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Title Page

Study Protocol Number: **MXP23001**

AIRB Approved
Kathleen DuVernay, LPN
Kathleen DuVernay DATE 9/29/2023

Study Protocol Title: **A Retrospective Review Evaluating the Matrix Pro Applicator for Treatment of Wrinkles**

NCT: NCT06219278

Study Device: **Profound Matrix System, Matrix Pro Applicator**

Study Sponsor: **Candela Corporation**
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Abbreviations and Definitions

AE	Adverse Event
cm	Centimeter
FST	Fitzpatrick Skin Type
FU	Follow Up
IRB	Institutional Review Board
J	Joule
MEND	Micro Epidermal Necrotic Debris
µbeam	Microbeam
µm	Micron
MTZ	Micro Thermal Zone
mJ	Millijoule
mm	Millimeter
ms	Millisecond
nm	Nanometer
NSR	Non-Significant Risk
UADE	Unanticipated Adverse Device Effect
SOP	Standard Operating Procedure
SPF	Sun Protection Factor
Tx	Treatment

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1. Study Synopsis

Study Information	
Study Type	Retrospective chart review
Study Device(s)	Profound Matrix System is a platform of 3 applicators: Sublime, Sublative RF and Matrix Pro. The Matrix Pro applicator, a new short pulse RF micro-needling device that treats with an array of RF micro-needles penetrating the skin, will be assessed in this retrospective analysis.
Indication(s)	Wrinkles
Treatment area(s)	Full face
Overall Study Objective	Evaluate the safety and efficacy of the Profound Matrix System with the Matrix Pro applicator for treatment of wrinkles
Target Enrollment	This is a retrospective chart review evaluating all subjects enrolled into the FUFT2002 source study meeting inclusion criteria and none of the exclusion criteria of this study protocol for retrospective analysis.
Study duration	N/A – this is a retrospective chart review
Study Site(s)	In the source study from which data for the current retrospective study will be extracted, subject enrollment occurred at up to five (5) clinical sites.
Study Design	This study is a retrospective analysis of de-identified subject data collected during implementation of the clinical study, "Functional Usability and Feasibility Testing of the Profound Matrix™ System (FUFT2002)" (source study). The FUFT2002 clinical study was a multi-site prospective clinical trial. The current retrospective study will analysis data extracted from the FUFT2002 database according to prespecified study selection criteria.
List of Measures	• Before and after photograph assessment • Subject satisfaction questionnaire • Pain/ discomfort during treatment using Numerical Rating Scale (NRS) • Adverse events evaluation
Primary Efficacy Endpoint(s)	The Primary Efficacy Endpoint is pre-defined as the percentage correct before and after photograph determinations made by blinded evaluators based on perception of facial wrinkles.

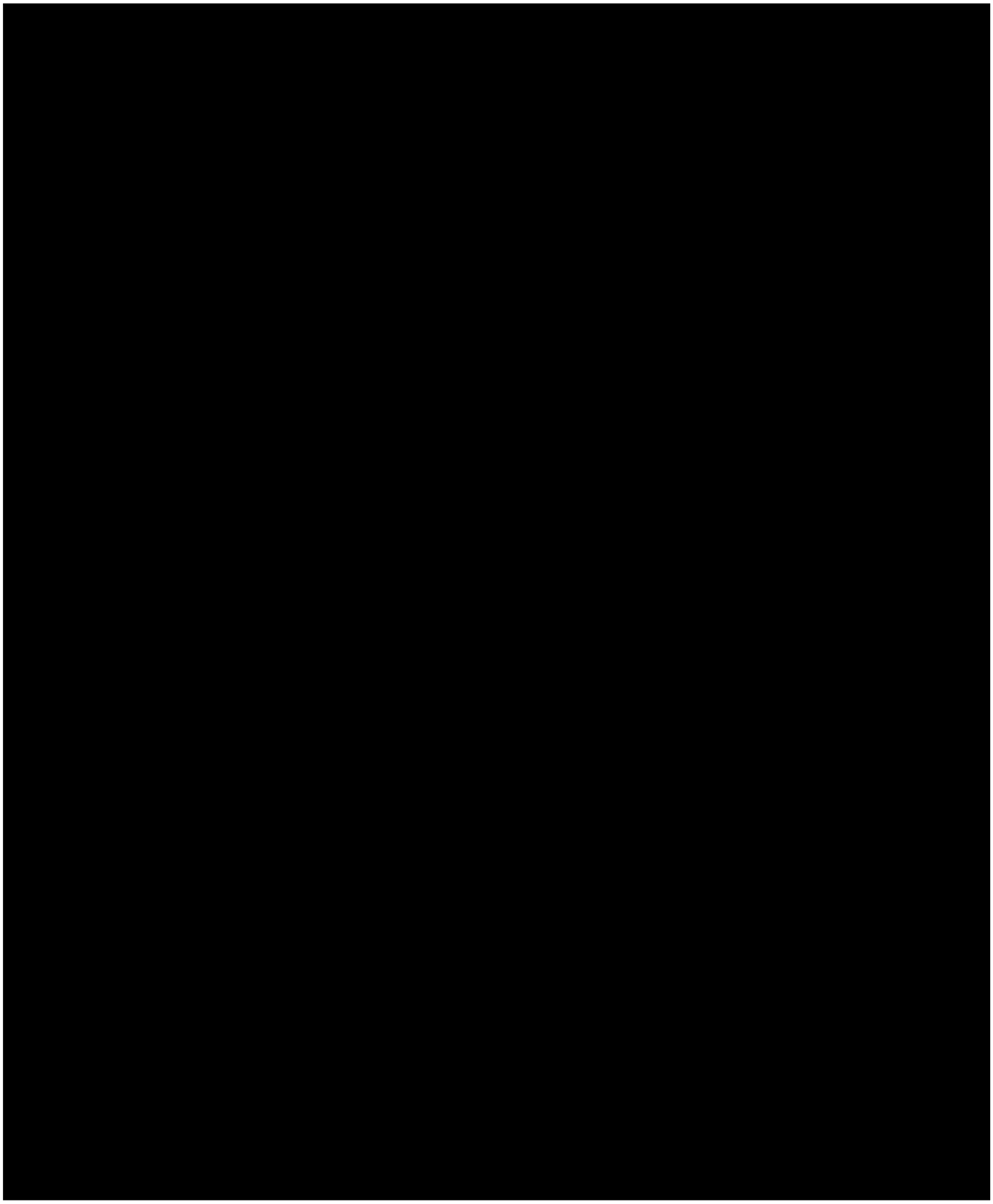
	There will be 3 independent blinded evaluators partaking in the study. Each will receive the set of subject photographs in de-identified coded randomized order (randomized for before and after treatment presentation order with respect to each subject photograph set, and with respect to order of subject set presentation). The blinded evaluators will be required to determine within each presented photographic set which of the images is the 'Before' image (prior to treatment initiation) and which is the 'After' image (post-treatment administration) based on his or her perception of the presentation of facial wrinkles. Each blinded evaluator will perform this task independently of the other. A minimum of 2 out of the 3 blinded evaluators correctly determining Before-After assignment for an individual subject's photograph set will indicate success for that individual subject with respect to positive treatment response. 70% overall individual responder rate will be positive for study success.
Secondary Efficacy Endpoint(s)	Subject satisfaction ratings at study endpoint.
Safety Endpoint(s)	Adverse events will be tabulated by type, incidence, severity, related to treatment, action taken and outcome
Tolerability Endpoint(s)	Subject assessment of treatment discomfort/pain immediately post-treatment via Numerical Rating Scale (NRS)
Exploratory Endpoint(s)	Skin response as assessed immediately after treatment by type and severity for all subjects

2. Study Introduction and Rationale

The objective of this retrospective chart review study is to extract existing de-identified data according to prespecified study selection criteria from that collected during implementation of the clinical study, "Functional Usability and Feasibility Testing of the Profound Matrix™ System (FUFT2002)", a multi-site prospective clinical trial. The goal of extracting this data is to evaluate the safety and efficacy of the Profound Matrix System Matrix Pro applicator for the treatment of wrinkles using pre-existing data from a clinical trial wherein the device to be evaluated for this indication was administered to study subjects per the intended treatment protocol to be administered for the treatment of wrinkles.

3. Study Device Description

Candela Corporation has developed its next generation radiofrequency (RF) system: Profound Matrix System (**Figure 1**) with Matrix Pro, Sublative RF and Sublime applicators (**Figure 2**).



Technical specifications for the Profound Matrix are provided in **Table 1**.

[redacted]

Regulatory Status

[redacted]

[redacted]

4. Investigation Plan

Study Design and Plan

A retrospective medical record (chart) review will be conducted at up to five (5) investigational sites that have prior experience treating patients with the Profound Matrix System (Candela Corporation, Marlborough, MA) for electrocoagulation and for treatment of wrinkles, acne scars or skin texture improvement. Data will be extracted from the medical records by a member of the clinical site study staff in a non-identifying manner and will include relevant demographic, safety and efficacy information but no patient identifiers. Data will be compiled and retrospectively analyzed to evaluate the treatment of wrinkles with the Matrix Pro applicator.

Study Endpoints and List of Measures

Safety will be assessed by analysis of the incidence, severity and relatedness of adverse events that were reported in the patient charts. Safety will include adverse events and optionally will include immediate skin response and discomfort during treatment.

Efficacy will be assessed by analysis of data collected by the sites from the patient chart review.

5. Study Population

Inclusion Criteria

[redacted]

Exclusion Criteria

1. Sun exposure during the course of the study
2. Aesthetic procedures and/or treatments during the course of the study
3. Any violation of study treatment instructions

4. Upon inspection, any differences in baseline and follow up photos that would not make evaluation of photos viable (e.g. chin placement, facial expression)
5. Any protocol deviation or change in study visit activities that would jeopardize reliability or validity of the retrospective review.

Study Participant Retention Plan

In the source FUFT2002 study, the study participant retention plan was the following: Subjects enrolled in the study can discontinue their participation at any time for any reason without prejudice or reduction in the quality of their medical care. The investigator or

Participant Compensation

As part of the FUFT2002 study, subjects received the Profound Matrix study treatment at no cost. There is no plan to compensate subjects for participation in this study.

6. Study Procedures

There are no visits for this study. FUFT2002 source study consisted of up to three treatment visits with treatment intervals 6 weeks ± 2 weeks and follow-up visits at 1 month (4 ± 2 weeks) and 3 month (12 ± 4 weeks) after last treatment).

7. Ethical Conduct of the Study

This study will be conducted only after receipt of determination of exempt status by a recognized Institutional Review Board (IRB). The IRB helps protect and ensure the rights and welfare of all research participants and ensures the research is conducted in an ethical manner.

This retrospective study qualifies for 'exempt' status under human subject regulations. Exempt studies are not subject to certain federal research requirements and do not require yearly recertification.

Additionally, this retrospective study meets Health Insurance Portability and Accountability Act (HIPAA) Privacy Requirements by satisfying the criteria for waiver of privacy authorization according to the following required criteria:

All data will be collected retrospectively from existing information already recorded in the study database from subjects who were consented, qualified, and enrolled in the completed prospective clinical study, "Functional Usability and Feasibility Testing of the Profound Matrix™ System (FUFT2002)", under approval of the Allendale IRB, (IRB #00005829).

Potential Benefits and Risks

As this is a retrospective chart review there are no anticipated risks or benefits to the subjects. The risk of breach of patient confidentiality will be mitigated by use of the de-identified Patient Study Number assigned by the clinical site. The Sponsor will not request access to the clinical sites' patient charts.

8. Adverse Events

Safety management, including adverse event evaluation and reporting, is not applicable to this retrospective study as all evaluations are being performed on prior existing data.

However, as the data being evaluated under this retrospective protocol will be sourced from a prior completed prospective clinical study, safety management, including adverse event evaluation, assessment, and reporting, as applicable, was in effect under that protocol. As such, any and all adverse event information for subjects in the source study whose data is being evaluated in this retrospective study will be extracted, assessed, and reported as part of the analysis under this retrospective study protocol.

The procedures for adverse event evaluation, assessment, and reporting for all clinical studies of Candela devices and which was employed in the source study are the following:

Adverse events, and unanticipated adverse device effects (UADE) are collected from the time of subject consent until the subject exits the study. A description of the adverse event or device event, date of onset, severity, action taken, relationship to study treatment and outcome are documented in the case report form.

The Investigator submits to Candela and to the reviewing IRB/EC a report of any unanticipated adverse device effect (UADE) as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (CFR 812.150(a)(1)).

Candela, upon learning of any unanticipated adverse device effect, shall immediately conduct an evaluation and report the results to FDA, all reviewing IRBs, and participating investigators within 10 working days after Candela first receives notice of the effect (CFR 812.46(b), 812.150(b)(1)).

9. Data Monitoring Plan

As this is a retrospective study, establishment of a data monitoring to ensure study and data compliance is not applicable.

The source study from which the data for analysis within this retrospective study is extracted; however, was executed under a pre-specified monitoring plan whose details were contained in the FUFT2002 source study's protocol and were in compliance with Candela Medical's Global Field Monitoring Procedure.

10. Data Management Plan

Procedures to Maintain Confidentiality

All study records and information will be identified by the subject number. All subject identifiers will be removed from all documents. Documents containing identifying information will be kept in locked files in the research staff's locked office. Limited access to electronic data will only be made available to members of the research team. No direct identifying information will be shared with any outside entities.

Protocol Deviations

All deviations will be tracked on a CRF and summarized in the progress report for the next continuing IRB/EC review.

Data Source

The data source in this study is existing information already recorded in the study database from subjects who were consented, qualified, and enrolled in the completed prospective clinical study, "Functional Usability and Feasibility Testing of the Profound Matrix™ System (FUFT2002)", under approval of the Allendale IRB, (IRB #00005829), and who the satisfy the retrospective study selection criteria. This study is a pure retrospective study. No additional information will be collected for any subject in this study other than the required information that is already existing in the database from the source study.

Data Collection Methodology

For extraction of qualifying subject data from the FUFT2002 clinical study database into the current retrospective study database, the FUFT2002 data will be queried for satisfaction of the retrospective study selection criteria (inclusion/exclusion criteria). Data extraction will be strictly limited to the subject data already existing in the FUFT2002 clinical study database, and furthermore restricted to only subject entries that satisfy the retrospective study selection criteria and to only the protocol-specified data elements for the qualifying subject records.

There will be no identifying information entered into the retrospective study database that could potentially connect an individual data record to an individual subject. Unique de-identified codes will be used for each subject data set extracted from the source study database and entered into the retrospective study database.

The collected retrospective data will only be used for the purposes of evaluating the efficacy, safety, and tolerability objectives of this study.

The parties who will have access to the retrospective and source study databases will be the designated Candela employees, and the study biostatistician. Access to the database will not be given to outside parties at any time during the data collation and analysis process or in the future for any reason.

Data Elements

The following data elements will be extracted from the qualifying identified existing subject data records in the FUFT2002 study database.

1) Subject Information

[redacted]

2) Treatment Variables

[redacted]

3) Outcome Variables

[redacted]

e) Adverse event and other safety information

Data Storage And Management

Primary records (source study database and documents) will continue to be maintained in the respective study sites and study site subject files as before. The study data elements extracted from the source study database will be directly entered into the retrospective study database to which only the designated Candela Medical study staff and the study biostatistician will have access.

Confidentiality and Privacy

All data and records generated during this study will be kept confidential in accordance with HIPAA regulations on subject privacy. Privacy of subjects and confidentiality of the collected data elements will be secured through use of a de-identified coding system that will comprise of study subject unique study identification number. The coded de-identifiers will be used for all data entries.

Providing Results to Subjects

Results will not be provided to subjects as there is no diagnostic or otherwise medical purpose associated with this retrospective analysis that could in any potential way benefit the subjects whose data was included in the analysis or alert them to potential risks or issues in any other regard.

11. Statistical Analysis Plan

Sample Size Determination and Justification

A sample size of 24 study subjects has been determined sufficient to provide an appropriate sample population for statistical analysis and generalizability of results.

Statistical justification for sample size determination and the success criteria determination on which it is based is presented below.

Primary Efficacy Endpoint is pre-defined as the percentage correct before and after treatment photograph determinations made by blinded evaluators based on perception of facial wrinkles.

There will be 3 independent blinded evaluators partaking in the study. Each will receive the set of subject photographs in de-identified coded randomized order (randomized for before and after treatment presentation order with respect to each subject photograph set, and with respect to order of subject set presentation). The blinded evaluators will be required to determine within each presented photographic set which of the images is the ‘Before’ image (prior to treatment initiation) and which is the ‘After’ image (3-months post-treatment administration) based on his or her perception of the presentation of facial wrinkles. Each blinded evaluator will perform this task independently of the other. A

minimum of 2 out of the 3 blinded evaluators correctly determining Before-After assignment for an individual subject's photograph set will indicate success for that individual subject with respect to positive treatment response. 70% overall individual responder rate will be positive for study success.

The rationale for selection of a minimum responder rate criterion of 70% (based on a 2 out of 3 blinded evaluator concordance) is based on the minimum requirement established by the United States Food and Drug Administration (U.S. FDA) to which Candela Corporation has been upheld and successfully employed previously to attain FDA market clearance for similar devices and indications.

Employing these parameters, the minimum pre-determined sample size to provide sufficient power for a statistical comparison of the proportion of treatment responders (P) versus a reasonable cutoff (P0) is based on a power calculation utilizing the (one proportion) binomial exact test and based on the following assumptions.

[redacted]

Therefore, a sample size of 24 study subjects is determined to be sufficient to provide appropriate sample population for statistical analysis such that the results of this retrospective study can be considered statistically and clinically meaningful and generalizable to the broader intended population.

General Overview of Statistical Plan

Efficacy analysis will be performed for both the primary modified intent-to-treat (mITT) and the secondary per protocol (PP) populations. Safety will be evaluated for the safety population. Each is defined below.

[redacted]

Handling Missing Data

Missing data will be handled using the Last Observation Carried Forward data imputation method. The number and proportion of subjects with missing data will be presented in a separate table tabulated with timepoint, date, and with reasons for the missing data provided.

Tools and Resources for Data Analysis

The data will be captured by transferring specified extracted data from the source database and any other applicable study documentation directly into a database created to capture data for this retrospective study. The final database will be verified against source case report forms and locked prior to writing the final clinical study report. Data may be analyzed using Microsoft Office Excel (Microsoft, Redmond, WA) or equivalent statistical software.

The clinical findings will be consolidated and communicated using the company's Clinical Study Report Template and other deliverables as applicable (clinical bulletins, white paper, publications, etc.)

The sample size calculation and statistical analysis plan was performed by an external clinical and regulatory consultant.

12. Publication Policy

Site and Investigator shall have the right to publish the results of the trial in accordance with the clause in the clinical trial agreement, if applicable, provided sponsor has given its prior written approval. Sponsor shall have the right to review for a minimum of thirty (30) days all proposed publications or announcements related to the study and shall further have the right to require removal of information from such publication or announcement if sponsor believes removal is necessary to comply with applicable regulatory responsibilities or to allow the sponsor sufficient time to protect its intellectual property rights (IPR), through the filing of patents or the pursuit of other protection. Sponsor reserves the right to remove all Confidential Information from any publications or presentations, or if sponsor deems that such removal does not sufficiently protect its intellectual property rights, to require that investigator refrain from making such publication or

presentation. Investigator agrees that if the trial is part of a multi-center trial, any publication by investigator of the trial results shall not be made before the first multi-center publication.

13. Roles and Responsibilities

Table 2. Roles and Responsibilities

Study Personnel	Role	Responsibilities
Maya Duffy	Study Manager	Oversee study related procedures
Bhumi Vinay Patel	Data Management Lead	Oversee data monitoring and management
Katherine Coleman, Liuping Li, and Nardeen Badarny	Clinical Research Associates	Oversee study related procedures, site monitoring, and collection of data
Elvira Cawthon	Clinical and Regulatory Consultant and Biostatistician for Sample Size Calculation and Data Analysis Plan	Provide statistics for sample size calculation and input to data analysis plan.
Dr. Konika Patel Schallen	Principal Investigator of FUFT2002 Source Study	Ensuring that the source clinical study is conducted according to the investigational plan, and applicable FDA regulations. Protecting the rights, safety, and welfare of study subjects.
Nicolle Dest	Senior Nurse Research Manager	Ensure study staff are following regulatory requirements and following protocol activities for source study. Providing de-identified clinical data to Candela
Raylene Piretti, Christina McCarthy-Greenwood, and Alexis Husson	Candela Institute for Excellence Study Staff	Adhere to regulatory requirements and protocol activities for FUFT2002 source study

14. Documentation Checklist

Retrospective chart review of de-identified FUFT2002 source study case report forms.

15. Reference List

Not applicable.

16. Appendices

Not applicable.