LEGXERCISE Professional

# CLINICAL EVALUATION OF A DEVICE ON LEG CIRCULATION



IntelliBrands
Smart Made For TV Products

# A TWO-WEEK CLINICAL EVALUATION OF A DEVICE ON LEG CIRCULATION

FINAL REPORT

**TYPE OF INVESTIGATIONAL DEVICE:** Passive exercise device
**INVESTIGATIONAL DEVICE NAME:** LEGXERCISE PROFESSIONAL

**INSTITUTE DEVICE CODE:** 084504-01
**STUDY CODE:** 084504_4362ITB
**REPORT CODE:** IRSI-E-ES-084504-01-03-21-RFV01-Rev01

**REPORT DATE**: 08/10/2021

**SPONSOR:** INTELLIBRANDS
9905 NW 17th St., Suite 108
Miami, FL 33172
Telephone: +1 (305) 223-3711

**STUDY SITE:** INTERNATIONAL RESEARCH SERVICES, INC.
222 Grace Church Street
Port Chester, NY 10573
Telephone: 914.937.6500
Fax: 914.937.8067
**Investigator in Charge:** Stephen R. Schwartz

# A TWO-WEEK CLINICAL EVALUATION OF A DEVICE ON LEG CIRCULATION

## SUMMARY

| | |
|---|---|
| **Investigational Device Name** | LEGXERCISE PROFESSIONAL |
| **Institute Device Code** | 084504-01 |
| **Study Code** | 084504_4362ITB |
| **Report Code** | IRSI-E-ES-084504-01-03-21-RFV01-Rev01 |
| **Sponsor** | INTELLIBRANDS |


| | |
|---|---|
| **OBJECTIVE OF THE STUDY** | The objective of this study was to evaluate the efficacy of a passive exercise device to improve leg circulation. |
| **METHODOLOGY** | On the initial visit (Baseline) the study subjects were evaluated by an expert grader to confirm the inclusion and non-inclusion criteria. A clinical efficacy assessment was carried out by the expert grader and instrumental measurements with the device GE Logiq e Ultrasound (Blood Flow) with imaging were also carried out by a trained technician. After the assessments, subjects were instructed to use the device, under a technician supervision, for the first time in-clinic for 45 minutes. After device use a new clinical efficacy assessment was performed and the subjects were instructed to answer to a subjective questionnaire (Immediate). Subjects received the device for use at home, under normal conditions of use, for 2 weeks ± 2 days and the device daily-log. During this period, subjects were instructed to record in the daily-log of the device use all the use performed and possible comments about the device. After 2 weeks of device use (Week 2), subjects returned to the Institute and a new clinical efficacy assessment was performed by an expert grader and the subjects were instructed to answer to a subjective questionnaire. Subjects used again the device for 45 minutes and after it a new clinical efficacy assessment and measurements with the device GE Logiq e Ultrasound With imaging were carried out (Week 2 Immediate). |
| **INVESTIGATOR IN CHARGE** | Stephen R. Schwartz. |
| **STUDY LENGTH** | Two weeks ± 2 days. |
| **APPLICATION SITE** | Legs. |
| **FREQUENCY OF APPLICATION** | Daily. |
| **INCLUDED STUDY POPULATION DESCRIPTION** | Female and male subjects, aged between 65 and 78 years old (mean age: 68 years old), with self-perceived health concerns and sedentary lifestyle, including but not limited to: self-perceived chronic leg pain (“Cramps”), little to no physical activity, prolonged periods of inactivity (i.e. >4 hours at a desk) for >4 days a week. |
| **NUMBER OF SUBJECTS** | A total of 45 study subjects were included in the study and a total of 44 completed the study. |
| **ETHICS** | This study was conducted in compliance with the Declaration of Helsinki principles, the applicable regulatory requirements, and according the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practices). |

**Expert Grading Assessments**
The device promoted an improvement in the appearance of lower leg skin discoloration after 2 weeks of use and after time-point Week 2 Immediate compared to time-points Baseline and Immediate.
The device did not promote an improvement of erythema.

**Laser Doppler Ultrasound**
The device promoted an improvement in blood flow after two weeks of use.

**Self-Assessment Questionnaire performed by the Study Subjects**

| | % of positive responses | |
|---|---|---|
| **Statement** | **Immediate** | **Week 2** |
| Helps to soothe lower leg pain. | 47.7% | 68.2% |
| Helps to reduce leg cramps in legs or feet | 47.1% | 70.6% |
| Helps to calm leg restlessness. | 60.9% | 65.2% |
| My legs feel more relaxed. | 81.8% | 77.3% |
| My muscles feel looser, less stiff. | 83.3% | 66.7% |
| Reduces joint stiffness. | 50.0% | 62.5% |
| I feel like I have exercised. | 59.1% | 63.6% |
| Increases the feeling of feeling stronger. | 38.6% | 56.8% |
| I feel like it is easier to walk. | 34.1% | 50.0% |

**RESULTS / CONCLUSION**

| | % of positive responses |
|---|---|
| **Statement** | **Week 2** |
| The device is easy to use | 97.7% |
| The device is safe to use | 97.7% |
| Reduces swelling in lower legs, ankles or feet | 55.0% |
| Reduces tingling in lower legs, ankles or feet | 64.7% |
| Reduces the feeling of heaviness in lower legs, ankles or feet | 78.9% |
| Reduces numbness in the lower legs, ankles or feet | 69.2% |
| Improves the appearance of skin discoloration in lower legs, ankles or feet | 50.0% |
| Improves the feeling of coldness in my lower legs, ankles or feet | 62.5% |
| Improves the feeling of itchiness in my lower legs, ankles or feet | 57.1% |
| Help to reduce “sleeplessness” caused by restless legs | 52.2% |
| Helps to reduce “sleeplessness” caused by leg cramps | 58.8% |
| Improves overall healthy feeling of legs | 61.4% |

Therefore, the following claims can be supported:

- *Improves lower leg blood flow (i.e. leg circulation)*; supported by the Laser Doppler Ultrasound Assessment;
- *Helps to reduce lower leg, ankle and feet swelling* supported by the Self-assessment questionnaire
- *Helps to reduce appearance of lower leg, ankle and feet skin discoloration*; supported by the Expert Grading Assessment;

- *Helps to reduce "cramps" in lower legs, and feet*; supported by the Self-assessment questionnaire;
- *Helps to reduce lower legs, pain sensations*; supported by the Self-assessment questionnaire;
- *Helps to reduce restless legs and sleeplessness caused by restless legs*; supported by the Self-assessment questionnaire;
- *Helps reduce leg and ankle joint stiffness*; supported by the Self-assessment questionnaire;
- *Improves leg restlessness, lower leg, ankles and feet coldness, tingling, swelling, numbness, heaviness and/or itchiness,* supported by the Self-assessment questionnaire;
- *Helps to reduce leg or feet cramps;* Supported by the self-assessment questionnaire;
- *Improves the perception of "loosening" leg muscles, feeling stronger, and relaxed legs*; supported by the Self-assessment questionnaire;
- *Improves overall healthy feeling of legs*; supported by the Self-assessment questionnaire;
- *The test device is easy and safe to use*, supported by the Self-assessment questionnaire.

**QUALITY ASSURANCE**

The study was conducted according to the Good Clinical Practices and in conformity with the Standard Operating Procedures of the Institute.

Data quality is assured, considering that our personnel is trained according to the study to be carried out, our equipment is always duly calibrated and the methods used are recognized and/or validated.

The Quality Assurance Department is in charge of auditing the Management System, and is fully available for any specific study monitoring carried out by the sponsor.

The signature below indicates that the study was carried out as described above and that the results were checked against the source documents.

Cristiane N.C. Moreira

Audited by: Cristiane Nunes Coelho Moreira
08/10/2021

**CONTENTS**

## 1. ABBREVIATION LIST

| | |
|---|---|
| ASTM | American Society for Testing and Materials |
| AE | Adverse Event |
| AIDS | Acquired Immune Deficiency Syndrome |
| CEO | Chief executive officer, |
| CFR | Code of Federal Regulations |
| Cm/s | Centimeter per second |
| COVID-19 | Coronavirus disease 2019 |
| Etc. | *Et cetera* |
| FDA | Federal Drug Administration |
| FL | Florida |
| GCP | Good Clinical Practice |
| HIPAA | Health Insurance Portability and Accountability Act |
| i.e. | That is |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonization |
| INC | Incorporated |
| IND | Investigational New Drug |
| IRSI | International Research Services, Inc. |
| Min. | Minute |
| NDA | New Drug Application |
| NY | New York |
| NW | North Western |
| PI | Principal Investigator |
| SAE | Serious Adverse Event |
| St. | Street |
| Vs | Versus |

## 2. INTRODUCTION

Over the last few years, the cosmetic industry has grown considerably, same as its concern in developing safe and effective products.

Industry awareness and consumer's and regulatory agencies requirements caused cosmetic manufacturers to adopt procedures that lead them to know better their products: to conduct clinical tests on safety and efficacy, which are coordinated by expert physicians, before marketing a product. These procedures provide cosmetic companies with greater safety, credibility and reliability among their consumers.

Efficacy studies allow us to assess the product's characteristics, detecting complaints and comments regarding its performance, as well as testing the quality control and the assured quality, analysis of competitors and claims support (what the product offers). In order to evaluate if a claim is appropriate, it is necessary to take into account the general consumers' impression concerning the presentation or the product advertisement (COLIPA, 2008). The claims must be supported by solid, clear and relevant evidences. Such evidences may result from experimental studies (biochemical / instrumental methods, sensory evaluations, technical evaluations and evaluations without the participation of study subjects, in vitro testing in cell cultures, use of hair locks, etc.), and consumers evaluations (ASTM E 1958-06, 2006).

For the efficacy assessment of products, clinical and/or self-assessment studies and instrumental studies can be used. The Self-Assessment by the study subjects is performed by following the "Standard Guide for Sensory Claim Substantiation" (ASTM E 1958-06, 2006), by using questionnaires. The ASTM (American Society for Testing and Materials) standards organization has been developed for over a century and represents one of the greatest voluntary organizations for standards development in the world, being a reliable source of technical standards of material, products, systems and services. Known by their high technical quality and relevance on market, ASTM standards have an important role in the infrastructure of the information guiding the study design, product manufacturing and commerce in global economy. The "Standard Guide for Sensory Claim Substantiation" is an ASTM standard that aims to disclose the good practices in sensory studies, approaching reasonable practices for executing sensory studies to validate product claims.

## 3. OBJECTIVE

The objective of this study was to evaluate the efficacy of a passive exercise device to improve leg circulation.

## 4. STUDY DESIGN

Monadic clinical study.

## 5. TEST SITE

The test device was used on the legs of the study subjects.

## 6. INVESTIGATIONAL DEVICE

Investigational device was provided by the sponsor and was labeled with appropriate codes and proper use instructions. All devices sent by the sponsor were initially stored in the samples room at the study site, with controlled temperature and restricted access. Devices' release was controlled by the principal investigator or by a previously designated technical staff. At the moment of receiving the device, the subjects were instructed on how to correctly store it, emphasizing the importance to keep it out of reach of children and/or animals.

### 6.1. Identification

Table 15. Investigational device identification

| Device Name | Device Type | Device Code | Batch |
|---|---|---|---|
| LEGXERCISE PROFESSIONAL | Passive Exercise device | 084504-01 | LEGX-012 |

### 6.2. Investigational Device Use Instructions

Sponsor-provided use instructions were verbally explained to subjects and provided in written study instructions along with a daily-log to record device use.

**At Home Use Instructions:**

Use device at least one time per day, for at least one hour on speed 2, following the directions in the manual included with the device.

**In-Clinic Instructions:**

Subjects should use device for 45 minutes on speed 2, following the direction in the manual included with the device.

#### 6.2.1. Investigational Device Use Compliance Check

The compliance of device use by the subjects was checked through the daily-log of device use completed by the subjects.

## 7. STUDY PERIOD

The total length of the study per subject was of 02 weeks ± 2 days.

- **Start of the First Group:** 03/29/2021;
- **End of the Last Group:** 04/13/2021.

## 8. STUDY SUBJECTS

### 8.1. Study Subjects Recruitment

The study subjects were recruited by the recruitment department of the study site that has a computerized and updated register system. The subjects registered into this system are interested in participating in clinical trials. They were contacted and asked to take part in the selection process and if they met all required criteria, they would be included in the study.

The study was performed in IRSI facilities and the subjects were informed about the site/address when they were contacted.

### 8.2. Selection and Admission of Study Subjects

During the subjects' selection for the study, the Institute certified that the subjects had no pathologies that could interfere with the study results. IRSI is also responsible for checking all inclusion and non-inclusion criteria for admission of the subject in the study.

### 8.3. Study Population

The population sample size predicted to be enrolled on the protocol was 44, aiming complete the study with 40 responses.

### 8.4. Inclusion Criteria

- Females/Males between ages of 65 and 85 years old, inclusive at enrollment;
- Self-perceived health concerns and sedentary lifestyle, including but not limited to:
  - Self-perceived chronic leg pain ("Cramps");
  - Little to no physical activity, prolonged periods of inactivity (i.e. >4 hours at a desk) for >4 days a week;
- Subjects will be able to read, understand and sign an informed consent form (includes HIPAA and State requirements);
- Willing to comply with all study instructions and requirements, including attendance at all scheduled study visits.

### 8.5. Non-Inclusion Criteria

- Athletes and active individuals, in good general health;
- Participating in any other clinical studies;
- Acute or chronic disease or medical condition, which could put him/her at risk in the opinion of the Principal Investigator or compromise study outcomes. Typical uncontrolled chronic or serious diseases and conditions which would prevent participation in any clinical trial are cancer, AIDS, renal impairment, mental illness, drug/alcohol addiction. (Per Sponsor, the following are permitted

in this clinical study: Arthritis, Bone on Bone, Recent Knee or Ankle Surgery, Pace Makers and Heart Conditions, High Cholesterol or Blood Pressure, Diabetes, Neuropathy, Lymphedema);

- Unreliable or unlikely to be available for the duration of the study;
- Immunocompromised subjects;
- (Women) Started Hormone Replacement Therapy within the last three months preceding the screening visit;
- Individuals unable to communicate or cooperate with the Principal Investigator due to language problems, poor mental development, or impaired cerebral function;
- Employees of IRSI or other testing firms/ laboratories, cosmetic or raw goods manufacturers or suppliers.

### 8.6. Permissions and restrictions during the study

- Initiation of use of any new vitamins, nutritional supplements or nutraceuticals is prohibited during the study, as is initiation of application of any new skin treatment device, or physical treatments (massage, physical therapy, device use, etc.) on legs.

## 9. METHODOLOGY

### 9.1. Materials and Equipment

- GE Logiq e Ultrasound (Probo Medical).

### 9.2. General procedures

On the initial visit (Baseline), the subjects were informed about the study objective, its methodology and duration, also about the possibly expected benefits and constraints related to the study and signed the Informed Consent Form (ICF) (APPENDIX 1). The study subjects were evaluated by an expert grader to confirm the inclusion and non-inclusion criteria.

For the subjects approved a clinical efficacy assessment was carried out by an expert grader and instrumental measurements with the device GE Logiq e Ultrasound (Blood Flow) with imaging were also carried out by a trained technician on a sub-group of subjects (Baseline). After the assessments, subjects were instructed to use the device, under a technician supervision, for the first time in-clinic for 45 minutes. After device use a new clinical efficacy assessment was performed and the subjects were instructed to answer to a subjective questionnaire (Immediate)

Subjects received the device for use at home, under normal conditions of use, for 2 weeks ± 2 days and the device daily-log. During this period, subjects were instructed to record in the daily-log of the device use all the use performed and possible comments about the device.

After 2 weeks of device use (Week 2), subjects returned to the Institute and a new clinical efficacy assessment was performed by an expert grader and the subjects were instructed to answer to a subjective

questionnaire. Subjects used again the device for 45 minutes and after it a new clinical efficacy assessment and measurements with the device GE Logiq e Ultrasound With imaging were carried out on a sub-group of subjects (Week 2 Immediate).

### 9.3. Procedure Schedule

Table 16. Study Schedule

| Procedures | | Screening/ Baseline | Immediate | Week 2 | Week 2 Immediate |
|---|---|---|---|---|---|
| **Study Initiation and Qualification** | Informed Consent and Medical History | X | - | - | - |
| | Inclusion/Exclusion Criteria reviewed | X | - | - | - |
| **Dispense/ Collect Device** | | D | - | - | *C* |
| **In Clinic Device Use** | | X (45 Min.) | - | X (45 Min.) | - |
| **Expert Grading** | - Skin Discoloration<br>- Erythema | X (pre-device use) | X | X | X (post-device use) |
| **Instrumental Evaluation** *Sub-Group, n=16* | GE Logiq e Ultrasound (Blood Flow) *With imaging* | X (pre-device use) | - | - | X (post-device use) |
| **Consumer Perception** | Subjective Questionnaire | - | X | X | - |

### 9.4. Methods

#### 9.4.1. Expert Grading Assessments

Clinical grading was performed through photos, using the standard 1 photograph, by an expert grader who is trained and validated in the procedure.

Ordinal scales were used to evaluate efficacy parameters and allowed a number to be directly and objectively attached to the quality of a given attribute. When responding to an ordinal scale item, the expert grader specifies their level of agreement to a statement by choosing a set grade, or level, on a 0-9 scale (skin discoloration) or a 0-4 scale (erythema).

The attributes and scales evaluated by the expert grader are described on the tables below.

Table 17. Skin attributes

| Attribute | Type of grading | Scale |
|---|---|---|
| Skin Discoloration | Visual | 0 – Uniform, even appearance;<br>9 – Uneven, blotchy, mottled. |
| Erythema | Visual | 0 - No erythema;<br>1 - Very slight erythema (barely perceptible);<br>2 - Well-defined erythema;<br>3 - Moderate to severe erythema;<br>4 - Severe erythema (beet redness) to slight eschar formation (injuries in depth). |

The evaluations were performed at the following time-points:

- Baseline - before device use;
- Immediate - after 45 min. of device use in clinic;
- Week 2 - after 2 weeks of device use;
- Week 2 Immediate - after 2 weeks of device use at home and 45 min. of device use in clinic.

### 9.4.2. Laser Doppler Ultrasound

The GE Logiq e Ultrasound quantifies the blood flow velocity (i.e. leg circulation). Assessments were performed on a subgroup of n = 16 subjects chosen at Baseline. Subjects were chosen to participate in the sub-group based on their anatomy and ability of the probe to capture valid reading at Baseline each subject's left or right lower lateral leg at the popliteal area (behind the knee). Determination of which leg was assessed for each subject was per a prepared randomization code at Baseline (APPENDIX 3). The location was recorded using a body map and the same leg was assessed at the following time-points (APPENDIX 5):

- Baseline - before device use;
- Week 2 Immediate - after 2 weeks of device use at home and 45 min. of device use in clinic.

### 9.4.3. Self-assessment Questionnaire Performed by the Study Subjects

The assessment by the subject were performed by following the "Standard Guide for Sensory Claim Substantiation" (ASTM E 1958-06, 2006), through the application of a questionnaire. The ASTM (American Society for Testing and Materials) standards organization has been developed for over a century and represents one of the greatest voluntary organizations for standards development in the world, being a reliable source of technical standards of material, products, devices, systems and services. Known by their high technical quality and relevance on market, ASTM standards have an important role in the infrastructure of the information guiding the study design, products manufacturing and commerce in global economy. The "Standard Guide for Sensory Claim Substantiation" is an ASTM standard that aims

to disclose the good practices in sensory studies, approaching reasonable practices for executing sensory studies to validate devices claims.

Subjective questionnaires allow the Sponsor to gauge the subjects' perceptions of the investigational device and its effects. Questions asked for subjects' agreement to a statement with a five-point scale.

The time-points, statements and scale of the self-assessment questionnaire are described in the table below.

Table 18. Self-assessment questionnaires time-points, statements and scale

| Time-point | Statement | Scale |
|---|---|---|
| Immediate / Week 2 | Helps to soothe lower leg pain. | 5 – Strongly Agree<br>4 – Agree<br>3 – Neutral<br>2 – Disagree<br>1 – Strongly Disagree |
| | Helps to reduce leg cramps in legs or feet | |
| | Helps to calm leg restlessness. | |
| | My legs feel more relaxed. | |
| | My muscles feel looser, less stiff. | |
| | Reduces joint stiffness. | |
| | I feel like I have exercised. | |
| | Increases the feeling of feeling stronger. | |
| | I feel like it is easier to walk. | |
| Week 2 | The device is easy to use | |
| | The device is safe to use | |
| | Reduces swelling in lower legs, ankles or feet | |
| | Reduces tingling in lower legs, ankles or feet | |
| | Reduces the feeling of heaviness in lower legs, ankles or feet | |
| | Reduces numbness in the lower legs, ankles or feet | |
| | Improves the appearance of skin discoloration in lower legs, ankles or feet | |
| | Improves the feeling of coldness in my lower legs, ankles or feet | |
| | Improves the feeling of itchiness in my lower legs, ankles or feet | |
| | Help to reduce "sleeplessness" caused by restless legs | |
| | Helps to reduce "sleeplessness" caused by leg cramps | |
| | Improves overall healthy feeling of legs | |

Subjects were also asked about the following complaints:

- Did you present lower leg, ankle and feet swelling before the study?
- Did you experience leg and ankle joint stiffness before the study?
- Did you experience leg restlessness before the study?
- Did you experience lower leg, ankles and feet coldness before the study?
- Did you experience lower leg, ankles and feet heaviness before the study?
- Did you experience lower leg, ankles and feet tingling before the study?

- Did you experience lower leg, ankles and feet numbness before the study?
- Did you experience lower leg, ankles and feet itchiness before the study?
- Did you experience lower leg, ankle and feet skin discoloration before the study?

For the statements related to these questions, only subjects who answered “yes” were considered. Thus, the number of answers varied according the statement.

### 9.5. Criteria and Procedures for Study Subjects Withdrawal

The removal of a study subject by the investigator may occur due to the following reasons:

- Study subjects not included: subjects who sign the ICF, but who do not meet the inclusion and non-inclusion criteria of the study;
- Subjects who present complications that affect their eligibility after the study consent;
- Subjects who present - at the Investigator's discretion - any problem that would prevent device use from continuing, at any time during the study;
- Consent withdrawal by the study subject, regardless of the reason;
- Lack of adhesion of the study subject to the study. A significant lack of adhesion will be recorded if the subject does not visit the study center for assessments;
- Serious Adverse Event;
- Concurrent disorder or treatment: any pathological process or treatment that occurred during the study period and that might interfere with the study device, such as a medication interaction or masking of results.

Those subjects removed from the study by the investigator were supervised in case they presented any event possibly related to the study, even after their removal. Those subjects removed due to occurrence of adverse event were continually supervised until the case is completely resolved.

Those subjects who were removed from study after the inclusion stage were not replaced.

## 10. ADVERSE EVENTS

Subjects will be advised to report all adverse events to the study personnel as soon as possible. An adverse event (AE) is any untoward medical occurrence experienced by a subject whether or not considered device related.

An adverse event must have an onset time after the subject is enrolled in the study and generally within one week after the subject's participation in the study has ended. The endpoint will depend on the nature of the device being tested.

An adverse event may consist of a:

- Disease or injury

- Exacerbation of pre-existing illness or condition
- Recurrence of an intermittent illness or condition
- Set of related signs or symptoms
- Single sign or symptom

Adverse events would be recorded on the appropriate case report form and include the Principal Investigator's assessment of device relationship as follows:

- 0 = Excluded;
- 1 = Unlikely;
- 2 = Not Clearly Attributable;
- 3 = Likely;
- 4 = Very likely.

### 10.1. Serious Adverse Events

A serious adverse event will be defined as any experience which is (any one or more of the following):

- Fatal;
- Life-threatening
- Persistent or significant disability/incapacity;
- Required or prolongs inpatient hospitalization;
- Results in congenital anomaly or birth defect.

### 10.2. Reporting of Adverse Events

Adverse events would be documented on the appropriate form and reported to the Sponsor within five business days if any relationship to the device(s) was determined by the PI.

The Sponsor would be notified of any serious adverse event (SAE) within 24 hours of recording the experience (when possible).

Proper judgment would be exercised in deciding whether expedited reporting is appropriate in other situations, such as events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should also usually be considered serious (FDA 21 CFR., Vol. 62, No. 194, 52243). Examples are:

- Overdose;
- Intensive treatment in an emergency room or at home for allergic bronchospasm;
- Development of drug dependency or drug abuse.

<u>Sponsor Contact for Reporting AEs and SAEs</u>

Contact: William Brand, CEO
INTELLIBRANDS
Address: 9905 NW 17th Street, Suite 108
Miami, FL 33172
Phone: 305-223-3711
E-Mail: william@intellibrands.tv

IRSI, IRSI staff and its Investigators do not assume Sponsor obligations for reporting SAEs to the FDA or other regulatory agencies.

## 11. APPLICABLE ETHICAL REMARKS

The study was conducted in compliance with the Declaration of Helsinki principles, the applicable regulatory requirements and according the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practice). This is not an IND / NDA clinical trial. IRSI does not assume any Sponsor obligations as stipulated in FDA GCP and ICH documents. This study is not intended for submission to the FDA.

Before the study starts, the subjects were informed about the study objective, its methodology and length, and about the possibly expected benefits and the constraints related to the study and signed the Informed Consent Form (ICF) (APPENDIX 1), elaborated according to the Declaration of Helsinki and FDA 21 CFR 50.25.

In order to maintain confidentiality of subjects' data, all data collected were identified by a number given to them at the beginning of the study. No personal information was disclosed in all data analysis. If required, the Investigator in charge must have allowed the study monitor to access all subjects study-related data. This included all documents containing the subject's clinical history for checking suitability for the study, diagnoses and any other document concerning the subject in the study.

All data that were found or proved by the study results are considered as being confidential information and sponsor's property. No information - as well as all documents generated during the study - will be copied or disclosed without a previous written consent of the sponsor. All information was kept confidential until the results were published.

The study technical documentation is in the Institute’s files, where it will be stored for a 2-year period.

## 12. STATISTICAL ANALYSIS

Exploratory data analysis (summary tables and graphs) was performed according the table below.

Table 19. Detailed statistical analysis

| Data Type | Statistical Method | Data Reported | Sample size |
|---|---|---|---|
| Demographics | Descriptive Statistics | Mean, standard deviation, minimum, maximum, frequencies and percentages | 44 |
| Expert grading | Descriptive Statistics<br>Paired T-test (monadic) | Mean, standard deviation, standard error, confidence interval, median, minimum and maximum<br>Mean percent improvement from Baseline<br>Percent of subjects improving<br>P-value (Time Interval vs. Baseline) | 44 |
| Instrumental Assessment (GE Logiq e Ultrasound) | | | 16 |
| Subjective Questionnaire | Descriptive Statistics | Frequency tables (n and %) of each response<br>Percent of positive response. | 44 |

*Please, refer to item 13.2.

The confidence level used on the comparative analysis was 95%.

Software: MINITAB 14 and XLSTAT 2021.

The raw data and statistical analysis can be found in APPENDIX 4.

## 13. RESULTS

### 13.1. Protocol Amendments

1) The SONOsite Titan Ultrasound machine listed in the protocol was rented from Probo Medical and was not operational, the GE Logiq e Ultrasound that was used in its place at the recommendation of the rental company.
2) Due to the temporary shutdown of the IRSI study site, as well as safety related precautions due to COVID-19 and the age range of the subjects (65-85 years) being in an “At Risk” group, the study was postponed and the study dates presented in the protocol were rescheduled.
3) The terminology of adverse event nexus was updated to align with IRSI SOP update, this was due to an internal documentation update.
4) The timepoints in which the GE Logiq e Ultrasound assessments were performed were updated per sponsor request. They were to be performed only at baseline, before the use of the device in-clinic and at the Week 2 visit immediately following device use in-clinic.
5) An additional claim was added to the proposed claim list per sponsor request: Helps to reduce leg cramps and sleeplessness caused by leg cramps, as assessed by subjective questionnaire results.
6) The protocol listed that all subjects would undergo ultrasound blood flow assessments, however due to limitations of the instrument (GE Logiq e) only a sub-group of subjects were selected to participate in this evaluation. Selection was based on the anatomy of the subject, and ability of the instrument to properly collect a reading of blood flow. A total of 20 subjects were selected to participate in this assessment.

### 13.2. Protocol Deviations

The protocol predicts the method of Tape measurement, however, per Sponsor request this data was not considered on the study.

.

The demographics variables of Sensitive Skin, Sensitive Eyes and Contact Lenses Wearer at time-point Baseline was not performed on subject 042, therefore, he was not considered for this assessment. The deviation does not impact the study results since the minimum number of subjects required by the protocol was achieved.

Only sixteen subjects were considered for the Laser Doppler Ultrasound analysis, all other subjects did not have their measurements collected

### 13.3. Population description and Adherence to the Study

Forty-five (45) subjects were included in the study, from them 44 completed the study. The summarized description of the population and the adherence to the study is available on the following table. The detailed description of the population is available in the APPENDIX 2.

Table 20. Included population and adherence to the study

| Included population | | | | | | | | | Adherence | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Recruited[1]** | **Non included[2]** | **Withdrawal[3]** | **Included[4]** | **Gender F** | **Gender M** | **Minimum Age (years)** | **Maximum Age (years)** | **Mean Age (years)** | **Absences[5]** | **Removed[6]** | **Completed the Study[7]** |
| 48 | 03 | 00 | 45 | 25 | 20 | 65 | 78 | 68 | - | 01 | 44 |
| **Subjects** | | | | | | | | | - | 007 | **-** |

*[1]subjects who attended the Institute and signed the ICF.*

*[2]subjects that not meet the inclusion criteria or presented any of the non-inclusion criteria.*

*[3] subjects that withdrew from the study after the study consent for personal reasons and were not included.*

*[4]subjects that did were approved in the study.*

*[5] subjects who missed the study for personal reasons unrelated to the study and to the investigational device*

*[6] subjects removed from the study are characterized as protocol deviation or another reason recorded by the investigator of the study*

*[7] subjects considered in the total who completed the study*

*Caption: F=Female; M=Male*

Subject 007 was removed from the study for presenting adverse event according to item 13.4.

The study achieved its objective to obtain, at its final, a minimum of 40 answers.

## 13.4. Demographics

Table 21. Demographics

| Variable | n | Mean ± SD | Min | Max |
|---|---|---|---|---|
| Age (years) | 44 | 67.8 ± 2.9 | 65 | 78 |
| Height (inches) | 44 | 5.4 ± 0.4 | 4.1 | 6.5 |
| Weight (pounds) | 44 | 176.5 ± 42 | 110 | 350 |
| | | | **n** | **Percent** |
| Sex | 44 | Male | 20 | 45.5% |
| | | Female | 24 | 54.5% |
| | | | **n** | **Percent** |
| Ethnicity | 44 | Hispanic or Latino | 2 | 4.5% |
| | | Not Hispanic or Latino | 42 | 95.5% |
| | | | **n** | **Percent** |
| Race | 44 | White | 36 | 81.8% |
| | | Black or African American | 4 | 9.1% |
| | | American Indian or Alaska Native | 2 | 4.5% |
| | | Asian | 2 | 4.5% |
| | | | **n** | **Percent** |
| Fitzpatrick Skin Type | 44 | Skin Type I | 3 | 6.8% |
| | | Skin Type II | 6 | 13.6% |
| | | Skin Type III | 22 | 50.0% |
| | | Skin Type IV | 10 | 22.7% |
| | | Skin Type V | 3 | 6.8% |
| | | | **n** | **Percent** |
| Facial Skin Type | 44 | Combination | 11 | 25.0% |
| | | Dry | 3 | 6.8% |
| | | Normal | 26 | 59.1% |
| | | Oily | 4 | 9.1% |
| | | | **n** | **Percent** |
| Body Skin Type | 44 | Normal | 31 | 70.5% |
| | | Dry | 11 | 25.0% |
| | | Very Dry | 2 | 4.5% |
| | | | **n** | **Percent** |
| Sensitive Skin | 43 | Yes | 8 | 18.6% |
| | | No | 35 | 81.4% |
| | | | **n** | **Percent** |
| Sensitive Eyes | 43 | Yes | 6 | 14.0% |
| | | No | 37 | 86.0% |
| | | | **n** | **Percent** |
| Contact Lenses Wearer | 43 | Yes | 3 | 7.0% |
| | | No | 40 | 93.0% |

### 13.5. Adverse Event

During the study 01 subject presented an adverse event. The adverse event is summarized on the following table.

Table 22. Adverse events

| Subject Number | Adverse event description | Intensity | Local | Action taken | Hypothesis / Rational | Nexus | Data Considered |
|---|---|---|---|---|---|---|---|
| 007 | Broken foot | Severe | Left foot | Subject Discontinued | Subject called to report she had a broken foot which occurred from a fall on 04/04/21. Subject had a follow-up appointment with her doctor on 05/04/21. Since subject was under the care of her own doctor, she did not require follow-up from IRSI. | Excluded | No |

### 13.6. Expert Grading Assessments

A statistically significant improvement of skin discoloration was observed at time-points Week 2 and Week 2 Immediate compared to Baseline. A statistically significant improvement of skin discoloration was observed at time-point Week 2 Immediate compared to Immediate.

No statistically significant improvement of erythema was observed at time-points Immediate, Week 2 and Week 2 immediate in relation to Baseline. No statistically significant improvement of erythema was observed at time-point Week 2 immediate in relation to time-points Immediate and Week 2.

Table 23. Descriptive statistics and results of the comparison in relation to Baseline and Week 2 Immediate

| Attribute | Statistic | Baseline | Immediate | Week 2 | Week2 Immediate | Immediate - Baseline | Week 2 - Baseline | Week 2 Immediate - Baseline | Week 2 immediate - Immediate | Week 2 immediate - Week 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Skin Discoloration | Mean | 0.64 | 0.61 | 0.42 | 0.39 | -0.03 | -0.22 | -0.25 | -0.22 | -0.03 |
| | Standard Error | 0.15 | 0.15 | 0.09 | 0.10 | 0.05 | 0.11 | 0.10 | 0.11 | 0.03 |
| | **% improvement (on the mean)** | | | | | **4.7** | **34.4** | **39.1** | **36.1** | **7.1** |
| | **% of subjects with improvement** | | | | | **15.9** | **31.8** | **36.4** | **38.6** | **13.6** |
| | **p-value** | | | | | **0.330** | **0.028*** | **0.009*** | **0.024*** | **0.161** |
| Erythema | Mean | 0.43 | 0.57 | 0.55 | 0.57 | 0.14 | 0.12 | 0.14 | 0.00 | 0.02 |
| | Standard Error | 0.08 | 0.08 | 0.08 | 0.08 | 0.09 | 0.08 | 0.08 | 0.09 | 0.08 |
| | **% improvement (on the mean)** | | | | | **-32.6** | **-27.9** | **-32.6** | **0.0** | **-3.6** |
| | **% of subjects with improvement** | | | | | **11.4** | **9.1** | **9.1** | **18.2** | **13.6** |
| | **p-value** | | | | | **0.932** | **0.916** | **0.945** | **0.500** | **0.607** |

* Significant at 5% (Student t test);

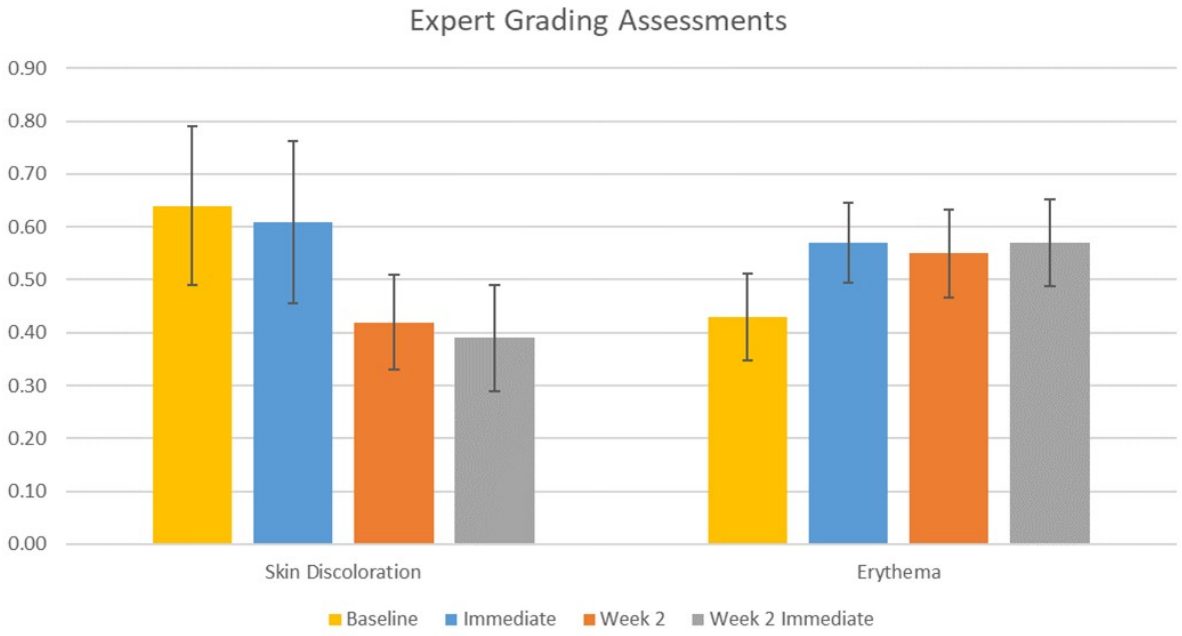


Figure 1 Mean and standard error per time-point and attribute

### 13.7. Laser Doppler Ultrasound

A statistically significant improvement (increase) was observed after two weeks of device use compared to baseline for systolic blood flow velocity and for diastolic blood flow velocity, indicating an improvement on the legs' blood flow.

Table 24. Descriptive statistics and comparison to Baseline

| Parameter | Statistics | Baseline | Week 2 Immediate | Week 2 Immediate - Baseline |
|---|---|---|---|---|
| Blood Flow Velocity (Systolic) | Mean | 57.3 | 62.8 | 5.5 |
| | Standard Error | 3.5 | 3.2 | 3.0 |
| | **Δ(%) on the mean to Baseline** | | | **9.6** |
| | **% of subjects with reduction** | | | **62.5** |
| | **p-value** | | | **0.043*** |
| Blood Flow Velocity (Diastolic) | Mean | 6.9 | 8.4 | 1.5 |
| | Standard Error | 1.0 | 0.9 | 0.8 |
| | **Δ(%) on the mean to Baseline** | | | **21.7** |
| | **% of subjects with reduction** | | | **62.5** |
| | **p-value** | | | **0.033*** |

* Significant at 5% (Student t test)

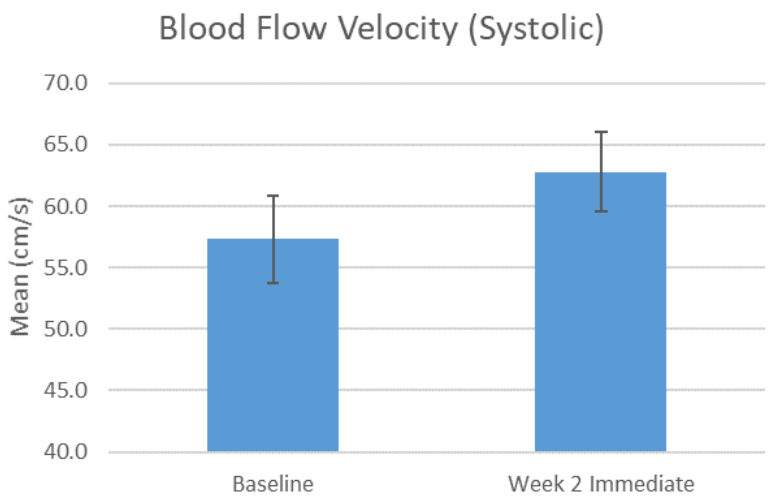


Figure 2 Mean and standard error per time-point and parameter of laser doppler ultrasound

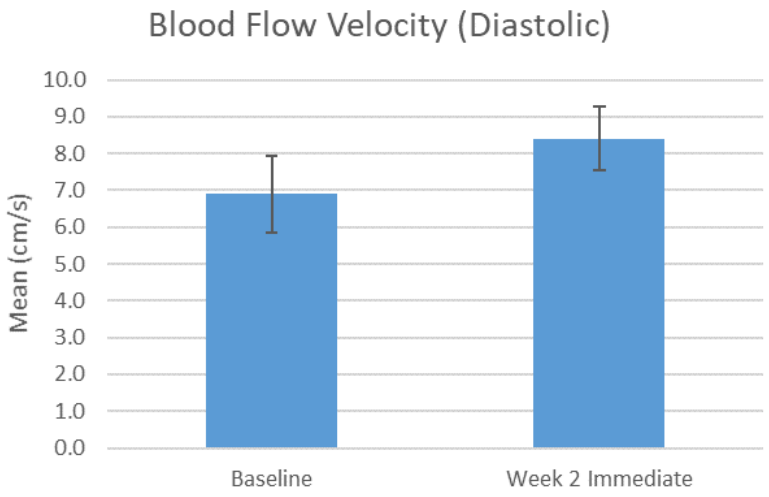


Figure 3 Mean and standard error per time-point and parameter of laser doppler ultrasound

## 13.8. Self-Assessment Questionnaire performed by the Study Subjects

The table and chart below present the percentage of subjects who stated to strongly agree and agree the attributes assessed after immediate and after 2 weeks of device use.

Table 25. Frequencies and percentages of positive responses (agreement)

| Statement | % (n) of positive responses | |
|---|---|---|
| | Immediate | Week 2 |
| Helps to soothe lower leg pain. | 47.7% (21) | 68.2% (30) |
| Helps to reduce leg cramps in legs or feet | 47.1% (8) | 70.6% (12) |
| Helps to calm leg restlessness. | 60.9% (14) | 65.2% (15) |
| My legs feel more relaxed. | 81.8% (36) | 77.3% (34) |
| My muscles feel looser, less stiff. | 83.3% (20) | 66.7% (16) |
| Reduces joint stiffness. | 50.0% (12) | 62.5% (15) |
| I feel like I have exercised. | 59.1% (26) | 63.6% (28) |
| Increases the feeling of feeling stronger. | 38.6% (17) | 56.8% (25) |
| I feel like it is easier to walk. | 34.1% (15) | 50.0% (22) |

Table 15. Frequencies and percentages of positive responses (agreement) – Week 2

| Statement | % (n) of positive responses |
|---|---|
| | Week 2 |
| The device is easy to use | 97.7% (43) |
| The device is safe to use | 97.7% (43) |
| Reduces swelling in lower legs, ankles or feet | 55.0% (11) |
| Reduces tingling in lower legs, ankles or feet | 64.7% (11) |
| Reduces the feeling of heaviness in lower legs, ankles or feet | 78.9% (15) |
| Reduces numbness in the lower legs, ankles or feet | 69.2% (9) |
| Improves the appearance of skin discoloration in lower legs, ankles or feet | 50.0% (2) |
| Improves the feeling of coldness in my lower legs, ankles or feet | 62.5% (5) |
| Improves the feeling of itchiness in my lower legs, ankles or feet | 57.1% (4) |
| Help to reduce “sleeplessness” caused by restless legs | 52.2% (12) |
| Helps to reduce “sleeplessness” caused by leg cramps | 58.8% (10) |
| Improves overall healthy feeling of legs | 61.4% (27) |

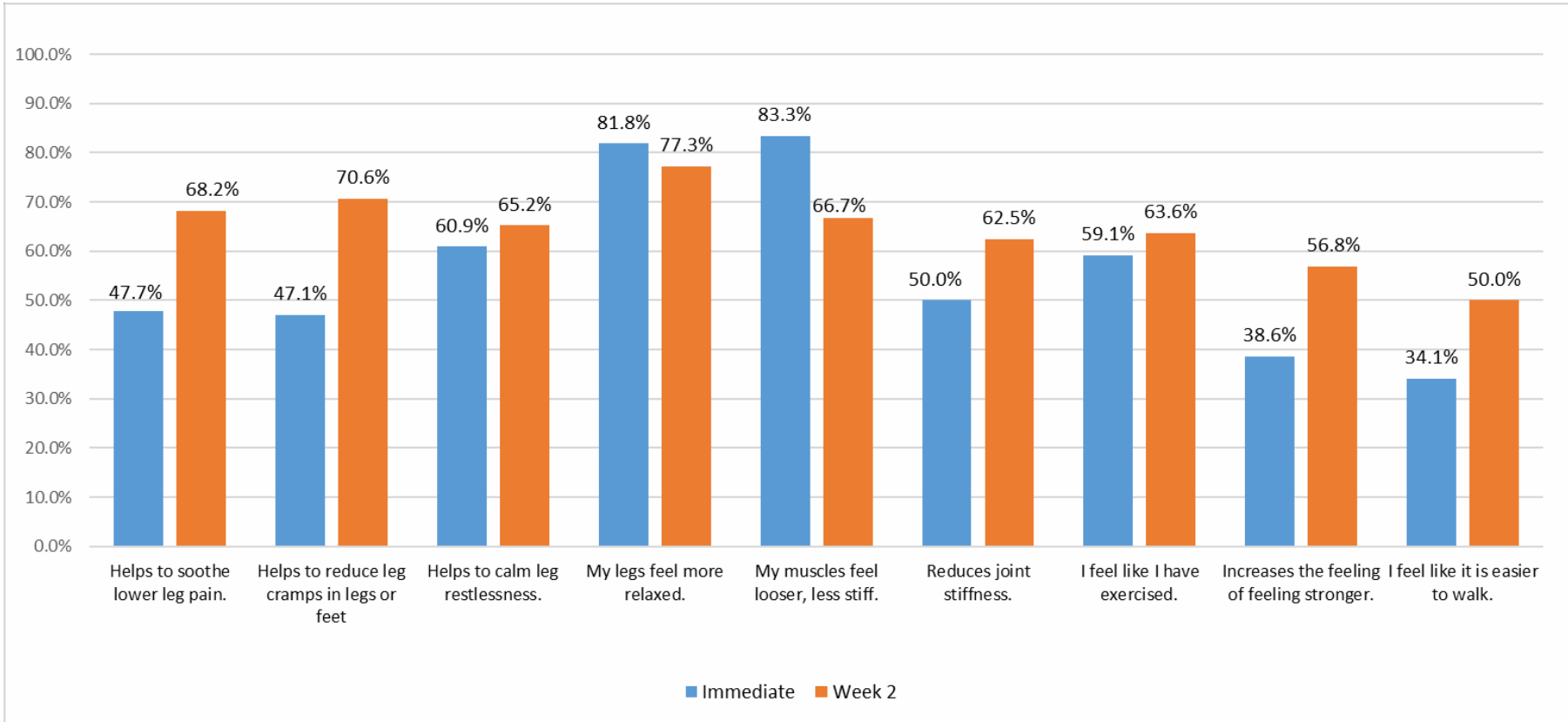


Figure 4 Percentage of positive responses by statement

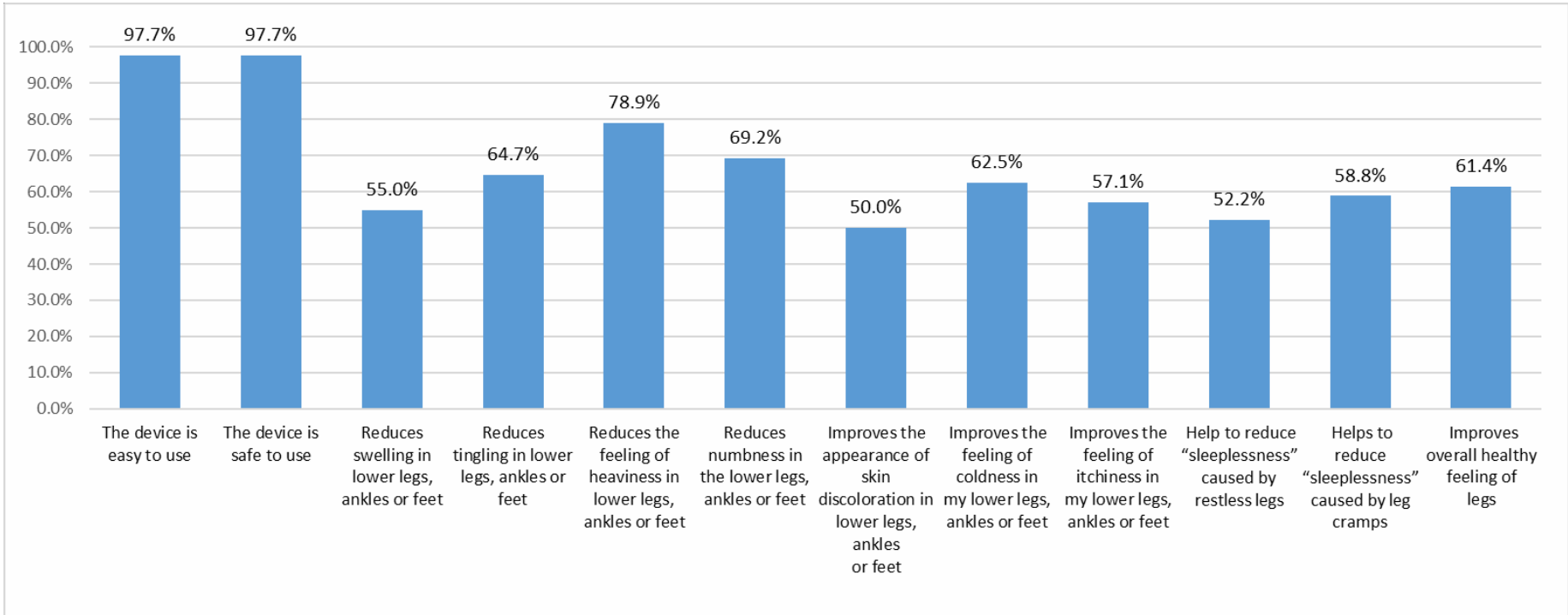


Figure 5 Percentage of positive responses by statement

## 14. CONCLUSION

According to the methodology used to assess the efficacy of the device **LEGXERCISE PROFESSIONAL**, submitted by the company **INTELLIBRANDS**, it could be concluded that:

### 14.1. Expert Grading Assessments

The device promoted an improvement in the appearance of lower leg skin discoloration after 2 weeks of use and after time-point Week 2 Immediate compared to time-points Baseline and Immediate.

The device did not promote an improvement of erythema.

### 14.2. Laser Doppler Ultrasound

The device promoted an improvement in blood flow after two weeks of use.

### 14.3. Self-Assessment Questionnaire performed by the Study Subjects

| | % of positive responses | |
|---|---|---|
| **Statement** | **Immediate** | **Week 2** |
| Helps to soothe lower leg pain. | 47.7% | 68.2% |
| Helps to reduce leg cramps in legs or feet | 47.1% | 70.6% |
| Helps to calm leg restlessness. | 60.9% | 65.2% |
| My legs feel more relaxed. | 81.8% | 77.3% |
| My muscles feel looser, less stiff. | 83.3% | 66.7% |
| Reduces joint stiffness. | 50.0% | 62.5% |
| I feel like I have exercised. | 59.1% | 63.6% |
| Increases the feeling of feeling stronger. | 38.6% | 56.8% |
| I feel like it is easier to walk. | 34.1% | 50.0% |

| | % of positive responses |
|---|---|
| **Statement** | **Week 2** |
| The device is easy to use | 97.7% |
| The device is safe to use | 97.7% |
| Reduces swelling in lower legs, ankles or feet | 55.0% |
| Reduces tingling in lower legs, ankles or feet | 64.7% |
| Reduces the feeling of heaviness in lower legs, ankles or feet | 78.9% |
| Reduces numbness in the lower legs, ankles or feet | 69.2% |
| Improves the appearance of skin discoloration in lower legs, ankles or feet | 50.0% |
| Improves the feeling of coldness in my lower legs, ankles or feet | 62.5% |
| Improves the feeling of itchiness in my lower legs, ankles or feet | 57.1% |
| Help to reduce “sleeplessness” caused by restless legs | 52.2% |
| Helps to reduce “sleeplessness” caused by leg cramps | 58.8% |
| Improves overall healthy feeling of legs | 61.4% |

Therefore, the following claims can be supported:

- *Improves lower leg blood flow (i.e. leg circulation)*; supported by the Laser Doppler Ultrasound Assessment;
- *Helps to reduce lower leg, ankle and feet swelling* supported by the Self-assessment questionnaire
- *Helps to reduce appearance of lower leg, ankle and feet skin discoloration*; supported by the Expert Grading Assessment;
- *Helps to reduce “cramps” in lower legs, and feet*; supported by the Self-assessment questionnaire;
- *Helps to reduce lower legs, pain sensations*; supported by the Self-assessment questionnaire;
- *Helps to reduce restless legs and sleeplessness caused by restless legs*; supported by the Self-assessment questionnaire;
- *Helps reduce leg and ankle joint stiffness*; supported by the Self-assessment questionnaire;
- *Improves leg restlessness, lower leg, ankles and feet coldness, tingling, swelling, numbness, heaviness and/or itchiness,* supported by the Self-assessment questionnaire;
- *Helps to reduce leg or feet cramps;* Supported by the self-assessment questionnaire;
- *Improves the perception of “loosening” leg muscles, feeling stronger, and relaxed legs*; supported by the Self-assessment questionnaire;
- *Improves overall healthy feeling of legs*; supported by the Self-assessment questionnaire;
- *The test device is easy and safe to use*, supported by the Self-assessment questionnaire.

Stephen R. Schwartz
Investigator in Charge
08/10/2021

José Marcos M. Vendramini
Statistician in Charge
08/10/2021

## 15. REFERENCES


ASTM, 2006 E 1958-06- Standard Guide for Sensory Claim Substantiation.

COLIPA GUIDELINES – Efficacy Evaluation of Cosmetic Products – May 2008.

FDA 21. Code of Federal Regulations. Title 21, Volume 1 – Food and Drugs, Chapter 1. Department of Health and Human Services. Subchapter A. April, 2019.

INTERNATIONAL CONFERENCE FOR HARMONIZATION (ICH) Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, 2016

ORGANIZACIÓN PANAMERICANA DE LA SALUD. BUENAS PRÁCTICAS CLÍNICAS: Documento De Las Américas, 2005

WORLD MEDICAL ASSOCIATION. Helsinki Declaration: Ethical principles for clinical research involving human beings, 52, 2000. Edinburgh: [y.n.], 2000. Amendment.

# APPENDIX 1. INFORMED CONSENT FORM

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

*This consent form may contain word(s) that you do not understand. Please ask the study staff to explain any word(s) or information that you do not clearly understand. You are entitled to a copy of this Consent Form and one will be provided to you at your first visit.*

**1.0 PURPOSE**

You are being asked to participate in a study to evaluate the efficacy of a device to improve Leg Circulation.

**2.0 ENROLLMENT**

Certain enrollment criteria are required for this study. If you do not meet these criteria you will not be enrolled in this study. Below is a list of enrollment requirements.

**Inclusion Criteria**

1. Females and males in good general health, between the ages of 65 and 85 years old, inclusive, at time of enrollment.
2. Self-perceived health concerns and sedentary lifestyle, including but not limited to:
   a. Self-perceived chronic leg pain ("Cramps"),
   b. Little to no physical activity, prolonged periods of inactivity (i.e. >4 hours at a desk) for >4 days a week
3. Able to read, understand and sign an informed consent form (includes HIPAA and State requirements) and to complete a brief personal medical history.
4. Willing to comply with all study instructions and requirements, including attendance at all scheduled study visits.

**Exclusion Criteria**

1. Athletes and active individuals, in good general health.
2. Participating in any other clinical studies
3. Acute or chronic disease or medical condition, which could put him/her at risk in the opinion of the Principal Investigator or compromise study outcomes. Typical uncontrolled chronic or serious diseases and conditions which would prevent participation in any clinical trial are cancer, AIDS, renal impairment, mental illness, drug/alcohol addiction. (*Per Sponsor, the following ARE permitted in this clinical study*: Arthritis, Bone on Bone, Recent Knee or Ankle Surgery, Pace Makers and Heart Conditions, High Cholesterol or Blood Pressure, Diabetes, Neuropathy, Lymphedema)
4. Unreliable or unlikely to be available for the duration of the study
5. Immunocompromised subjects
6. (Women) Started Hormone Replacement Therapy within the last three months preceding the screening visit
7. Unable to communicate or cooperate with the Principal Investigator due to language problems, poor mental development, or impaired cerebral function
8. Employees of IRSI or other testing firms/ laboratories, cosmetic or raw goods manufacturers or suppliers

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

**3.0 PROCEDURES**

You are being asked to voluntarily participate in a two visit study. Each visit will last for approximately one hour. The study will include approximately Forty (40) test subjects. At today's visit you will be asked to read and sign this informed consent prior to receiving any study instructions. You will also be asked to complete a brief medical/personal history form. Qualification for study participation will be evaluated by an IRSI technician using information collected from your medical history as well as an inclusion/ exclusion checklist. If qualified, you will be enrolled into the study. You will complete Visual Grading/Photography, Tape Measurement, and SONOS Titan Laser Doppler assessment. After all baseline assessments are complete, you will be provided with the study device as well as verbal and written use instructions. You will use the device for the first time onsite and then undergo SONOS Titan Laser Doppler assessment. You will also complete a questionnaire after use. Following completion of the post use assessments, you will receive an appointment for your Week 2 visit and be dismissed from the site.

**3.1 PRODUCT**

All subjects will receive the test device to use at home for two weeks. You will also use the device for the first time at today's visit and again at the Week 2 visit. You must bring the device to the Week 2 visit.

You will use the device for 45 minutes on speed 2 during the clinic visit, following the direction in the manual included with the device. You will use the device at home at least one time per day, for at least one hour on speed 2, following the directions in the manual included with the device.

**3.2 SUBJECTIVE QUESTIONNAIRE**

You will answer a questionnaire at the Baseline visit, after use of the device and at the Week 2 visit, after two weeks of repeated use. You will be asked to answer questions regarding leg circulation and your level agreement with statements about product performance.

**3.3 LASER DOPPLER ULTRASOUND**

All subjects will have Laser Doppler (GE Logiq e Ultrasound) performed to assess blood the blood flow velocity (i.e. leg circulation). Assessments will be performed on each subject's left or right lower lateral leg at the popliteal area (behind the knee) at Baseline, before the use of the device in-clinic and at the Week 2 visit immediately following device use in-clinic. Determination of which leg is to be assessed for each subject will be per a prepared randomization code at Baseline. The same leg will be assessed again at the Week 2 visit.

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

**3.4 TAPE MEASUREMENTS**

The area directly above the ankles will be measured with a tape measure pre-device use at Baseline and post-device use at Week 2.

**4.0 COMPENSATION**

You will receive $80.00 for completing the study as directed. If you are not qualified for this study you will not be compensated. If you are present and qualified, but not enrolled due to overbooking, you will be paid $20.00. Please note that it is the policy of IRSI to overbook all studies due to high rates of cancellations and no-shows. Completing the study paperwork does not guarantee enrollment into the study, even if you meet the entry criteria and qualify. If you are discontinued from the study you may be paid on the basis of the visits you have completed, at approximately $40.00 per visit.

If you withdraw from this study for personal reasons unrelated to the test materials, you will not be compensated. If you are disqualified for refusal to obey rules, follow instructions or attend all visits as scheduled, you will not be compensated.

This is a voluntary study and you may withdraw at any time without obligation or prejudice. The sponsor and/or investigative staff may remove you from this study at any time for any reason without loss of benefits, except as stated above.

**5.0 POTENTIAL BENEFITS**

You may notice an improvement in lower leg blood flow, reduction in lower leg, ankle and feet swelling, reduction in lower leg ankle and feet skin discoloration, reduction in "cramps" in lower legs, ankles and feet, lower pain sensations in lower leg, ankles and feet, reduction in restless legs and sleeplessness caused by restless legs, reduction in leg and ankle joint stiffness, improvement in lower leg, ankle and feet coldness, tingling, swelling, numbness, heaviness and/or itchiness, improvement of the perception of "loosening" leg muscles, and improvement in overall healthy feeling of legs. However, the amount is unknown and will vary among participants.

**6.0 POTENTIAL RISKS**

The products are for you ONLY to use.

You may notice an increase in muscle discomfort. If you do, you should contact IRSI immediately.

Reactions, if any, usually occur at or around the test area (feet and/or legs) but are not limited to this area. Reactions may persist in some individuals. In the event of a reaction you should **immediately** contact:

**Jennifer, Study Coordinator at (914) 937-6500, Ext. 133**

In the event of a medical emergency, you should seek medical attention first and then contact IRSI.

If you experience an injury as a direct result of administration of the test material, the study sponsor agrees to pay medical expenses necessary to treat such injury: (1) To the extent you are not otherwise reimbursed by your own medical insurance, (2) provided you have followed the directions of the investigator before and after the

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

injury occurred. Additional financial compensation will not be provided. Medical follow-up will be provided until the investigator or study coordinator determines you have recovered.

If you withdraw due to personal reasons related to product usage other than a response judged by IRSI staff to be a reaction to test product or instructions, you may not be paid. If, in the judgment of the investigative staff, it is best to discontinue your participation for reasons such as a documented medical condition not related to study materials, product failure or study termination, you will be paid for that portion of the study you have completed (pro rata), according to the number of scheduled visits made to the office. If your participation in the study is stopped due to an adverse reaction related to use of the test material or test instructions, you will be paid the full stipend amount.

If you are pregnant or planning on becoming pregnant or at significant risk of becoming pregnant during this test, you should not enroll in the test. Although no side effects to pregnancy are expected from the test materials the risks are unknown. If you become pregnant during the test you will immediately stop product use and notify IRSI.

For safety reasons, even if you drop from this study you may be asked to make follow-up visits to the study facility or to a physician. In the event of a reaction this is especially important for your safety and so that accurate information can be obtained.

**7.0 CONFIDENTIALITY OF RECORDS**

Reports prepared by IRSI use statistical information only and at no time will your name be used in these reports. The sponsor, the FDA and others in certain legal action, may inspect the records of this study which will include your name, medical records and, if applicable, personal information relating to your participation.

By signing this consent form you authorize the release of your medical records, only for treatment of illnesses and injuries related to this study to IRSI, and the study sponsor. IRSI will not release any information in your medical records except as stated in this consent.

**8.0 COVID-19 Addendum:**

IRSI is monitoring the COVID-19 situation in the New York area closely and have prepared for an outbreak in our area or office building. In the event that this study in whole or in part cannot be completed due to an outbreak of COVID-19 in the New York area or our office building, you will be informed immediately via phone and/or e-mail. Do not discontinue use of your test product unless otherwise instructed by an IRSI staff member.

In the event the study in whole or in part cannot take place as scheduled due to a stay at home order or closure to our office building one or more of the following may occur:

- The study may be cancelled.
- Visit(s) may be postponed or rescheduled, or moved to another local location.
- You may be required to complete at-home subjective questionnaires (via phone, website, or mail) for the remaining study visits.
- You may be asked to provide self-portraits using your smartphone (if applicable).
- You may be asked to remain on the study longer and resume visits once order is lifted.

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

- If needed additional test products may be provided to you via curbside pickup or mailed to your home.

In case of a change to the study due to COVID-19, you will be contacted via phone and or email, please make sure to check your messages regularly especially in the event of another outbreak reported in our area.

All efforts will be made to accommodate schedule changes, however failure to complete the study including at home subjective questionnaires or other study changes may result in your discontinuation of the study.

If you or someone in your household, or someone you come in contact with experiences symptoms of COVID-19 we ask that you contact IRSI immediately and cancel or reschedule your appointment until your 2-week self-quarantine is complete. If you or someone in your household TESTS POSITIVE for COVID-19, please contact IRSI immediately.

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

**8.0 USE OF PERSONAL INFORMATION (HIPAA) AUTHORIZATION**

Your participation in this study will involve disclosing some of your personal data and medical information (allergies, medications, illnesses, conditions and demographics {age, sex, race, and occupation}) as well as name, address, email address, Social Security Number, and phone number to IRSI.

The Study Coordinator, Investigator or authorized staff member may ask you for this information. By signing this consent form you authorize the release of your medical records (for treatments, illnesses and injuries as a direct result of test material use) to IRSI.

The same staff and management that write IRSI's reports will review or use the medical information you report. At no time will your name, address, phone number, email address or social security number be published in a report. The study Sponsor and the FDA may be granted access to your personal information regarding this study. IRSI will use the medical information you provide in order to conduct this study.

Additionally, IRSI will use the medical information in its database so that IRSI may be able to contact you to participate in future studies. Therefore, your authorization to IRSI to use the medical information and data you provide has no end date.

You have the right to revoke this authorization so long as IRSI has not already relied on or used the information you provided for this study. At your written request, IRSI will not contact you for future studies. Only employees who have signed a confidentiality agreement are permitted to access the database. IRSI does not sell the identifying information in the database. Even if you take back your consent to participate in this study the Use of Personal Information authorization will remain in effect.

**Your signature below indicates you have read the above privacy statement.**

| Signature: | Date: |
|---|---|
| | |

Subject Initials: _____

| | INFORMED CONSENT FORM | Study Number | 084504_4362ITB |
|---|---|---|---|
| | A Two-Week Clinical Evaluation of a Device on Leg Circulation | Subject Initials: | |
| | | Subject ID: | |

**9.0 CONSENT OF SUBJECT**

I have read and fully understand this consent and what is required of me during this study. I understand the risks, benefits and procedures and that I am free to ask questions at any time. I have no questions at this time. Additional information regarding the test material may become available to me during this study. If additional information becomes available or the study procedures are changed and this affects my well-being a new consent form will be provided to me. By signing this consent, I authorize the release of my medical records in the event of an illness, injury or reaction related to this study. The investigator or a member of the staff will be available at (914) 937-6500 to answer my questions. I have read this consent and I freely and voluntarily agree to participate in this study as described to me. By signing this form, I forfeit none of my legal rights.

| | | | |
|---|---|---|---|
| Signature: | | Date: | |
| Print Name:<br>Last: | First: | M.I: | |
| Street Address: | City: | State: | Zip: |
| Home Phone: | Cell Phone: | Work Phone: | |
| E-Mail Address: | | | |
| Social Security Number: | | | |

DO NOT WRITE BELOW THIS LINE

**********

**Witness Signature:** Person Administering Consent (IRSI Personnel)

| | | |
|---|---|---|
| Signature: | | Date: |
| Print Name:<br>Last: | First: | |

## APPENDIX 2. STUDY GROUP

| SUBJECT | AGE (YEARS) | GENDER | STATUS |
|---|---|---|---|
| 001 | 67 | M | I |
| 002 | 66 | M | I |
| 003 | 65 | M | I |
| 004 | 70 | F | I |
| 005 | 68 | M | I |
| 006 | 69 | F | I |
| 007 | 67 | F | I |
| 008 | 65 | M | I |
| 009 | 69 | F | I |
| 010 | 66 | M | I |
| 011 | 65 | M | I |
| 012 | 69 | M | I |
| 013 | 66 | F | I |
| 014 | 69 | F | I |
| 015 | 68 | F | I |
| 016 | 67 | F | I |
| 017 | 67 | F | I |
| 018 | 65 | M | I |
| 019 | 67 | F | I |
| 020 | 69 | F | I |
| 021 | 69 | F | I |
| 022 | 70 | F | I |
| 023 | 68 | F | I |
| 024 | 65 | F | I |
| 025 | 70 | F | I |
| 026 | 67 | M | I |
| 027 | 65 | F | I |
| 028 | 65 | F | I |
| 029 | 78 | M | I |
| 030 | 66 | F | I |
| 031 | 66 | M | I |
| 032 | 77 | M | I |
| 033 | 70 | F | I |
| 034 | 65 | F | I |
| 035 | 70 | M | I |
| 036 | 65 | M | I |
| 037 | 65 | M | I |
| 038 | 72 | M | I |

## STUDY GROUP (CONTINUATION)

| SUBJECT | AGE (YEARS) | GENDER | STATUS |
|---|---|---|---|
| 039 | 68 | F | I |
| 040 | 66 | F | I |
| 041 | 66 | M | I |
| 042 | 66 | F | I |
| 043 | 67 | F | I |
| 044 | 65 | M | I |
| 045 | 73 | M | I |
| 046 | 68 | F | NI |
| 047 | 69 | F | NI |
| 048 | 66 | F | NI |

Caption

**F**= female

**M**= Male

**I** = Included

**NI** = Not Included (to present any non-inclusion and/or not present some of the inclusion criteria).

## APPENDIX 3. RANDOMIZATION

| SUBJECT | SIDE |
|---|---|
| 001 | Right |
| 002 | Right |
| 003 | Right |
| 004 | Left |
| 005 | Left |
| 006 | Right |
| 007 | Left |
| 008 | Left |
| 009 | Left |
| 010 | Right |
| 011 | Right |
| 012 | Left |
| 013 | Right |
| 014 | Right |
| 015 | Left |
| 016 | Left |
| 017 | Right |
| 018 | Left |
| 019 | Right |
| 020 | Right |
| 021 | Left |
| 022 | Right |
| 023 | Right |
| 024 | Left |
| 025 | Right |
| 026 | Left |
| 027 | Right |
| 028 | Left |
| 029 | Left |
| 030 | Left |
| 031 | Right |
| 032 | Right |
| 033 | Right |
| 034 | Left |
| 035 | Right |
| 036 | Right |
| 037 | Left |
| 038 | Right |
| 039 | Left |
| 040 | Left |
| 041 | Left |
| 042 | Right |
| 043 | Left |
| 044 | Left |
| 045 | Left |

## APPENDIX 4. RAW DATA AND STATISTICAL ANALYSIS

### Expert Grading Assessments

Table 16. Raw Data and difference from baseline and from Week 2 Immediate – Skin Discoloration

| Subject | Baseline | Immediate | Week 2 | Week 2 Immediate | Immediate - Baseline | Week 2 - Baseline | Week 2 Immediate - Baseline | Week 2 immediate - Immediate | Week 2 immediate - Week 2 |
|---|---|---|---|---|---|---|---|---|---|
| 001 | 4.0 | 4.0 | 2.0 | 2.5 | 0.0 | -2.0 | -1.5 | -1.5 | 0.5 |
| 002 | 0.5 | 0.5 | 1.5 | 1.5 | 0.0 | 1.0 | 1.0 | 1.0 | 0.0 |
| 003 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 004 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | -0.5 | -0.5 | -0.5 | 0.0 |
| 005 | 2.5 | 2.5 | 1.5 | 1.0 | 0.0 | -1.0 | -1.5 | -1.5 | -0.5 |
| 006 | 0.5 | 0.5 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 008 | 4.0 | 4.0 | 2.0 | 2.5 | 0.0 | -2.0 | -1.5 | -1.5 | 0.5 |
| 009 | 1.5 | 1.0 | 0.5 | 0.5 | -0.5 | -1.0 | -1.0 | -0.5 | 0.0 |
| 010 | 0.5 | 0.0 | 0.5 | 0.5 | -0.5 | 0.0 | 0.0 | 0.5 | 0.0 |
| 011 | 0.0 | 0.5 | 0.5 | 0.0 | 0.5 | 0.5 | 0.0 | -0.5 | -0.5 |
| 012 | 0.0 | 0.0 | 1.0 | 0.5 | 0.0 | 1.0 | 0.5 | 0.5 | -0.5 |
| 013 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 014 | 2.5 | 3.0 | 1.0 | 1.0 | 0.5 | -1.5 | -1.5 | -2.0 | 0.0 |
| 015 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 016 | 2.0 | 2.5 | 0.0 | 0.0 | 0.5 | -2.0 | -2.0 | -2.5 | 0.0 |
| 017 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | -0.5 | -0.5 | -0.5 | 0.0 |
| 018 | 0.5 | 1.0 | 0.5 | 0.5 | 0.5 | 0.0 | 0.0 | -0.5 | 0.0 |
| 019 | 1.5 | 0.5 | 0.5 | 0.5 | -1.0 | -1.0 | -1.0 | 0.0 | 0.0 |
| 020 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 021 | 1.0 | 0.0 | 1.0 | 0.5 | -1.0 | 0.0 | -0.5 | 0.5 | -0.5 |
| 022 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 023 | 0.5 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | -0.5 | -0.5 | -0.5 |
| 024 | 0.0 | 0.5 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | -0.5 | 0.0 |
| 025 | 0.0 | 0.5 | 0.5 | 0.0 | 0.5 | 0.5 | 0.0 | -0.5 | -0.5 |
| 026 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 027 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 028 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | -0.5 | -0.5 | -0.5 | 0.0 |
| 029 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 030 | 0.5 | 0.0 | 0.0 | 0.0 | -0.5 | -0.5 | -0.5 | 0.0 | 0.0 |
| 031 | 1.5 | 1.0 | 1.5 | 2.0 | -0.5 | 0.0 | 0.5 | 1.0 | 0.5 |
| 032 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 033 | 0.5 | 0.5 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 034 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

Table 17. Raw Data and difference from baseline and from Week 2 Immediate – Skin Discoloration (Continuation)

| Subject | Baseline | Immediate | Week 2 | Week 2 Immediate | Immediate - Baseline | Week 2 - Baseline | Week 2 Immediate - Baseline | Week 2 immediate - Immediate | Week 2 immediate - Week 2 |
|---|---|---|---|---|---|---|---|---|---|
| 035 | 0.0 | 0.0 | 1.5 | 1.5 | 0.0 | 1.5 | 1.5 | 1.5 | 0.0 |
| 036 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 037 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 038 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | -0.5 | -0.5 | -0.5 | 0.0 |
| 039 | 1.0 | 0.5 | 0.0 | 0.0 | -0.5 | -1.0 | -1.0 | -0.5 | 0.0 |
| 040 | 0.5 | 1.0 | 0.0 | 0.0 | 0.5 | -0.5 | -0.5 | -1.0 | 0.0 |
| 041 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 042 | 0.0 | 0.0 | 0.5 | 0.5 | 0.0 | 0.5 | 0.5 | 0.5 | 0.0 |
| 043 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 044 | 0.5 | 0.5 | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 045 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Mean | 0.6 | 0.6 | 0.4 | 0.4 | 0.0 | -0.2 | -0.3 | -0.2 | 0.0 |
| SE | 0.2 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 |
| 95% CI | [0.3; 0.9] | [0.3; 0.9] | [0.2; 0.6] | [0.2; 0.6] | [-0.1; 0.1] | [-0.4; 0] | [-0.5; -0.1] | [-0.4; 0] | [-0.1; 0.1] |
| S.D. | 1.0 | 1.0 | 0.6 | 0.7 | 0.3 | 0.7 | 0.7 | 0.7 | 0.2 |
| Median | 0.5 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Min. | 0.0 | 0.0 | 0.0 | 0.0 | -1.0 | -2.0 | -2.0 | -2.5 | -0.5 |
| Max. | 4.0 | 4.0 | 2.0 | 2.5 | 0.5 | 1.5 | 1.5 | 1.5 | 0.5 |

Table 18. Raw Data and difference from baseline and from Week 2 Immediate – Erythema

| Subject | Baseline | Immediate | Week 2 | Week 2 Immediate | Immediate - Baseline | Week 2 - Baseline | Week 2 Immediate - Baseline | Week 2 immediate - Immediate | Week 2 immediate - Week 2 |
|---|---|---|---|---|---|---|---|---|---|
| 001 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 002 | 0.0 | 0.0 | 1.0 | 1.0 | 0.0 | 1.0 | 1.0 | 1.0 | 0.0 |
| 003 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 004 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | -1.0 |
| 005 | 1.0 | 1.0 | 0.0 | 1.0 | 0.0 | -1.0 | 0.0 | 0.0 | 1.0 |
| 006 | 0.0 | 1.0 | 0.0 | 1.0 | 1.0 | 0.0 | 1.0 | 0.0 | 1.0 |
| 008 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 009 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | -1.0 | -1.0 | -1.0 |
| 010 | 0.0 | 1.0 | 0.0 | 1.0 | 1.0 | 0.0 | 1.0 | 0.0 | 1.0 |
| 011 | 0.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 |
| 012 | 0.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 |
| 013 | 0.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 |
| 014 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 015 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 016 | 1.0 | 1.0 | 0.0 | 1.0 | 0.0 | -1.0 | 0.0 | 0.0 | 1.0 |

Table 17. Raw Data and difference from baseline and from Week 2 Immediate – Erythema (Continuation)

| Subject | Baseline | Immediate | Week 2 | Week 2 Immediate | Immediate - Baseline | Week 2 - Baseline | Week 2 Immediate - Baseline | Week 2 immediate - Immediate | Week 2 immediate - Week 2 |
|---|---|---|---|---|---|---|---|---|---|
| 017 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | -1.0 | 0.0 |
| 018 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 019 | 1.0 | 0.0 | 1.0 | 1.0 | -1.0 | 0.0 | 0.0 | 1.0 | 0.0 |
| 020 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | -1.0 | 0.0 |
| 021 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | -1.0 |
| 022 | 0.0 | 0.0 | 1.0 | 1.0 | 0.0 | 1.0 | 1.0 | 1.0 | 0.0 |
| 023 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | -1.0 | -1.0 | -1.0 |
| 024 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | -1.0 | -1.0 | -1.0 |
| 025 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | -1.0 | -1.0 | -1.0 |
| 026 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | -1.0 | 0.0 |
| 027 | 0.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 1.0 | 1.0 |
| 028 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 029 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 030 | 1.0 | 0.0 | 1.0 | 1.0 | -1.0 | 0.0 | 0.0 | 1.0 | 0.0 |
| 031 | 2.0 | 1.0 | 2.0 | 2.0 | -1.0 | 0.0 | 0.0 | 1.0 | 0.0 |
| 032 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 033 | 0.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 |
| 034 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 035 | 0.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 |
| 036 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 037 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 038 | 1.0 | 0.0 | 0.0 | 1.0 | -1.0 | -1.0 | 0.0 | 1.0 | 1.0 |
| 039 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 040 | 1.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 041 | 1.0 | 1.0 | 0.0 | 1.0 | 0.0 | -1.0 | 0.0 | 0.0 | 1.0 |
| 042 | 1.0 | 0.0 | 1.0 | 1.0 | -1.0 | 0.0 | 0.0 | 1.0 | 0.0 |
| 043 | 0.0 | 1.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | -1.0 | 0.0 |
| 044 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 045 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Mean | 0.4 | 0.6 | 0.5 | 0.6 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 |
| SE | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| 95% CI | [0.2; 0.6] | [0.4; 0.8] | [0.3; 0.7] | [0.4; 0.8] | [-0.1; 0.3] | [-0.1; 0.3] | [-0.1; 0.3] | [-0.2; 0.2] | [-0.2; 0.2] |
| S.D. | 0.5 | 0.5 | 0.5 | 0.5 | 0.6 | 0.5 | 0.6 | 0.6 | 0.5 |
| Median | 0.0 | 1.0 | 1.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Min | 0.0 | 0.0 | 0.0 | 0.0 | -1.0 | -1.0 | -1.0 | -1.0 | -1.0 |
| Max | 2.0 | 1.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

## Laser Doppler Ultrasound

Table 18. Raw Data and descriptives statistcs

| Subject | Blood Flow Velocity (Systolic) | | | Blood Flow Velocity (Diastolic) | | |
|---|---|---|---|---|---|---|
| | Baseline | Week 2 | Week 2 - Baseline | Baseline | Week 2 | Week 2 - Baseline |
| 002 | 59.3 | 59.3 | 0.0 | 7.3 | 5.0 | -2.3 |
| 003 | 48.1 | 70.5 | 22.4 | 7.3 | 5.6 | -1.7 |
| 006 | 64.6 | 57.0 | -7.6 | 3.4 | 5.6 | 2.2 |
| 008 | 55.9 | 52.6 | -3.3 | 6.2 | 7.3 | 1.1 |
| 015 | 71.6 | 72.7 | 1.1 | 6.2 | 9.5 | 3.3 |
| 018 | 52.6 | 53.7 | 1.1 | 14.0 | 14.0 | 0.0 |
| 020 | 31.9 | 58.2 | 26.3 | 2.8 | 5.6 | 2.8 |
| 023 | 43.1 | 76.6 | 33.5 | 2.8 | 6.2 | 3.4 |
| 026 | 78.9 | 85.6 | 6.7 | 16.2 | 13.4 | -2.8 |
| 030 | 57.3 | 49.2 | -8.1 | 9.0 | 6.7 | -2.3 |
| 034 | 40.8 | 46.4 | 5.6 | 1.1 | 5.0 | 3.9 |
| 037 | 46.4 | 45.9 | -0.5 | 8.4 | 5.6 | -2.8 |
| 040 | 53.7 | 56.5 | 2.8 | 5.0 | 9.0 | 4.0 |
| 041 | 64.3 | 71.6 | 7.3 | 8.4 | 14.0 | 5.6 |
| 043 | 63.2 | 64.3 | 1.1 | 2.2 | 8.4 | 6.2 |
| 045 | 85.6 | 84.4 | -1.2 | 9.5 | 13.4 | 3.9 |
| Mean | 57.3 | 62.8 | 5.5 | 6.9 | 8.4 | 1.5 |
| SE | 3.5 | 3.2 | 3.0 | 1.0 | 0.9 | 0.8 |
| 95% CI | [49.8; 64.8] | [56; 69.6] | [-0.8; 11.8] | [4.7; 9.1] | [6.6; 10.2] | [-0.2; 3.2] |
| S.D. | 14.1 | 12.8 | 11.9 | 4.2 | 3.4 | 3.1 |
| Median | 56.6 | 58.8 | 1.1 | 6.8 | 7.0 | 2.5 |
| Minimum | 31.9 | 45.9 | -8.1 | 1.1 | 5.0 | -2.8 |
| Maximum | 85.6 | 85.6 | 33.5 | 16.2 | 14.0 | 6.2 |

## Subjective Questionnaire

| Subject | Did you present lower leg, ankle and feet swelling before the study? | Did you experience leg and ankle joint stiffness before the study? | Did you experience leg restlessness before the study? | Did you experience lower leg, ankles and feet coldness before the study? | Did you experience lower leg, ankles and feet heaviness before the study? | Did you experience lower leg, ankles and feet tingling before the study? | Did you experience lower leg, ankles and feet numbness before the study? | Did you experience lower leg, ankles and feet itchiness before the study? | Did you experience lower leg, ankle and feet skin discoloration before the study? |
|---|---|---|---|---|---|---|---|---|---|
| 001 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 003 | No | No | No | No | No | No | No | No | No |
| 004 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No |
| 005 | Yes | Yes | Yes | No | Yes | No | No | No | No |
| 006 | No | No | No | No | No | No | No | No | No |
| 007 | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No |
| 008 | Yes | Yes | Yes | No | Yes | Yes | Yes | No | No |
| 009 | No | No | No | No | No | No | No | No | No |
| 010 | Yes | No | No | No | No | No | No | No | No |
| 011 | No | No | No | No | No | No | No | No | No |
| 012 | No | No | No | No | No | No | No | No | No |
| 014 | Yes | Yes | Yes | No | No | No | No | No | No |
| 015 | Yes | Yes | Yes | No | No | No | Yes | Yes | No |
| 016 | Yes | No | No | No | No | No | No | No | No |
| 017 | No | Yes | No | No | No | No | No | No | No |
| 018 | Yes | No | Yes | No | No | Yes | No | No | No |
| 019 | Yes | Yes | Yes | No | Yes | Yes | Yes | No | No |
| 020 | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| 021 | Yes | Yes | Yes | No | Yes | Yes | Yes | No | No |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 022 | No | No | No | No | No | No | No | No | No |

| Subject | Did you present lower leg, ankle and feet swelling before the study? | Did you experience leg and ankle joint stiffness before the study? | Did you experience leg restlessness before the study? | Did you experience lower leg, ankles and feet coldness before the study? | Did you experience lower leg, ankles and feet heaviness before the study? | Did you experience lower leg, ankles and feet tingling before the study? | Did you experience lower leg, ankles and feet numbness before the study? | Did you experience lower leg, ankles and feet itchiness before the study? | Did you experience lower leg, ankle and feet skin discoloration before the study? |
|---|---|---|---|---|---|---|---|---|---|
| 025 | No | No | No | No | No | No | No | No | No |
| 023 | Yes | Yes | Yes | No | Yes | No | No | No | No |
| 024 | No | Yes | Yes | No | Yes | Yes | Yes | No | No |
| 027 | Yes | Yes | Yes | No | Yes | Yes | Yes | No | No |
| 028 | No | Yes | Yes | No | No | No | No | No | No |
| 029 | Yes | No | Yes | No | Yes | Yes | Yes | Yes | No |
| 030 | No | No | No | No | Yes | No | No | No | No |
| 031 | Yes | Yes | No | Yes | Yes | Yes | No | Yes | Yes |
| 032 | Yes | Yes | No | Yes | No | Yes | No | No | No |
| 033 | No | No | Yes | Yes | No | No | No | No | No |
| 034 | No | Yes | Yes | No | Yes | No | No | No | No |
| 036 | No | Yes | Yes | No | Yes | Yes | No | No | No |
| 037 | No | No | Yes | No | No | No | No | No | No |
| 038 | Yes | Yes | No | No | No | Yes | No | No | No |
| 039 | No | Yes | Yes | No | Yes | Yes | Yes | No | No |
| 040 | Yes | Yes | Yes | No | Yes | Yes | Yes | No | No |
| 041 | No | No | No | No | No | No | No | Yes | No |
| 042 | No | Yes | Yes | Yes | No | Yes | No | No | No |
| 043 | Yes | Yes | No | Yes | Yes | Yes | Yes | No | Yes |
| 044 | No | Yes | Yes | No | Yes | No | No | Yes | No |

Table 19. Frequencies and percentages – Immediate

| Statement | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
|---|---|---|---|---|---|
| Helps to soothe lower leg pain. | 2.3% (1) | 0% (0) | 50% (22) | 36.4% (16) | 11.4% (5) |
| Helps to reduce leg cramps in legs or feet | 0% (0) | 5.9% (1) | 47.1% (8) | 35.3% (6) | 11.8% (2) |
| Helps to calm leg restlessness. | 0% (0) | 4.3% (1) | 34.8% (8) | 56.5% (13) | 4.3% (1) |
| My legs feel more relaxed. | 2.3% (1) | 2.3% (1) | 13.6% (6) | 68.2% (30) | 13.6% (6) |
| My muscles feel looser, less stiff. | 0% (0) | 8.3% (2) | 8.3% (2) | 75% (18) | 8.3% (2) |
| Reduces joint stiffness. | 0% (0) | 8.3% (2) | 41.7% (10) | 41.7% (10) | 8.3% (2) |
| I feel like I have exercised. | 4.5% (2) | 11.4% (5) | 25% (11) | 31.8% (14) | 27.3% (12) |
| Increases the feeling of feeling stronger. | 4.5% (2) | 9.1% (4) | 47.7% (21) | 22.7% (10) | 15.9% (7) |
| I feel like it is easier to walk. | 0% (0) | 9.1% (4) | 56.8% (25) | 27.3% (12) | 6.8% (3) |

Table 20. Frequencies and percentages – Week 2

| Statement | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
|---|---|---|---|---|---|
| The device is easy to use | 0% (0) | 0% (0) | 2.3% (1) | 6.8% (3) | 90.9% (40) |
| The device is safe to use | 0% (0) | 0% (0) | 2.3% (1) | 11.4% (5) | 86.4% (38) |
| Reduces swelling in lower legs, ankles or feet | 0% (0) | 0% (0) | 45% (9) | 20% (4) | 35% (7) |
| Reduces tingling in lower legs, ankles or feet | 0% (0) | 0% (0) | 35.3% (6) | 17.6% (3) | 47.1% (8) |
| Reduces the feeling of heaviness in lower legs, ankles or feet | 0% (0) | 0% (0) | 21.1% (4) | 42.1% (8) | 36.8% (7) |
| Reduces numbness in the lower legs, ankles or feet | 0% (0) | 0% (0) | 30.8% (4) | 30.8% (4) | 38.5% (5) |
| Improves the appearance of skin discoloration in lower legs, ankles or feet | 0% (0) | 0% (0) | 50% (2) | 25% (1) | 25% (1) |
| Improves the feeling of coldness in my lower legs, ankles or feet | 0% (0) | 12.5% (1) | 25% (2) | 25% (2) | 37.5% (3) |
| Improves the feeling of itchiness in my lower legs, ankles or feet | 0% (0) | 14.3% (1) | 28.6% (2) | 28.6% (2) | 28.6% (2) |
| Helps to soothe/alleviate lower leg pain | 2.3% (1) | 2.3% (1) | 27.3% (12) | 47.7% (21) | 20.5% (9) |
| Helps to reduce/alleviate leg cramps in legs or feet | 0% (0) | 5.9% (1) | 23.5% (4) | 23.5% (4) | 47.1% (8) |
| Reduces joint stiffness | 0% (0) | 12.5% (3) | 25% (6) | 37.5% (9) | 25% (6) |
| Helps to calm/alleviate leg restlessness | 0% (0) | 13% (3) | 21.7% (5) | 34.8% (8) | 30.4% (7) |
| Help to reduce “sleeplessness” caused by restless legs | 0% (0) | 13% (3) | 34.8% (8) | 21.7% (5) | 30.4% (7) |
| Helps to reduce “sleeplessness” caused by leg cramps | 0% (0) | 5.9% (1) | 35.3% (6) | 29.4% (5) | 29.4% (5) |
| I feel like I have exercised | 4.5% (2) | 13.6% (6) | 18.2% (8) | 25% (11) | 38.6% (17) |
| I have an increased feeling of feeling stronger | 4.5% (2) | 9.1% (4) | 29.5% (13) | 20.5% (9) | 36.4% (16) |
| My muscles feel looser, less stiff | 0% (0) | 4.2% (1) | 29.2% (7) | 37.5% (9) | 29.2% (7) |
| My legs feel more relaxed | 2.3% (1) | 0% (0) | 20.5% (9) | 43.2% (19) | 34.1% (15) |
| I feel like it is easier to walk | 2.3% (1) | 6.8% (3) | 40.9% (18) | 20.5% (9) | 29.5% (13) |
| Improves overall healthy feeling of legs | 2.3% (1) | 0% (0) | 36.4% (16) | 29.5% (13) | 31.8% (14) |

## APPENDIX 5. LASER DOPPLER ULTRASOUND IMAGES

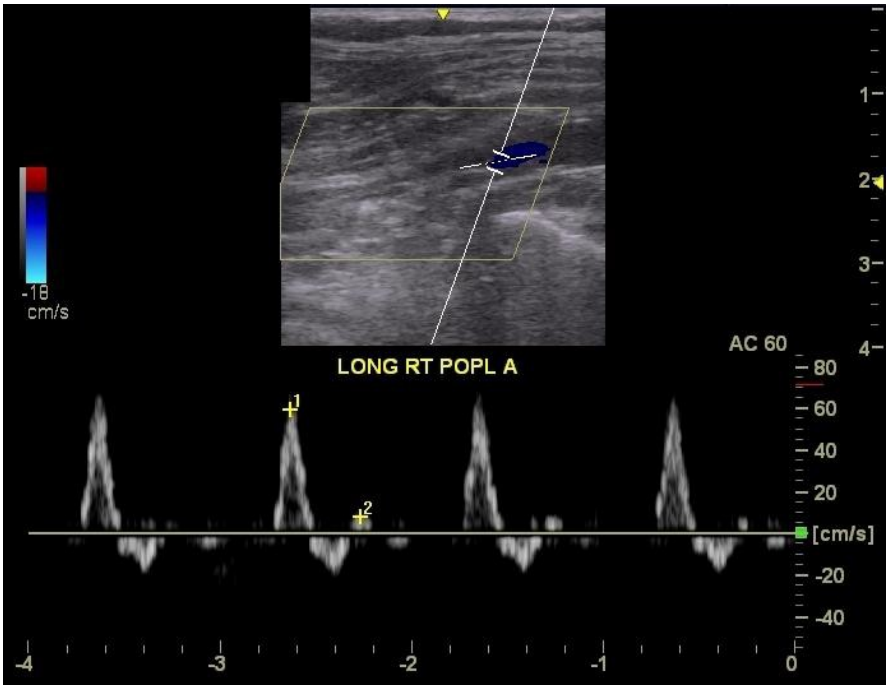


Figure 6 002_Baseline

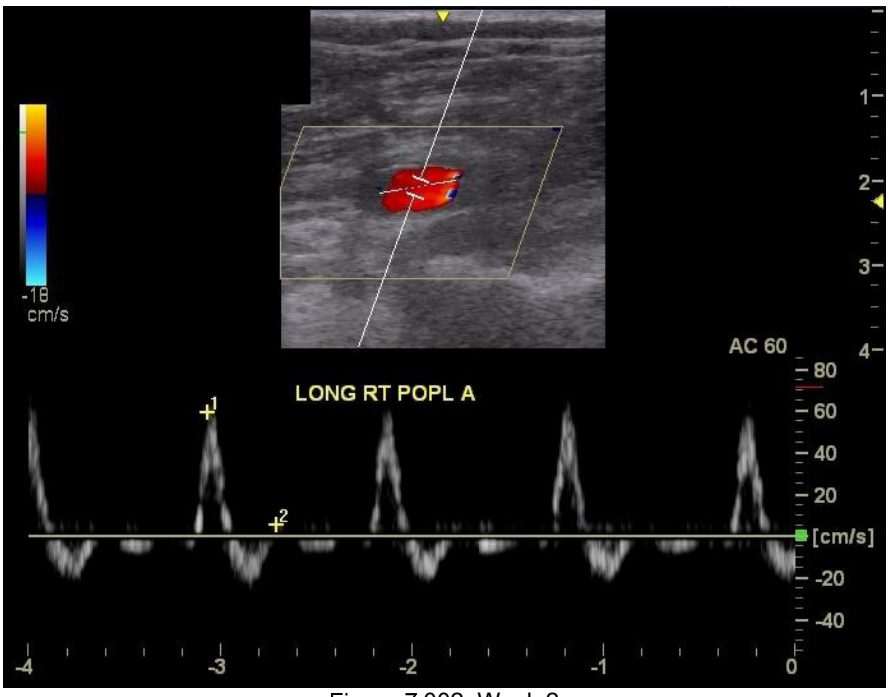


Figure 7 002_Week 2

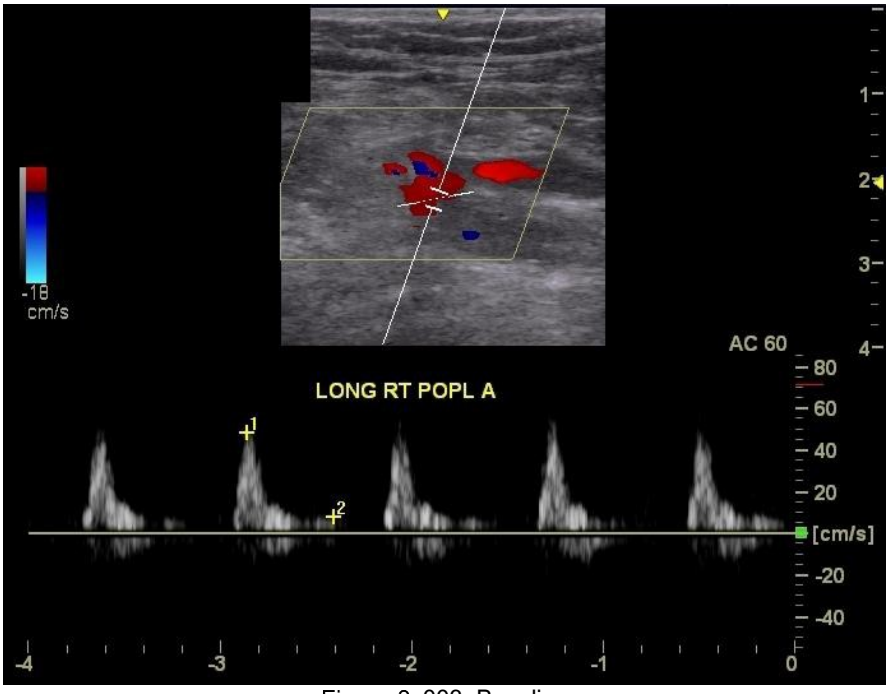


Figure 8 003_Baseline

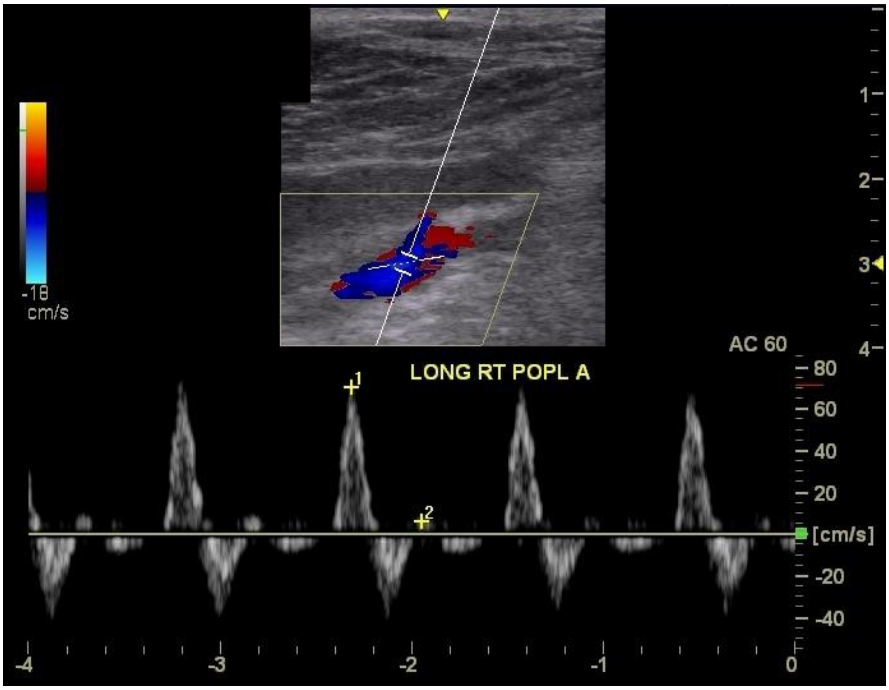


Figure 9 003_Week 2

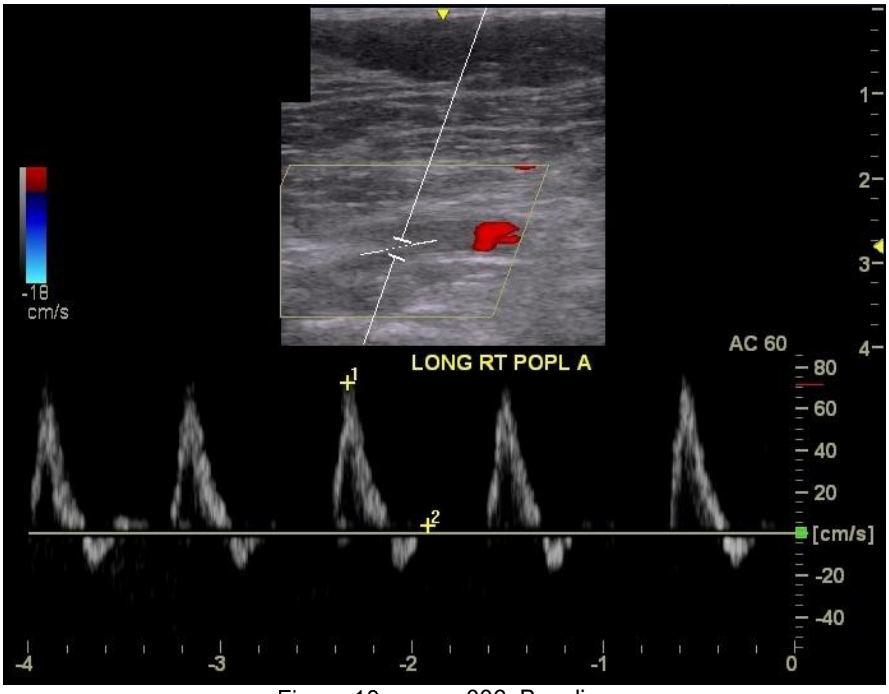


Figure 10 006_Baseline

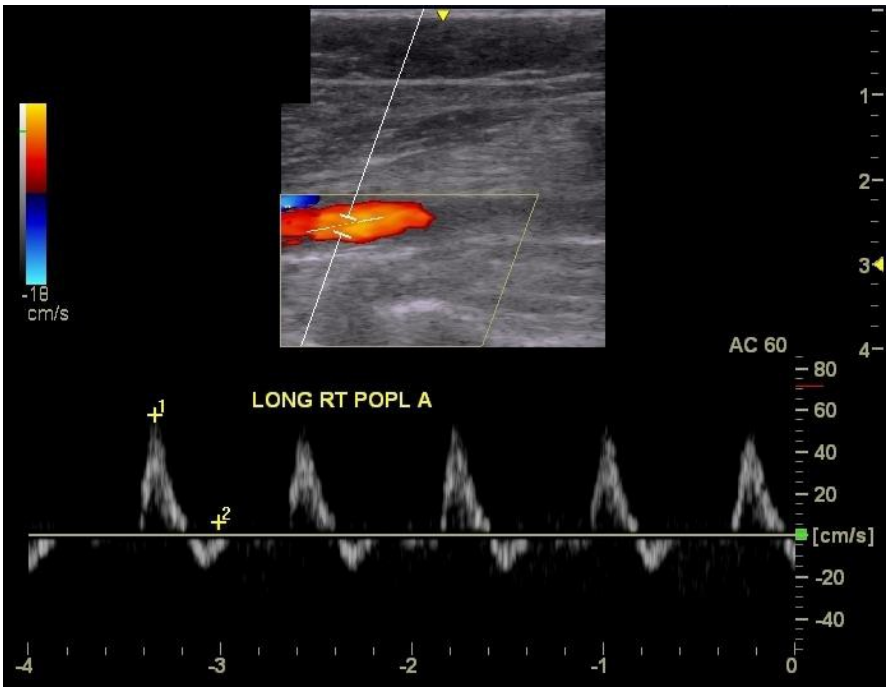


Figure 11 006_Week 2

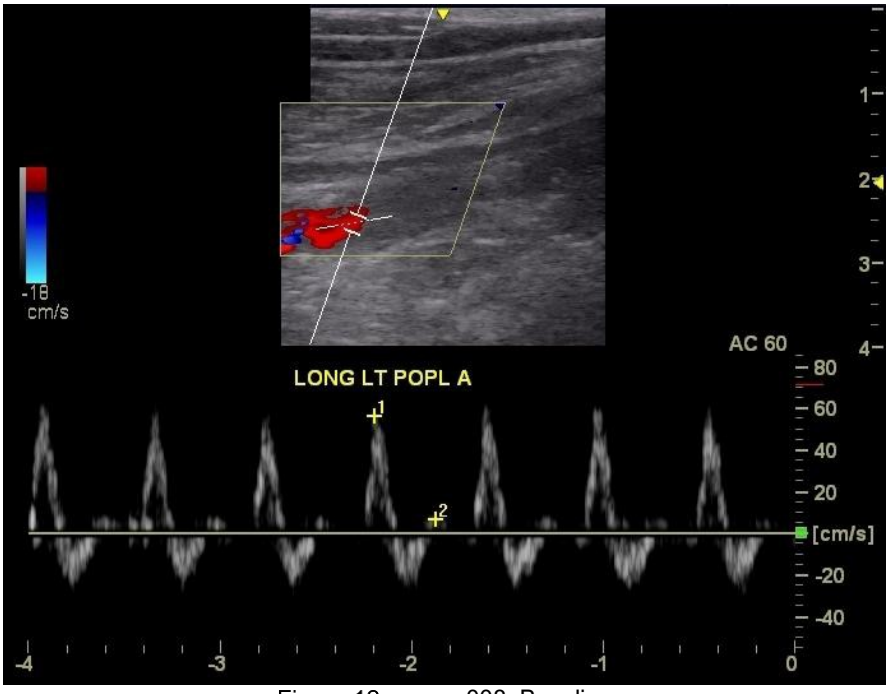


Figure 12 008_Baseline

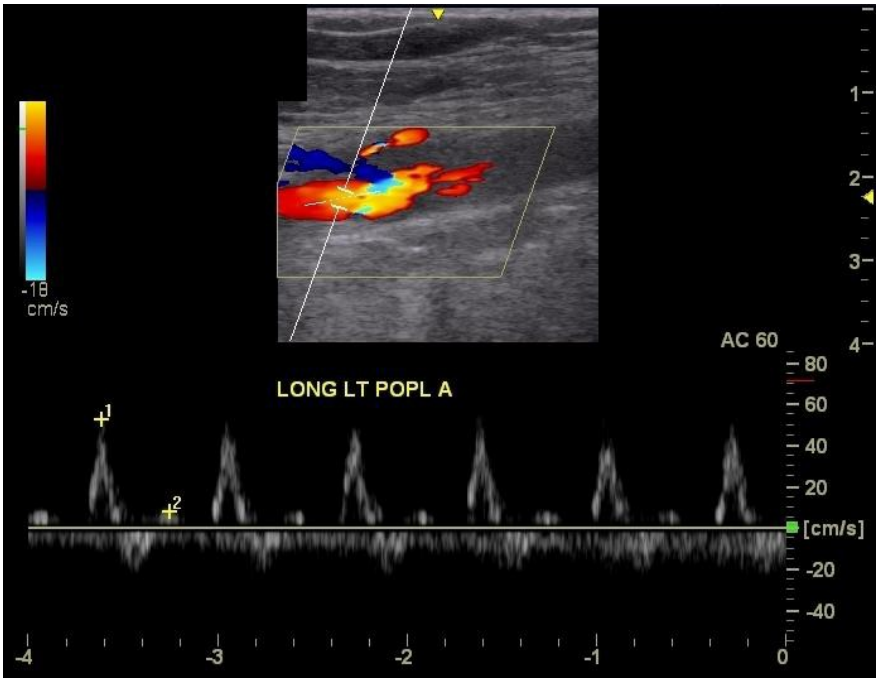


Figure 13 008_Week 2

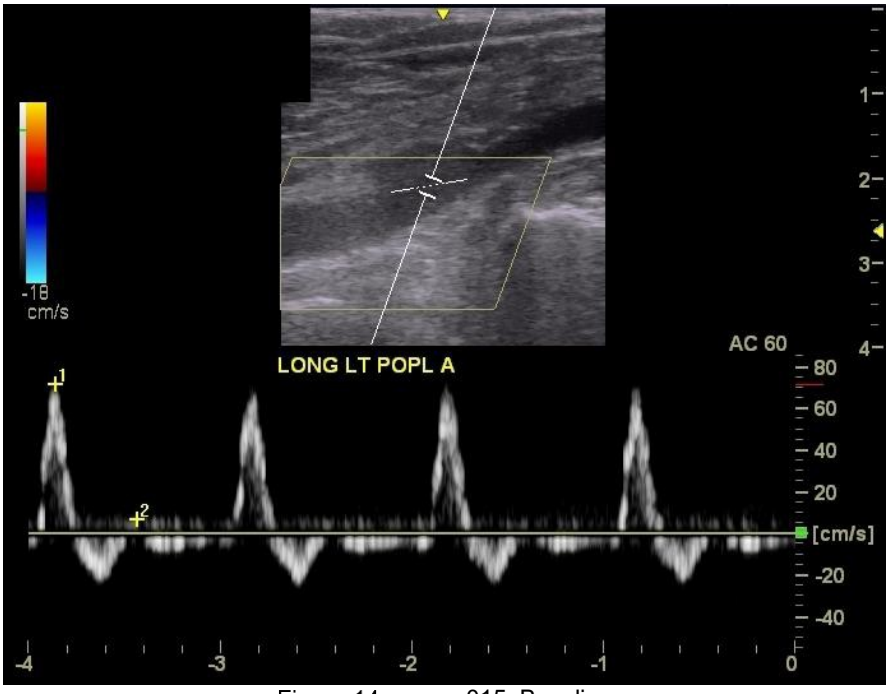


Figure 14 015_Baseline

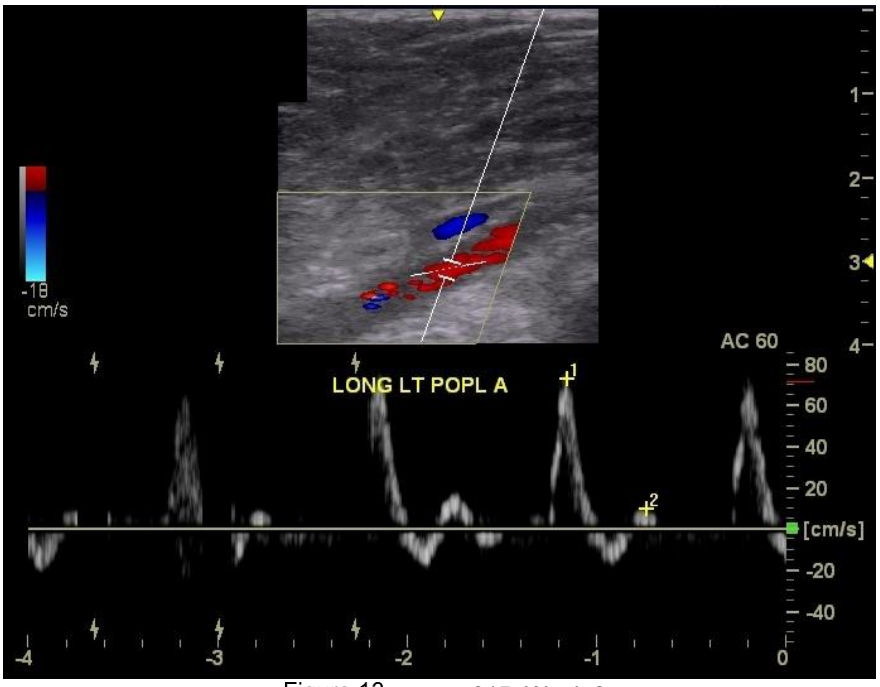


Figure 13 015_Week 2

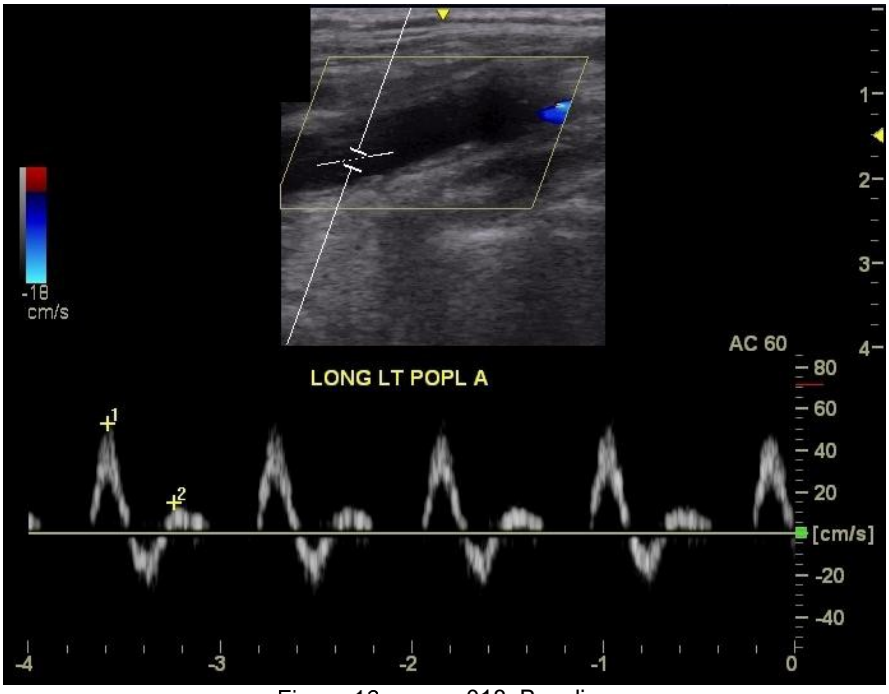


Figure 16 018_Baseline

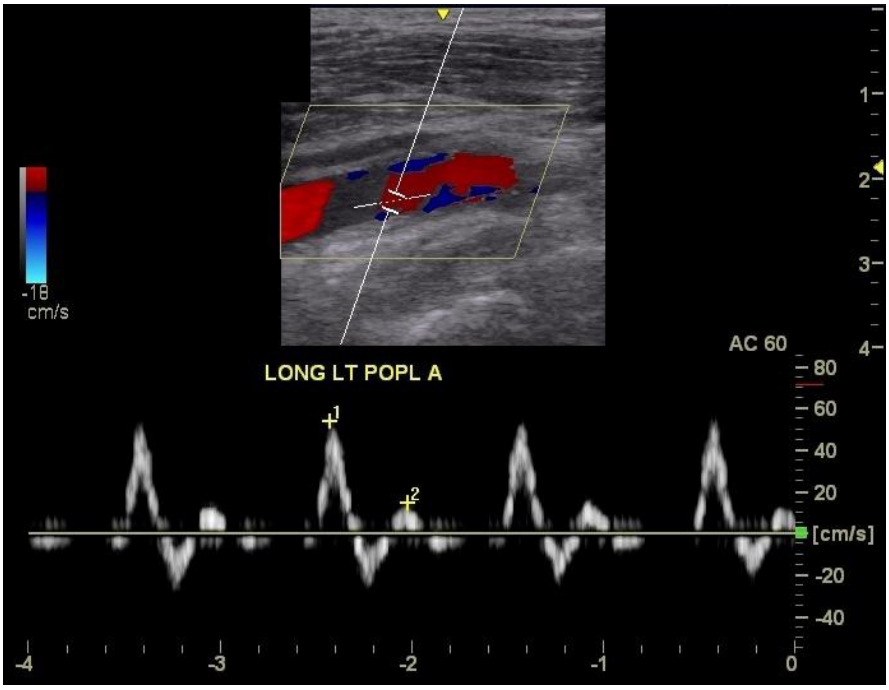


Figure 17 018_Week 2

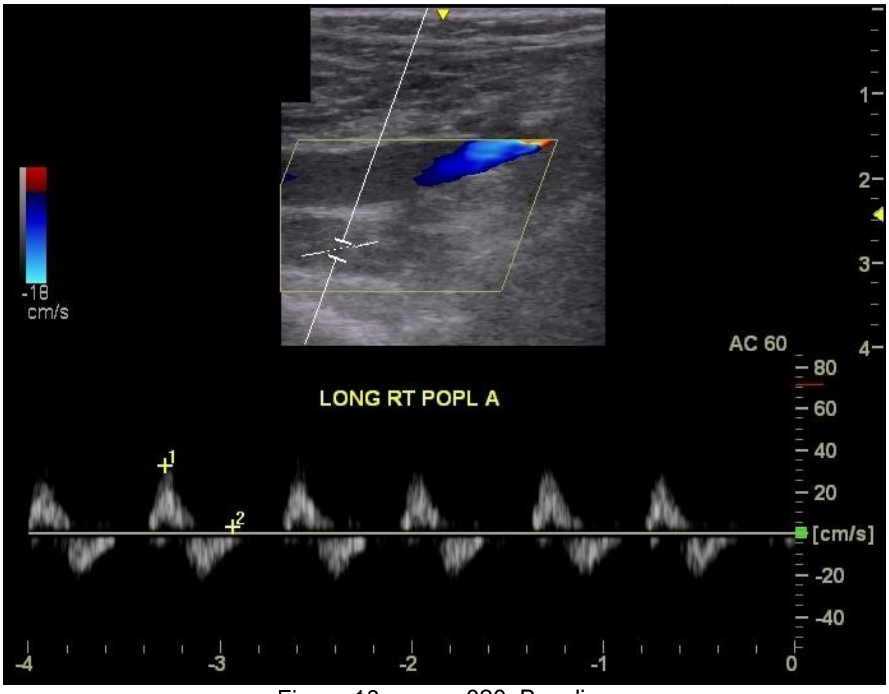


Figure 18 020_Baseline

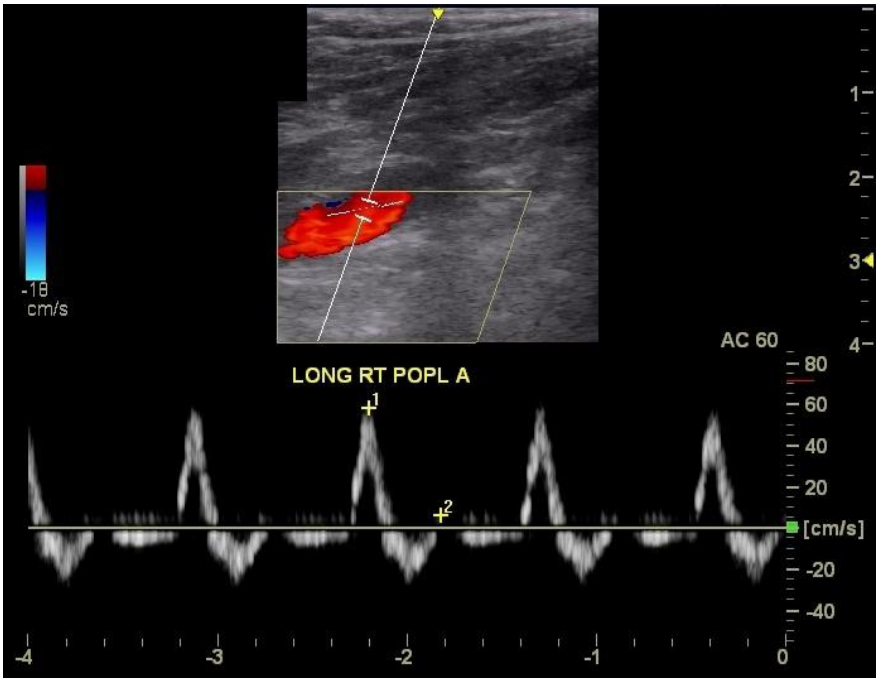


Figure 19 020_Week 2

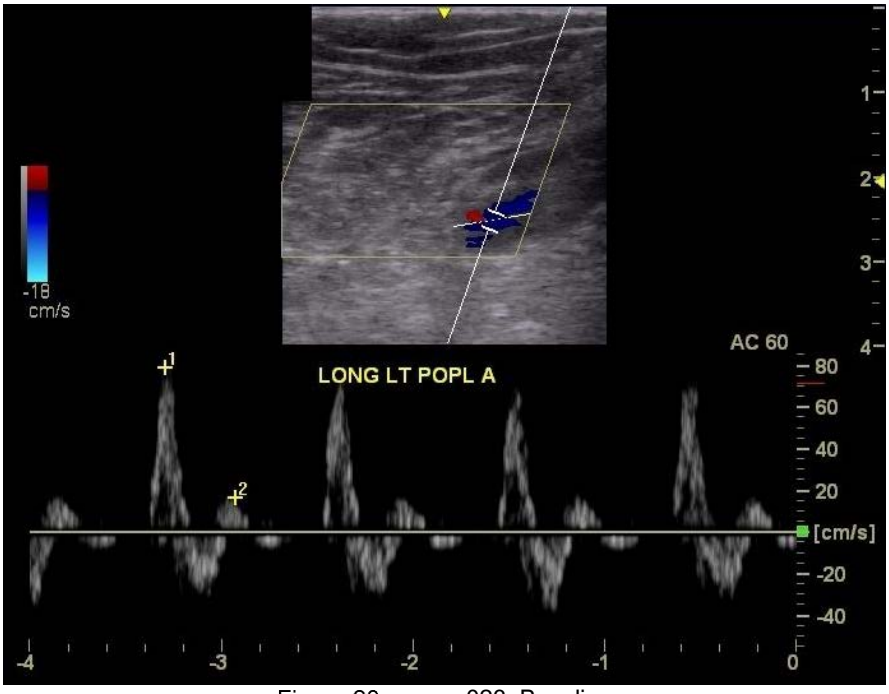


Figure 20 023_Baseline

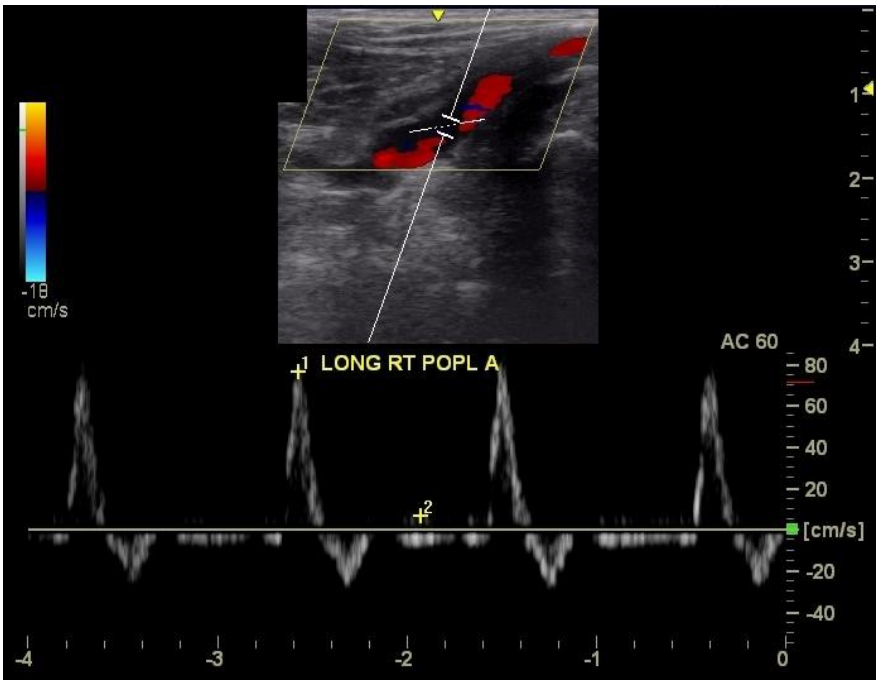


Figure 19 023_Week 2

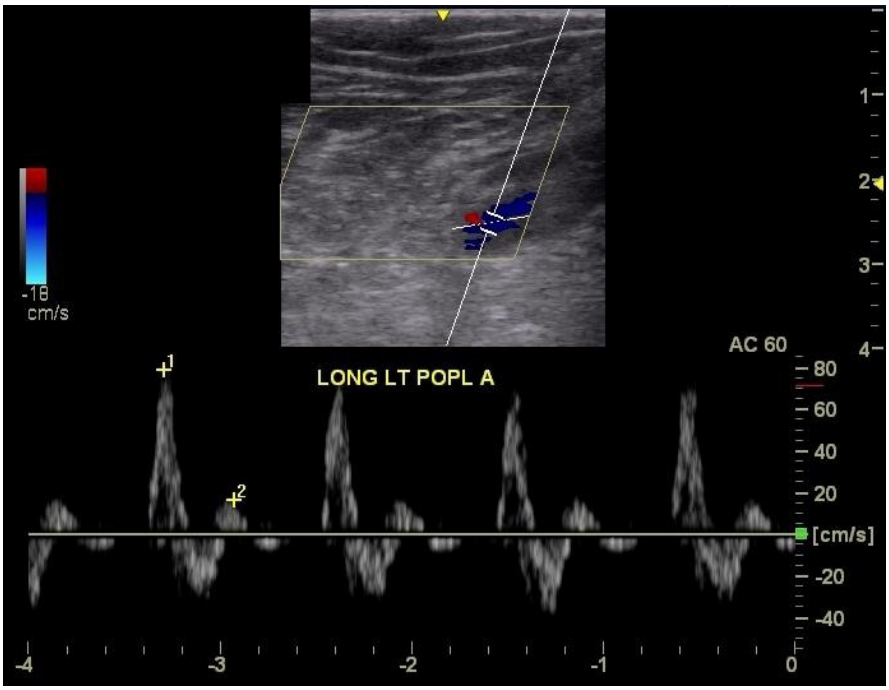


Figure 22 026_Baseline

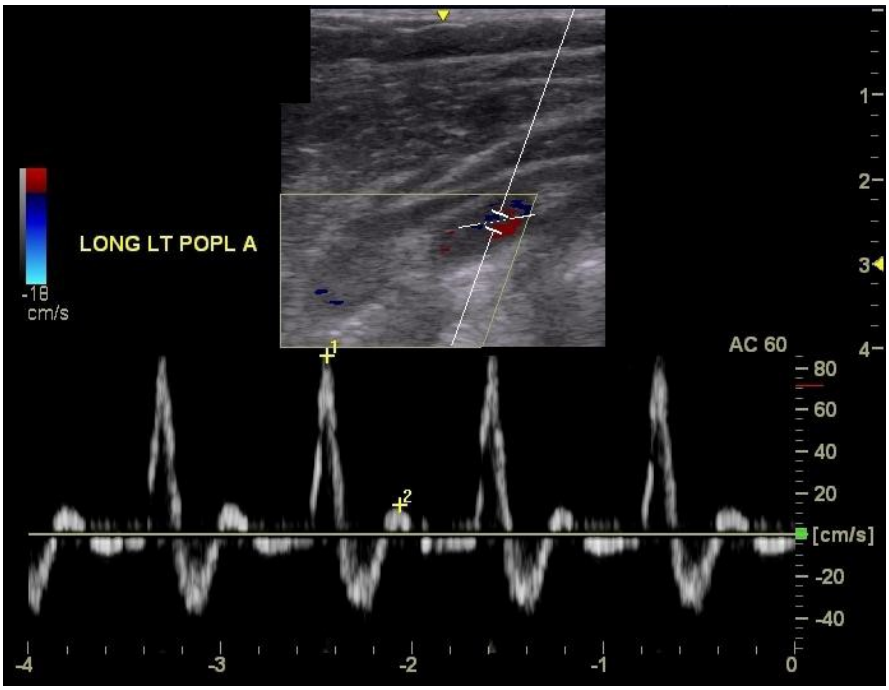


Figure 23 026_Week 2

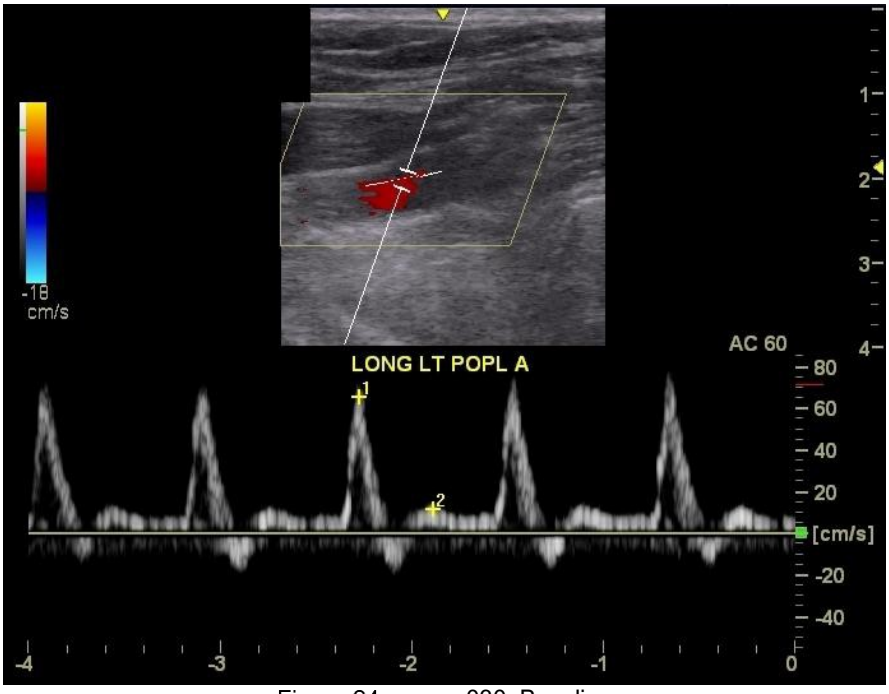


Figure 24 030_Baseline

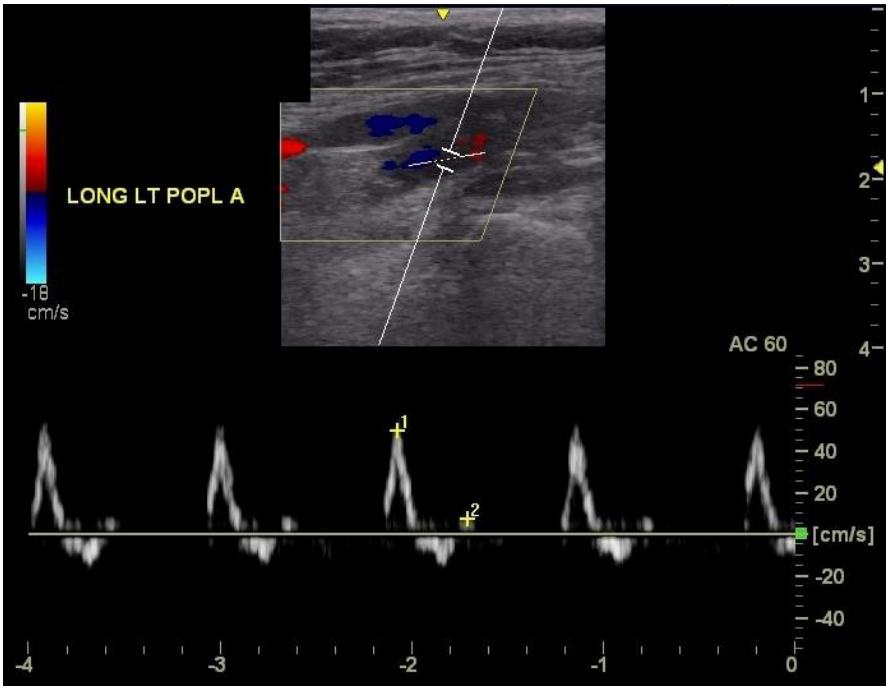


Figure 25 030_Week 2

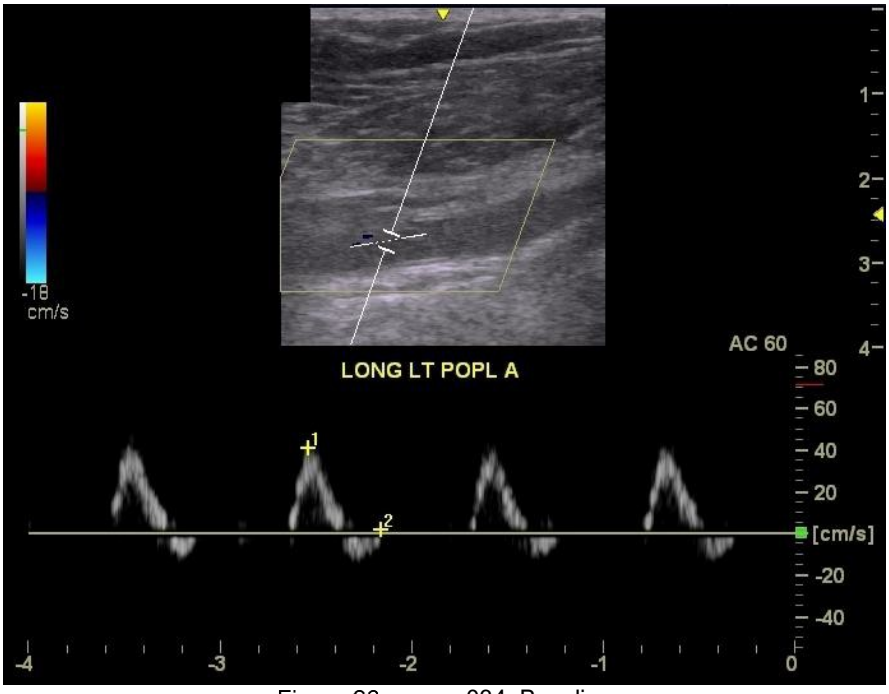


Figure 26 034_Baseline

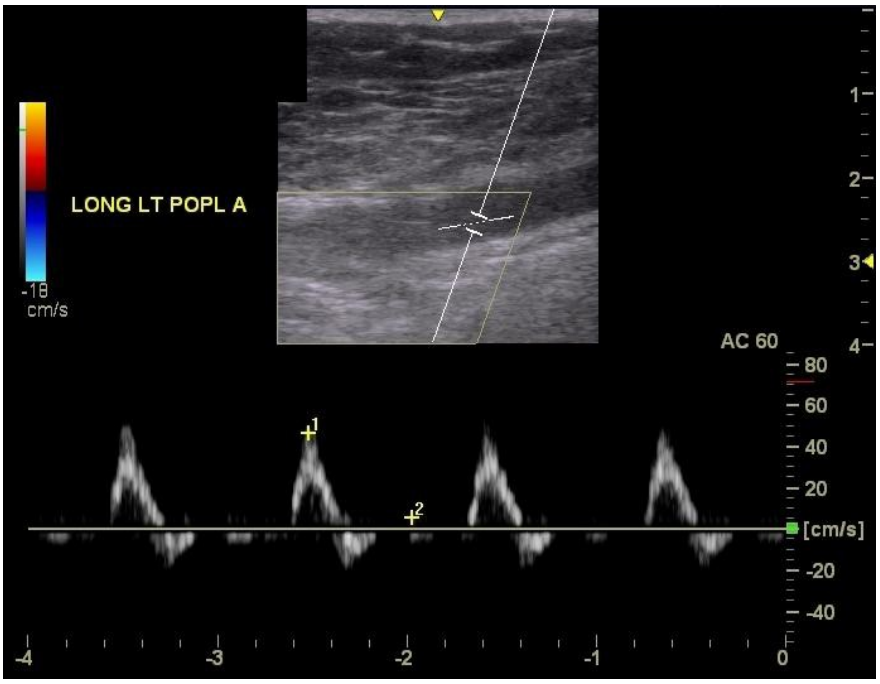


Figure 27 034_Week 2

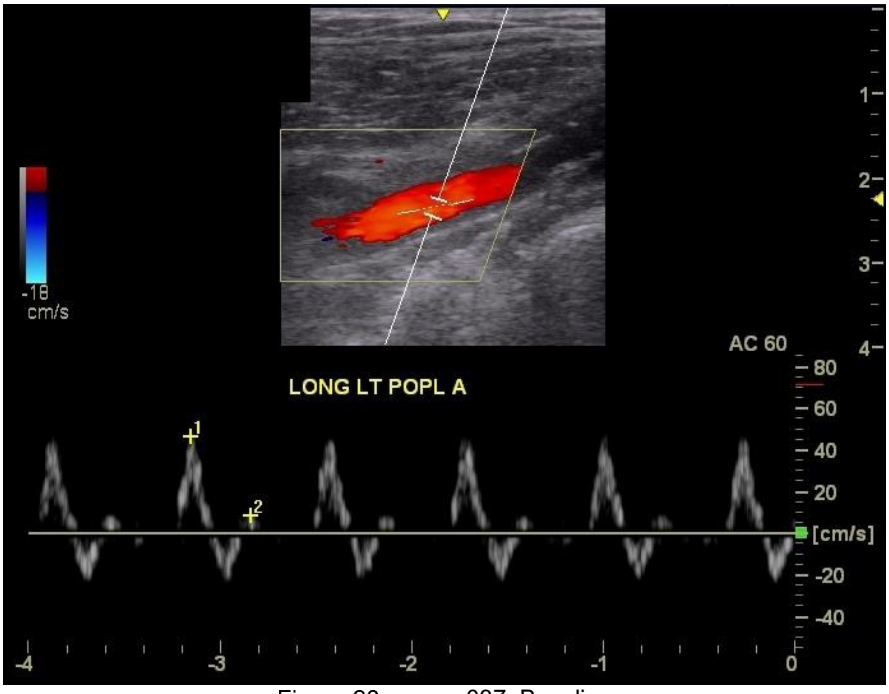


Figure 28 037_Baseline

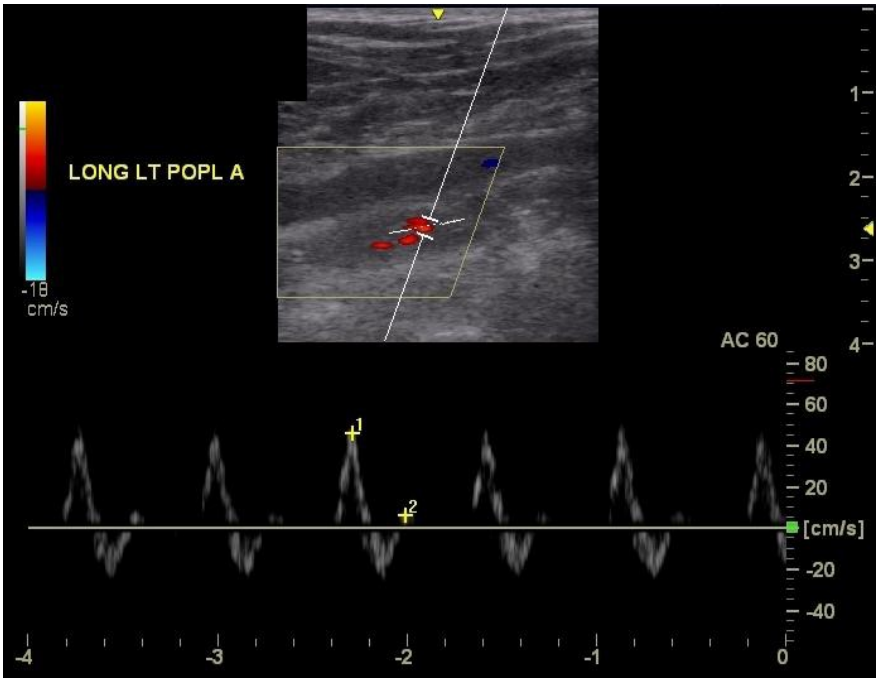


Figure 27 037_Week 2


Figure 30 040_Baseline

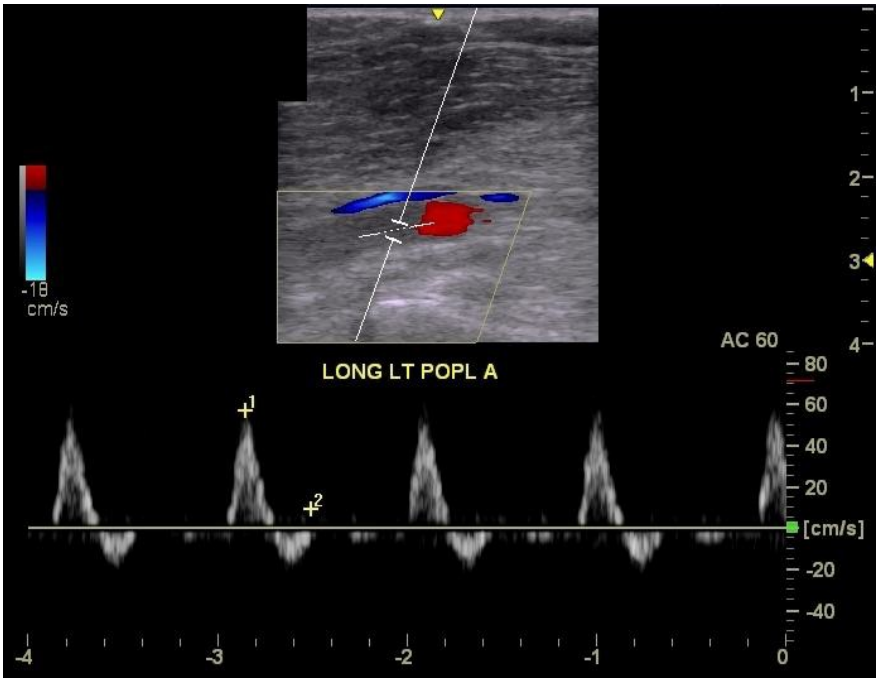


Figure 27 040_Week 2


Figure 32 041_Baseline

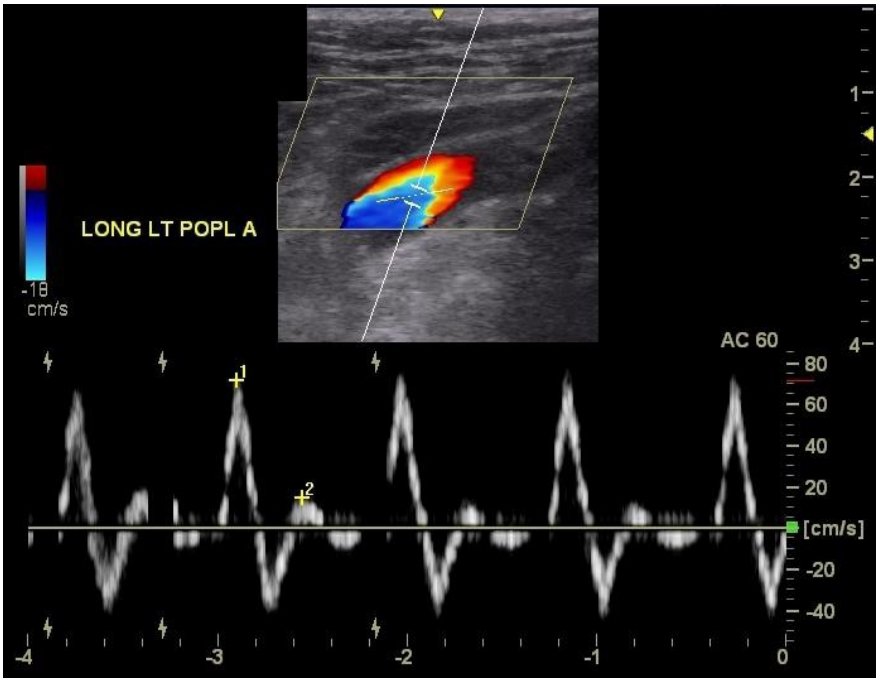


Figure 27 041_Week 2

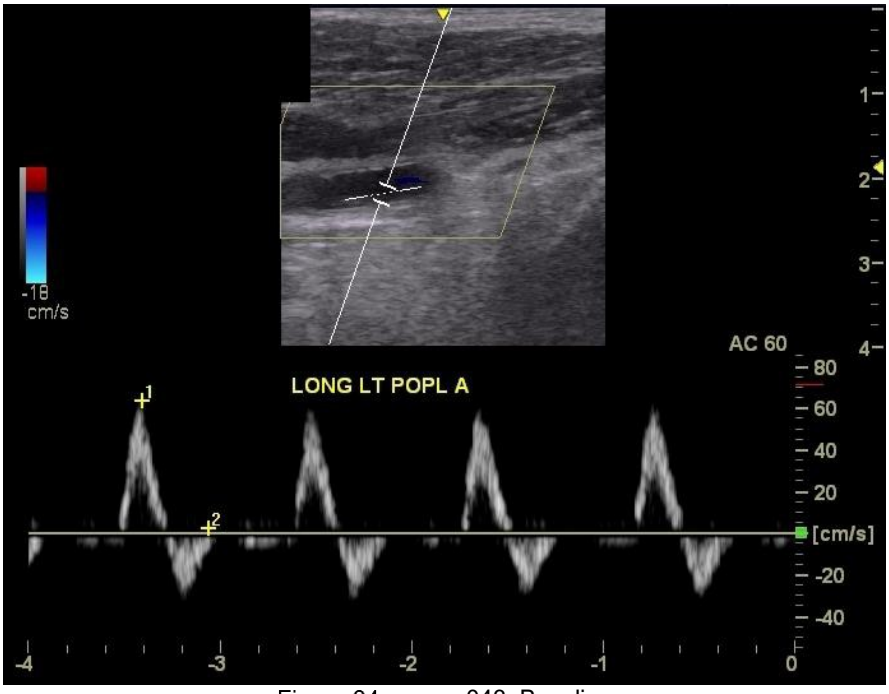


Figure 34 043_Baseline

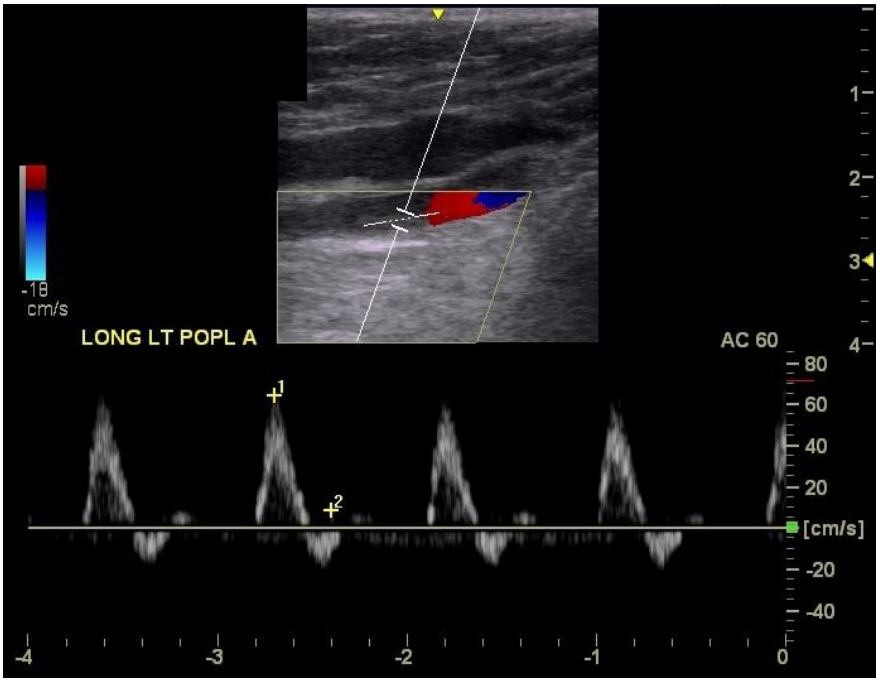


Figure 27 043_Week 2

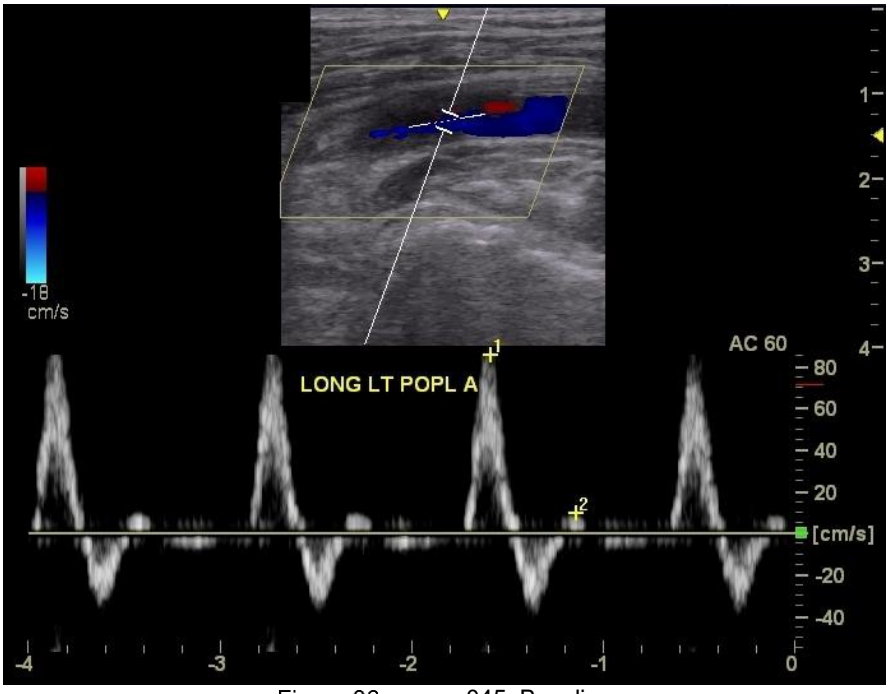


Figure 36 045_Baseline

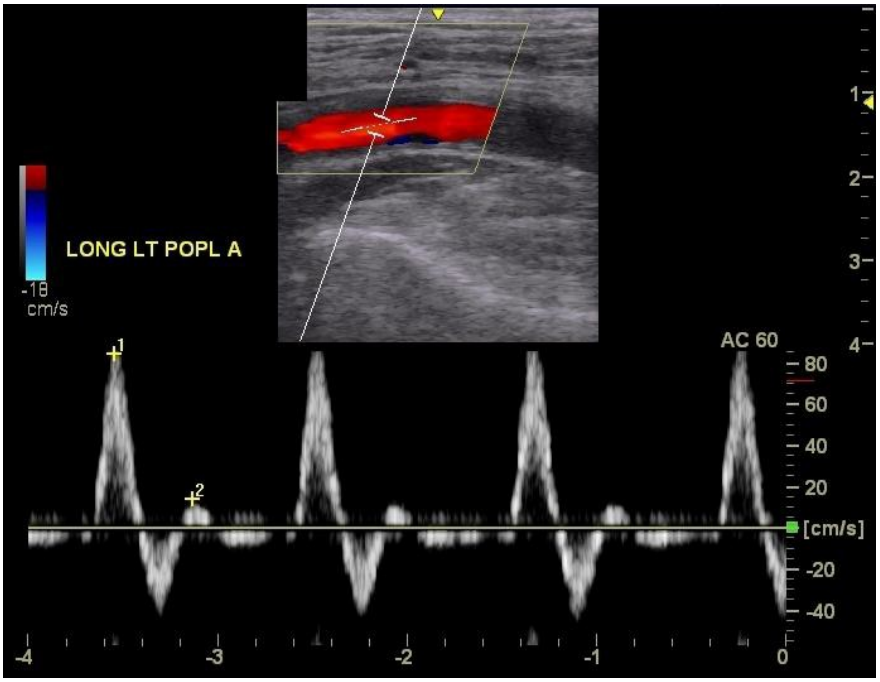


Figure 27 045_Week 2