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Statistical Analysis Plan

Sundt™ Carotid Shunt Retrospective Post Market Clinical Follow-up Study (PMCF)

PROTOCOL NO.: C-SCS-001
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Title: Sundt™ Carotid Shunt Retrospective Post Market Clinical Follow-up Study (PMCF)

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Prepared By:

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Signature Date Time Zone

INTEGRA LIFESCIENCES CORPORATION SIGNATURE PAGE

The undersigned have approved this Statistical Analysis Plan for use in this study.

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TABLE OF CONTENTS

1. LIST OF ABBREVIATIONS

Abbreviation	Term
BMI	Body Mass Index
CFR	Code of Federal Regulations
eCRF	Electronic Case Report Form
EMR	Electronic Medical Records
FDA	Food and Drug Administration
GCP	Good Clinical Practices
ICF	Independent Consent Form
Integra	Integra LifeSciences Corporation
IRB	Institutional Review Board
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
PMCF	Post Market Clinical Follow-up.
PP	Per Protocol
QC	Quality Control
SAE	Serious Adverse Event (As further defined in section 5.1)
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SCS	Sundt™ Carotid Shunt
SD	Standard Deviation
SOP	Standard Operating Procedures
SV	Screening Visit
TLA	Transient Ischemic Attack
USA	United States of America

2. INTRODUCTION

This document provides a detailed description of the statistical methods and procedures to be implemented during the analysis of the clinical study. The methods and procedures are intended to support the generation of study report, including detailed descriptions of the populations and methodologies, as well as summary tables, listings and graphics.

This statistical analysis plan (SAP) is based on Version 1.0 of the Protocol# C-SCS-001.

3. STUDY OBJECTIVES

The primary objective of this study to retrospectively investigate the safety and efficacy of the Integra Sundt™ carotid shunt during endarterectomy procedures.

3.1. Primary Study Endpoint

The primary endpoint of this study is evidence of injury to the artery or cerebral ischemia secondary to shunt placement and removal.

4. STUDY DESIGN

This is a non-randomized, multi-center, single-arm, all-comers retrospective Post Market Clinical Follow-up study investigating subjects who received a Sundt™ carotid shunt during a carotid endarterectomy before study initiation at the site. The study duration from the first patient's chart review to the completion of the last patient's chart review is expected to be 1 year. The study will end when the data for 100 subjects has been collected.

5. STUDY PROCEDURE

This study is a retrospective review of patients who have undergone a carotid endarterectomy procedure with the use of the Sundt™ carotid shunt prior to study initiation.

Eligible subjects for the study should be identified by the 3-digit site number followed by the 3-digit subject ID. Numbering of the subjects should be done in a reverse chronological order with the most recent subject being 001 followed by the second most recent being 002 and so forth.

Required information will be collected through a review of the patient chart or electronic medical records (EMR) by the Principal Investigator or delegated personnel. The delegated staff member shall collect demographics, details surrounding the procedure, and the post-operative assessment.

6. SAMPLE SIZE DETERMINATION

100 patients will be enrolled at up to 10 centers, with up to a maximum of 40 consecutive patients enrolled at each center. Patients will be enrolled at a minimum of 3 centers. This study will take place in the United States only.

7. STATISTICAL ANALYSES

7.1. General Statistical Considerations

The PMCF is a retrospective chart review. All analyses will be descriptive in nature. No formal statistical analyses will be performed. The study objectives will be presented by summary statistics.

Summary statistics (mean, standard deviation, quintiles, counts, and percentages) will be presented for all demographic (i.e. age, gender, etc.), clinical baseline characteristics (medical history, surgical history, medications), surgical procedures (procedures performed, duration of surgery) and complications.

The primary objective will be evaluated by summarizing the incidence of injury to the artery or cerebral ischemia secondary to shunt placement.

All statistical analysis will be conducted using SAS® for Windows, version 9.4 or later.

7.2. Study Subjects

7.2.1. Disposition of Patients and Protocol Deviation

This study is a retrospective PMCF study. The numbers of subjects who met the inclusion and exclusion criteria the study will be summarized.

7.2.2. Analysis Populations

7.2.1.1. Efficacy population

Not applicable

7.2.1.2. Safety population

The safety population will consist of the patients who undergone a carotid endarterectomy with the Sundt™ carotid shunt. All analysis will be based on the safety population.

7.2.3. Demographics

Baseline

- Age
- Gender
- Height
- Weight
- BMI

7.2.4. Medical History

Medical History data will be summarized by the following categories, by subject listings will be provided for each subject.

- Relevant Past Medical History
  - Transient Ischemic Attack (TIA)
  - Stroke
  - Asymptomatic Carotid Stenosis
  - Bleeding Disorder
  - Diabetes
  - Smoking
  - Other relevant past medical history per the investigator's opinion
- Past Surgical History
  - Previous Head or Neck Surgery
  - Previous Head or Neck Radiation
  - Previous Vascular Surgery
  - Other relevant surgical history per the investigator's opinion
- Diagnosis / Indication for Surgery
- Concomitant Medications

7.2.5. Operation Procedure

- Operative details are to be summarized and/or listed. These variables include: Procedure(s) performed
- Duration of surgery
- Device information, including lot number
- Medications
- Any complications noted in the operative report and in the investigator's opinion determined to be related to the device

7.2.6. Post-operative Assessment (up to 60 days post-procedure)

Post-operative assessment will be summarized, details will be listed by subject.

- Evidence of cerebral ischemia as indicated by post-operative neurological exam
- Evidence of injury to artery as seen on post-operative imaging of the carotid artery either by carotid duplex ultrasound or angiogram

7.2.7. Device Performance

The following device performance questions will be summarized using descriptive statistics by visit

1. Was the shunt use routine or selective? If selective, specify the test and the result that led to use of the shunt.
2. Was there any delay in surgery or complication due to preparation of the device for surgery? If yes, please explain.
3. What was the clamping method type for shunt insertion?
4. How long was the carotid artery cross clamped for shunt insertion?
5. Was there any device-related damage to the artery during insertion of the shunt? If yes, please explain.
6. Was there evidence of clot formation within the shunt at any point during the procedure? If yes, describe how this was detected and what was the remedy. What was the impact to the procedure?

7. Was there any evidence of reduced flow within the shunt other than clot formation (e.g. due to kinking, malposition within the artery)?

8. Was there any evidence of excessive bleeding around the shunt after initial placement? If yes, what was the remedy and the result of that remedy?

9. Did removal of the shunt cause vessel injury or complicate closure? If yes, please explain.

10. Was there evidence of post-operative cerebral ischemia noted in the neurological exam?

11. Did the subject experience injury to the artery due to the device as evidenced by the imaging of the carotid artery either by carotid duplex ultrasound or angiogram?

12. Were there any other device-related complications not previously recorded in the case report forms? If yes, please explain.

7.2.8. Analysis of Safety Data

The summary of safety results will be summarized and presented by subject. listing will also be provided for all adverse events.

7.3. Missing Data

No imputations is planned for missing data. All summaries will be based on the non-missing data.

8. REFERENCES