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An Open-Label, Single Center Clinical Study to Evaluate the Efficacy of Periorbital Rejuvenation with a 1927 nm Diode Laser Treatment

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Introduction

The chromophore of the 1927 nm diode laser is mainly water, which can be used for skin rejuvenation.[1-3] This study intends to use the Solta CLEAR+BRILLIANT Laser System, featuring a 1927 nm diode laser with 5 mJ energy, a treatment spot of 140 μm, a treatment depth of 170 μm, and a treatment coverage of approximately 5% per energy level after four rounds of treatment using the patented Intelligent Optical Tracking® System (IOTs). The purpose of this research project is to investigate the treatment design, therapeutic effects and safety of the 1927 nm laser for the rejuvenation of the skin around the eyes.

Study objectives and endpoints

- **Objectives**: The objective of this study is to evaluate the treatment design, therapeutic effects and safety of the 1927 nm laser for the rejuvenation of the skin around the eyes.
- **Primary endpoint**
    1. Change from baseline in texture score at visit 4 (follow-up session)
- **Secondary endpoints**
    1. Change from baseline in color measurements (L*) at visit 4 (follow-up session)
    2. Change from baseline in pigmentation score at visit 4 (follow-up session)
    3. Change from baseline in pores' index at visit 4 (follow-up session)
    4. Change from baseline in physician assessment of Global Aesthetic Improvement Score (GAIS), at visit 4 (follow-up session)
    5. Change from baseline in patient assessment of Global Aesthetic Improvement Score (GAIS), at visit 4 (follow-up session)
    6. Change from baseline in texture score at visit 2
    7. Change from baseline in color measurements (L*) at visit 2
    8. Change from baseline in pigmentation score at visit 2
    9. Change from baseline in pores' index at visit 2
    10. Change from baseline in physician assessment of Global Aesthetic Improvement Score (GAIS), at visit 2
    11. Change from baseline in patient assessment of Global Aesthetic Improvement Score (GAIS), at visit 2
    12. Change from baseline in texture score at visit 3
    13. Change from baseline in color measurements (L*) at visit 3
    14. Change from baseline in pigmentation score at visit 3
    15. Change from baseline in pores' index at visit 3
    16. Change from baseline in physician assessment of Global Aesthetic

Improvement Score (GAIS), at visit 3

17. Change from baseline in patient assessment of Global Aesthetic Improvement Score (GAIS), at visit 3
18. Adverse reaction after each treatment
19. Visual Analogue Scale (VAS) during treatment
20. Change from baseline in self-reported satisfaction with the skin around the eyes

Investigational plan

- **Study Design**

This is an open-label, single center clinical study to evaluate the efficacy of periorbital rejuvenation with a 1927 nm diode laser treatment. The trial administrator will assign the subjects into different treatment groups (Group A: 2-week interval between treatments, or Group B: 4-week interval between treatments) .

- **Randomization**

This study is designed as a randomized clinical trial. The randomization of subjects will be generated by computer algorithm prior to the start of the trial. The trial administrator will assign the subjects into different treatment groups (Group A: 2-week interval between treatments, or Group B: 4-week interval between treatments) based on the order of enrollment and the corresponding randomization code.

- **Screening**

Upon obtaining the signed informed consent form, the trial staff will record the subjects' basic information, medical and surgical history, medication history, and Fitzpatrick skin type. Women will undergo pregnancy testing, and inclusion and exclusion criteria will be reviewed.

- **Treatment Visits**
  - Visit 1

    Before the first treatment, a camera photograph and Antera 3D assessment will be performed, and the subjects will complete a self-assessment questionnaire for skin conditions. EMLA Cream 5% will be applied topically for 20 minutes. Ocular laser shields will then be placed over the eyes following the application of Alcaine Ophthalmic Solution 0.5%. Clear + Brilliant™ Permea device periorbital treatment will then be performed. After the treatment, the subjects will complete a visual analog scale (VAS) for pain and use moisturizing skincare products.

- Visit 2

  Before the second treatment, a camera photograph and Antera 3D assessment will be performed, and the subjects will complete a self-assessment questionnaire for skin conditions, the Global Aesthetic Improvement Scale (GAIS) for overall aesthetic improvements, and a treatment safety questionnaire. EMLA Cream 5% will be applied topically for 20 minutes. Ocular laser shields will then be placed over the eyes following the application of Alcaine Ophthalmic Solution 0.5%. Clear + Brilliant™ Permea device periorbital treatment will then be performed. After the treatment, the subjects will use moisturizing skincare products.
- Visit 3

  Before the third treatment, a camera photograph and Antera 3D assessment will be performed, and the subjects will complete a self-assessment questionnaire for skin conditions, GAIS for overall aesthetic improvements, and a treatment safety questionnaire. EMLA Cream 5% will be applied topically for 20 minutes. Ocular laser shields will then be placed over the eyes following the application of Alcaine Ophthalmic Solution 0.5%. Clear + Brilliant™ Permea device periorbital treatment will then be performed. After the treatment, the subjects will use moisturizing skincare products.
- Visit 4

  Four weeks after the third treatment, a follow-up assessment will be performed, including a camera photograph and Antera 3D assessment, self-assessment questionnaire for skin conditions, GAIS for overall aesthetic improvements, and a treatment safety questionnaire.

- **Time of Each Visit**

  Each visit lasts approximately 40 minutes, including 20-minute topical anesthesia, 15-minute laser treatment, and 5-minute photography.

- **Laser treatment**

  Solta CLEAR+BRILLIANT Laser System, featuring a 1927 nm diode laser with 5 mJ energy, a treatment spot of 140 μm, a treatment depth of 170 μm, and a treatment coverage of approximately 5% per energy level after four rounds of treatment using the patented Intelligent Optical Tracking® System (IOTs). We will perform laser treatment on the periorbital area.
- **Imaging Record**s

  Each visit will include:
  - Camera photograph: One photograph of periorbital area in half-face position (from the eyebrows to the lower nose).

- Antera 3D photography: Two photographs of both sides of the periorbital area (5.6 x 5.6 cm), along with L*, texture, pigmentation, and pore indices. A total of eight photographs will be taken.

- **Other Study Procedures**
  - Basic information survey, including date of birth, gender, fitzpatrick skin type, and medication history.
  - Height and weight
  - Medical and surgical history, including a survey of past and current illnesses, allergies, and surgical history.
  - Medication history, concurrent use of medications, or related aesthetic treatments
  - Pregnancy test: urine pregnancy test (only performed on women before menopause).
  - Self-assessment questionnaire for skin condition
  - Global aesthetic improvement scale (GAIS) from subjects and investigator
  - Treatment safety questionnaire
  - Pain VAS (Pain Visual Analogue Scale)
  - Antera 3D camera

    Antera 3D® (a product of PSET BioMed and Miravex Limited, Ireland) is a non-invasive inspection tool that uses "image capture" technology to analyze and examine skin. The principle of obtaining the structure of skin texture is based on the colorimetric shape-from-shading (SFS) method, which is widely used to eliminate strong light on the skin and improve the accuracy of the inspection data. With this method, texture reconstruction can be used for skin analysis and quantification, such as measuring wrinkle depth and width, skin damage, and overall roughness. The captured spectral data can also be used to create maps that confirm the distribution and concentration of melanin and hemoglobin. The testing method for subjects involves comparing a fixed area of skin.

	1st treatment (visit 1)	2nd treatment (visit 2)	3rd treatment (visit 3)	Follow-up (visit4)
Group A	Week 0	Week 2	Week 4	Week 8
Group B	Week 0	Week 4	Week 8	Week 12
Camera photograph	V	V	V	V
Pain VAS	V			
Antera 3D assessment	V	V	V	V
Self-assessment questionnaire for skin condition	V	V	V	V
Investigator Global Aesthetic Improvement Scale (GAIS)		V	V	V
Subjects Global Aesthetic Improvement Scale (GAIS)		V	V	V
Treatment safety questionnaire		V	V	V

Study activities

- **Eligibility Criteria**
  - Inclusion Criteria:
    - ✓ aged between 30 and 65 years old;
    - ✓ no significant skin lesions or inflammation on the facial skin;
    - ✓ willing and able to comply with study requirements, instructions, and restrictions;
    - ✓ signed informed consent form.
  - Exclusion Criteria:
    - ✓ underwent facial active treatment, such as using laser, intense pulsed light, radiofrequency skin tightening, ultrasound skin tightening, botulinum toxin, or dermal fillers injection, within the previous six months;
    - ✓ have chronic skin diseases such as atopic dermatitis, psoriasis, chronic urticaria, vitiligo, rosacea, or keloid;
    - ✓ pregnant or breastfeeding;
    - ✓ suffered from acute illnesses or infections requiring treatment within 14 days before entering the study;
    - ✓ have had serious illnesses (such as heart disease, lung disease, brain disease, or liver disease) within the previous three months;

- ✓ allergic to Lidocaine or Prilocaine used in topical anesthetic cream or suffer from methemoglobinemia;
- ✓ used any skin medication on the face within 30 days before the trial, deemed by the principal investigator to affect the study results;
- ✓ deemed unsuitable for the study by the principal investigator.

- **Limitations and Cooperation Requirements for Study Participants**
  - Limitations for study participants during the trial
    - ✓ Participants are not allowed to undergo other chemical peels, beauty injections or phototherapy around the eyes during the trial.
    - ✓ Participants should avoid sun exposure or the use of tanning machines on their face during the trial.
    - ✓ Participants should maintain their original skincare routine during the trial and avoid using new facial skin products or topical/ingested whitening agents that claim to have whitening, spot-fading, or wrinkle-fighting effects.
  - Cooperation requirements for study participants during the trial
    - ✓ Participants should use umbrellas or wear hats to protect themselves from the sun when going outside on days with high UV index.
    - ✓ Participants can clean their faces as usual, but they must maintain a similar cleaning pattern every day.
    - ✓ Participants can use facial moisturizers, sunscreens, makeup, and makeup removers as usual, but they must maintain a similar pattern every day.
  - Consequences of failure to comply with trial limitations or cooperation requirements
    - ✓ If participants use the above limited items or fail to cooperate with the above requirements during the trial, they should inform the researchers actively. The principal investigator will assess whether the products or treatments used by the participants have any impact on the trial's test results and safety, as well as the feasibility of the participants continuing to participate in the trial.

Adverse Reactions and Management in Clinical Settings

- Allergic contact dermatitis caused by topical anesthetic cream has an incidence rate of less than 0.1%, which may result in skin redness, swelling, mild burning or itching. Topical steroid cream can be used for treatment.
- This device may cause local transient pain (lasting about one to several

hours) and redness and swelling (lasting about one to two days). Most of these side effects will disappear on their own. If the symptoms persist, symptom relief medication such as oral pain relievers like acetaminophen or non-steroidal anti-inflammatory drugs can be used.

- Small scabs the size of a needle tip may appear, which will fall off on their own within a week.
- If inflammation and pigmentation occur due to the constitution or sun exposure, topical or oral whitening products can be used for treatment for 1-3 months.

Data Collection, Processing, Evaluation, and Statistical Analysis Methods

- **Data Confidentiality**

  To maintain data confidentiality, data will be entered into a computer using a numbering system, and the data will be stored on an encrypted computer in the lead investigator's institution. The study lead investigator and research team members have a duty of confidentiality regarding information about the subjects and follow the rule that data cannot be taken out of the hospital.
- **Protection of Subjects' Privacy**

  The research team will use a study code to represent the identity of the subjects, and only the lead investigator and relevant research team members will know the link between the code and the name. If the trial/research results are published, the subjects' identities will still be kept confidential.
- **Statistical analysis**
  - For the analysis of numerical data, we will use either an independent t-test or Mann-Whitney U test to compare differences between the two groups. Additionally, a paired t-test or Wilcoxon signed-rank test will be used to compare differences between before and after treatment.
  - For categorical data, we will present the data in the form of frequency and contingency tables. To determine if there are significant differences in rates between the two groups, we will use either the chi-square test or Fisher's exact test.
  - All reported P-values will be from two-sided tests, and statistical significance will be determined at a threshold of $P < 0.05$.

Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, Operations Manual,

International Council for Harmonisation (ICH) guidelines, applicable regulations, and guidelines governing clinical study conduct and the ethical principles that have their origin in the Declaration of Helsinki.

Completion of the study

The end-of-study is defined as the date of the last subject's last visit.

References

1. Alharbi MA. 1927 nm Thulium Laser Successfully Treats PostInflammatory Hyperpigmentation in Skin of Color. Dermatol Res Pract 2021;2021:5560386.
2. Kim SM, Hwang S, Almurayshid A, Park MY, Oh SH. Non-Ablative 1927 nm Fractional Thulium Fiber Laser: New, Promising Treatment Modality for Riehl's Melanosis. Lasers Surg Med 2021;53:640-6.
3. Kurmuş G, Tatlıparmak A, Aksoy B, Koç E, Aşiran Serdar Z, Ergin C. Efficacy and safety of 1927 nm fractional Thulium fiber laser for the treatment of melasma: a retrospective study of 100 patients. J Cosmet Laser Ther 2019;21:408-11.