaration of Helsinki) รายงานเบลมองต์ (Belmont Report) แนวทางจริยธรรมสากลสำหรับการวิจัยในมนุษย์ของสภาองค์การสากลด้านวิทยาศาสตร์การแพทย์ (CIOMS) และแนวทางการปฏิบัติการวิจัยที่ดี (ICH-GCP)

วันที่รับรองด้านจริยธรรมของโครงร่างการวิจัย: 27 เมษายน 2564

วันสิ้นสุดการรับรอง: 26 เมษายน 2565

ความถี่ของการส่งรายงานความก้าวหน้าของการวิจัย: 1 ปี

ลงนาม .....

(รองศาสตราจารย์ พลตรีหญิง แพทย์หญิง แสงแข ชำนาญวนกิจ)
ประธานคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง

The Mae Fah Luang University Ethics Committee on Human Research
333 Moo 1, Thasud, Muang, ChiangRai 57100
Tel. (053) 917-170 to 71 Fax. (053) 917-170 E-mail: rec.human@mfu.ac.th

ผู้วิจัยที่โครงร่างการวิจัยผ่านการรับรองจากคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง ต้องปฏิบัติดังต่อไปนี้

(1) ดำเนินการวิจัยตามที่ระบุในโครงร่างการวิจัยอย่างเคร่งครัด

(2) ใช้เอกสารชี้แจงข้อมูลแก่อาสาสมัครที่เข้าร่วมในโครงการวิจัย และเอกสารแสดงเจตนายินยอมเข้าร่วมการวิจัย / แบบสอบถาม / แบบบันทึกข้อมูล ที่มีตราประทับของคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง เท่านั้น

(3) ผู้วิจัยต้องส่งรายงานความก้าวหน้าของการวิจัย (AP 05/2019) ตามระยะเวลาที่คณะกรรมการฯ กำหนด และอย่างน้อย 30 วัน ก่อนหมดอายุการรับรอง ในกรณีที่การวิจัยยังไม่เสร็จสิ้น ผู้วิจัยต้องส่งจดหมายขอต่ออายุการรับรอง

(4) เมื่อมีการแก้ไขเพิ่มเติมโครงร่างการวิจัย ผู้วิจัยต้องส่งรายงานส่วนแก้ไขเพิ่มเติมโครงร่างการวิจัย (AP 06/2019) และโครงร่างการวิจัยที่มีการแก้ไขเพิ่มเติม เพื่อแจ้งให้คณะกรรมการฯ พิจารณารับรองก่อนดำเนินการตามที่ได้แก้ไขเพิ่มเติม (ยกเว้นในกรณีที่การแก้ไขเพิ่มเติมนั้นกระทำเพื่อความปลอดภัยของอาสาสมัคร)

(5) เมื่อมีเหตุการณ์ไม่พึงประสงค์ชนิดร้ายแรง "ในสถาบัน" ผู้วิจัยต้องส่งรายงานเหตุการณ์ไม่พึงประสงค์ชนิดร้ายแรง (AP 07/2019) ตามข้อกำหนดของ ICH-GCP

(6) เมื่อมีการเบี่ยงเบนหรือไม่ปฏิบัติตามโครงร่างการวิจัยที่ได้รับการรับรอง ผู้วิจัยต้องส่งรายงานการเบี่ยงเบนหรือไม่ปฏิบัติตามข้อกำหนด (AP 08/2019)

(7) เมื่อมีการยุติโครงการวิจัยก่อนกำหนดเวลาที่กำหนด ผู้วิจัยต้องส่งเอกสารแจ้งการยุติโครงการวิจัยก่อนกำหนด

(8) เมื่อการวิจัยเสร็จสิ้น ผู้วิจัยต้องส่งรายงานปิดโครงการวิจัย และ/หรือ สรุปผลการวิจัย (AP 09/2019)

ข้าพเจ้าในฐานะ ผู้วิจัย ยินยอมที่จะปฏิบัติตามข้อกำหนดดังกล่าว

.....

(แพทย์หญิงหาชิน แทด ทิน)

วันที่ 27.4.21

หมายเหตุ สามารถ Download แบบรายงานต่าง ๆ ได้ที่ https://ethic.mfu.ac.th

The Mae Fah Luang University Ethics Committee on Human Research
333 Moo 1, Thasud, Muang, ChiangRai 57100
Tel: (053) 917-170 to 71 Fax: (053) 917-170 E-mail: rec.human@mfu.ac.th

CERTIFICATE OF APPROVAL

COA: 081/2021

Protocol No: EC 20249-20

Title: The effectiveness of Hyaluronic acid filler injection in the treatment of gummy smile

Principal investigator: Thazin Thet Tin, M.D.

School: Anti-Aging and Regenerative Medicine

Funding support: -

Approval:

1) Research protocol — Version 3 Date April 18, 2021
2) Information sheet for research project participants — Version 2 Date February 28, 2021
3) Informed consent form — Version 1 Date December 24, 2020
4) Case record form and Assessment form — Version 1 Date December 24, 2020
5) Research participant recruitment information — Version 2 Date February 28, 2021
6) Principal investigator and Co-investigators
   - Thazin Thet Tin, M.D.

The aforementioned documents have been reviewed and approved by the Mae Fah Luang University Ethics Committee on Human Research in compliance with international guidelines such as Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use - Good Clinical Practice (ICH - GCP)

Date of Approval: April 27, 2021

Date of Expiration: April 26, 2022

Frequency of Continuing Review: 1 year

(Assoc. Prof., Maj. Gen. Sangkae Chamnanvanakij, M.D.)

Chairperson of the Mae Fah Luang Ethics Committee on Human Research

The Mae Fah Luang University Ethics Committee on Human Research
333 Moo 1, Thasud, Muang, ChiangRai 57100
Tel. (053) 917-170 to 71 Fax. (053) 917-170 E-mail: rec.human@mfu.ac.th

For all investigators approved by the Mae Fah Luang University Ethics Committee on Human Research (MFU EC) must comply with the followings:

1. Strictly conduct the research as required by the protocol
2. Use only the information sheet, consent form, questionnaire and case record form bearing the MFU EC stamp of approval
3. Send a progress report (AP 05/2019) for continuing review and for renewing the approval at least 30 days before expiration date.
4. When there are changes of the protocol, the investigator must send an amendment report (AP 06/2019) with amended protocol for MFU EC approval before implementing any changes in the research (unless those changes are required urgently for the safety of the research subjects).
5. When there is any unanticipated problem or severe adverse event, the investigator must send a safety report (AP 07/2019) as set forth in the ICH-GCP.
6. When there is any deviation or non-compliance with the approved protocol, the investigator must send a protocol deviation/non-compliance report (AP 08/2019).
7. When the research stops before planned schedule, the investigator must send a premature termination document.
8. When the research finishes, the investigator must send a final report (AP 09/2019).

I, as an investigator, agree to comply with the above obligation.

.....

(Thazin Thet Tin, M.D.)

Date 27.4.21

Please go to https://ethic.mfu.ac.th to download MFU EC forms for reporting.

APPENDIX B

GRAPH

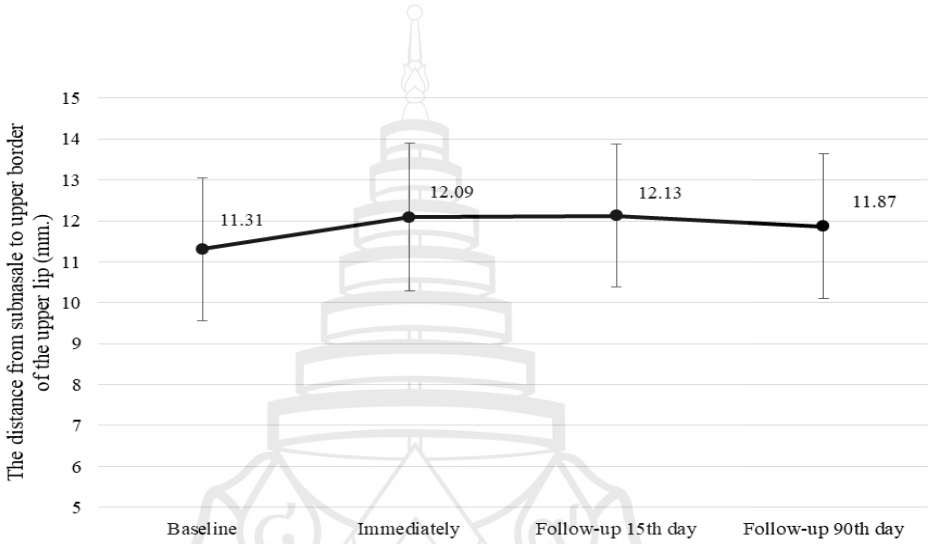

Figure A1 Line graph showing distance from subnasale to upper border of the upper lip

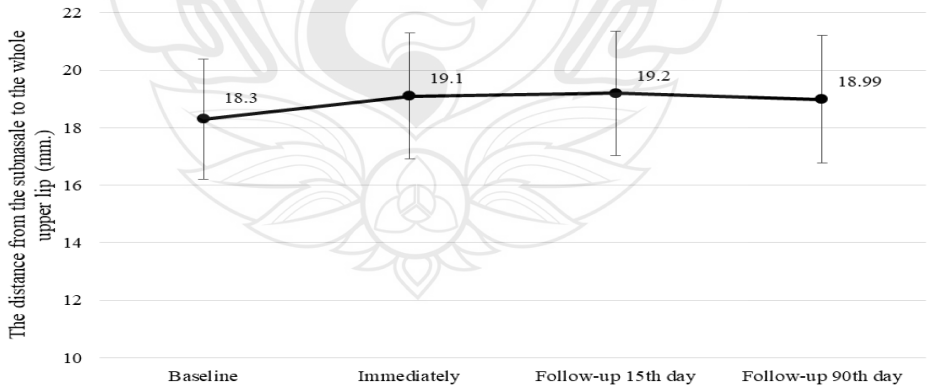

Figure A2 Line graph showing distance from the subnasale to the whole upper lip

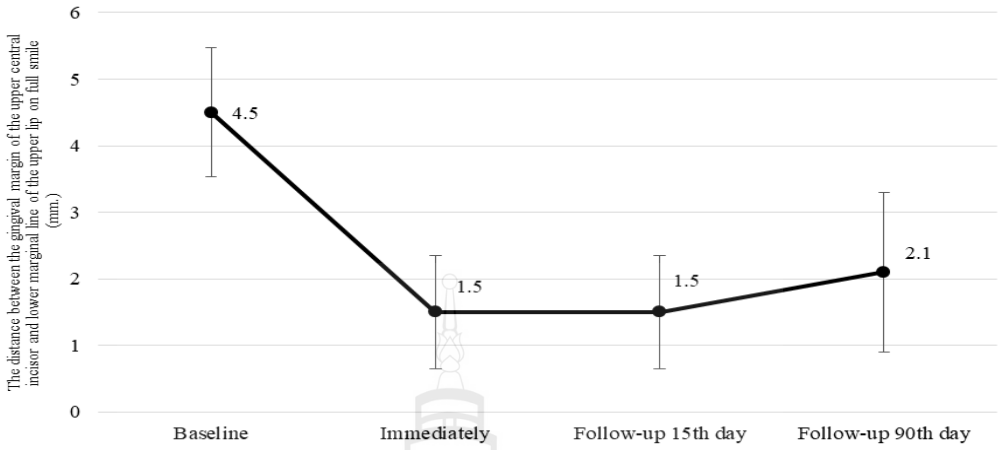

Figure A3 Line graph showing distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile

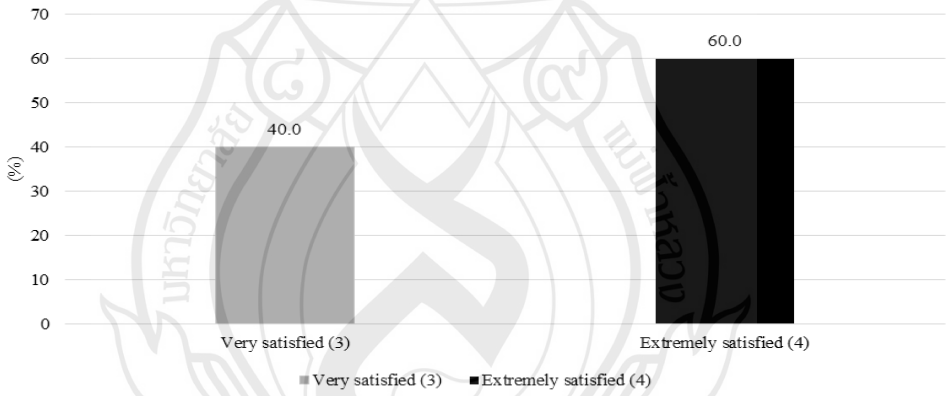

Figure A4 Bar chart revealing the percentage of subject's satisfaction on follow-up 90th day

APPENDIX C

CASE REPORT FORM, QUESTIONNAIRE, SATISFACTION RECORD FORM

RESEARCH PROFILE (CONFIDENTIAL)

Volunteer Number……..

General information (Only official)

1. Date
2. Name
3. Hospital number
4. Address
5. Tel
6. Email
7. Gender
8. Age .....year
9. Occupation
   - .....1. Government officer
   - .....2. Employer
   - .....3. Housewife
   - .....4. Student
   - .....5. Employee
   - .....6. Others
10. Underlying disease
11. allergy to hyaluronic acid filler
12. allergy to lidnocaine
13. previous history of botox treatment within 6months No ( ) Yes ( )
14. previous history of filler treatment within 6months No ( ) Yes ( )
15. history of surgery of face or nose
16. Personal medication and supplement
    a. Active inflammatory skin disease, open wound in the treatment area
    b. History of malignant or premalignant lesions in the treatment area
13. History of food or drug allergy
14. Current facial product use
15. History of following treatment before the study
    - .....1. Yes (Identify.....)
    - .....2. No

    O Ablative and non-ablative laser
    O Intense pulse light
    O Microdermabrasion
    O Skin needling
    O Chemical peeling
    O Facial whitening treatment
    O Facial whitening agent

RESEARCH RECORD: RESEARCHER'S PART
CASE RECORD FORM, CRF

1. **Measure the length of gummy smile during smiling by using the dental Vernier caliper**

   A the distance from subnasale to upper border of the upper lip

   B the distance from the subnasle to the whole upper lip.

   C the distance between the gingival margin of the upper central incisor and lower marginal line of the upper lip on full smile

By use of dental Vernier caliper	No.	Length in mm
Week 0, before treatment	A	
	B	
	C	
Week 0,immediately after treatment	A	
	B	
	C	
Day 15th	A	
	B	
	C	
Day 90th	A	
	B	
	C	

By reducing the length of "C" at each visit shows the improvement of the treatment.

2. **Treatment Satisfaction Score**

Satisfactory evaluation by Volunteers (Please draw the circle on 12th Week)

0	1	2	3	4

Score 0= no satisfaction
Score 1= little satisfaction
Score 2= average satisfaction
Score 3= more satisfaction
Score 4= most satisfaction

3. **Side Effect Record (for researcher's evaluation)**

Side effect (if has) ..... in week .....
Treatment.....
Result.....

CURRICULUM VITAE

CURRICULUM VITAE

NAME	Miss Thazin Thet Tin
DATE OF BIRTH	16 August 1991
ADDRESS	No 19/A, Boyarnyunt Street, Dagon Township, Yangon, Myanmar

ADUCATIONAL BACKGROUND

2014	Bachelor of Medicine and Bachelor of Surgery, MBBS Yangon, University of Medicine, Myanmar

WORKING EXPERIENCE

2018	Medical, Singaporean aesthetic clinic in yangon (novu clinic), Myanmar
2016-2017	Medical, Korean aesthetic clinic in yangon (cosmo clinic), Myanmar
2015	Medical, Polyclinic in yangon, Myanmar