A single-center study evaluating the feasibility of a specific block of the two distal branches of the tibial nerve for forefoot surgery.

DISTIB

INTERVENTIONAL RESEARCH PROTOCOL WITH MINIMAL RISKS AND LIMITATIONS

GENERAL INFORMATION

PROTOCOL REFERENCES

Protocol code number assigned by the sponsor: 2018/03
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Version number: Version 3.0 dated April 30, 2019
NCT03504462

STUDY SPONSOR

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PROTOCOL SIGNATURE PAGE

Study Title: Single-center study evaluating the feasibility of a specific block of the two distal branches of the tibial nerve for forefoot surgery.
Protocol code: 2018/03
Version: V3.0 dated 04/30/2019

This protocol was read and approved on the date noted below.
Both parties agree to conduct the research in accordance with the protocol, good clinical practice, and applicable laws and regulations.

FOR THE SPONSOR

NAME: Dominique BOULANGÉ,
President of CMC Ambroise Paré and Pierre Cherest

Date: _ _ / _ _ / _ _ _ _

Signature:

THE PRINCIPAL INVESTIGATOR

NAME: Dr. Sébastien BLOC

Date: _ _ / _ _ / _ _ _ _

Signature:

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1. ABBREVIATIONS

AL: Local Anesthesia
ALR: Regional Anesthesia
ANSM: French National Agency for Medicines and Health Products Safety
ARC: Clinical Research Associate
CMC: Medical-Surgical Center
CNIL: National Commission for Information Technology and Civil Liberties
CPP: Committee for the Protection of Persons
ECG: Electrocardiograph
ENA: Analog-to-Digital Scale
ENR: Digital Recognition Scale
HV: Hallux Valgus
MR: Reference Methodology
NIBP: Non-Invasive Blood Pressure
RICAP: Research and Innovation at the Ambroise Paré Medical Center
SpO2: Pulse Oximetry
PIVC: Peripheral Intravenous Catheter

2. SCIENTIFIC RATIONALE AND GENERAL DESCRIPTION OF THE RESEARCH

2.1. Study Context

Surgery for forefoot conditions (such as hallux valgus, ingrown toenails, foot wounds, metatarsal fractures, Morton's neuroma, etc.) is a painful procedure typically performed on an outpatient basis. Effective pain management is crucial, and regional anesthesia (RA) is currently the gold standard technique (1–3). Blockade of the sciatic nerve and/or its branches is the most appropriate analgesic technique. The innervation of the foot depends exclusively on this nerve.

The sciatic nerve block has long been performed in the popliteal fossa or on the thigh (4). However, this technique causes motor block of the tibialis anterior and triceps surae muscles. The former causes a steppage gait, while the latter results in an inability to lock the knee. Early resumption of walking therefore requires the use of a knee brace and canes (5). This technique, long used for hospitalized patients, is therefore poorly suited for outpatient forefoot surgery.

Trunk blocks of the distal branches of the sciatic nerve (tibial and fibular) at the ankle have been considered to maintain ankle joint mobility, thereby facilitating early discharge home while ensuring effective pain relief (6,7) (Figures 1 and 2). The tibial nerve block at the ankle allows for anesthesia of the various branches of this nerve: the medial plantar branch (medial plantar nerve), the lateral plantar branch (lateral plantar nerve), and the calcaneal branches. This block is combined with blocks of the deep and superficial peroneal nerves. This technique is an effective alternative for forefoot surgery. Nevertheless, the loss of cutaneous sensation and deep (or proprioceptive) sensation in the heel theoretically carries a risk of falling. Indeed, the loss of proprioception results in the abolition of the medial plantar reflex (flexion of the toes upon percussion of the plantar arch), as well as an absence of muscle contraction of the triceps surae. Early discharge is therefore feasible, either without weight-bearing using crutches, or with cautious weight-bearing and crutches, for patients who have been informed of the risk of falling.

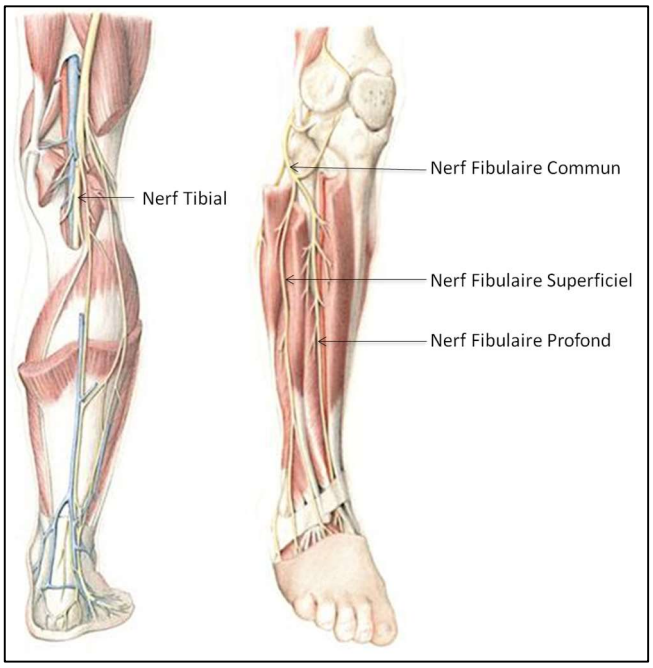


Figure 1: Anatomy of the sciatic nerve

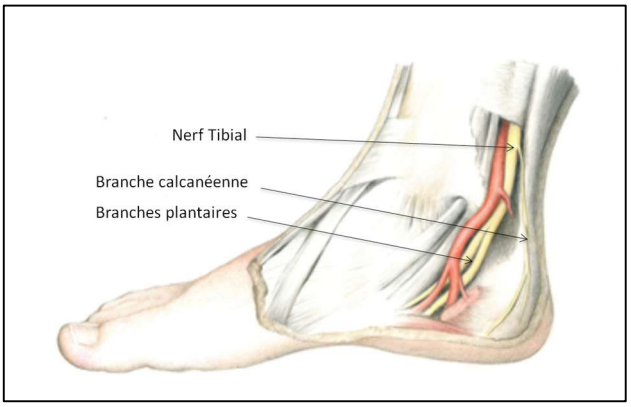


Figure 2: Branches of the sciatic nerve at the ankle

2.2. Research Hypothesis

Specific anesthesia of the distal foot, sparing the heel, would allow for both effective pain relief and safe resumption of walking with exclusive heel support in a postoperative off-loading shoe (such as a Barouk shoe).

Ultrasound allows for precise localization of the nerves and their distal branches. The specific localization and anesthesia of the branches innervating the forefoot (medial and lateral plantar nerves) could meet this dual objective: effective pain relief and safe resumption of walking.
A specific approach to these two distal branches of the tibial nerve could be considered at the medial border of the foot, along a line connecting the center of the medial malleolus and the medial calcaneal tuberosity (MC axis = flexor retinaculum) (Figure 3). The calcaneal branch of the tibial nerve generally originates in the medial retromalleolar region, above the MC axis.

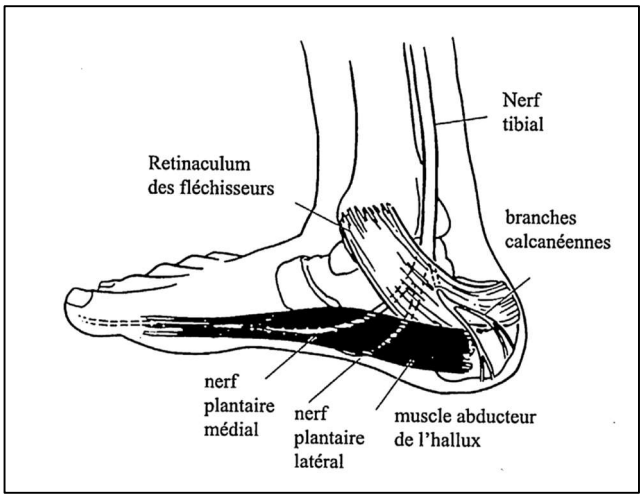


Figure 3: Anatomy of the flexor retinaculum

The objective of this study is to evaluate the feasibility and safety of a specific anesthesia of the distal foot, preserving sensation in the heel, for forefoot surgery.

2.3. Summary of benefits, if any, and foreseeable and known risks for participants in the study

2.3.1. Expected benefits for the patient

The objective of this study is to provide long-lasting analgesia for forefoot surgery, while promoting early resumption of unassisted walking (without crutches or splints) and rapid discharge from the hospital.

2.3.2. Predictable and known risks

These include the risks associated with any anesthesia and surgery that are independent of the research. They are explained to patients during anesthesia and surgical consultations.

There are no risks specific to the study.

2.4. Description of the study population

Adult patients scheduled for forefoot surgery, such as metatarsal osteotomy, surgical treatment of ingrown toenails, foot wounds, foot infections, metatarsal fractures, or Morton's neuroma.

3. RESEARCH OBJECTIVES

3.1. Primary objective

The primary objective of the study is to evaluate the feasibility and safety of a specific anesthesia technique for the distal foot, preserving sensation in the heel.

3.2. Secondary objectives

1. To evaluate the feasibility of forefoot surgery.
2. To assess the ability to identify the plantar nerves at the ankle.
3. To assess patient satisfaction.
4. To evaluate the complication rate.

4. EVALUATION CRITERIA

4.1. Primary Endpoint

The primary endpoint is the success of the procedure, defined as the successful selective block of the plantar branches of the tibial nerve, anesthesia of the distal foot while preserving heel sensation, and the absence of paresthesia.

The success of the selective block of the plantar branches of the tibial nerve will be assessed using a sensation score for each branch of the tibial nerve.

A cold test and a touch test will be performed every 10 minutes for 40 minutes following the injection of local anesthetics.
The touch test will be performed using a 2-point sensitivity measurement device (Touch-Test).
The cold test will be performed using a cold roller (Rullo “Oerlikon” nizell.ch).
The tests will be performed on specific areas of the tibial nerve:

- calcaneal branches: calcaneus;
- medial plantar nerve: medial part of the arch of the foot;
- lateral plantar nerve: lateral part of the arch of the foot.

A contralateral assessment will be performed to accurately determine the sensory score.
Score/Contralateral side: 2: normal sensation, 1: decreased sensation, 0: total loss of sensation.

The success of the selective block will be confirmed if the following results are obtained at 40 minutes:

- calcaneal branches = 2
- medial plantar nerve = 0
- lateral plantar nerve = 0

At 40 minutes, a precise mapping of the plantar arch will be performed to determine the exact extent of sensory loss (Figure 4).

The degree of paresthesia during the procedure will be assessed by asking the patient about any sensations of discomfort: tingling, numbness, or other prickling sensations.

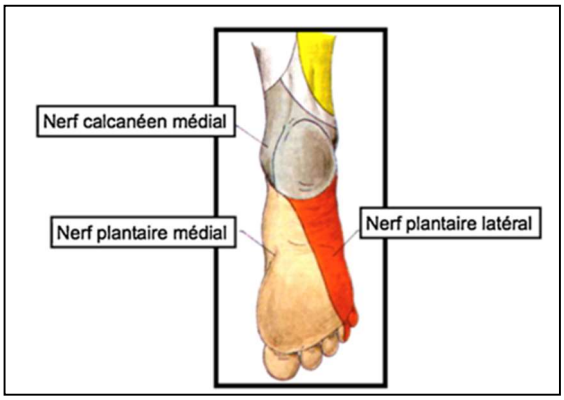


Figure 4: Example of a plantar arch mapping

4.2. Secondary endpoints

Regarding Secondary Objective 1:
The feasibility of forefoot surgery using a specific block of the two distal branches of the tibial nerve, combined with a block of the superficial and deep peroneal nerves and the saphenous nerve, will be assessed by the fact that no additional anesthetic technique is required to perform the surgery.

Regarding Secondary Objective 2:
Ultrasound identification of the plantar arteries and plantar nerves below the midfoot axis will be assessed using a Numerical Scale for Identification of the Medial and Lateral Plantar Nerves (ENR-Plantar Nerves): a numerical scale ranging from 0 (no visualization) to 100 (extremely easy visualization).

Regarding Secondary Objective 3:
Patient satisfaction and comfort during the ALR procedure will be assessed using three numerical scales:
- Patient satisfaction is assessed using an Analog Numeric Scale (ANS-Satisfaction) ranging from 0 (very dissatisfied) to 100 (very satisfied).
- Pain assessment during regional anesthesia uses a Numerical Analog Scale (NAS-R) ranging from 0 (no pain) to 100 (extremely painful).
- Pain assessment during peripheral venous access (PVA) uses an ANS (ANS-PVA) ranging from 0 (no pain) to 100 (extremely painful). It will serve as a reference for the ANS-ALR.

Regarding secondary objective 4:
Any sensory-motor complications will be assessed using a questionnaire (Appendix 1) during a phone call with the patient on Day 15±4 and at 1 month during the follow-up visit with the surgeon.

5. RESEARCH METHODOLOGY

5.1. Study Type

Single-center, prospective, non-randomized, open-label study.
This is a pilot study seeking to demonstrate the feasibility of a specific block of the two distal branches of the tibial nerve for forefoot surgery, while preserving heel sensation.

5.2. Research Procedure

The research protocol includes the following steps:

5.2.1. Inclusion

The patient will be informed of the protocol by an investigator during the anesthesia consultation. Clear and accurate information will be provided to the patient both verbally and in writing (see information sheet). The physician will verify the inclusion and exclusion criteria.
If the patient agrees to participate in the study after a reflection period they deem sufficient, a consent form will be provided to them. This form must then be dated and signed by the investigator and the patient.

5.2.2. In the operating room

a) Anesthesia

Patient preparation:
Upon arrival in the operating room, the patient will be positioned under the conditions necessary and recommended for performing the ALR:

- Placement of a peripheral intravenous line (PIVC),
- Low-flow nasal oxygen therapy,
- Strict aseptic technique,
- Monitoring: ECG, NIBP, and SpO2.

Pain assessment at the time of PIVC placement will be obtained from the patient using the ENA-PIVC scale.

Patients will not receive premedication or deep sedation during the LAR procedure. However, in cases of significant discomfort, light sedation may be offered, as is standard for all LAR techniques.
The ALR will be performed systematically under ultrasound guidance.

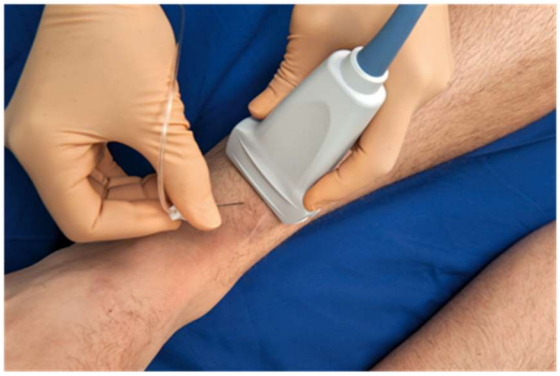
Performing ultrasound-guided ALR:
The ALR will be performed 45 minutes before surgery, and its effectiveness will be verified before transfer to the operating room.
The patient will be placed in the supine position for the various procedures. All procedures will be performed using an ultrasound machine (Logic E – General Electric). The transducer (L8-18 linear transducer – General Electric) will be positioned to provide an axial view of the nerves. 22-gauge, 50-mm needles (BBraun – Stimuplex Ultra 360) designed for regional anesthesia will also be used. The needle will be inserted either in the ultrasound plane (IP) or out of the ultrasound plane (OOP). Prior to each procedure, skin disinfection will be performed using an alcoholic iodine solution. 5 to 7 mL of 0.375% naropeine, a local anesthetic (LA), will be injected at the point of contact with each nerve.
All patients will receive a block of the superficial and deep fibular nerves, a saphenous nerve block, as well as the lateral and medial plantar nerves below the MC axis.
Pain assessment during ALR will be collected from the patient using the ENA-ALR.

- *Performing the deep peroneal nerve block*

The ultrasound probe will be positioned on the anterior edge of the ankle. The dorsal artery of the foot will be initially identified, and the deep peroneal nerve will be located in contact with it. The local anesthetic will be injected in contact with the artery or the nerve.

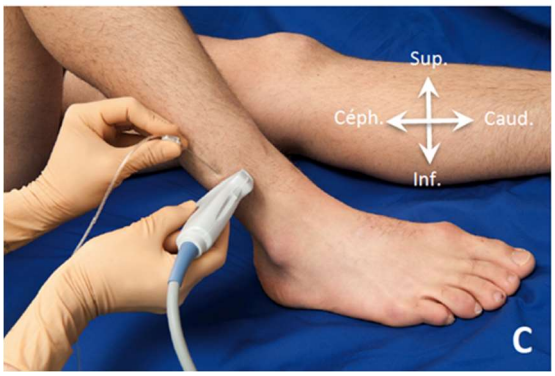
- *Performing the superficial peroneal nerve block*

The superficial peroneal nerve is specifically blocked at the lateral border of the leg directly over the fibula, beneath the superficial fascia.



Performing the deep peroneal nerve block

E Albrecht, S Bloc, H Cadas, V Moret.
Based on the Practical Manual of Ultrasound-Guided Regional Anesthesia
Elsevier - Masson, Paris, 2014



Performing a superficial peroneal nerve block

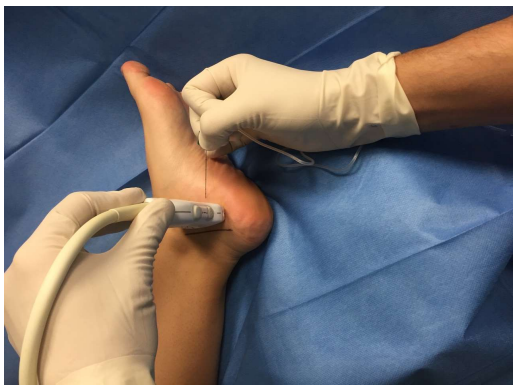
E Albrecht, S Bloc, H Cadas, V Moret.
dapted from Practical Manual of Ultrasound-Guided Regional Anesthes
Published by Elsevier-Masson, Paris, 2014

- *Performing a saphenous nerve block*

An infiltration of the medial edge of the foot will be performed systematically.

- *Performing the specific lateral and medial plantar nerve block*

The line connecting the center of the medial malleolus and the medial calcaneal tuberosity (MC axis) will be marked prior to performing the block.
The ultrasound probe will be positioned at the medial edge of the foot below this line. The two plantar branches of the tibial nerve will be identified, as well as the tibial plantar arteries. The local anesthetic will be injected in contact with the neurovascular bundle.
The anesthesiologist will assess the identification of the plantar arteries and nerves below the MC axis using the ENR-Plantar Nerves protocol.



Position of the ultrasound probe for performing a block of the distal branches of the tibial nerve at the ankle

Sensory tests:
The cold test and touch test will be performed every 10 minutes for 40 minutes following the injection of local anesthetics into the specific territories of each nerve.
The anesthesiologist will record the sensory score for each branch of the tibial nerve.

At 40 minutes, a detailed sensory map of the sole of the foot will be created.

Recording of potential complications:
The occurrence of any paresthesia, indicative of nerve damage, will be noted. The anesthesiologist will ask the patient during the procedure about any sensations of discomfort: tingling, numbness, or other prickling sensations.

If regional anesthesia fails—defined as the inability to perform the surgery—the anesthesiologist will use the standard anesthesia technique: a tibial nerve block at the ankle above the mid-calf line.

b) Surgery

The surgical procedure will be performed according to standard practice.
Any intraoperative complications will also be noted.
The patient's satisfaction score will be assessed at the end of surgery.

5.2.3. End of the study

The follow-up period ends after recording any complications at 15±4 days via a phone call with the patient, and then at 1 month during the follow-up visit with the surgeon.

5.3. Study Design

Steps	Inclusion Visit		Day 0 In the operating room	Day 15±4	Follow-up visit with the surgeon at 1 month
	Anesthesia consultation	Pre-anesthesia visit			
Information	X				
Consent		X			
Verification of inclusion and exclusion criteria	X	X			
Specific plantar nerve block			X		
Sensory tests			X		
ENR-Plantar nerves			X		
ENA-VVP ENA-ALR ENA-Satisfaction			X		
List of possible complications			X	X (phone call)	X

5.4. Expected duration of participant involvement, description of the timeline and duration of the study

The study itself begins when the patient and the investigator sign the consent form. It ends after checking for complications during the follow-up visit with the surgeon 1 month post-surgery.
The study is scheduled to take 24 months to complete, starting from the date of the first enrollment. The enrollment period is expected to last 23 months.

5.5. Identification of Participants

As part of this study, participants will be identified as follows:
Upon signing the consent form, the investigator logs into the secure eCeric website and creates a patient record. An alphanumeric "patient identifier" enrollment number is then automatically generated by the application. It consists of the patient's initials (first letter of the last name and first letter of the first name)

followed by a sequential enrollment number. This reference is unique and will be retained for the duration of the study.
The investigator creates an enrollment table; this table allows the patient's identity to be unambiguously linked to an enrollment sequence number. This unique number identifies the study data pertaining to the patient.

5.6. Description of measures taken to reduce or avoid bias

To avoid selection bias, this study will be offered to all eligible patients seen in the anesthesia clinic. For eligible patients who are not included, the reason for exclusion will be noted.
The evaluation criterion is sufficiently objective to avoid any assessment bias.

5.7. Description of the rules for permanently or temporarily terminating a person's participation in the research, procedures for monitoring these individuals, and procedures for replacing these subjects, if necessary

Any subject included in the study may decide to withdraw their consent to participate in the study at any time and for any reason, without having to provide explanations or justifications and without this affecting the care they are receiving or will receive. The investigator must indicate in the patient's eCRF the date and, if applicable, the reason for the termination of participation in the research. Withdrawal of consent prohibits the use of medical data obtained after the withdrawal of consent. Data already collected regarding the subject may be used.

The investigator may temporarily or permanently suspend a subject's participation in the research for any reason that impacts their safety or that is in the patient's best interest. Data already collected regarding the subject may be used in the analysis of the study results.

A subject's withdrawal from the study will not alter their usual care.

A patient who withdraws prematurely from the study will be replaced, and a study withdrawal form will be completed, including the reason for withdrawal (Consort flow diagram).
Once the protocol-specified sample size is reached, the investigator must halt recruitment for the study. However, patients who have already signed a consent form may still be included in the study.

5.8. Identification of all data collected directly in the study's eCRF and for which no other source documents exist

Sensory scores, assessment of plantar nerve recognition, patient satisfaction and comfort scores, as well as data obtained during the telephone call on Day 15±4 by a healthcare professional, are recorded directly in the eCRF.

6. SELECTION OF RESEARCH PARTICIPANTS

6.1. Inclusion Criteria

The following patients will be included:

- Aged 18 years or older,
- Scheduled for forefoot surgery (metatarsal osteotomy, surgical treatment of ingrown toenails, foot wounds, foot infections, metatarsal fractures, or Morton's neuroma),
- Having given their consent to participate in accordance with regulations,
- Covered by social security.

6.2. Exclusion criteria

The following will not be included:

- Minors,
- Pregnant or breastfeeding women,
- Patients under guardianship or conservatorship,
- Patients unable to understand,
- Patients unable to read or write in French,
- Patients with communication difficulties or neuropsychiatric disorders,
- Patients with intolerance to nonsteroidal anti-inflammatory drugs,
- Patients with peripheral neuropathy,
- Patients with a history of allergy to local anesthetics,
- Patients with coagulation disorders,
- Patients with impaired renal function,
- Patients who chronically use opioids,
- Patients with chronic pain syndromes or fibromyalgia,
- Patients with an ASA score of 4.

6.3. Exclusion criteria

None

6.4. Recruitment procedures

All patients coming to the clinic for scheduled forefoot surgery who meet the eligibility criteria will be offered the opportunity to participate in the study. They will be informed during the anesthesia consultation. Informed consent will be obtained after taking the time to verify that the information provided has been properly understood. Patients unable to understand the content of the information provided will not be included in the study.

6.5. Simultaneous participation in another study, exclusion period

The patient may participate in another study simultaneously if the inclusion and exclusion criteria are met. There is no exclusion period for individuals participating in this study.

7. SAFETY ASSESSMENT

In the context of interventional research involving minimal risks and constraints, the medical procedures or strategies that are the subject of the research are part of standard practice and are used in accordance with their indications. Potential adverse events or incidents are therefore those related to the patient's routine care (care-related) and do not require specific reporting by the research coordinator.

These events must follow the standard reporting procedure established by current regulations and implemented within the institution:

• Adverse effects that may be related to a medication must be reported to the Regional Pharmacovigilance Center,

• Incidents or potential incidents resulting from the use of a medical device that must be reported to the local medical device vigilance coordinator,

• Other (reporting of nosocomial infections).

These reports are mandatory for all physicians (or other relevant healthcare professionals), both within the context of this study and outside of it.

As part of this study, the occurrence of adverse events will nevertheless be recorded and reported in the eCRF during a telephone call at Day 15±4 and during the follow-up visit with the surgeon at 1 month.

8. STATISTICS

8.1. Description of the planned statistical methods

The planned analysis will take place in 3 stages:

- **Descriptive statistics**

The number and percentage of patients approached, enrolled, withdrawn early, and who completed the entire trial will be provided. A CONSORT diagram will be created.
A general description of the population will be provided. For categorical variables, the total number of subjects and the number in each category, as well as the corresponding proportions and their confidence intervals, will be provided. For continuous variables, the sample size, mean, and standard deviation will be provided for normally distributed variables; the sample size, median, and first and last quartile limits will be provided for non-normal distributions. Ordinal variables will be analyzed as categorical variables (sample size and percentage) to better clarify the available data.

- **Study Design**

This is an exploratory study of a sample, without a comparison group. The primary endpoint is based on a binary qualitative variable (yes/no). The statistical method selected is based on estimating a population proportion with a 95% confidence interval. For secondary endpoint 1 (surgical feasibility), the same type of analysis will be used as above for the primary endpoint. For the other secondary endpoints, the statistical analysis will be primarily descriptive.

- **Exploratory analysis**

To the extent that the study statistician or investigators deem it helpful in clarifying the results obtained, an exploratory phase may be conducted using bivariate (correlation coefficient) or multivariate (multiple regression, logistic regression, or correspondence analysis) tests to determine the relationships between variables.

This phase will be the subject of a written description that will be appended to the study's statistical analysis plan.
In the analysis report, the tests performed are clearly identified as post-hoc tests. Consequently, the probabilities obtained are for guidance only.

8.2. Estimated number of participants to be included in the study, with statistical justification

This is an exploratory study, which makes it difficult to calculate the number of subjects to include. Based on recruitment capacity, the objective is to quickly determine the value of the method so that, if necessary, a comparative study can be conducted, and to ensure sufficient statistical power. A sample of 50 patients allows, if the proportion is between 0.1 and 0.5, for 95% confidence intervals of a reasonable width (see table below).

Confidence intervals	N	Interval width	Proportion (P)	Lower limit	Upper limit
0.95	50	0.166	0.10	0.017	0.183
0.95	50	0.198	0.15	0.051	0.249
0.95	50	0.222	0.20	0.089	0.311
0.95	50	0.240	0.25	0.130	0.370
0.95	50	0.254	0.30	0.173	0.427
0.95	50	0.264	0.35	0.218	0.482
0.95	50	0.272	0.40	0.264	0.536
0.95	50	0.276	0.45	0.312	0.588
0.95	50	0.278	0.50	0.361	0.639

We will therefore estimate the number of patients needed to obtain 50 informed consents.

8.3. Expected significance level

This is a two-sided significance level of 0.05.

8.4. Statistical criteria for stopping the study

No interim analysis is planned that could lead to the study being discontinued.

8.5. Method for handling missing, unused, or invalid data

No specific method for imputing missing data is planned.

8.6. Management of changes to the initial statistical plan

Any modification to this plan will be documented in writing, stating the reasons for the changes. The analysis plan and, if applicable, the document(s) modifying the initial statistical analysis plan will be appended to the analysis report.

8.7. Selection of subjects to be included in the analyses

All patients approached for the study will be included in the CONSORT diagram for the study.

Any patient in the study population who has signed a consent form, completed the study, and for whom there is no protocol violation likely to critically affect the results of the analysis will be included in the analyses.

8.8. Principal Investigator

Dr. Pierre Squara, CMC Ambroise Paré

9. RIGHTS OF ACCESS TO DATA AND SOURCE DOCUMENTS

9.1. Access to Data

The sponsor has obtained the agreement of all parties involved in the research to ensure direct access to all research sites, source data, source documents, and reports for the purpose of quality control and audit by the sponsor and/or the competent authorities.

Investigators shall make the individual documents and data strictly necessary for the monitoring, quality control, and audit of the research available to persons authorized by the sponsor in accordance with applicable laws and regulations (Articles L.1121-3 and R.5121-13 of the Public Health Code).

9.2. Source documents

Source documents are defined as any original document or item that serves to prove the existence or accuracy of data or facts recorded during the research. They shall be retained for 15 years by the healthcare facility where the research was conducted in accordance with regulations.

9.3. Data confidentiality

In accordance with the provisions regarding the confidentiality of data to which persons responsible for quality control of research involving human subjects have access (Article L.1121-3 of the Public Health Code), and in accordance with the provisions regarding the confidentiality of information concerning, in particular, the nature of investigational drugs, trials, the participants, and the results obtained (Article R. 5121-13 of the Public Health Code), individuals with direct access to this data shall take all necessary precautions to ensure the confidentiality of information regarding the participants, particularly with respect to their identity, as well as the results obtained. Those responsible for quality control, just like the investigators themselves, are bound by professional secrecy (under the conditions defined by Articles 226-13 and 226-14 of the Penal Code).

During the course of the research or upon its completion, the data collected on the participants and transmitted to the sponsor by the investigators (or any other specialized personnel) will be anonymized. Patients will be identified only by an identification number containing their initials and their study entry number. These details are recorded in the observation log. The data collected is strictly confidential. It is accessed only by the medical team, persons duly authorized by the study sponsor, and, if necessary, by representatives of the competent health and judicial authorities. The identity of participants will not be disclosed in any report or publication resulting from this study.

The sponsor will ensure that each person participating in the research has given written consent for access to and use of their individual data, which is strictly necessary for the quality control of the research.

The sponsor declares that it will process the study data in accordance with the CNIL's reference methodology (MR001).

10. QUALITY CONTROL AND ASSURANCE

10.1. Quality Control

The sponsor appoints a Clinical Research Associate (CRA) to conduct monitoring visits, who will ensure that:

- the rights, safety, and protection of the individuals participating in the research are upheld,
- the critical elements necessary for the analysis of the primary and secondary objectives are present,
- the reported data are accurate, complete, and consistent with the source documents,
- the research is conducted in accordance with the protocol, Good Clinical Practice (GCP), applicable laws and regulations, and in accordance with the Standard Operating Procedures established by the Research and Innovation Team at CMC Ambroise Paré (RICAP), the study sponsor.

The investigator and members of his team agree to make themselves available during visits conducted by the ARC.

During these visits, the following items will be reviewed:

- Written informed consent;
- Compliance with the research protocol and the technical procedures defined therein;

- Quality of the data collected in the observation log: accuracy, missing data, consistency of the data with the "source" documents (medical records, appointment logs, original laboratory results, etc.).

10.2. eCRF

All information required by the protocol will be recorded in an electronic case report form (eCRF), with data hosted on a central, secure server. Data will be collected as it is obtained by the investigator and/or personnel designated by the investigator.

10.3. Quality assurance

Quality control for the trial is conducted under the responsibility of the Ambroise Paré Clinical Research Center. An audit may be conducted at any time by individuals appointed by the sponsor who are independent of the research team. Except in special cases, the investigator is notified of the planned audit well in advance. The same applies to an inspection conducted by the Competent Authority. The purpose of these procedures is to ensure the quality of the research, the validity of its results, and compliance with applicable laws and regulations.

Those who direct and oversee the research agree to comply with the requirements of the sponsor and the Competent Authority regarding an audit or inspection of the research.

11. ETHICAL CONSIDERATIONS

11.1. Statement indicating that the research will be conducted in accordance with the protocol, good clinical practice, and applicable laws and regulations

The protocol complies with the ethical principles established by the 18th World Medical Assembly (Helsinki 1964) and by the amendments established at the 29th (Tokyo 1975), 35th (Venice 1983), 41st (Hong Kong 1989), 48th (Somerset West 1996), 52nd (Edinburgh 2000), 53rd (Washington 2002), 55th (Tokyo), 59th (Seoul), and revised at the 64th World Medical Assembly (Fortaleza, Brazil, October 2013) . It will be conducted in accordance with the ICH guidelines on Good Clinical Practice.

11.2. Procedures for informing and obtaining consent from research participants

No interventional research may be performed on a person without their free and informed consent, obtained in writing after all relevant information has been provided to them orally and prior to any procedure specified in the protocol and related to the research.

The research is presented orally to the patient by an anesthesiologist-investigator during the anesthesia consultation. During this visit, patients will receive complete and honest information, in understandable terms, regarding the study's objectives and constraints, the potential risks involved, the necessary monitoring and safety measures, their right to refuse to participate in the study, and the possibility of withdrawing at any time without this affecting the care they receive. An information sheet corresponding to the information provided to the patient is given to the patient. After answering any questions the patient may have, and after ensuring that the patient has had sufficient time to reflect, the patient's consent is obtained by the anesthesiologist-investigator prior to the patient's inclusion in the study, during the pre-anesthesia visit.
A copy of the consent form, dated and signed by the participant and the investigator, is provided to the participant prior to their participation in the study. The investigator retains the original copy of the dated and signed informed consent form. At the end of the study, a copy of the signed consent form will be

placed in a tamper-proof, sealed envelope containing all consent forms, which will be archived by the sponsor.

Changes to the protocol that result in an amendment will be reflected by corresponding changes in the informed consent form and the information provided verbally to the patient.

11.3. Compensation for Participants

No compensation is provided for patients in this study.

11.4. Legal obligations

11.4.1. Roles of the sponsor

The CMC Ambroise Paré is the sponsor of this study and is responsible for its conduct. The sponsor reserves the right to discontinue the study at any time for medical or administrative reasons; except in cases of force majeure, the investigator's opinion on this decision will be obtained and recorded in the trial documentation.

11.4.2. Approval of the Protocol and Amendments

Prior to the start of the study, the protocol, the information sheet, the informed consent form, and any other relevant documents will be submitted to the Institutional Review Board (IRB) for review. Notification of the HPC's favorable opinion will be forwarded to the study sponsor and the health authorities. This document must include a list of the HPC members who were present on the day the opinion was issued, along with their positions and qualifications.

The sponsor will notify the French National Agency for Medicines and Health Products Safety (ANSM) of the study.

The study may only be initiated after the sponsor has received all documents required from an ethical and regulatory standpoint, and in particular the favorable opinion of the CPP.

Any substantial modification to the protocol concerning the study's objectives, design, study population, or significant administrative aspects will require the approval of the coordinating investigator and the sponsor, as well as a favorable opinion from the CPP.

11.4.3. Commitment to Compliance with the "Reference Methodology" MR-001

The CMC Ambroise Paré, the research sponsor, has signed a commitment to comply with the "Reference Methodology" MR-001.

11.4.4. Final Research Report

The final research report is prepared and signed by the sponsor and the principal investigator. A summary of the report, drafted in accordance with the Competent Authority's reference template, must be submitted to the Competent Authority within one year of the end of the research, corresponding to the end of the participation of the last person enrolled in the study.

12. DATA PROCESSING AND RETENTION OF RESEARCH-RELATED DOCUMENTS AND DATA

12.1. Data Entry and Processing

The data required to conduct the study are listed in the table below, which specifies, for each document, its format, processing method, and content.

The computerized processing of personal data complies with the provisions of the amended French Data Protection Act No. 78-17 of January 6, 1978. Each participant may exercise their right of access and rectification guaranteed by Articles 39 and 40 of the aforementioned law by contacting the physician who is treating them in the context of this research and who knows their identity. The identity of participants will not be disclosed in any report or publication resulting from this study.

The investigator's center has a secure archive, accessible only to investigators, for the local storage of protocol data and personal data. Data transmission is secure (CMC Ambroise Paré IT Department).

The data contained in the trial database and in the eCRF will be transferred by the principal investigator to the sponsor responsible for creating the database used for statistical analysis. Until this transfer, the data will be processed under the sole responsibility of the trial staff.

	Support	Processing	Content
Consent form	Paper	Document completed by the patient and archived: - by the investigational site in a secure location, - by the sponsor in a sealed envelope.	It contains proof of the patient's informed consent.
Inclusion form	Digital	A document completed by the center and used to notify the sponsor of a new patient's inclusion in the study.	This form contains the patient's identification number but not their identity.
Data collected by the investigator	Digital	e-CRF	This data does not contain any information that would reveal the patient's identity.
List of enrolled patients	Paper	Confidential document retained by each investigator.	Document containing identifying data available only to the investigator; it allows the patient to be contacted if necessary. It also allows the study-specific enrollment number to be linked to the patient's medical record.

12.2. Data processing (CNIL) in France

This research is conducted in accordance with the "Reference Methodology" (MR-001). The processing of personal data for this research falls within the scope of Articles 53 through 61 of Law No. 78-17 of January 6, 1978, as amended, relating to information technology, files, and civil liberties. This change was approved by a decision dated January 5, 2006.

Each participant may exercise their right of access and rectification guaranteed by Articles 39 and 40 of the aforementioned law by contacting the physician who is treating them as part of this research and who knows their identity.

The identity of participants will not be disclosed in any report or publication resulting from this study.

In accordance with the Law of March 4, 2004, on patients' rights, and if they so desire, participants in this research may be informed of the study's results once it is completed.

The CMC Ambroise Paré, the research sponsor, has signed a commitment to comply with this "Reference Methodology."

12.3. Archiving

The specific research documents will be archived under the study name in the premises designated for this purpose by the sponsor until the end of the period of practical utility. These documents are:
- Protocol and Appendices (including the patient information sheet and the consent form), Any amendments,
- CPP opinion and ANSM notification form,
- Original signed consent forms in a sealed envelope,
- Inclusion criteria,
- Copy of the computer files containing individual data,
- Any follow-up documents,
- Statistical analyses,
- Final study report.

At the end of the period of practical use, all documents to be archived, as defined in the CMC Ambroise Paré procedure for "filing and archiving documents related to research involving human subjects," will be transferred to the premises designated for this purpose by the sponsor. They will remain under the sponsor's responsibility for 15 years after the study's completion, in accordance with institutional practices.

No removal or destruction may be carried out without the sponsor's consent. At the end of the 15-year period, the sponsor will be consulted regarding destruction.

All data, documents, and reports may be subject to an audit or inspection.

Electronic data will be burned onto a physical medium (CD-ROM or DVD) and printed on paper, after which it will be erased from the sponsor's electronic media. The sponsor agrees to have, during the specified archiving period, the necessary equipment to read these physical media. The sponsor may also decide to produce a printout of this data.

12.4. Ownership of Data

The CMC Ambroise Paré is the owner of the data, and no use or transmission to a third party may be made without its prior written consent.

12.5. Identification of all data to be collected in the observation log

Demographic data:
- Age
- Gender
- Height
- Weight

Preoperative data:
- Date of surgery
- Type of surgery
- Intraoperative events: Use of standard anesthesia technique
- Volume of local anesthetic per nerve
- Time of regional anesthesia, time of surgery, time of surgery completion
- Sensory scores (from the cold test and touch test) recorded every 10 minutes during the 40 minutes following local anesthetic injection,
- Mapping of the plantar arch based on sensory scores,

- ENR-Plantar nerves
- ENA-VVP
- ENA-ALR
- ENA-Satisfaction
- Intraoperative complications

Postoperative data:

- Possible complications (see Appendix 1: questionnaire)

13. FUNDING AND INSURANCE

13.1. Study funding

The costs associated with conducting this research are the responsibility of the sponsor.

13.2. Insurance

The Sponsor shall take out insurance for the entire duration of the research (under policy number WIBCLT17615 with Lloyd's) covering its own civil liability as well as that of the investigators responsible for directing and supervising the conduct of the research on behalf of the Insured, and of any other party involved in this research on behalf of the Insured. This insurance policy, in accordance with Article L.1121-10 of the Public Health Code, is taken out with **Lloyd's,** 8/10 rue Lamennais, 75008 Paris, France.

14. PUBLICATION RULES

The research will be registered on the ClinicalTrials.gov website.
This study will be published in the form of abstracts and original articles. The order of authorship will be determined by Dr. Sébastien Bloc, the principal investigator.

15. REFERENCES

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16. APPENDIX 1: QUESTIONNAIRE TO IDENTIFY POTENTIAL COMPLICATIONS AT DAY 15±4

Questionnaire to identify potential complications at Day 15±4

Patient enrollment number: I__I__I__I__I

Date the questionnaire was completed: ___/___/_____

	Since surgery,	Yes	No
Q1	Have you experienced a decrease in sensitivity in your foot?	☐	☐
Q2	Do you experience tingling and/or prickling and/or numbness and/or itching?	☐	☐
Q3	Do you have difficulty moving your toes?	☐	☐