Original Article

A Comparative Study of Nasolabial Fold Depth Measurements Using Clinical Grading, Photography, and Ultrasound

WEIWEI DONG[1], SOPHIA SI LING HENG[2], FIRDAUS HAYATI[3]*

[1]Phd Candidate, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS88400 Kota Kinabalu, Sabah, Malaysia. 88450
Email: dongweiwei0805@gmail.com
ORCID ID: https://orcid.org/0009-0006-2462-8320
[2]MD, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS88400 Kota Kinabalu, Sabah, Malaysia. 88450
Email: sophia.hsl@ums.edu.my
ORCID ID: https://orcid.org/0000-0001-6522-3705
[3]Associate Professor, MD, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS88400 Kota Kinabalu, Sabah, Malaysia. 88450
Email: m_firdaus@ums.edu.my
ORCID ID: https://orcid.org/0000-0002-3757-9744

Abstract

Objective: The present study conducted to assess and compare the comparative study of nasolabial fold depth measurements using clinical grading, photography, and ultrasound. **Methodology**: A total 0f 150 participants was included men and women aged 20-65 who will seek regenerative therapies to improve NLF. The sample size was determined based on power analysis, taking into account the expected effect size, the required level of statistical significance, and statistical power. Recruitment of participants was carried out through collaboration with aesthetic clinics and centers specializing in facial rejuvenation surgery. The treating investigator administered HA filler Restylane (Q-Med) to all participants in the study. The evaluations were conducted using the Modified Fitzpatrick Wrinkle Scale (MFWS), a clinical scoring system that relies on photographic scales, high-frequency ultrasound imaging, and the Modified Fitzpatrick Wrinkle Scale. **Results:** A cohort of 150 participants (25 males and 125 females) with an average age of 45.1±7.8 years. A notable enhancement of the Modified Fitzpatrick Wrinkle Scale in relation to the baseline was seen across all treatment indications examined after 21 days of intervention (all $p<0.0001$). The scores for the nasolabial fold and marionette lines shown substantial improvement in comparison to the initial measurements throughout all subsequent visits ($p \leq 0.001$ for all). The average values for nasolabial folds shown a significant improvement, decreasing from an initial mean of 5.0±0.5 to 2.0±.05 after 21 days. The use of soft-tissue fillers for nasolabial folds resulted in significant enhancements in collagen levels and increased density of newly formed collagen, as seen using high-frequency dermal ultrasonography. There was a notable rise in dermal density, specifically tissue echogenicity, in the nasolabial folds at all subsequent visits compared to the first measurement (all $p \leq 0.001$). **Conclusion:** This research shows the first evaluation of clinical assessment/grading has easy and accurate outcome as ultrahigh frequency ultrasound (UHFUS) and photograph.

Keywords: Nasolabial Fold Depth, Clinical Grading, Photography, Ultrasound

Introduction

The process of facial ageing is a multifaceted phenomenon characterised by a multitude of structural and physiological alterations occurring in both the skin and underlying tissues. The deepening of nasolabial folds (NLF) is a prevalent aesthetic issue among individuals as they exhibit evident indicators of facial ageing. The nasolabial fold (NLF) is a facial feature that spans from the lateral aspects of the nose to the commissures of the mouth. As individuals progress in age, the formation of these creases intensifies and manifests as more prominent features, hence contributing to the perception of ageing and weariness. (Figure 1).

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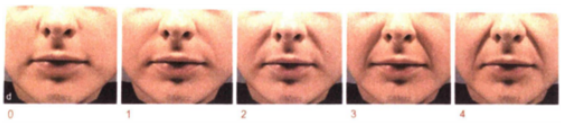

Figure 1: Nasolabial fold[1]

In recent times, there has been an increasing scholarly focus on medical aesthetic regenerative therapies that target the ageing process of nasolabial folds (NLF). Nevertheless,

Address for Correspondence: Associate Professor, MD, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS88400 Kota Kinabalu, Sabah, Malaysia. 88450
Email: m_firdaus@ums.edu.my

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there exists a dearth of standardised assessment systems tailored specifically for Asian populations, with a particular emphasis on the Chinese demographic. Current assessment approaches frequently depend on subjective evaluations or generic measures that may not sufficiently capture the distinct attributes of non-linear fluid ageing within this demographic. The global medical cosmetology industry experienced a notable expansion in its market size, increasing from $126 billion in 2017 to $142 billion in 2021. This rise can be attributed to an average annual growth rate of around 3%. The market size of the medical beauty business is expected to rise due to the development of individuals' living standards and the increasing popularity of the "beauty economy". According to projections, the worldwide aesthetic medicine market is expected to surpass $120 billion by the year 2023. Hence, the establishment of an ageing assessment system for nasolabial folds (NLF) specifically tailored to Asian populations, particularly the Chinese, is imperative. This system should encompass a thorough examination of facial anatomical characteristics and age-related changes in the nasolabial folds among Chinese individuals. Its primary objective would be to furnish clinicians with a quantitative and objective tool for assessing NLF, enabling them to devise personalised treatment strategies and monitor the efficacy of interventions. Wrinkles are characterised as depressions on the epidermal layer of the skin, exhibiting a range of textures and exhibiting varying degrees of prominence, contingent upon their respective levels of depth. This research will focus on Asian communities, primarily Chinese populations, in order to investigate their unique face features and cultural influences. The scope of the project will encompass a comprehensive review of relevant literature, an analysis of existing methods for assessing nasolabial folds (NLF), and the development of tailored assessment tools.

Nasolabial folds, also known as the lines that manifest bilaterally adjacent to the lips, serve as a prominent indicator of the ageing process in the facial region. The formation of these folds can be ascribed to physiological alterations in fibroblasts, specialised cells accountable for the synthesis of collagen, elastin, and glycosaminoglycan (GAG). The alterations encompass the deterioration of collagen and elastin fibres, the thinning of the skin, the drop in levels of hyaluronic acid (HA) leading to a reduction in skin volume, and the dryness of the dermis.

Hyaluronic acid (HA) plays a crucial role in preserving the skin's hydration and elasticity. This glycosaminoglycan is primarily responsible for these functions. The process of HA binding with water molecules results in substantial skin hydration. Moreover, hyaluronic acid (HA) plays a pivotal function in cellular proliferation and the formation of the intercellular matrix within the dermis. Additionally, it aids in the creation of a viscoelastic framework that establishes a connection between collagen and elastin fibres. Due to the aforementioned advantages, hyaluronic acid (HA) is widely recognised as a superior option for dermal fillers. Facial rejuvenation procedures primarily aim to restore volume in order to enhance the features of the face.

The reduction of wrinkles and the attainment of a more youthful appearance can be accomplished by the application of injectable dermal fillers. These substances efficiently diminish the visibility of wrinkles, so enhancing the overall aesthetic of an individual. Injectable fillers, such as hyaluronic acid (HA), are commonly employed within the field of plastic surgery and cosmetic medicine. These compounds encompass a wide array of substances and can be supplied using various injection techniques in order to target wrinkles and improve skin laxity. The phenomenon of facial ageing comprises a multitude of elements that impact the various tissues within the facial region. The natural phenomenon is subject to several influences, including as bone remodelling, muscle atrophy, deflation and relocation of fat compartments, as well as the decline in skin elasticity, wetness, and smoothness. The user's material is insufficient in length to be reformulated academically. The age-related alterations that contribute to the clinical signs of facial ageing encompass lip atrophy, marionette lines, and an augmented nasolabial fold. The aforementioned alterations have been associated with a decline in perceived beauty, psychological well-being, and general life satisfaction. The given sequence encompasses the set of integers.

Consequently, therapies frequently sought in clinical practise encompass operations intended to augment lip volume and contour, as well as ameliorate the severity of nasolabial folds and marionette lines. When expertly administered, the use of hyaluronic acid-based soft-tissue fillers is a cost-effective, safe, reliable, and reproducible strategy for meeting patients' aspirations for facial rejuvenation through minimally invasive techniques. The numeral 8 is now under discussion.

Given the extensive array of injectable medical devices currently accessible in the market, it is imperative to undertake clinical outcome studies to examine the immediate and long-term effects of these devices. Conducting such studies is crucial in order to support informed decision-making processes and assist both patients and practitioners in choosing the most appropriate goods.

In contemporary times, the utilisation of three-dimensional (3D) imaging and advanced ultrasound technology has demonstrated its efficacy as a valuable method for evaluating the nasolabial fold (NLF). This methodology is particularly advantageous due to its noninvasive nature, expeditiousness, and capacity to provide precise outcomes. The study focuses on individuals aged 17 to 21 years. However, the measurement of changes in the NLF may provide challenges due to its complicated nature and lack of clearly defined boundaries. The evaluation process is complex, and the results may vary depending on the specific attributes of the NLF.

The objective of this study is to examine and contrast different clinical grading methods, including photography and ultrasonography, for the assessment of the depth of nasolabial folds (NLF) in Asian individuals, namely those of Chinese descent.

Scope of the Study

The study will specifically target Asian populations, with a particular emphasis on Chinese populations due to their

distinct facial features and cultural factors. The research will encompass a thorough examination of relevant literature, an evaluation of existing methods for assessing nasal alar flare (NLF), and the creation of customized assessment systems.

Significance of the Study

With the increasing trend of population aging and the uniqueness of Asian facial aesthetics, Asian people are gradually paying more attention to nasolabial creases. However, current nasolabial crease assessment tools are mainly based on studies in Western populations, and their applicability and accuracy have not been fully validated in Asian populations. Therefore, this study aims to establish an assessment system for nasolabial crease aging focusing on Asian populations (Chinese), to deeply study the facial anatomical features and age-related nasolabial crease changes in Asian populations (Chinese), and to provide clinicians with a reliable assessment tool to address the current gap in NLF aging assessment in Asian populations,

Literature Review

Assessment of Nasolabial Crease

In facial aesthetic treatments, the most important indicator to measure the outcome of the treatment is patient satisfaction. However, given the uncertainty of patient perception and outcome expectations, as well as the lack of treatment goals that are easily defined or standardized, any assessment of postoperative efficacy is necessarily subjective. The recognition of the need for evidence-based approaches to assessing the effectiveness of different aesthetic treatments requires a more objective and quantitative approach to patient-relevant measurement and evaluation tools.

The assessment of nasolabial crease usually includes two methods: primary and objective observation evaluation. The main observation evaluation method uses the wrinkle scale to score (Figure 2). The depth, length, width, etc. of the nasolabial crease are evaluated by a professional doctor based on comparative photographs or direct observation of the patient's facial features, and a corresponding score is given. Meanwhile, objective observation evaluation method: uses imaging and biophysical measurement. Imaging measurement is an objective evaluation of the shape, depth, width, etc. of nasolabial creases using various medical imaging equipment, whereas, biophysical measurement is the use of biophysical measurement techniques to measure the tissue properties of the nasolabial fold to assess the degree of change (Fig 2).

Rating Score	Wrinkle Severity at Rest	Description
0	Absent	No visible wrinkles
1	Minimal	Minimal wrinkles, within 1.5 cm radius of the lateral canthus and may be minimally etched
2	Mild	Shallow wrinkles, extending between 1.5 to 2.5 cm radius of the lateral canthus and may be minimally etched
3	Moderate	Moderately deep wrinkles, extending between 1.5 to 2.5 cm radius of the lateral canthus and moderately etched
4	Severe	Very deep wrinkles, exceeding 2.5 cm radius of the lateral canthus and may be deeply etched

Figure 2 :The Wrinkle Severity Rating Scale[2]

Table 2,3,4 summarize different nasolabial crease evaluation scales using multiple approaches. Table 1 summarizes descriptive grading methods where the applications of each evaluation criterion were highlighted such method highly depends on the experience and subjective opinion of the practitioners. Table 2 summarizes the photo grading method where the practitioners observes the severity of NLF depending on the available photo. Table 3 summarizes the self-assessment method where the patients' satisfaction post treatments are taken into consideration. In the revolution of the beauty industry, multiple cutting-edge imaging instruments were employed to evaluate the NLFs (Table 4) where more objective bases outcomes could be performed. Pro and cons of each instrument-based method are enlisted. The biophysical measurement methods where there are non-invasive methods had been employed to evaluate the hydro-contain and skin laxity (Table 5).

Table 1: Short listed descriptive grading of the main observation method of nasolabial creases

No	Evaluation method	Assessment structure	Clinical application	Reference
1	Glogau Scale	● Grade I (no wrinkles). ● Il grade (wrinkles appear when doing movements). ● Grade III (wrinkles that appear at rest). ● Grade IV (wrinkle only, i.e. almost no wrinkle-free skin).	Assess the degree of aging of facial skin	Monheit GD *et al.*[7]
2	Fitzpatrick Wrinkle Scale(FWS):	● Grade 1 is shallow wrinkles, score 1-3 points, mild degeneration of elastic tissue, that is, subtle tissue changes with slightly deepened skin lines ● Grade 2 is shallow to medium-deep wrinkles, moderate number, moderate degeneration of elastic tissue, that is, obvious papular elastic tissue degeneration, yellow translucent papules, skin discoloration ● Grade 3 is shallow to deep wrinkles, massive, with or without skin folds, severe degeneration of elastic tissue, i.e., polypapular and fusion elastic tissue degeneration, thickening, yellow or pale rhomboid skin on the neck	Evaluation of the effect of laser skin remodeling	Shoshani D *et al.*[8]
3	Nasolabial fold wrinkle scale (NCWS).	● Grade 0: No wrinkles or only fine superficial wrinkles. ● Grade 1: Mild wrinkles, but not yet noticeable. ● Grade 2: Moderate wrinkles, visible on static or minor expressions. ● Grade 3: Severe wrinkles, visible at static or slight expressions. ● Grade 4: Extremely severe wrinkles, visible at rest.	Assess the condition of nasolabial fold tissue in people of different ages and genders	Stefura T *et al.*[6]

Table 2: Short listed photo grading method for the main observation and evaluation of nasolabial creases

No.	Evaluation method	Assessment structure	Clinical application	Reference
1	Wrinkle Severity Rating Scale (WSRS)	● 1. Absent: No visible fold. continuous skin line. ● 2. Mild: Shallow but visible fold with a slight indentation; minor facial feature. Implant is expected to produce a slight improvement in appearance. ● 3. Moderate:Moderately deep folds. Clear facial features visible at normal appearance but not when stretched. Excellent correction is expected from injectable implants. ● 4. Severe Very long and deep folds; prominent facial features. Less than 2mm visible fold when stretched. Significant improvement is expected from injectable implant. ● 5. Extreme Extremely deep and long folds are detrimental to facial appearance.2-4mm Visible V-shaped fold when stretched. Unlikely to have satisfactory correction with injectable implant alone.	It is used to evaluate wrinkles at rest	Monheit GD *et al.*[7]
2	Modified Fitzpatrick Wrinkle Scale (MFWS).	● 0F: No wrinkle. No visible wrinkle; contin- uous skin line. ● 0.5F: Very shallow yet visible wrinkle. ● 1F: Visible wrinkle and slight indentation. ● 1.5F: Visible wrinkle and clear indentation. o1-mm wrinkle depth *. ● 2F: Moderate wrinkle. Clearly visible wrin- kle, 1- to 2-mm wrinkle depth * ● 2.5F: Prominent and visible wrinkle. ● 3F: Deep wrinkle. Deep and furrow wrinkle; more than 3-mm wrinkle depth.	It is used to evaluate wrinkles at rest	Shoshani D *et al.*[8]
3	Merz Nasolabial Fold Scale (MNLF)	● 0F: No wrinkles ● 1F: Slightly wrinkled ● 2F: Moderate wrinkles ● 3F: Visible wrinkles ● 4F: Severe wrinkles	Used to evaluate facial wrinkles at rest	Pruettijarai U *et al.*[9]

Table 3: Patient self-test satisfaction scale

No.	Evaluation method	Assessment structure	Clinical application	Reference
1	Global Aesthetic Improvement Scale, GAIS	● Deteriorate(0):The appearance is not as good as the initial state. ● Invalid(1):The appearance is basically the same as the initial state. ● Slightly Improved(2):Compared with the initial state, the appearance is obviously improved, but still needs to be trimmed. ● Significantly Improved(3): Compared with the initial state, patients at this level have significantly improved, but the best improvement effect has not been achieved. ● Completely Improve(4):The patients of this level have achieved the best cosmetic effect through implant materials.	Patients subjectively evaluate their satisfaction with the effect after treatment	Kopera D *et al.*[10]

Table 4: Imaging modalities for the observation and evaluation of nasolabial creases

No.	Evaluation method	Principle	Merit	Shortcoming	Clinical application
1	High-frequency ultrasound	Probe ultrasonic waves with frequencies exceeding 10MHz	● Non-invasive,real-time,dynamic monitoring, long-term follow-up. ● Clear and visible layers of skin	● Affected by the patient's position and operator's technique. ● In China, it is necessary to establish an ultrasound imaging department and professional medical staff to operate.	Monitor tissue for abnormalities and foreign bodies
2	3D scanning technology 3D	through high-speed scanning measurement, obtain the three-dimensional coordinate data of the surface of the measured object, and establish a three-dimensional image model of the object	● Short scanning time ● High scanning and measurement accuracy and repeatability ● fast and realistic stereo reconstruction, and wide application range	● The equipment is expensive, ● the equipment hardware and built-in software are uneven, and computer software is required to program and measure.	Prosthesis placement surgery or facial tissue reconstruction
3	Computer Tomography CT	X-ray is used to scan a certain area of the human body and a three-dimensional reconstruction image is obtained after computer processing	● Rebuilding bone tissue has good advantages	● The accuracy of soft tissue reconstruction is low. ● it has higher energy radiation, has carcinogenic effects. ● cannot be widely accepted by patients	Orthopedic surgery for the face

Table5: Biophysical measurement of nasolabial creases

No.	Evaluation method	Pprinciple	Merit	Shortcoming	Clinical application
1	Bioelectrical impedance method	A technique for determining human body water by electrical methods	● Non-invasive ● simplified measurement, ● repeatable	● There are many influencing factors: such as skin temperature, humidity and thickness, body position, inaccuracy, current passage, children and people with heart disease, foreign body implants or catheters, pregnant women and other people are not suitable.	A technique for determining human body water by electrical methods
2	Skin elastometer	A testing instrument for detailed analysis of human skin rheology Using a capacitive electron system, the degree of pulling is measured by lifting and pulling by applying a pulling force to the skin vacuum, to measure the degree of skin laxity	● Non-invasiv ● simplified measurement ● repeatable	● The operation is relatively complex, requires certain skills, ● It is affected by the operator's technology.	The elasticity of the skin can be measured very accurately, through digital data feedback

Methodology

The flow of the study has been explained in the Fig 3

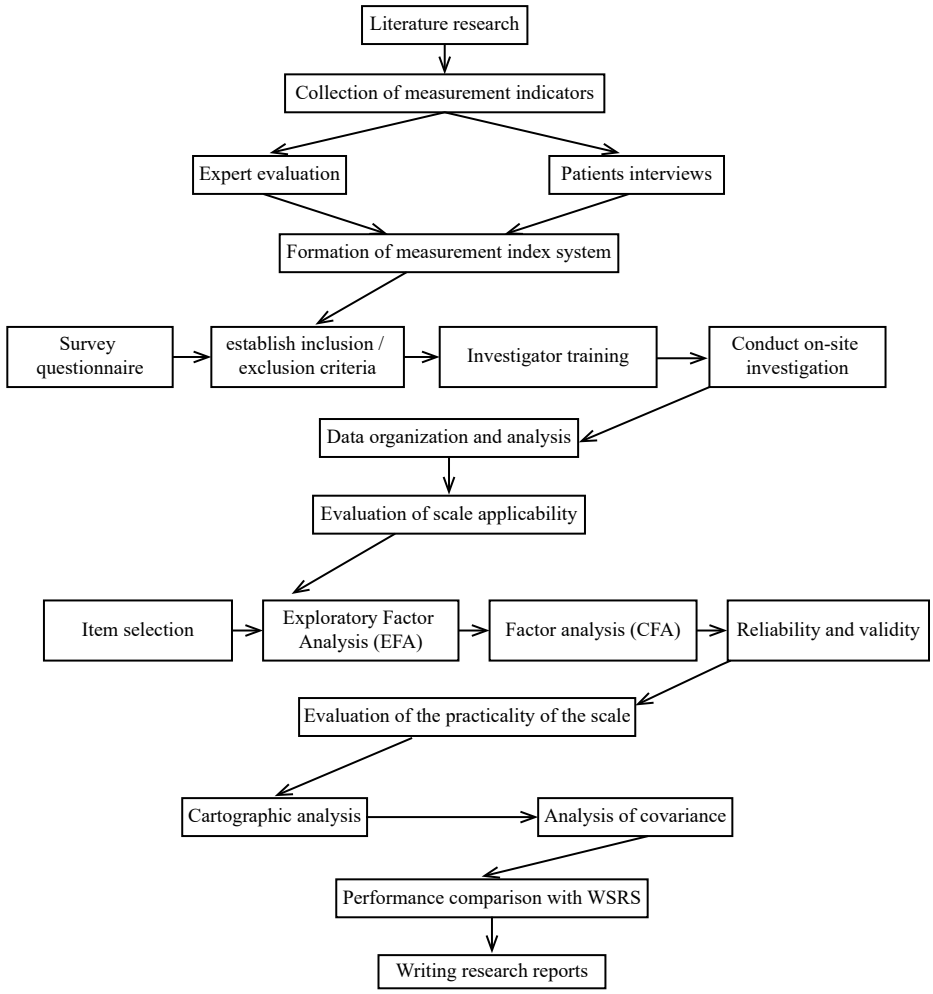

Figure 3: work flowchart

Study Type and Design

This study used a prospective observational design to establish a nasolabial fold (NLF) aging assessment system with a focus on Asian populations (Chinese) for before and after regenerative treatment. This study collected data from individuals seeking NLF improvement through rejuvenation therapy. The assessment system was developed on the basis of a comprehensive review of the available literature, analysis of NLF characteristics in Asian populations, and the inclusion of objective indicators and standardized assessment tools.

Study Population and Sample Size

The study targeted the Asian population, with a particular focus on Chinese population. A total 0f 150 participants was included men and women aged 20-65 who will seek regenerative therapies to improve NLF. The sample size was determined based on power analysis, taking into account the expected effect size, the required level of statistical significance, and statistical power. Recruitment of participants was carried out through collaboration with aesthetic clinics and centers specializing in facial rejuvenation surgery.

Inclusion and Exclusion Criteria

Inclusion Criteria

1) Asians, especially Chinese**,** Chinese women or men over the age of 20-65;
2) In the evaluation of the researcher, there are obvious, bilateral or nearly symmetrical wrinkles in the nasolabial groove;
3) Able to follow research guidance and willing to complete all required visits;
4) The pregnancy test was negative and there was no pregnancy plan during the study period;
5) Sign the informed consent form.

Exclusion Criteria

1) Facial hair may affect the visual observation score of wrinkle severity;
2) There are obvious acne scars, active inflammation, infection, cancer or precancerous lesions, or unhealed wounds in the injection area;
3) Have undergone facial tissue transplantation, or silicone, liposome (fat) injection or other permanent use Or semi permanent or temporary dermal filler;
4) Botulinum toxin cosmetic injection, laser skin replacement, light modulated intense pulsed light, radio frequency, skin abrasion, chemical skin replacement or other ablation or non ablation operations were performed within 6 months before the study treatment;
5) Have used any new over-the-counter drugs or prescription drugs, oral or topical wrinkle removal products in the study treatment area (right and left nasolabial fold) within 3 months before treatment.

Injection Technique

The treating investigator administered HA filler Restylane (Q-Med) to all participants in the study. Before the administration process, the injection sites were prepped by using an antiseptic solution. Subsequently, the administration of Restylane took place by means of a 27-gauge sharp needle, targeting the dermis of the nasolabial fold (NLF) region. The needle was introduced into the designated location and then withdrawn during the administration of the filler substance. In order to minimise the risk of HA leakage, the injection procedure was promptly stopped following the withdrawal of the needle. The treating investigator provided guidance that the appropriate quantity of Restylane filler for a single side of the nasolabial fold (NLF) should be below 1.5 mL, however the specific volume was established at their discretion. After the administration of the injection, a manual manipulation was conducted at the injection site in order to achieve a consistent dispersion of the filler substance. Participants were directed to provide ice to the designated injection sites both before to and during the intervention in order to mitigate any potential discomfort. In instances where no discernible improvement was noted one month after the original injection, a supplementary injection was delivered. The collection of data pertaining to adverse events occurred at each visit conducted during the duration of the injection and subsequent follow-up period.

Assessment Follow-ups

The participants were monitored and assessed for a period of 18 months. The evaluation of aesthetic repair was place three weeks post-injection. The durability of the correction was assessed at intervals of 3, 6, 9, 12, 15, and 18 months.

Nasolabial Crease Evaluation Scales

The objective evaluation method for nasolabial folds is precise but complex and costly, making it difficult to promote on a large scale. The subjective evaluation method is more suitable for clinical application, and currently remains the most convenient, cost-effective, and widely used evaluation method.
The following is an introduction to the 3 typical nasolabial crease evaluation scales:
WSRS (wrinkle severity rating scale): The scale has been divided into 5 levels (Table 6), the scale is judged by the length of nasolabial creases And the assessment in the resting state is not comprehensive and perfect (Fig 4).

Figure 4: Wrinkle severity rating scale

Table 6: The Wrinkle Severity Rating Scale

Score	Describe
5. Extreme	Extremely deep and long folds are detrimental to facial appearance. 2-4mm Visible V-shaped fold when stretched. Unlikely to have satisfactory correction with injectable implant alone.
4. Severe	Very long and deep folds; prominent facial features. Less than 2mm visible fold when stretched. Significant improvement is expected from injectable implant.
3. Moderate	Moderately deep folds. Clear facial features visible at normal appearance but not when stretched. Excellent correction is expected from injectable implants.
2. Mild	Shallow but visible fold with a slight indentation; minor facial feature. Implant is expected to produce a slight improvement in appearance.
1. Absent	No visible fold. continuous skin line.

Figure 3: Schematic diagram of WSRS indexing for nasolabial creases[2]

The Modified Fitzpatrick Wrinkle Scale: Modified Indexing

Based on the WSRS score, nasolabial fold wrinkles are further subdivided into the following 7 levels (Table 7): This scale is judged by the depth of the nasolabial fold, and the assessment in the resting state is not comprehensive and perfect. (Fig 5)

Table 7: The Modified Fitzpatrick Wrinkle Scale

Class	Describe
0F	No wrinkle. No visible wrinkle; contin- uous skin line.
0.5F	Very shallow yet visible wrinkle.
1F	Visible wrinkle and slight indentation.
1.5F	Visible wrinkle and clear indentation. o1-mm wrinkle depth *.
2F	Moderate wrinkle. Clearly visible wrin- kle, 1- to 2-mm wrinkle depth *
2.5F	Prominent and visible wrinkle.
3F	Deep wrinkle. Deep and furrow wrinkle; more than 3-mm wrinkle depth.

*Wrinkle depth is based on assessors' estimation rather than physical measurement.

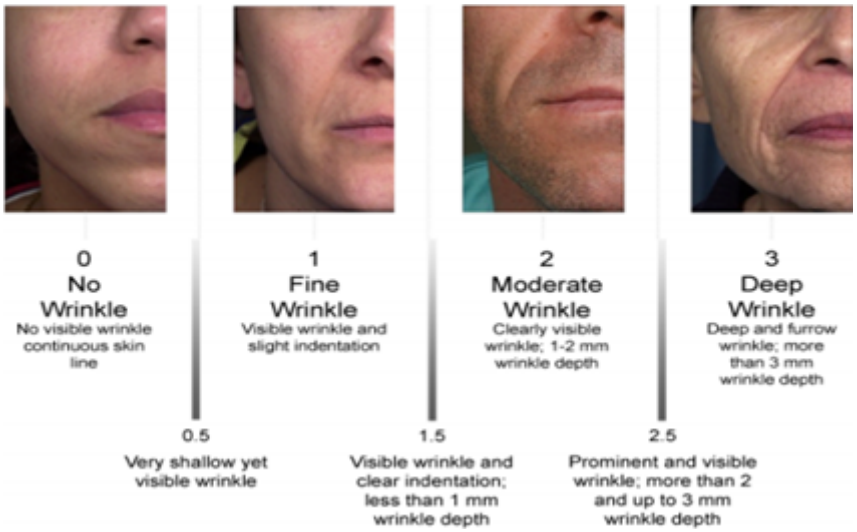

Figure 5: Reference photographs of the four main classes for MFWS and descriptions for all classes.

High-frequency ultrasound imaging

High-frequency ultrasound imaging, specifically at a frequency of 20 MHz, The DermaScan C USB (also known as Monaderm) is a device that generates 2D visualisations for the purpose of measuring dermal density in terms of percentage. The number 12 is the numerical representation of a quantity. The dermal density was evaluated on each visit for a sample of 16 participants who were randomly chosen from the population of individuals who had nasolabial fold injections. The evaluation of the strength of the reflected echoes, which corresponds to the density of the tissue, was conducted using a CPU that was built into the system. The results were then visualised using the integrated software, which presented the information as color-graded 2D pictures. The echogenicity colour spectrum, spanning

from hyperechogenic to hypoechogenic, encompasses a variety of colours including white-yellow, red, green, blue, and black.

Digital Photographs

Standardized digital photography was performed at each visit

Statistical Analysis

The collected data will be analyzed using appropriate statistical methods to evaluate the efficacy and outcomes of rejuvenation therapy of the NLF aging assessment system focusing on the Asian population (China). Descriptive statistics will be used to summarize demographic characteristics and baseline NLF measurements. The paired t-test or Wilcoxon sign rank test will be used to compare pre- and post-treatment NLF measurements. Subgroup analyses can be performed based on factors such as age, sex, and severity of NLF. The statistical significance will be set to $p<0.05$. Statistical software (e.g. SPSS, R) will be used for data analysis.

The specific statistical tests and models used will depend on the nature of the data and research question and will be adjusted appropriately to account for potential confounding variables. Results will be presented using descriptive statistics, tables, and charts to provide a clear and concise summary of the findings. Through rigorous statistical analysis, this study aims to provide objective evidence for the effectiveness of the NLF aging assessment system focused on the Asian population (China) and the effect of rejuvenation treatment on NLF improvement in this specific population.

Results

Disposition and Demographics of the Study Participants

A cohort of 150 participants (25 males and 125 females) with an average age of 45.1 ± 7.8 years (ranging from 25 to 70) and an average BMI of 22.1 ± 1.2 (ranging from 17.8 to 30.7) received the experimental device through injection. Additional demographic information is included in Table 1. The most often treated areas were the nasolabial folds, which were addressed in 120 participants. This was followed by the marionette lines, which were treated in 30 cases. The participants were administered an average of 2.0±0.5 ml of soft-tissue filler injection. Table 2 illustrates the average amount of injected product per unit area. Out of the patients who were involved in the trial, a total of 120 people successfully finished the study, which corresponds to a duration of 18 months (Table 8, 9 and Fig 6).

Table 8: Baseline variables

Variable	
Mean age (years)	45.1 ± 7.8
Gender (*n*)	
Male	25
Female	125
Average Mean weight (kg)	59.8
Average Mean height (cm)	158.9
Average Mean BMI (kg/m^2)	22.1
Skin Phototype	
I	3
II	56
III	70
IV	19
Missing data	2

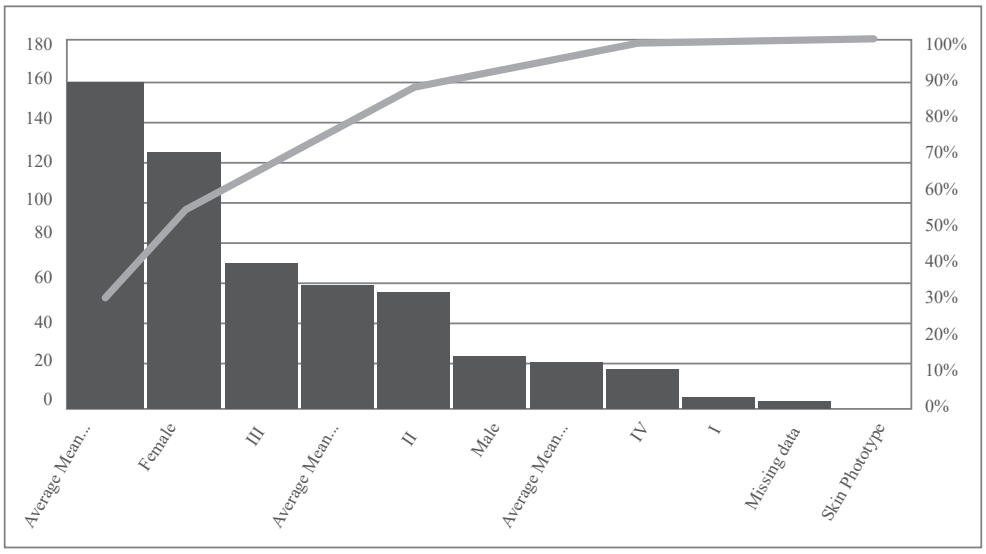

Figure 6: Baseline variables

Table 10: Volume of injected product per area

	Nasolabial folds	Marionette lines	All (sum of all the injected volumes for the same patient)
N	120	30	76
Mean Volume (ml)	1.7	0.9	2.1
Standard deviation	0.3	0.3	0.7

Modified Fitzpatrick Wrinkle Scale (MFWS): The concept of the Modified Fitzpatrick Wrinkle Scale (MFWS) refers to the systematic evaluation and assessment of aesthetic outcomes in clinical settings. This approach involves the comprehensive examination and rating of several aesthetic parameters to provide a holistic perspective on the overall aesthetic A notable enhancement of the Modified Fitzpatrick Wrinkle Scale (MFWS) in relation to the baseline was seen across all treatment indications examined after 21 days of intervention (all $p<0.0001$). The average difference in means and medians for nasolabial folds, marionette lines, and lips was about one grade (equivalent to 0.5 points on a scale ranging from 0 to 3). The greatest success rates were seen in the nasolabial folds (99.1%), followed by the marionette lines (90.1%) as shown in Table 10 and Fig 7. The success rates seen in this study were found to be in accordance with the outcomes reported in the intention-to-treat (ITT) population.

Table 9: Modified Fitzpatrick Wrinkle Scale (MFWS)

Modified Fitzpatrick Wrinkle Scale (MFWS)		Nasolabial folds		Marionette lines	
		Basepoint	After 3weeks	Basepoint	After 3weeks
0	*N*	-	4	-	1.6
	%	-	7%	-	4%
0.5	*N*	-	4	-	1.6
	%	-	7%	-	4%
1	*N*	-	26	-	8
	%	-	41%	-	26%
1.5	*N*	1	17	1	7
	%	2%	26%	2%	20%
2	*N*	6	14	6	12
	%	10%	21%	10%	15%
2.5	*N*	24	7	12	4
	%	33%	10%	26%	12%
3	*N*	22	-	17	-
	%	60%	-	50%	-
p-Value			<0.0001		<0.0001

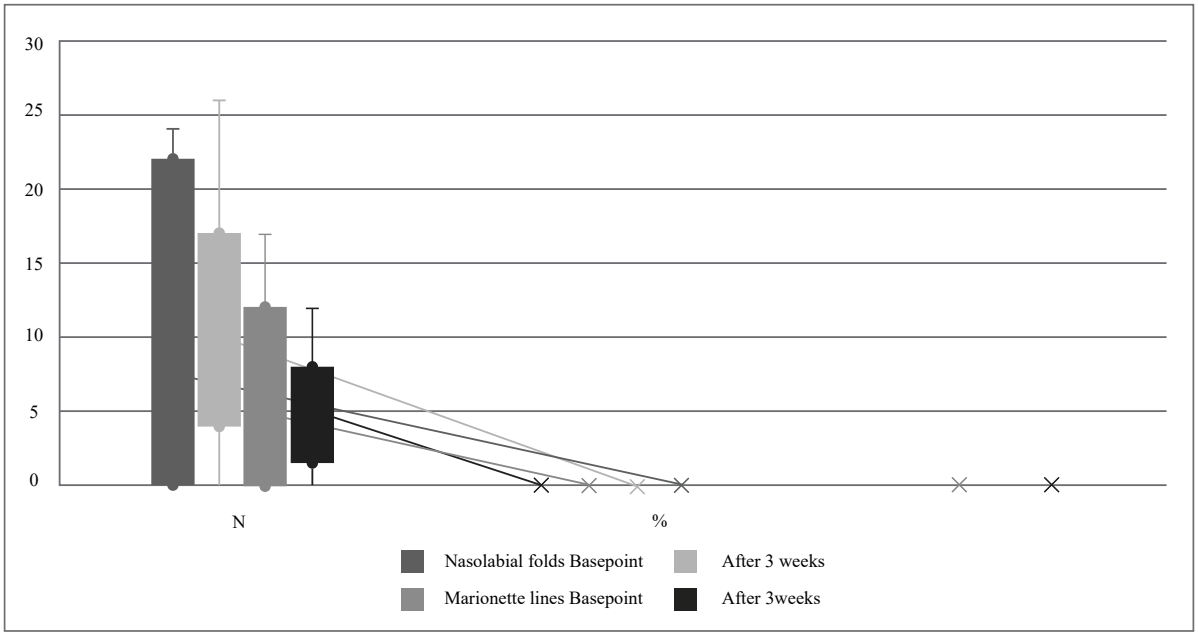

Figure 7: Modified Fitzpatrick Wrinkle Scale (MFWS)

Photographic Assessment

The scores for the nasolabial fold and marionette lines shown substantial improvement in comparison to the initial measurements throughout all subsequent visits ($p\leq0.001$ for all). The average values for nasolabial folds shown a significant improvement, decreasing from an initial mean of 5.0±0.5 to 2.0±.05 after 21 days, and further improving to 1.9±1.0 at the 18-month mark after the injection. The average values for marionette lines shown a significant improvement, decreasing from an initial mean of 4.9±0.7 to 2.5±1.1 after a period of 21 days. Furthermore, during the 18-month follow-up, the mean value further improved to 3.0±0.8. The MLFS demonstrated statistically significant improvement relative

to the baseline at all follow-up visits ($p < 0.001$).

Assessment of Nasolabial Fold by Ultrasound

The use of soft-tissue fillers for nasolabial folds resulted in significant enhancements in collagen levels and increased density of newly formed collagen, as seen using high-frequency dermal ultrasonography. There was a notable rise in dermal density, specifically tissue echogenicity, in the nasolabial folds at all subsequent visits compared to the first measurement (all $p \leq 0.001$) (Figures 8). The maximum density was seen at 9 weeks, with a mean value of 55.1%± 12.4%. Subsequently, the density exhibited a continual drop until 18 weeks, when it reached a mean value of 46.1%± 10.7%. In comparison, the density at baseline was found to be 30.1%± 8.7%.

Ultrarasound

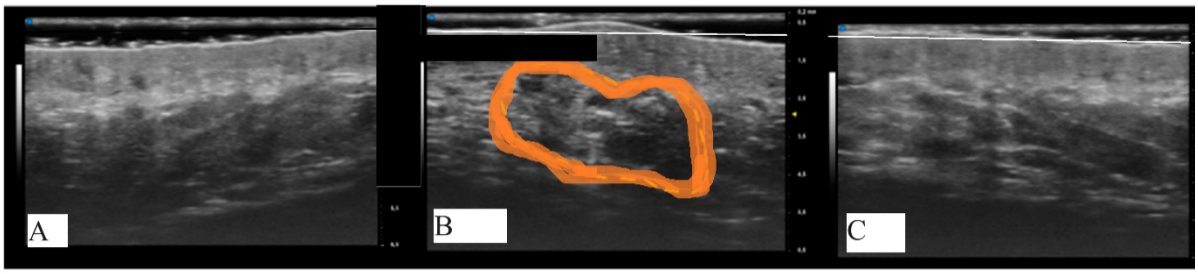

Figure 8: ultra-high-frequency ultrasound (UHFUS) prior to the injection of hyaluronic acid (HA) filler. Following the injection. Subsequently, UHFUS was performed again 6 months after the injection to evaluate any changes.

A significant proportion of local responses were resolved within a period of threeweeks. Following the 3rd visit, it was observed that in four participants who had lip injections, there were instances of irregular palpation and/or excessive correction. However, all other local responses had subsided. The individual exhibited overcorrection and irregularity upon palpation after treatment for nasolabial folds and marionette lines, as seen on the 3rd visit. All responses were successfully resolved towards the conclusion of the research.

Discussion

The current investigation was undertaken to evaluate and juxtapose the comparative analysis of nasolabial fold depth measures utilising clinical grading, photography, and ultrasound techniques. While all injections yielded positive results, significant disparities in efficacy were seen depending on the precise facial area targeted, in relation to clinical criteria. The administration of injections into the nasolabial fold yielded the most favourable success rates and significant improvements in outcome measures, encompassing subjective and objective evaluations, during both the immediate and extended timeframes. A recent systematic evaluation was conducted to evaluate the aesthetic outcomes achieved through the use of soft-tissue fillers for the treatment of the nasolabial fold. The assessment employed the Wrinkle Severity Rating Scale (WSRS) and the Modified Fitzpatrick Wrinkle Scale to quantitatively measure the observed results. The findings given in this study demonstrate that the average MFWS scores, obtained by pooling data, were 1.27 at the 12-month follow-up visit after the injection. This observation might be contrasted with the average values documented in this study, which were 0.96 and 1.16 for the evaluator and participant assessment, respectively. The inclusion of an 18-month follow-up period in the experiment being described can be considered a notable benefit. A study was undertaken by Rzany *et al.*[3] to investigate the efficacy of two hyaluronic acid-based soft tissue fillers in treating nasolabial folds, with a focus on comparing the follow-up lengths. The response rates, as determined by the WSRS assessment, were observed to be approximately 80% at the 18-month mark following the initiation of therapy, according to the researchers' observations. The evaluations conducted in this research were based on the General Adaptation Syndrome (GAS), and the success rates seen within the study group achieved a remarkable 93% without necessitating any additional adjustments or re-administrations. The efficacy of administering injections specifically targeting marionette lines yielded favourable outcomes among the studied group. Nevertheless, the efficacy of lip therapy shown a much shorter duration. The perceived discrepancy in outcomes can be ascribed to the limited approved volume of injection (up to 1.0 ml) for lip augmentation, as well as the relatively higher degree of mobility exhibited by the lip region compared to other facial locations, such as the nasolabial fold and marionette lines. Czumbel *et al.*[4] did a comprehensive meta-analysis examining the efficacy and safety of hyaluronic acid-based dermal fillers in the context of lip augmentation. In accordance with the results presented in this study, the authors observe that the effectiveness of the therapies remained present in around 50% of the participants who were administered said treatments for a period of one year.

The temporal efficacy of fillers is a critical consideration that both patients and practitioners carefully evaluate prior to the administration of injections. Hyaluronic acid experiences enzymatic and nonenzymatic degradation mechanisms as a result of its occurrence within the extracellular matrix of the skin. The physiological mechanism outlined presents a restriction on the longevity of hyaluronic acid-based soft

tissue fillers, hence constituting a noteworthy restraint in their application. A multitude of research have been conducted to investigate the durability of soft-tissue fillers based on hyaluronic acid (HA). As a result, it has been discovered that the pace of deterioration is significantly impacted by various physico-chemical characteristics, including the extent of cross-linking, concentration of the gel, cohesiveness, hardness, and ability to swell. The numerical sequence provided by the user encompasses the consecutive numerals 19, 20, 21, and 22. In the current study, it is important to highlight that a standardised product was utilised across all perioral regions, therefore raising questions regarding the underlying causes that may account for the observed discrepancies in longevity. Several potential factors can influence the extent of product degradation in relation to facial anatomy, mobility of the treated area, injection volume, and injection technique with respect to the injection site. The role of facial expressions in the process of product degradation is widely recognised. Prior studies have demonstrated that the rheological properties of soft-tissue fillers can be modified under the influence of shear pressures, as evidenced by tests conducted by scholars in the respective domain.

The mouth cavity is a dynamic anatomical region that exhibits substantial mobility, playing a crucial role in vocal and nonverbal communication, as well as the processes of food intake and digestion. The orbicularis oris muscle complex demonstrates continuous stretching and compression of the lips, leading to shear stresses that could potentially contribute to the deterioration of HA-fillers. Therefore, it is imperative to provide correction operations for the lips more frequently and in bigger volumes, in contrast to facial folds which are commonly perceived as being more stable. Future research efforts should focus on further investigating and expanding upon the findings of this study. Specifically, it is important to evaluate the long-term effectiveness and durability of the hyaluronic acid-based soft-tissue filler when used in different anatomical locations and administered by various injection techniques. These investigations will yield additional knowledge and understanding on the subject under consideration.

Prior studies have posited that the utilisation of high-frequency ultrasound imaging presents a feasible approach for the objective evaluation of skin tissue structure. The assessment of dermal density, which includes the components of the extracellular matrix including collagen, elastin, and hyaluronic acid, holds importance in evaluating the advancement of regeneration following rejuvenation procedures. The findings of the study demonstrate a significant increase in dermal density across all subsequent visits, as compared to the initial measurement. The aforementioned discovery offers factual evidence in favour of the phenomenon of structural tissue remodelling that takes place following the application of hyaluronic acid (HA) filler. The Tri-Hyal technology, which integrates three distinct types of hyaluronic acid (HA), appears to have a notable impact on this process of remodelling.

The soft-tissue filler employed in this study is synthesised utilising three discrete sizes of hyaluronic acid chains obtained from non-animal origins. The included hyaluronic acid (HA) molecules encompass BDDE cross-linked very-long chain and long-chain HA, as well as free HA. Several advantages have been discussed with regard to this specific production procedure. Multiple studies have demonstrated that the reduction in the utilisation of cross-linking agents can potentially yield beneficial effects in terms of mitigating potential toxicity. Furthermore, it has been observed that the progressive distribution of complimentary hyaluronic acid (HA) has the ability to induce the synthesis of extracellular matrix by fibroblasts, hence facilitating the advancement of skin maturation over a prolonged duration. The numerical values 27, 28, and 29 are under discussion. However, further scientific investigation is required to provide a more accurate understanding of the molecular mechanisms by which Tri-Hyal technology-based soft-tissue fillers improve skin quality.

The Modified Fitzpatrick Wrinkle Scale was utilised to assess the magnitude of nasolabial wrinkles and the effectiveness of cosmetic procedures. The MFWS, which is a validated outcome measure in clinical settings, is frequently employed to assess facial wrinkles and the effectiveness of soft-tissue augmentation.[5] In contrast, the Multidimensional Feedback and Wellness Scale (MFWS) is a comprehensive five-point scale that spans a spectrum of responses, ranging from notable enhancement (1) to considerable decline (5). Stefura *et al*.[6] did a previous meta-analysis to investigate the effectiveness of tissue filler treatment in the nasolabial region. The findings demonstrated a statistically significant average enhancement in the Wrinkle Severity Rating Scale (WSRS) score following a period of 6 months. Furthermore, a slight increase in the score of the Modified Fitzpatrick Wrinkle Scale was observed at the six-month mark. The utilisation of three-dimensional (3D) pictures enabled the achievement of a greater level of precision and complexity that would have been unattainable using traditional two-dimensional (2D) imaging methods. In addition, the use of three-dimensional (3D) images facilitated a thorough assessment of the nasolabial folds, providing valuable insights into the long-term viability of the results over time. This remark underscores the effectiveness and durability of the injection, stressing its favourable impact on the patient's facial aesthetics. The utilisation of this additional evaluation method exhibits notable efficacy within the realm of aesthetic medicine, particularly in procedures involving alterations to volume. As a result, these procedures may be measured with accuracy and objectivity. Additional investigation is necessary in forthcoming research endeavours to examine the association between ultrahigh-frequency ultrasound (UHFUS) images and three-dimensional (3D) imaging.

This study is not without limitations. The research lacks the essential characteristics of a blinded, randomised, controlled trial, hence reducing its academic merit. The failure to carry

out evaluations by investigators who are blinded represents a missed chance to strengthen the reliability and validity of the data. Additionally, the inclusion of objective volume analysis through the utilisation of advanced three-dimensional surface analysis techniques could have offered additional objective verification for the findings obtained in this study. The safety attributes of the hyaluronic acid-based soft-tissue filler now being studied are consistent with the safety profiles of other frequently employed devices for facial rejuvenation. The frequency of adverse events that arise as a result of hyaluronic acid-based soft-tissue filler injections was in line with anticipated outcomes. Furthermore, in most cases, these events resolved within a period of 21 days following the injection.

Based on an analysis of the assessment structure, clinical applications, and the advantages and disadvantages associated with evaluating nasolabial creases, the following conclusions can be drawn.

The conventional nasolabial crease scale is a clinically practical and non-invasive tool. However, its research and development process has been considerably time-consuming, with the most recent scale being introduced in 2015. Regrettably, no updates have been made in the past five years. Nonetheless, advancements in medical aesthetic technology have continued to progress. The realm of aesthetics is constantly evolving, with changes occurring on a daily basis. However, the modernization of traditional scales has not been able to keep up with the rapid pace of these changes.

The assessment fields and dimensions of conventional scales primarily focus on static nasolabial creases and loose nasolabial creases. However, Table 2.3 reveals that there exist five distinct types of nasolabial creases, indicating that the traditional scale is inadequate for evaluating all variations of nasolabial creases.

One notable benefit of objective evaluation lies in its ability to provide accurate and unbiased assessments, as exemplified by clinical grading.

Ultrasound instruments, which appear to be universally utilised, necessitate the expertise of trained medical personnel for their operation.

Conclusion

This research shows the first evaluation of clinical assessment/grading has easy and accurate outcome as ultrahigh frequency ultrasound (UHFUS) and photograph. The advent of capturing photos with extraordinarily high resolution offers a unique opportunity, not previously explored in existing literature, to accurately identify anatomical landmarks and HA dermal filler with an unprecedented level of precision. This enables careful descriptions with an accuracy that extends to the millimetre scale. One further innovation of this method is in its potential to provide precise visualisation of the anatomical locations where fillers are administered, hence presenting intriguing avenues for future advancements. One notable advancement in the field is the use of echo-guided filler injections, which have shown a substantial reduction in the occurrence of serious adverse effects. In conclusion, we suggest using clinical grading as a means of monitoring patients who have had HA (hyaluronic acid) filler injections. This recommendation is based on the non-invasive nature of the diagnostic tool and its exceptional accuracy in identifying the distribution of the specific product used.

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