Statistical Analysis Plan (SAP)

A Prospective, Randomized, Controlled, Multi-Center Evaluation of a Powered Vascular Stapler in Laparoscopic Nephrectomies and Nephroureterectomies

Protocol Number: ESC-15-002

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SAP Version: 1.0
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Revision History

Version Number	Version Date	Reasons for Revision
1.0	October 11, 2017	Original Document

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This is the Statistical Analysis Plan (SAP) for the final analysis of data collected under Protocol ESC-15-002. This SAP describes in detail the statistical methodology and statistical analyses for this protocol.

1 Study Overview

1.1 **Study Objectives**

The primary objective of the trial is to demonstrate that the frequency of hemostatic interventions/procedures required intra-operatively or post-operatively related to the transection of the renal artery (RA) and renal vein (RV) during laparoscopic nephrectomies and nephroureterectomies with the powered vascular stapler (PVS) is not increased when compared to the standard of care (SOC) stapling device.

1.2 **Study Design**

This was a prospective, randomized, controlled, multi-center, open-label study that planned to collect and compare data from the surgeon's current SOC stapler (for RA/RV transection) and PVS. Prospective subjects were informed about the nature of the research, given the informed consent document (ICD) to read, and if the subject understood the consent, were asked to provide written consent.

2 Treatment Assignment

Subjects were assigned to either the surgeon's current SOC stapler or PVS. The ECHELON FLEX™ PVS with Advanced Placement Tip is a sterile, single use instrument that simultaneously cuts and staples tissue. There are four staggered rows of staples, two on either side of the cut line. The ECHELON FLEX™ PVS with Advanced Placement Tip and reloads have a staple line that is approximately 35 mm long and a cut line that is approximately 30 mm long. The shaft can rotate freely in both directions and an articulation mechanism enables the distal portion of the shaft to pivot to facilitate lateral access to the operative site. The powered vascular stapler has been cleared for marketing by the FDA and is CE marked which allows for commercial distribution in the European Union. The device was used in accordance with its product labeling and Instructions for Use.

3 Randomization and Blinding Procedures

Subjects were randomized to either the surgeon's current SOC stapler or PVS in a 1:1 ratio. Randomization could have occurred at any time prior to surgery up to transection of the vessel(s). Sites were instructed to wait until as close as possible to the actual time of vessel transection so as to minimize randomized drops within the study.

Randomization was accomplished through utilization of envelopes at the study site. Randomization envelopes were created according to the "Work Instructions for the Creation of Randomization Envelopes", document number WE001625, based on a randomization schedule generated by the Ethicon Biostatistics group. The randomization schedule was generated using a validated program that incorporated variable block sizes, and treatment assignment was balanced within each study site. This was an open-label study and therefore no blinding procedures were required.

4 Interval Windows

Interval windows are not defined for the purpose of analysis in this study as the collection of data for the primary performance endpoint occurred intra-operatively and the collection of data for the primary safety endpoint occurred through hospital discharge and subsequent follow-up at the final visit. The final visit occurred approximately 4 weeks after surgery, thus no interval windows need to be defined given the absence of long-term follow-up in this study. The study protocol specified a window of 5 days around the scheduling of the 4-week follow-up visit, and any information entered in the eCRFs at this visit will correspond to the 4-week visit. There will be no assigning of observations to time points outside of the visit to which they are recorded in the eCRFs. The complete Schedule of Events for this study can be found in the Synopsis of the study protocol.

5 Primary and Secondary Endpoints

5.1 Primary Performance Endpoint

The primary performance (effectiveness) endpoint in this study was defined as the occurrence of hemostatic interventions/procedures completed for intra-operative bleeding related to the transection of the RA and RV with the use of either the SOC or PVS stapler. Hemostasis interventions or procedures were defined as bleeding detected and controlled intra-operatively (additional stapling, over-sewing, clip placement, compression, use of suture, sealant, and/or buttress, and/or use of energy); or bleeding that occurred intra-operatively requiring blood or blood product transfusion or an additional surgical procedure (e.g. conversion to open). No hemostasis intervention was defined as no bleeding at the staple line or bleeding that stopped after initial blotting of the staple line.

5.2 Primary Safety Endpoint

The primary safety endpoint was defined as the occurrence of hemostatic interventions/procedures completed for post-operative bleeding related to the transection of the RA and RV with the use of SOC or PVS. Hemostasis intervention was defined as bleeding that occurred post-operatively requiring blood or blood product transfusion or an additional surgical procedure (related to RA and RV transection). No hemostasis intervention was defined as no interventions needed for post-operative bleeding (related to RA and RV transection). This endpoint was recorded at the subject level as it was based on post-operative interventions and not specific to any individual firing.

5.3 Secondary and Additional Endpoints

Key additional endpoints in this study include: Surgeon Task Load Index, adverse events, and device usability questionnaires.

6 Levels of Significance

Evaluation of the acceptance criterion for this study is being accomplished through estimation of a 95% confidence interval. No hypotheses are specified for this study and no p-values are being calculated, therefore no level of significance is specified. All estimation of additional endpoints will be performed using 95% confidence intervals.

7 Analysis Sets

There will be three analysis sets defined:

- The Full Analysis Set (FAS) will consist of all randomized subjects who had a procedure performed and provide data on the number of surgical interventions.
- The Per Protocol (PP) Analysis Set will consist of all subjects in the FAS who had no major protocol violations. Determination of major deviations are conducted by the study Medical Director, Clinical Operations Trial Leader, Franchise Clinical Study Lead, and Biostatistician. A major deviation is defined as: A departure from the study protocol that has the potential to affect the scientific validity of the study (including deviations that: a) impact the analysis of the primary endpoint, or b) are due to inappropriate enrollment of a subject that does not meet the inclusion/exclusion criteria) or the safety, rights and welfare of the enrolled subject.
- The Safety Analysis Set consists of all randomized subjects on whom a procedure is started.

The primary performance endpoint analysis will be performed on the Full Analysis Set and subjects will be classified according to their randomized treatment group. The primary performance endpoint analysis will also be performed on the PP set as a sensitivity analysis to the results on the FAS. The analysis of additional endpoints will also be performed on the Full Analysis Set. Analysis of the primary safety endpoint and adverse events summaries will be performed on the Safety Analysis Set.

8 Sample Size Justification

Approximately 250 subjects were planned to be randomized in the study in a 1:1 ratio to SOC or PVS. Historical clinical study data on a similar powered surgical stapler demonstrated a need for staple line interventions in approximately 6% of firings on the pulmonary artery or pulmonary vein. This data also showed an average of 2.6 to 2.9 firings per subject, and it is expected, given differences in device design and procedure, that each subject would have required 2 to 3 firings on the renal vein or renal artery in the current study.

Given that it was expected to have a minimum of 300 firings in each group, the sample size of approximately 250 subjects total was considered adequate for descriptive summarization of the primary performance endpoint, i.e. number and frequency of intra-operative surgical interventions. Assuming an approximate background intervention rate of 6%, the given sample size was to have provided reasonable precision in the estimation of the intervention rate to an expected margin of error for a 95% confidence interval of at most 2.9% for each group.

During development of the protocol with the Notified Body (TUV) following their decision to grant CE mark to the device, a formal hypothesis was not defined for the study; however, to establish that the hemostasis intervention rate of PVS is not increased compared to SOC, an acceptance criterion was developed and a 95% confidence interval for the difference in the proportion of firings requiring interventions for PVS minus SOC will be calculated. The powered vascular stapler will be considered to have acceptable performance if the upper bound of the 95% confidence interval does not exceed 3%.

While the given sample sizes were expected to provide reasonable precision for estimation of the hemostasis intervention rate within each treatment group, the study was not sufficiently powered for demonstrating that the between treatment group comparison could achieve the 3% acceptance criterion. The given sample sizes are not large enough to control expected variability of the difference in rates between groups with a high probability, even if the true intervention rates are equivalent, thus increasing the likelihood of not meeting this acceptance criterion.

Given the increased risk of not meeting the acceptance criterion due to an undersized study, additional analyses are being prospectively planned to help provide additional information on the types and severity of interventions that may be needed in each treatment group. These are detailed in Section 10.4.1 below.

9 Data Monitoring Committee (DMC)

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

10 Analyses to be Conducted

10.1 General Conventions

Subject data will be summarized using listings and tables. 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 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 version 9.4 or higher. During the course of analysis programming of tables that are mocked up 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. Amendment of the SAP is required in any case where changes to statistical analyses that were planned in the original signed SAP are proposed.

10.2 Disposition of Study Subjects

Subject disposition will be summarized by randomized treatment group and overall using counts and percentages. The number and percentage of subjects in each analysis set will be tabulated. Additionally, the number and percentage of subjects completed and discontinued will be tabulated along with the specific reasons for discontinuation.

10.3 Demographic, Baseline, and Surgical Characteristics

Summary statistics of subject demographics (age, gender, race, and ethnicity) will be presented by randomized treatment group and overall for the Full Analysis Set. Surgical characteristics including, at minimum, type of surgery (nephrectomy or nephroureterectomy), number of ports used, number of renal arteries transected, number of drains placed, ASA physical status, estimated blood loss, conversion to open, requirement for blood transfusion, procedure duration, and drain duration will be summarized by randomized treatment group and overall. Results of tumor assessments performed by the pathology laboratory (including tumor stage, maximum tumor diameter, and maximum tumor depth) will also be summarized by randomized treatment group and overall.

10.4 Primary Endpoint Analyses

For the primary performance endpoint, summary statistics and 95% confidence intervals will be provided for the number and frequency of interventions by randomized treatment group. An intervention is defined as any firing which required a hemostasis intervention.
To account for the potential dependence among firings within a subject, the 95% confidence interval within each treatment group will be estimated using a bootstrap approach. For each subject, the outcome of each firing will be represented by a vector of 0's (indicating no intervention needed) and 1's (indicating an intervention was needed). This vector will be re-sampled with replacement to generate a bootstrap sampled vector of observations for each subject. Then, the proportion of observations requiring intervention for each subject will be calculated from this bootstrap vector. After obtaining a sample proportion of firings requiring intervention for each subject, the mean of these sample proportions will be calculated across all subjects within that treatment group to provide an estimated sample proportion of firings requiring intervention based on 1 iteration of the bootstrap process. This process will then be repeated a minimum of 5000 times to generate a sampling distribution for the proportion of firings requiring intervention within each treatment group. The mean of this sampling distribution will be provided as the point estimate of the

proportion of firings requiring intervention for that treatment group and the 95% confidence interval will be estimated by the lower 0.025 and upper 0.975 percentiles of this sampling distribution.

The table below demonstrates 1 iteration of this bootstrap process within a treatment group.

Subject ID	Observed Data Vector	Bootstrap Sampled Vector	Bootstrap-Based Sample Proportion
1	(0, 0, 1, 0, 0)	(0, 1, 0, 1, 0)	0.40
2	(0, 0, 0)	(0, 0, 0)	0.0
3	(0, 1, 0, 0)	(1, 0, 0, 0)	0.25
4	(0, 0, 1, 0, 0)	(0, 0, 0, 0, 0)	0.0
5	(0, 0)	(0, 0)	0.0
…	…	…	…
…	…	…	…
125	(1, 0, 0, 1, 0)	(0, 1, 0, 0, 0)	0.20
Summary			Average of above proportions to get 1 observation in the sampling distribution of the proportion of firings requiring intervention.

The above re-sampling process will then be repeated a minimum of 5000 times to estimate the sampling distribution for each treatment group.

For each of the 5000 iterations, the difference in bootstrap estimated sample proportions (PVS – SOC) will be calculated and these values will be used to estimate the sampling distribution of the difference between PVS and SOC in the proportion of firings requiring intervention. The mean of this sampling distribution will be provided as the point estimate for the difference of the proportion of firings requiring intervention between groups and the one-sided upper-tailed 95% confidence interval limit for the difference will be estimated by the upper 0.95 percentile of this sampling distribution.

A secondary estimate of the proportion of firings requiring intervention will be provided under the assumption of independence of firings within a subject. This will be performed based on the total number of firings and the percentage will be calculated as the number of firings requiring an intervention divided by the total number of firings. The following SAS code will be used to generate two-sided 95% confidence intervals for the individual treatment groups and a one-sided upper-tailed 95% confidence interval for the difference between groups:

```
proc sort data=hemo_interv;
  by TrtGroup descending event;
run;
```

```
*two-sided exact 95% confidence interval for within treatment summary;
proc freq data=hemo_interv order=data;
  tables TrtGroup*event/binomial riskdiff exact;
run;
*one-sided exact 95% confidence interval for between treatment summary;
proc freq data=hemo_interv order=data;
  tables TrtGroup*event/binomial riskdiff alpha=0.10;
  exact riskdiff;
run;
```

This code assumes that the dataset hemo_interv contains one record per firing, the variable 'TrtGroup' contains the identifier for randomized treatment group (the SOC group should be listed in the first row of the table), and the variable 'event' identifies an occurrence of the primary endpoint with a 1 and no occurrence of the primary endpoint with a 0. The resulting output in the Column 1 Risk Estimates table in the SAS Output Window provides the individual confidence intervals for each treatment group as well as the confidence interval for the difference between groups. The above approach utilizes the exact methodology of Clopper and Pearson for estimation of the confidence intervals within each group as well as the difference between groups.

Additional summaries will be provided to tabulate the total number of vessels transected as well as the specific type of vessel that was transected – renal artery or renal vein. The specific types of interventions that were performed will also be tabulated by randomized treatment group.

The primary safety endpoint, the occurrence of hemostatic interventions/procedures completed for post-operative bleeding related to the transection of the RA and RV, is measured at the subject level and will be analyzed using the same methodology as described above for independent observations. A similar dataset will be created that contains one record per subject and an indicator for whether or not the subject experienced a post-operative intervention event. The SAS code provided above will be utilized in a similar manner for this analysis.

10.4.1 Additional Analysis of Primary Performance Endpoint

In consideration of the types of hemostasis interventions that may be observed and recognizing the differing degrees of severity that exist among the types of interventions, each firing will be further classified into one of the following three categories:

- No interventions: No bleeding or bleeding that stops after initial blotting of staple line;
- Hemostasis controllable: bleeding detected and controlled intra-operatively (additional stapling, over-sewing, clip placement, compression, use of suture, sealant, and/or buttress, and/or use of energy);
- Hemostasis intervention: bleeding that occurs intra-operatively requiring blood or blood product transfusion or an additional surgical procedure (e.g. conversion to open).

The number and percentage of firings in each of these categories will be summarized separately for each treatment group. Hemostasis interventions clearly represent the most significant types of interventions from a device performance and subject safety point of view. This summary will be used to supplement the primary performance endpoint analysis where all interventions, regardless of severity, are grouped together and utilized for assessing the acceptance criterion.

10.5 Plans for Interim Analysis

No interim analyses were planned or performed for this study.

10.6 Handling of Missing Data

All summaries will be performed only on subjects undergoing the surgical 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.

10.7 Sensitivity Analyses

Analyses of the primary performance and safety endpoints will be replicated on the Per Protocol Set to assess the primary results in the set of subjects with no major protocol violations.

10.8 Subgroup Analysis

No subgroup analyses are planned for this study.

10.9 Assessment of Site Homogeneity

No summaries or adjustments by study site are planned for this study.

10.10 Additional Endpoint Analyses

Device usage details will be summarized with counts and percentages for subjects in whom the device was articulated during the surgical procedure. Summaries will be provided by randomized treatment group and in total. Similar summaries will also be provided for the surgeon satisfaction questionnaire and the surgeon device questionnaire (administered only in PVS cases).

Summary statistics will be provided for the Surgery Task Load Index (Surg-TLX). Surgeons are asked to rate 6 specific components after each surgery performed. The 6 components are – mental fatigue, physical fatigue, hurried/rushed pace, procedure complexity, anxious while performing procedure, and distracting operating environment. Each component is scored on a 0 to 100 scale with lower scores representing a ‘Low’ response on that component and higher scores indicating a ‘High’ response on that component. Summaries will also be provided for an overall score which is calculated as the average of the six components for each surgery.

The total number of protocol deviations will be tabulated by treatment group and in total. Specific types of protocol deviations will also be summarized with counts and percentages. The number and percentage of subjects with at least one protocol deviation will also be summarized.

10.11 Safety Analyses

Safety will be assessed through the incidence of adverse events (AEs) and serious adverse events (SAEs), which will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The number and percentage of subjects reporting AEs and SAEs will be summarized at the MedDRA system organ class and preferred term level by treatment group and overall. Similar summaries will also be provided for AEs and SAEs related to the study device, as well as for AEs and SAEs related to the study procedure. Related events are those where the relationship is indicated as Possibly, Related, or Unknown. The incidence of AEs will also be summarized by maximum severity. All reported adverse events will be listed.

Appendix: Table Shells and List of Listings to be Generated

Table shells are provided below for all summaries to be generated for this study. Additionally, a list of all listings to be created is provided corresponding to the eCRFs that were used during this study. All fields collected will be listed.

Table 1
Subject Disposition
All Subjects

	Standard of Care Stapler	Powered Vascular Stapler	Total
Signed Informed Consent			xx
Randomized	xx	xx	xx
Safety Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Full Analysis Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued from the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation			
Withdrawal of consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Surgical	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Site or Study Termination	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: All percentages are based on the number of subjects in the Safety Set as the denominator.

Table 2
Subject Demographics
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Race			
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity			
Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Non-Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Age (years)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Gender			
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 3
Protocol Deviations
Safety Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total Number of Protocol Deviations	xxx	xxx	xxx
Specific Types of Protocol Deviations [1]			
Informed Consent Process	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Inclusion/Exclusion Criteria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Randomization	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Procedure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Visit Out of Window	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sponsor Assessment of Protocol Deviations [1]			
Minor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Major	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number (%) of Subjects With at Least 1 Protocol Deviation [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

1. Denominator used is the total number of protocol deviations reported.
2. Denominator used is the total number of subjects in the column header.

Table 4
Surgical Characteristics
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Type of Surgery			
Laparoscopic Nephrectomy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Laparoscopic Nephroureterectomy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Renal Arteries Transected			
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Ports			
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Drains Placed Intraoperatively			
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ASA Physical Status			
Class I	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Class II	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Class III	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 4
Surgical Characteristics
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Estimated Blood Loss (mL)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Transfusion of Blood or Blood Product Required?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Procedure Converted to Open?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Procedure Duration (min)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Drain Duration (nights)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Programming Note: Chest tube duration is calculated from date of surgery to date of final chest tube removal

Table 5
Tumor Assessment – Pathology Lab
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Tumor Stage, Confirmed by Pathology			
Stage 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIIA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIIB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IV	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Maximum Tumor Diameter (cm)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Maximum Tumor Depth (cm)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Primary Tumor TNM Classification			
TX	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tix	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T1a	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T1b	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 5
Tumor Assessment – Pathology Lab
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
TNM Classification for Regional Lymph Node			
NX	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Distant Metastasis Present?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tumor Confirmed by Pathology as Non-Small Cell Lung Cancer?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 6
Intra-Operative Interventions on Renal Artery or Renal Vein
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total Number of Vessels Transected	xxx	xxx	xxx
Renal Artery	xxx	xxx	xxx
Renal Vein	xxx	xxx	xxx
Bootstrap Based Estimate of Number of Vessel Transections Requiring Intervention			
n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Two-sided 95% Confidence Interval for Percent	xx.x%, xx.x%	xx.x%, xx.x%	xx.x%, xx.x%
Difference (One-sided 95% CI Upper Limit) for Percent Requiring Transection [2]	xx.x% (xx.x%)		
Independent Samples Estimate of Number of Vessel Transections Requiring Intervention [1]			
n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Two-sided 95% Confidence Interval for Percent	xx.x%, xx.x%	xx.x%, xx.x%	xx.x%, xx.x%
Difference (One-sided 95% CI Upper Limit) for Percent Requiring Transection [2]	xx.x% (xx.x%)		
Type of Intervention, n (%) [3]			
Additional Stapling	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Over-sewing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Compression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Use of Suture	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sealant	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Buttress	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Use of Energy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Clip Placement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Product Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Additional Surgical Procedure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Intervention	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Intervention Category, n (%) [4]			
No Intervention	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hemostasis Controllable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hemostasis Intervention	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Denominator for calculation of percentage is the total number of vessels transected in that group.
[2] Difference is calculated as Powered Vascular Stapler minus Standard of Care Stapler.
[3] Denominator for calculation of percentage is the total number of vessels requiring intervention in that group.
[4] Hemostasis Controllable includes additional stapling, over-sewing, compression, use of suture, sealant, buttress, use of energy, clip placement, or other intervention. Hemostasis Intervention includes blood product transfusion and additional surgical procedure.

Table 7
Post-Operative Interventions or Procedures Related to Renal Artery or Renal Vein Bleeding
Safety Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Number of Subjects Requiring Post-Operative Intervention Related to Renal Artery or Renal Vein Bleeding			
n (%) [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
95% Confidence Interval for Percent	xx.x%, xx.x%	xx.x%, xx.x%	xx.x%, xx.x%
Type of Intervention, n (%) [2]			
Blood Product Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Additional Surgical Procedure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Intervention	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Denominator for calculation of percentage is the total number of subjects in that group.
[2] Denominator for calculation of percentage is the total number of subjects requiring intervention in that group.

Table 8
Device Usage Details
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Number of Subjects Where Device Was Articulated	xxx	xxx	xxx
Did Articulation Make it Easier to Perform Surgery? [1]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Was Articulation Essential to Performing the Surgery? [1]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Was the Angle Range of the Device Sufficient? [1]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

1. Denominator used is the total number of subjects in whom the device was articulated.

Table 9
Surgery Task Load Index (SURG-TLX)
Full Analysis Set

Characteristic	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Overall Score			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Mentally Fatiguing			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Physically Fatiguing			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Similar summaries for remaining components:			
Hurried/Rushed Pace			
Procedure Complexity			
Anxious While Performing Procedure			
Distracting Operating Environment			

Note: Each component is scored on a 0 to 100 scale with lower scores representing a ‘Low’ response and higher scores representing a ‘High’ response.

Table 10
Surgeon Satisfaction Questionnaire
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
How Satisfied Were You With Device Usability?			
Very Unsatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unsatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Amount of Tissue Slippage			
No Tissue Slippage	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Some Tissue Slippage	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Extensive Tissue Slippage	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 11
Surgeon Device Questionnaire
Full Analysis Set

Question Response	Powered Vascular Stapler (N = ##)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip enables easier placement of the device on vessels compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip has the potential to reduce the amount of dissection required (otomy) around the vessel to place the stapler compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip has the potential to reduce the surgeon stress during the most challenging step of the procedure, which is the renal artery/renal vein transection, compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip allows for the precise control and placement of the end effector on the target vessel compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)

Table 12
Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class	Preferred Term	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 3		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 4		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The following tables will have the same format as Table 12:

Table 13	Serious Adverse Events by System Organ Class and Preferred Term Safety Set
Table 14	Adverse Events Related to the Study Device by System Organ Class and Preferred Term Safety Set
Table 15	Serious Adverse Events Related to the Study Device by System Organ Class and Preferred Term Safety Set
Table 16	Adverse Events Related to the Study Procedure by System Organ Class and Preferred Term Safety Set
Table 17	Serious Adverse Events Related to the Study Procedure by System Organ Class and Preferred Term Safety Set

Table 18
Adverse Events by System Organ Class, Preferred Term and Maximum Severity
Safety Set

System Organ Class	Preferred Term	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The following listings will be generated for this study:

Listing 1	Inclusion/Exclusion Criteria All Subjects
Listing 2	Demographics All Subjects
Listing 3	Medical History All Subjects
Listing 4	Surgical History All Subjects
Listing 5	Inclusion/Exclusion at Surgery and ASA Status All Subjects
Listing 6	Procedure Details All Subjects
Listing 7	Procedure Time Duration All Subjects
Listing 8	Intra-Operative Interventions on Renal Artery and Renal Vein All Subjects
Listing 9	Intra-Operative Interventions Not on Renal Artery and Renal Vein All Subjects
Listing 10	Device Usage Details All Subjects
Listing 11	Tumor Assessment Log All Subjects
Listing 12	Surgeon Device Questionnaire (PVS Only) All Subjects
Listing 13	Surgery Task Load Index All Subjects
Listing 14	Surgeon Satisfaction Questionnaire All Subjects
Listing 15	Post-Operative Interventions on Renal Artery and Renal Vein All Subjects

Listing 16	Drain Details Log All Subjects
Listing 17	Adverse Events All Subjects
Listing 18	Concomitant Medications All Subjects
Listing 19	Concomitant Procedures/Interventions All Subjects
Listing 20	Protocol Deviations All Subjects
Listing 21	Completion/Withdrawal All Subjects
Listing 22	Study Visits All Subjects