STATISTICAL ANALYSIS PLAN

Clinical Investigation Plan number: QS-IS-G-H-2201

PROSPECTIVE CLINICAL INVESTIGATION ON THE EVALUATION OF PERFORMANCE AND SAFETY OF THE EPIONE ASSISTED CT-GUIDED PERCUTANEOUS PROCEDURES IN THE LUNGS

Role	Name	Signature	Date
Quantum Surgical: Study Manager	Marion CHASSOUANT		
Delta Consultants: Study Biostatistician	Marie GEOFFRAY		
Delta Consultants: Quality Control Biostatistician	Adrien FRANCAIS		

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1. ABBREVIATIONS

ANSM	L'Agence nationale de sécurité du médicament et des produits de santé
ADE	Adverse Device Effect
AE	Adverse Event
CE	European Conformity
CRF	Case Report Form
CSR	Clinical Study Report
CT	Computed Tomography
DRM	Data Review Meeting
eCRF	electronic Case Report Form
GGO	Ground Glass Opacity
ITT	Intention to Treat
LTP	Local Tumor Progression
MAM	Minimal Ablation Margin
NSCLC	Non-Small Cell Lung Cancer
PP	Per Protocol
PMCF	Post Market Clinical Follow-up
PT	Preferred Term
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SAP	Statistical Analysis Plan
SIR	Society Interventional Radiology
SOC	System Organ Class
SOP	Standard Operating Procedure
TNM	Tumor Nodule Metastasis

2. INTRODUCTION

The purpose of the Statistical Analysis Plan (SAP) is to describe:

- The statistical methodology.
- The calculated/derived variables.
- The general rules and conventions.
- The tables and listings to be included in the Clinical Investigation Report (CIR).

The SAP is based on the Clinical Investigation Plan version 2.0 dated 9th September 2022 and the Case Report Form (CRF) version 2.0 dated 31st March 2023.

3. CLINICAL INVESTIGATION PLAN SUMMARY

The following definitions concern the study:

Designation	Definition
Needle tip	The distal extremity of the inserted needle (sharp end)
Target	The point in the scanner aimed at during the intervention; the point where the operator decides to place the needle tip during the planning phase
Adjustment	A manipulation of the needle by the operator after the insertion phase guided by the EPIONE® device in order to obtain an acceptable trajectory to continue the intervention. This does not include the manipulation of a needle initially and voluntarily planned and/or inserted at a distance from the target by the operator. The adjustment can be: MINOR: Adjustment in depth, in the axis of the needle (advance or retrieve). MEDIUM: Lateral adjustment, the needle does not entirely leave the patient's body. MAJOR: Total removal of the needle(s) from the patient's body and reinsertion of the needle following the same planned trajectory, or a new trajectory to reach the target.

3.1. Study objectives

Primary objective:

The primary objective of the study is to demonstrate the **feasibility of the Epione® device** in assisting needle insertion in CT-guided intervention in the lungs.

The primary endpoint to feasibility is the technical success of the intervention per lesion assessed from **the percentage of robotically assisted lesion targeting and needle placements that were accurate enough to allow the percutaneous intervention.**

The technical success of the intervention will be described by lesion with a Boolean, YES or NO answer to the question:
"Is/are the needles positioned accurately enough to allow next step of the intervention?".

Secondary objectives:

The secondary performance objectives are the following:

- Assessment of the needle placement accuracy.
- Assessment of the number and grading of needle adjustments.
- Assessment of immediate post-intervention ablation success (ablation only).
- Assessment of the long-term performance of ablation: local tumor progression (LTP) rate (ablation only).

The secondary safety objectives are the following:

The safety assessment is based on the reporting of all AEs (serious and non-serious, including deficiency or dysfunction) and AEs related to device or intervention (see Clinical Investigational Plan Section 8 for definition and recording/reporting modalities including severity and causality SIR classification).

3.2. Study design

3.2.1. Study design and device

This is an interventional, prospective, non-comparative, non-randomized and single-arm study of a CE marked device, used outside of its intended use according to the Medical Devices Regulation MDR (EU) 2017/745.
The Epione® device is a Class IIa, non-invasive device and, as such, falls into Case #1 of the ANSM categorization (pre-market study category 1).

Eligible patients scheduled for an Epione® CT-guided intervention in the lung from the investigator's site will be proposed to participate. If they agree, they are enrolled. In case

the prescribed intervention is not maintained, the patient will be removed from the study without any impact on the inclusion window.

The inclusion period (recruitment) is estimated as 6 months for 25 patients (*i.e.* at least 25 CT-guided interventions in the lungs: at least 1 per patient). The inclusion rate will depend on the number of sites using the Epione® device routinely. Two study sites in France are expected to participate in this clinical investigation, Gustave Roussy (Villejuif) will be the coordinating center and a second site will be the Hôpital de La Timone (Marseille).

Considering the main criteria is feasibility, a technical failure of the whole intervention (for all the lesions planned in case of multiple lesions) leads to patient's premature end of study and study withdrawal. In this case, the only data available and analysable will be the technical success of lesion treatment (primary endpoint).

The study device is a user-controlled, stereotactic accessory intended to assist in the planning and manual advancement of the needle, as well as aiding the verification of needle position during CT-guided percutaneous ablation procedures.

The operating principle of the investigational device is detailed in section 6.2 of the protocol.

Five visits will be recorded in the CRF.

- **Visit 1** (within one month before treatment): the first visit is planned to screen the patient, present the study, and deliver the information notice and informed consent form.
- **Visit 2** (treatment): the second visit consists of recovery of the signed informed consent form, confirmation of enrolment, validation of screening, and collection of demographic and tumor characteristics. Pre-intervention CT-guided image, planning of needle trajectory and insertion of needle into targeted area using study device, per-intervention CT-guided image and post-intervention CT-guided image will all be performed.
- **Visit 3**: Follow-up at 1 month (between 2 weeks and 6 weeks after treatment).
- **Visit 4**: Follow-up at 6 months (between 4 months and 8 months after treatment).
- **Visit 5**: Follow-up at 12 months (between 10 months and 14 months after treatment), end of study.

See Section 9 of the Clinical Investigation Plan for a detailed description of each visit.

Technical success is defined as:
When the needle(s) tip(s) reach(es) the target(s) with sufficient accuracy to pursue the intervention, and:

- Robotic needle insertion is performed without adjustment.

- Robotic insertion with only minor or medium adjustment(s).
- Robotic insertion is performed with one robotic major adjustment.

Technical failure is defined as:
When the needle tip does not reach the target with sufficient accuracy to pursue the intervention:

- If insertion of one or several needle(s) from the skin is fully manual.
- Failure of a robotic major adjustment.
- Note: if a lesion cannot be treated because of a major pneumothorax on the previous lesions treated, the lesion is excluded from the study and is not taken into account in feasibility statistics.

3.2.2. Study population

Inclusion criteria

The inclusion criteria are the following:

- Patient ≥18 years.
- Patient for whom a CT-guided intervention in lung has been prescribed and consensually agreed by a multidisciplinary team of radiologists, surgeons and clinicians.
- Patient with a signed informed consent.
- Patient covered by a social security system.

Exclusion criteria

The exclusion criteria are the following:

- Patient unable to undergo general anesthesia.
- Pregnant or nursing female.
- Patient already participating in another clinical study.

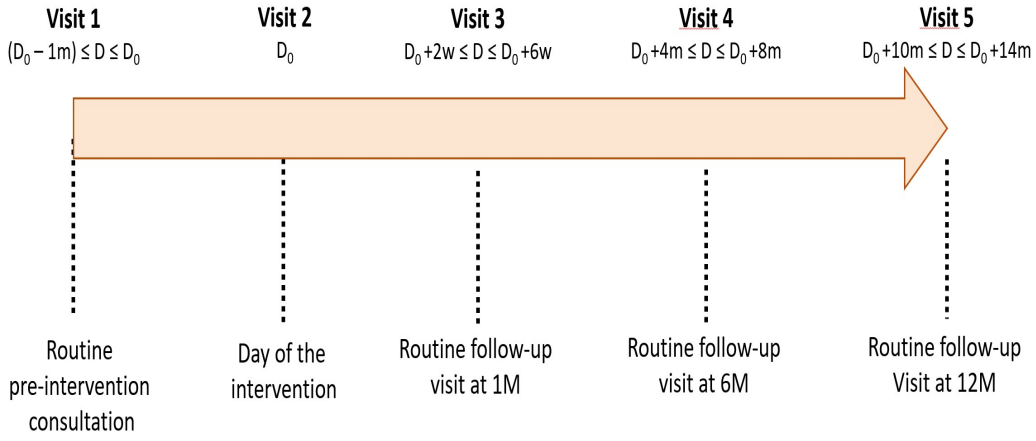
3.2.3. Study duration and flow chart

Study duration per patient

The study will last from patient's informed consent form signature to Visit 5.

Duration can be 10 months to 15 months, depending on the day of patient's informed consent retrieval and the day of Visit 5.

Flow chart of the study



3.3. Investigational device

The investigational sites have an Epione® device in their interventional radiology department. Quantum Surgical will provide the required training and support to the hospital staff, to enable an adequate use of the device for the clinical investigation considering the new destination of use. Furthermore, operators must have performed CT-guided interventions with Epione® on at least five patients to envisage their participation to the investigation. During the study, if any defect in the investigational device is observed, the study manager must be informed.

The Epione® device is an image-guided robotized device that assists the physician during CT-guided interventions. It provides guidance of rigid straight instruments compatible with the diameter of the needle guide supplied by Quantum Surgical. It allows the physician to plan the insertion of needles or probes from medical images and provides stable, accurate and reproducible guidance in accordance with the planning.

See Clinical Investigation Plan Section 6 for complete investigational device description.

3.4. Sample size justification

The sample size rationale is the following:

The previous pilot study on the Epione® was performed on 20 PP patients (22 ITT) with one or two liver lesions [1].

In addition, a clinical study was conducted on the MAXIO by Smakic *et al.* in 2018 [2], which evaluated all types of interventions with the device, and was performed on a consecutive series of 55 patients using the Robot CT-Guided arm (and then compared to retrospective data from manual interventions).

A PMCF study (QS-NIS-G-H-2101) on the Epione® device is in progress in 2022, it aims to collect clinical data on the performance and safety of the procedures performed with the Epione® device in the abdomen with a target of 55 patients with various indications.

The present study aims to collect clinical data on the performance and safety of procedures performed with the Epione® device used outside of its current indication, for an extension of the indication to the thorax (lungs). Thus, it was decided to define the sample size by an inclusion window of 8 months, with a target of 25 patients (at least one CT-guided intervention in the lungs per patient) considering the inclusion rate of the center.

3.5. Criteria for evaluation planned in the clinical investigation plan

3.5.1. Primary Variable

The primary objective of the study is the the **feasibility of the Epione® device** in assisting needles insertion in CT-guided intervention in the lungs.

The primary endpoint to feasibility is the technical success of the intervention per lesion assessed from **the percentage of robotically assisted lesion targeting and needle placements that were accurate enough to allow the percutaneous intervention.**

The technical success of the intervention will be described by lesion with a Boolean, YES or NO answer to the question:
"Is/are the needles positioned accurately enough to allow next step of the intervention?

3.5.2. Secondary Performance Variables

- **Needle placement accuracy per needle after adjustment(s):**

Estimation of distance from target on the planning (planned needle tip position) to real needle tip on the control CT-scan (scan 3) performed after complete robotic needle(s) insertion and adjustment(s).
Estimation of distance from planned needle tip position to target tumor center compared to needle tip position to target tumor center on the final CT-scan performed after complete robotic needle(s) insertion and adjustment(s).

Estimated deviation distance: method
The operator will perform an estimation of the deviation between planned needle and the corresponding inserted needle on the control CT-scan (scan 3) performed after complete robotic needle(s) insertion and adjustment(s), to be representative of the

practice (the interventional radiologist only carries out the intervention when he/she considers the needle position being acceptable in regard with his/her objectives).

On the final CT-scan, the operator identifies the point he/she targeted on the planning, the presumed position is located by memory with the help of anatomical structures surrounding the area. Following collected distances are:

- 3D deviation (3D distance from inserted needle point to planned needle point): estimation and measure.
- Lateral deviation (distance from orthogonal projection of planned needle point to needle axis): estimation and measure.
- Depth deviation (distance from orthogonal projection of planned needle point to inserted needle point on needle axis): estimation and measure.

In addition, the 3D distance from needle tip to lesion center (estimation) is also collected.

- **The number of needle adjustments and grading to reach the target**

The adjustment can be:

  - MINOR: Adjustment in depth, in the axis of the needle(s) (advance or retrieve).
  - MEDIUM: Lateral adjustment, the needle does not leave the patient's body.
  - MAJOR: Total removal of the needle(s) from the patient's body and reinsertion of the needle following the same planned trajectory, or a new trajectory to reach the target.

- **Post-intervention ablation success (ablation only)**

The per-intervention ablation assessment is performed between the pre-interventional and final post-interventional CT-scan (scan 4), in order to determine if the ablation is complete, incomplete or unclear, defined as the following:

  - COMPLETE ABLATION: Ground glass opacity (GGO) induced by the ablation completely covers the targeted tumor minimal 5 mm ablation margins.
  - INCOMPLETE ABLATION: GGO covers the targeted tumor but with a margin of <5 mm.
  - UNCLEAR ABLATION: Margins cannot be assessed, or the delimitation is not identifiable.

- **Long-term local performance of ablation at 6 and 12 months (ablation only)**

Long-term local performance of ablation is based on local tumor progression (LTP) evaluated from CT images at the 6 and 12 months' Follow-up visit. Follow-up visit at 1 month will be taken as baseline.

3.5.3. Secondary Safety Variables

All AEs related to the device or the intervention will be collected.

AEs are categorized in six classes defined below:

Minor complications

- A: No therapy or nominal (non-substantial) therapy.
- B: Moderate escalation of care, requiring substantial treatment, under conscious sedation, blood product administration, extremely prolonged outpatient observation or overnight admission after outpatient intervention not typical for the intervention.

Major complications

- C: Marked escalation of care, *i.e.* hospital admission or prolongation of existing hospital admission for > 24 hours, hospital admission that is atypical for the intervention, inpatient transfer from regular floor/telemetry to intensive care unit or complex intervention performed requiring general anesthesia in previously non-intubated patient (< 48 h).
- D: Marked escalation of care, *i.e.* hospital admission or prolongation of existing hospital admission for > 24 hours, hospital admission that is atypical for the intervention, inpatient transfer from regular floor/telemetry to intensive care uni, or complex intervention performed requiring general anesthesia in previously non-intubated patient (> 48 h).
- E: Life-threatening or disabling event.
- F: Patient death or unexpected pregnancy abortion.

3.5.4. Other Variables

- Demographic data (age, gender).
- Physical examination (weight, height, body mass index).
- Pregnancy test result (if applicable, confirmed by the operator, no test required for the investigation)
- Medical/surgical history (related to disease for the previous 3 months).
- Concomitant treatment/therapy (potentially impacting the intervention for the previous 3 months).
- Comorbidities (potentially impacting the intervention for the previous 3 months).
- Type of intervention planned to require percutaneous needle placement in the thorax (ablation, biopsy, fiducial markers insertion, abscess drainage).

- Targeted tumor for lung intervention: primary cancer (type, stage) or metastatic (origin) or unidentified.
- Information of targeted lesions: number, size(s), location(s), side, lobe, estimated intra parenchymal distance, intervention performed).
- Tumor ablation (type of thermal ablation, material used, duration, post-ablation CT scan).
- CT-guided needle placement (date, operator name, needle identification and size, images pre-and intra-intervention, intervention timing from beginning of the robotically-assisted intervention (switch subject device on) to per-intervention image assessment, intervention timing from beginning of the planning to per-intervention image assessment, device malfunction(s).

3.6. Coding

All AEs will be coded using MedDRA version 25.1 (September 2022).
All concomitant treatments will be coded using WHODrug version March 2022.

4. CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

4.1. Changes in the conduct of the study

Any amendment to the clinical investigation plan will be described in the study report.

4.2. Changes in the planned analyses

Any major/minor changes from the SAP will be discussed in the study report.

Definitions of the Per Protocol population and the Safety Population have been slightly modified from the definition in the protocol, indeed it has been clarified by the Sponsor that treated patients include all patients with an assistance of at least one needle placement with EPIONE®, even if the procedure (ablation, biopsy, fiducial placement or abscess drainage) was not performed using the EPIONE® device in accordance with protocol specifications.

5. GENERAL ANALYSIS METHODOLOGY

5.1. Study periods

First patient included: 30 November 2022.

Planned recruitment time: 6 months.

Planned last patient completed: Q1 2024.

5.2. Definition of protocol deviations

The protocol deviations will be listed by the statisticians when data collection ends. The deviations will then be categorized as major or minor during the interim/final Data Review Meeting (DRM) prior to locking database.

5.3. Analysis populations

Four different analysis populations are foreseen:

Screened Population
All patients who are proposed to enter the study.

Intention-to-Treat (ITT) Population
All screened patients who have confirmed their signed informed consent and are planned to be treated using the Epione® device.

Per Protocol (PP) Population
All patients in the ITT population treated by the Epione® device, including those for which the procedure was not completed with the Epione® device, without any major deviation.

Safety Population
All patients in the ITT population treated by the Epione® device, including those for which the procedure was not completed with the Epione® device.

5.4. Database lock

Interim and final database locks will be executed after resolution of all queries related to data and after the DRM is held. Database locks will be performed electronically using ENNOV Clinical V8.0 by Delta Consultants' data management team following Delta Consultants' SOPs.

5.5. Statistical concerns

The statistical analysis will be performed by an external CRO (Contract Research Organization: Delta Consultants, Eybens, France). All statistical analyses will be produced using SAS® 9.4 software (Cary, NC, USA).
Results will be presented using tables and listings in two Word documents.

5.5.1. Summary statistics

Description of relevant study variables will be performed using n, number of missing data, mean, standard deviation, median, min and max for quantitative variables and

using number of missing data, frequency and percentage of non-missing for qualitative variables.

Analyses will be presented by patient, by lesion (when relevant) and/or by needle (trajectory). The statistical analysis will take into account data clustering (*e.g*. several procedures for a given patient) in case of inferential statistics.

5.5.2. Level of significance

A 5% significance threshold will be used.

5.5.3. Adjustments for covariates

No adjustment for covariates is planned for this study.

5.5.4. Handling of dropouts and missing data

Missing data will not be imputed, except dates (missing day) if needed in order to calculate durations.

5.5.5. Interim analyses

Two interim analyses are planned to gather early evidence on the performance and safety of the device. The interim reports will be integrated in the clinical data pool of the Sponsor for regulatory purposes.

- The first interim analysis will be performed when the first 10 patients have been included in the study and have undergone the planned robotic intervention with data recorded and validated in the eCRF, enabling the primary and secondary endpoints related to the intervention to be analyzed. All possible tables and listings will be produced (summarized in table below).
- The second interim analysis will be performed when all 25 patients expected have been included in the clinical investigation, with the identical conditions detailed in the previous point. All possible tables and listings will be produced (summarized in table below).

Objective	Endpoint	Population	Method	1st interim	2nd interim	Final
Feasibility	Technical success of the intervention	PP and ITT	Lesion	X	X	X
Performance	Needle placement accuracy	PP and ITT	Needle	X	X	X
	Number and grading of needle adjustments	PP and ITT	Needle, Lesion, Patient	X	X	X
	Immediate post intervention ablation success	PP and ITT	Lesion, Patient	X	X	X
	Long-term performance of ablation using the LTP rate	PP and ITT	Lesion			X
Safety	Number of AE recorded	SP		X	X	X
	Number of SAE recorded	SP		X	X	X
	Number of SADE recorded	SP		X	X	X

5.5.6. Multicentre studies

No comparison between the two sites is planned.

5.5.7. Multiple comparisons/multiplicity

No handling of multiple comparisons will be performed.

5.5.8. Examination of subgroups

No subgroup analyses are planned.

5.6. Patient data listings

Individual data listings will be provided in Word format. Patient data listings are listed in Section 13 of this SAP.

6. STUDY PATIENTS

6.1. Disposition of patients

The disposition of patients according to populations of analysis (Screened, ITT, PP, Safety) and visits (Visit 1 – Screening, Visit 2 – Intervention, Visit 3 – Follow up at 1 month, Visit 4 – Follow-up at 6 months and Visit 5 – Follow-up at 12 months, End of study) will be presented using frequency and percentages.

End of study information (normal end of follow-up (Visit 5 performed), AEs, screen failures, patient's will to withdraw from study, lost to follow-up, device deficiency or dysfunction, death and other) will be presented using frequency and percentages.

6.2. Protocol deviations

Validation of inclusion/exclusion criteria will be presented using frequency and percentages. All protocol deviations will be presented in patient data listings. Major deviations leading to exclusion from a population will be described as frequency and percentage of patients in the Screened population.

7. DEMOGRAPHIC AND BASELINE CHARACTERISTICS

Demographic and lung tumor characteristics will be presented on the ITT population using summary statistics for qualitative or quantitative parameters:

- Demographic data: age (years), gender, height (cm), weight (kg), Body Mass Index (kg/m^2).
- Planned intervention: side of targeted lung (left, right or both [together/separately]), type of CT-Guided percutaneous treatment to be planned:
    - Ablation.
    - Biopsy.
    - Abscess drainage.
    - Fiducial marker insertion.
- Lung tumor type:
    - Primary tumor: NSCLC subtype, TNM stage (or other).
    - Metastatic tumor: primary cancer location.
    - Unidentified.
- Lung lesions:
    - Number of lesions intended to be treated per lung per patient.
    - Lesion details: lung side (left or right) and lobe (upper, lower or medium), lesion location (<10mm to mediastinum, <10mm to hilum, <10mm to pleura), tumor size (cm), estimated intra parenchymal distance (cm), intervention type performed (ablation, biopsy, abscess drainage, fiducial marker insertion).
- Planning with the Epione® device:
    - Number of needle trajectories
    - Needle identification information.

In addition, the following duration parameters will be presented only for the final analysis:

- Procedure time (post-intervention - pre-interventional CT-scan).
- Duration of Epione® device use (end of trajectory guidance – start of procedure planning).
- Duration of guidance (end of trajectory guidance - start of trajectory guidance).

Medical history, comorbidities, concomitant treatments (for the last 3 months) and planning with the Epione® device at inclusion will be described in patient data listings.

8. MEASUREMENT OF TREATMENT COMPLIANCE

Not applicable.

9. PERFORMANCE ANALYSES

Performance analyses will be conducted on the ITT and PP populations.

9.1. Primary endpoint

9.1.1. Definition of the primary variable

The primary endpoint is the technical success by lesion of each intervention.

Technical success by lesion is defined as:
When the needle(s) tip(s) reach(es) the target(s) with sufficient accuracy to pursue the intervention, and:

- Robotic needle insertion is performed without adjustment.
- Robotic insertion with only minor or medium adjustment(s).
- Robotic insertion is performed with one robotic major adjustment.

Technical failure by lesion is defined as:
When the needle tip does not reach the target with sufficient accuracy to pursue the intervention:

- If insertion of one or several needle(s) from the skin is fully manual.
- Failure of a robotic major adjustment.

The parameter of the primary endpoint consists of the percentage of robotically assisted lesion targeting and needle placements that were accurate enough to allow the percutaneous intervention.

The investigator will describe the technical success of the procedure for each lesion on a 2-point scale:

- "Is/are the needles positioned accurately enough to allow next step of the intervention?" ="Yes"
- "Is/are the needles positioned accurately enough to allow next step of the intervention?" ="No"

The performance endpoint is defined by "Is/are the needles positioned accurately enough to allow next step of the intervention?" = "Yes".

Note: if a lesion cannot be treated because of a major pneumothorax on the previous lesions treated, the lesion is excluded from the study and is not taken into account in feasibility statistics (negative answer to the question "Was the CT-Guided intervention maintained" with "pneumothorax" as reason specification).

9.1.2. Statistical evaluation of the primary variable

Performance of the investigational device:
Frequency and percentage with **"Is/are the needles positioned accurately enough to allow next step of the intervention?" = "Yes"** reported by the investigator will be described by lesion. 95% CI of the percentage will be provided.

9.2. Secondary performance endpoints

9.2.1. Needle placement accuracy

The needle placement accuracy defines how accurately the operator has positioned the needle with respect to the planned needle trajectory.

On the control CT-scan (scan 3), the operator identifies the point he/she targeted on the planning, the presumed position is located by memory with the help of anatomical structures surrounding the area. Distance is estimated from the needle tip:

- 3D deviation (3D Distance from inserted needle point to planned needle point): estimation and measure.
- Lateral deviation (distance from orthogonal projection of planned needle point to needle axis): estimation and measure.
- Depth deviation (distance from orthogonal projection of planned needle point to inserted needle point on needle axis): estimation and measure.

In addition, the 3D distance from needle tip to lesion center (estimation) is also collected.

The assessment will be performed during (estimation) and after (measure) the intervention.

<u>During the intervention:</u>

- The operator will perform an evaluation of distances from target on the planning (planned needle tip position) to real needle tip on the final CT-scan performed after complete robotic needle(s) insertion and adjustment.
- The distances from planned needle tip position to tumor center will be compared to needle tip position to tumor center on the final CT-scan performed after complete robotic needle(s) insertion and adjustment.

<u>After the intervention:</u>
The same images will be reviewed and both the above will be measured using a ruler tool of the Epione® or equivalent, except for 3D distance to lesion center for which only the estimation per-operation is available (in case of multi-needle intervention, this estimation is not applicable and will not be presented).

Needle placement accuracy (mm) estimations and measures (seven parameters) will be described by needle as quantitative data.

9.2.2. Number and grading of needle adjustments

During or after each intervention, the number of needle adjustments will be reported, if necessary.
The number of needle adjustments to reach the target will be presented using qualitative and quantitative descriptive statistics:

- per needle.
- per lesion (sum per lesion).
- per patient (sum per patient).

Grading of adjustment(s) (minor, medium and major, refer to Section 3.5.2 for definitions) will be presented using frequency and percentage:

- per needle (at least one per needle).
- per lesion (at least one per lesion).
- per patient (at least one per patient).

In addition, quantitative descriptive statistics on the estimated corrective distance (mm) will be presented separately for each grading of adjustment (minor and medium):

- per needle (the highest per needle).
- per lesion (the highest per lesion).
- per patient (the highest per patient).

The highest distance was considered as the worst distance.

Finally, method of adjustment (using Epione® or other [CT guided, freehand]) will be presented in a listing.

9.2.3. Immediate post-intervention ablation success (ablation only)

This secondary criterion determines if the ablation is complete, incomplete or unclear. In a complete ablation, the ablation volume completely covers the lesion, with sufficient MAM of 5 mm. Ablation assessment tool of EPIONE will be collected (complete ablation, incomplete ablation, unclear ablation) and summary statistics for qualitative parameters will be provided per lesion and per patient (the best result per patient).

9.2.4. Long-term performance of intervention using the Local Tumor Progression rate (ablation only)

Patients with tumor ablation will be evaluated for Local Tumor Progression (LTP) on follow-up CT imaging by the physician during the routine follow-up visits. This will be presented by lesion only.

Frequency and percentage of patients with any visible LTP on control imaging will be presented at approximately 6 months and 12 months. 95% CIs will be provided. The CT images of the ablation zone obtained at 1 month-FU routine visit will be considered as baseline imaging. The evaluation at later follow-up visits will be performed by comparing follow-up CT-scans to the baseline.

10. SAFETY ANALYSES

The secondary safety analysis will be conducted on the Safety population.

10.1. Adverse events

All detailed AEs will be listed by patient.

10.1.1. Summary of AEs

Throughout the study, the investigator will report the presence or absence of AEs and SAEs in the CRF.

A summary of AE occurrence (number of AEs, number of patients, percentage of patients) will be presented overall, by intensity, by severity and by relationship with the device or procedure.

A summary table with all AEs will be presented by System Organ Class (SOC) and Preferred Term (PT). The same table will be provided for ADEs (Adverse Device Effects), SAEs (Serious Adverse Events) and SADEs (Serious Adverse Device Effects).

Individual listings of AEs (related or not) will be presented by patient with all characteristics recorded from the CRF.

10.1.2. Device dysfunction

Individual listing of device dysfunction will be presented by patient with all characteristics recorded from the CRF.

10.2. Deaths, other serious adverse events (SAEs) and other significant adverse events

Individual listings for ADEs, SAEs, pregnancies (if any) and SADEs will be presented including all details recorded in the AE form in the CRF.

10.3. Clinical laboratory evaluation

Not applicable.

10.4. Vital signs, physical findings and other observations related to safety

Not applicable.

11. DOCUMENTATION OF STATISTICAL METHODS

11.1. Hardware and Software

Statistical analyses will be performed by Delta Consultants, Eybens, France. All analyses will be carried out using SAS® version 9.4 run under Microsoft® Windows 10®.

11.2. Inferential statistics

Statistical inference will be used to estimate CIs for the statistical endpoints described in the SAP.

12. TABLES

The list of tables is provided below.

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Table 3.1.2. Primary endpoint: Percentage of lesions with the needle(s) positioned accurately enough to allow the next step of the intervention – PP Population

Table 3.2.1. Needle placement accuracy measured during intervention (estimation) – ITT population

Table 3.2.2. Needle placement accuracy measured during intervention (estimation) – PP population

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1. Patient disposition

2. Demography and baseline characteristics

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Listing 2.2. Medical history and comorbidities – ITT population
Listing 2.3. Lung tumor characteristics – ITT population
Listing 2.4. Lung lesion details – ITT population
Listing 2.5. Planning with the Epione® device – ITT population
Listing 2.6. Procedure timing and duration – ITT population
Listing 2.7. Follow-up visits – ITT population

3. Primary and secondary performance endpoint evaluations

Listing 3.1. Primary endpoint: Needle(s) positioned accurately enough to allow the next step of the intervention – ITT Population
Listing 3.2. Needle placement accuracy measured during intervention – ITT population
Listing 3.3.1. Number and grading of needle adjustments – General information – ITT population
Listing 3.3.2. Number and grading of needle adjustments – By patient – ITT population
Listing 3.3.3. Number and grading of needle adjustments – By lesion – ITT population
Listing 3.3.4. Number and grading of needle adjustments – By needle – ITT population
Listing 3.4. Immediate post-intervention ablation success (ablation only) – ITT population
Listing 3.5. Long-term performance of the intervention using the Local Tumor Progression rate (ablation only) – ITT population

4. Secondary safety endpoint evaluations

Listing 4.1. Adverse Events (summary during intervention) – Safety population
Listing 4.2. Adverse Events (details) – Safety population
Listing 4.3. Adverse Device Effects (ADEs) – Safety population
Listing 4.4. Serious Adverse Events (SAEs) – Safety population
Listing 4.5. Serious Adverse Device Effects (SADEs)– Safety population
Listing 4.6. Device dysfunction – Safety population

5. Other Listings

Listing 5.1. Concomitant medications – ITT population
Listing 5.2. Concomitant treatments related to AE/SAE – ITT population
Listing 5.3. CT-scan details – ITT population

14. REFERENCES

1. Multicenter study to evaluate the safety and performance of the Quantum Surgical robotic device for image-guided percutaneous needle placement in liver tumors. 2021. Internal document.
2. Smakic et al. Performance of a robotic assistance device in computed tomography-guided percutaneous diagnostic and therapeutic procedures. Cardiovasc. Intervent. Radiol. 2018; 41:639-644.

15. APPENDICES

15.1. Template of results tables and listings

Table 2.2. Demographic Data

Variable	Modality	Statistic	Patient (N=XX)
Age (years)		N	XX
		Missing	XX
		Mean (SD)	XX.X (XX.X)
		Median (Q1 ; Q3)	XX (XX ; XX)
		Min ; Max	XX ; XX
Weight (kg)		N	XX
		Missing	XX
		Mean (SD)	XX.X (XX.X)
		Median (Q1 ; Q3)	XX (XX ; XX)
		Min ; Max	XX ; XX
Height (cm)		N	XX
		Missing	XX
		Mean (SD)	XX.X (XX.X)
		Median (Q1 ; Q3)	XX (XX ; XX)
		Min ; Max	XX ; XX
BMI (kg/m²)		N	XX
		Missing	XX
		Mean (SD)	XX.X (XX.X)
		Median (Q1 ; Q3)	XX (XX ; XX)
		Min ; Max	XX ; XX

Analysis table : ADSL
Programme : <F:\LABOS\QUANTUM\H2201\H2201_sas\H2201_prog\H2201_prog_Stat\H2201_Tables.sas>
Date and hour of program execution : DDMMM2023 HH:MM; Date and hour of AD programme : DDMMM2023 HH:MM

Listing 1. Protocol deviations and study populations

Patient	Screened population	ITT population	PP population	Safety population	Deviation ID	Description of deviation	Minor / major
01-001	Yes	Yes	Yes	Yes	XXXX	xxxxxxx	Minor
…							

Analysis table : ADDV
Programme : <F:\LABOS\QUANTUM\H2201\H2201_sas\H2201_prog\H2201_prog_Stat\H2201_Listings.sas>
Date and hour of program execution : DDMMM2023 HH:MM; Date and hour of AD programme : DDMMM2023 HH:MM