Statistical Analysis Plan

Initial Experience of the Treatment of Kidney Stones with the MONARCH™ Platform, Urology

Protocol Number: 2021-URO-0001
Protocol Version: C, October 18, 2022

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The following individuals have reviewed this version of the Statistical Analysis Plan and are in agreement with the content:

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1 Introduction

This is the Statistical Analysis Plan (SAP) for the final analysis of data collected under Protocol 2021-URO-0001. This SAP describes in detail the statistical methodology and statistical analyses for this protocol.

1.1 Study Objectives

The aim of the study is to collect descriptive performance data on the use of the MONARCH™ Platform, Urology (hereafter referred to as MONARCH™) for robotic mini-Percutaneous Nephrolithotomy (PCNL) procedures. Data gathered from this study will be used to optimize the robotic platform and inform training and education material for future users.

1.2 Study Design

This is a single-center, prospective, single-arm study to collect descriptive data on the robotic-assisted mini-PCNL removal of kidney stones using the MONARCH™ system.

The study will enroll up to 20 patients. Each enrolled subject will be followed up to 30 days ± 7 days post procedure.

2 Treatment Assignment

This is a single-arm study where all enrolled subjects will have the MONARCH™ system utilized for removal of kidney stones via a mini-PCNL procedure.

3 Randomization and Blinding Procedures

As this is a single-arm study, no randomization occurred, and no blinding procedures are required.

4 Interval Windows

Interval windows for the purpose of analysis in this study are not defined outside of those already specified in the protocol for visit scheduling where the collection of data for the primary and safety endpoints occurs.

Table 1 Schedule of Assessments in the protocol specifies the following visit windows:

- Screening/baseline: approximately 30 days prior (allowing up to 60 days prior) to the procedure
- Pre-operative imaging, no longer than 30 days pre-procedure
- Post-operative 30 days follow-up (± 7 days)

Any information entered in the electronic Case Report Forms (eCRFs) at a given visit will correspond to the scheduled visit. There will be no assigning of observations to time points outside of the visit to which they are recorded in the eCRFs.

5 Levels of Significance

No hypotheses are specified for this study and no p-values are being calculated, therefore no level of significance is specified. All estimation of endpoints will be performed using 95% confidence intervals where indicated below.

6 Analysis Sets

The summary of all performance and safety endpoints will be performed on the set of subjects in whom the MONARCH™ system is utilized during the procedure. This will be labeled as the Full Analysis Set (FAS) and will be identified by having a time recorded in the "When was the Ureteroscope introduced (timestamp)?" field on the Procedure: Ureteroscopy and Percutaneous Access eCRF.

7 Sample Size Justification

The study is expected to enroll up to 20 subjects. No formal hypothesis is being tested and therefore the sample size determination is not based on a statistical power calculation, but rather is deemed sufficient for a descriptive summary of safety and primary endpoints in this first-in-human experience with the study device.

8 Analyses to be Conducted

8.1 General Conventions

Subject data will be summarized in tables and presented in further detail in listings. All eCRF data will be listed per subject for all subjects. Descriptive statistical analyses will be provided for pre-specified study endpoints. Summaries for continuous variables will include a minimum of number of observations (n), mean, standard deviation, median, minimum, and maximum. Summaries for categorical variables will include number and percentage.

Analyses will be conducted using SAS software. During the course of programming of tables for summaries that are described in this SAP, minor modifications may become necessary. Examples of these minor modifications include, but are not limited to, re-wording of a footnote, addition of a footnote, re-labeling of a column, or addition or removal of a column from a listing. In cases where modifications to tables or listings are not related to a change in statistical analysis methodology or conclusions that could be made on the originally proposed methodology, then no amendment of the SAP is necessary. Changes to planned analyses

specified in the protocol or alterations of an approach that is described herein, will require an amendment to the SAP.

During the course of study enrollment, one subject was enrolled into the study at two separate times to accommodate stone removal in each kidney. Follow-up for the initial unilateral procedure was completed prior to the second contralateral procedure to allow for the ability to obtain a complete safety follow-up per study protocol, and thereby minimize or eliminate any confounding factors that may occur with the performing of concurrent study procedures. For simplicity in analysis, data obtained on this subject during these procedures will be treated independently; therefore a procedure-level analysis will be the same as a subject-level analysis and data from subjects 101-001 and 101-003 will be assumed to be independent.

8.2 Disposition of Study Subjects

Subject disposition will be summarized in total using counts and percentages. The number and percentage of subjects in the FAS who completed and discontinued will be tabulated along with the specific reasons for discontinuation.

8.3 Demographic and Baseline Characteristics

Summary statistics of subject demographics (age, sex, race, and ethnicity) will be presented for the FAS. Vital signs (height, weight, body mass index, systolic blood pressure, diastolic blood pressure, heart rate and ASA score) will be summarized in a similar manner.

Counts and percentages will be provided for medical history terms included on the Relevant Medical History eCRF including Diabetes, Recently on blood thinners, Prior history of stone disease, Anatomic abnormalities, and Prior urinary tract infections. Data collected in the Other Relevant Medical History and Urologic or Other Relevant Procedure History eCRFs will be listed.

Summary statistics will be provided for quantitative parameters collected in the Complete Blood Count (CBC) and Complete Metabolic Panel (CMP) blood draws reported at the Screening/Baseline Visit. Urinalysis and culture test results will be listed.

8.4 Clinical Characteristics

Pre-operative clinical characteristics as well as procedure day measurements will be summarized at both the subject level as well as the kidney stone level given that many subjects present with more than one stone for treatment in the study. At the subject level, counts and percentages will be provided for whether the left or right kidney is being treated, as well as the number of stones per subject, and the number of kidney regions with stones. Summary statistics will be provided for cumulative stone burden, defined as the sum of the longest dimension of all stones, estimated percutaneous tract length, subject weight prior to the procedure and oxygen saturation as reported in the Pre-Procedure Setup eCRF.

At the stone level, counts and percentages will be provided for the pole location and sub-location and summary statistics will be provided for the longest linear dimension, as well as the remaining dimensions in decreasing order, and stone radio density.

8.5 Primary Endpoint and Associated Hypotheses

No formal hypotheses are specified for this study.

The primary endpoint is the successful completion of the robotic-assisted mini-PCNL kidney stone removal procedures including:

- Gaining safe concomitant (i.e., retrograde and antegrade) access to the upper urinary tract
- Locating and visualizing the kidney stones
- Enabling fragmentation of stones by standard of care method
- Evacuating stone fragments and dust

Successful completion is identified by answering "Yes" to each of these questions on the Investigator Assessment form. The number and percentage of subjects experiencing successful completion will be summarized and an exact 95% confidence interval will be estimated. Counts and percentages will also be provided for each of the four components of the primary endpoint.

8.6 Secondary Endpoints and Associated Hypotheses

There are no secondary endpoints specified in the study protocol. Analysis of additional data collected is described in subsequent sections.

8.7 Additional Endpoints

Summary statistics will be provided for the following:

- Procedure duration: defined as the difference between "When was the patient's percutaneous wound closed?" from the Mini-PCNL eCRF and "When is the Cystoscope introduced?" from the Pre-Procedure Setup eCRF
- Cumulative stone burden at the 30-day follow-up visit as well as change in stone burden from the Screening/Baseline visit; Change in cumulative stone burden (%) will also be summarized and is defined as 100*(Change/Baseline)
- Stone radio density at 30 days
- Duration of stent placement in days: defined as the difference between "Date of stent extraction" from the Physical Exam and Vital Signs eCRF at the 30-day visit and "Did you place a ureteral stent in this patient?" from the Mini-PCNL eCRF + 1
- Subject weight post-procedure as well as change from pre-procedure weight
- Length of stay in nights: defined as "Date of hospital discharge" – "Date of hospital admission"
- CBC and CMP results at the 30-day visit as well as change from the Screening/Baseline visit

- Selected labs taken immediately post procedure (sodium, creatinine, hematocrit) as well as change from the Screening/Baseline visit

Counts and percentages will be provided for the following:

- Conversion to conventional (non-robotic) treatment methods from the Investigator Assessment eCRF
- At the subject level, the number, location, individual sizes of post-operative stones, and cumulative stone burden of any post-operative stones will be provided.
- Estimated stone free rate at 30 days: defined as the number of subjects with no reportable stone size (or size reported as zero in all three dimensions) on the Radiology Imaging II eCRF at the 30-day visit
- Number of Randall's plaques in each of the Upper Pole, Interpole, and Lower Pole as reported in the Investigator Assessment eCRF
- Subjects requiring retreatment for stone removal with the duration of the study, as reported within the Concomitant Procedure eCRF

8.8 Safety Analyses

All adverse events (AE) and serious adverse events (SAE) will be monitored once the patient is enrolled (signs informed consent) through the end of follow-up. Given the small, planned sample size for this study, the summaries described below will only be provided if five or more AEs are reported during the study. If fewer than five are reported, then only listings of reported AEs will be provided.

An overview table of all AEs will be generated that includes the total number of AEs, number and percentage of subjects with at least one AE, number and percentage of subjects with at least one SAE, number and percentage of subjects with at least one AE related to the study device, as well as related to the study procedure. Related AEs are those identified as having a relationship of causal, probable or possible reported in the corresponding field of the AE eCRF.

Furthermore, separate AE summary tables will be provided by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC) and Preferred Term (PT) for all AEs. Separate AE summary tables will also be provided to show a breakdown of AEs by MedDRA SOC and PT and relationship to study device, as well as relationship to study procedure. SAEs will be summarized in a similar manner.

Summaries by MedDRA SOC and PT will also be provided for events classified as major (Clavien-Dindo Class III or higher) and minor (Clavien-Dindo Class I or II). Separate summaries by individual Clavien-Dindo grade will be provided.

Listings will be provided for concomitant medications, concomitant procedures, physical examination findings and vital signs during follow-up.

8.9 Plans for Interim Analysis

No interim analysis was planned for this study that had the intention of altering study design or execution. Three summaries of data were provided to support abstract writing that described the initial experiences of the device use in subjects.

8.10 Handling of Missing Data

All summaries will be performed only on subjects undergoing the scheduled procedure and only observed data will be summarized. There will be no imputation of data for early terminated subjects or for missing data within the database.

8.11 Adjustments for Multiplicity

No adjustments for multiplicity are necessary for this study given the absence of any formal hypothesis testing.

8.12 Sensitivity Analyses

No sensitivity analysis is planned for this study.

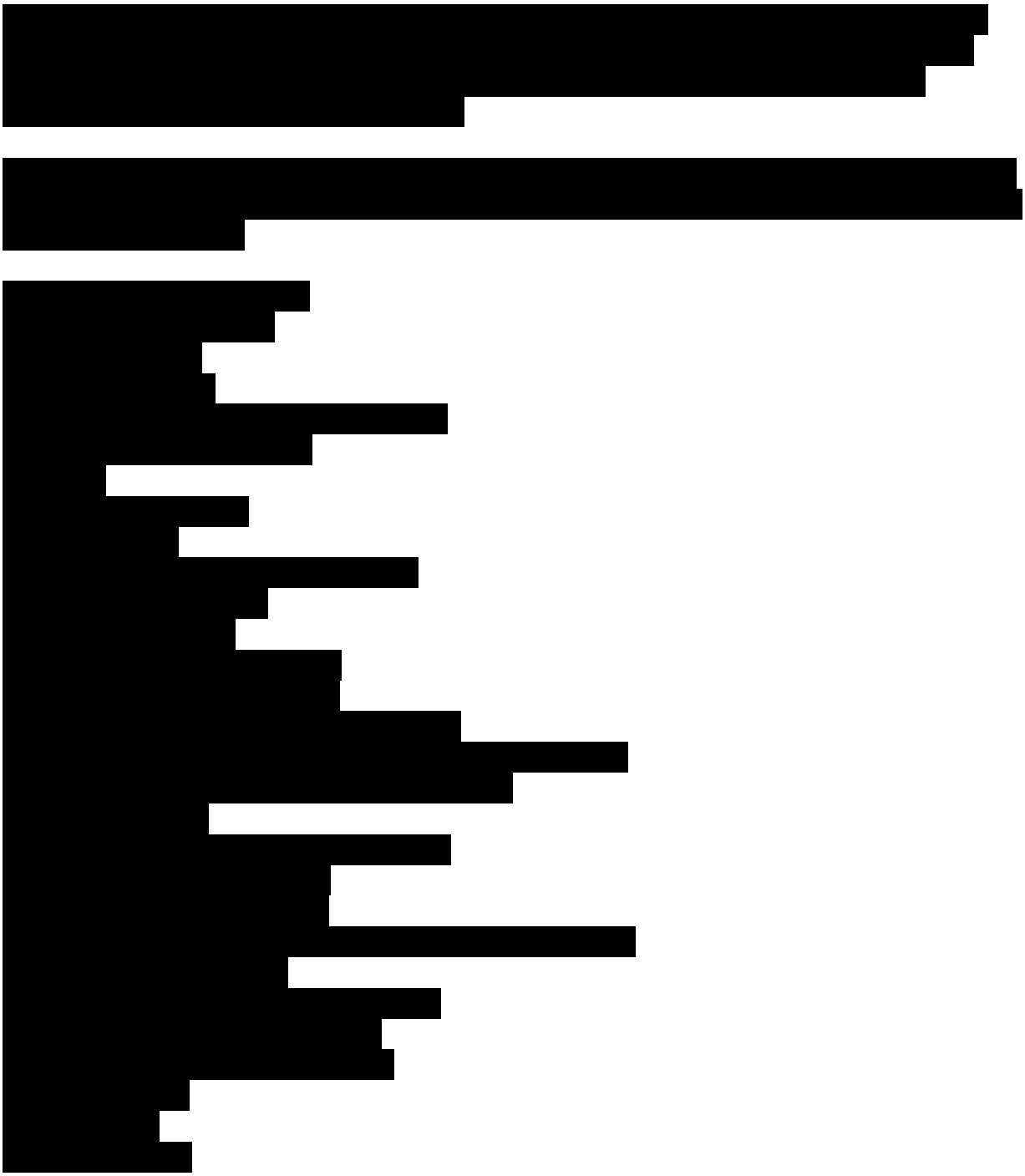
8.13 Subgroup Analysis

No subgroup analysis is planned for this study.

8.14 Assessment of Site Homogeneity

No summaries or adjustments by study site are planned for this study as there is only one site enrolling subjects into the trial.

8.15 Exploratory Analyses



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9 Data Monitoring Committee (DMC)

No Data Monitoring Committee was planned or utilized during this study.

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