Elana Surgical Kit$_{HUD}$

HDE: H080005

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Pediatric Advisory Committee
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Presentation Outline

- **Device Description, Regulatory History & Pre-Market Clinical Data:**

  Mohamad Bydon, M.D.

- **Postmarket Medical Device Reporting (MDR) & Post-approval Study (PAS):**

  Cara J. Krulewitch, CNM, Ph.D., FACNM

Indications for Use

The Elana Surgical Kit_{HUD} is indicated **for creating arteriotomies during an intracranial vascular bypass procedure in subjects 13 years of age or older** with an **aneurysm or a skull base tumor** affecting a large [> 2.5 mm], intracranial artery that **failed balloon test occlusion, cannot be sacrificed, or cannot be treated with conventional means due to local anatomy or complexity**.

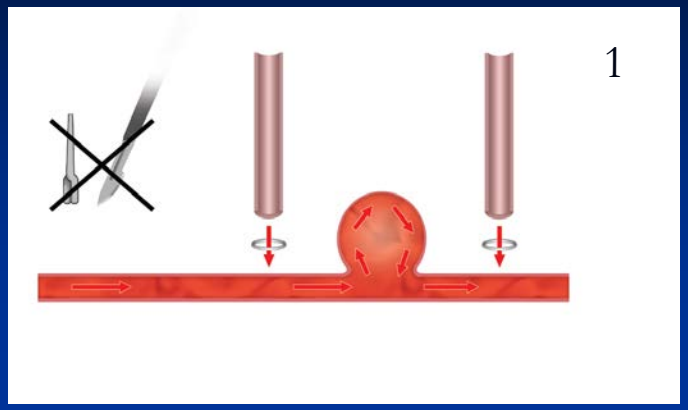
Device Description

Main Components

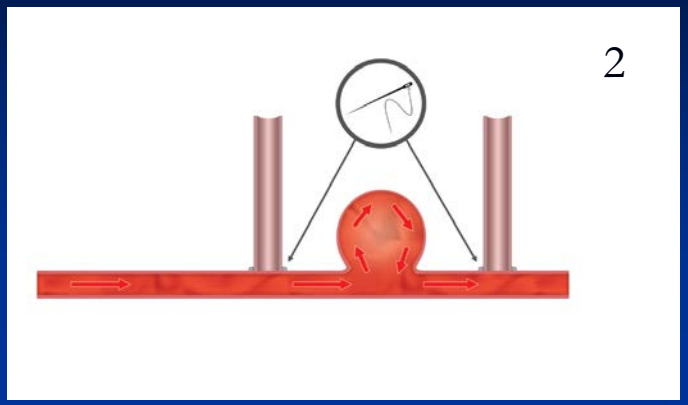
- **Elana Ring:**
  - implanted platinum flat ring
  - available in two diameters based on vessel size
  - defines the exact location of the arteriotomy site on the recipient vessel and helps ensure a flush interface between the laser tip and the arteriotomy site
- **Elana Catheter 2.0:**

  Provides vacuum through the central lumen, and delivers laser light to cut an arteriotomy.
- The Elana Catheter 2.0 is attached to the legally-marketed **Spectranetics XeCl (Xenon-Chloride) Excimer Laser System, Model CVX-300**.

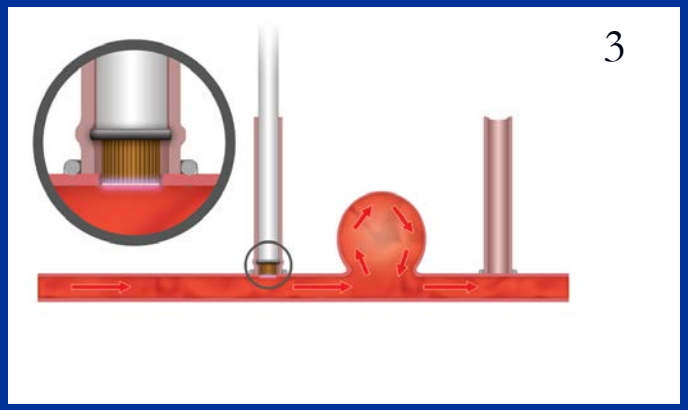
Device Description - Operating Steps



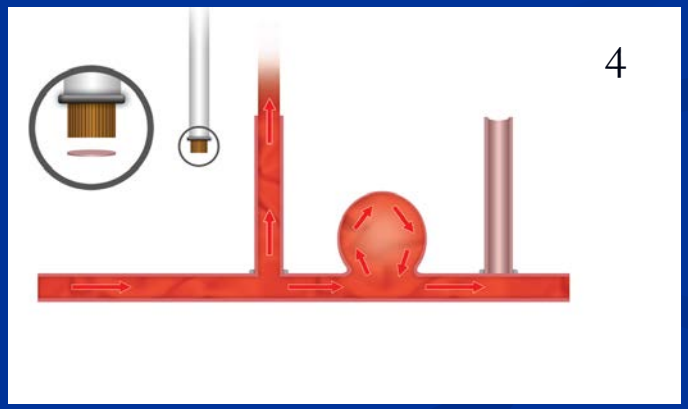
Step 1 – Suture Ring to graft



Step 2 –Suture Ring with donor graft to artery wall

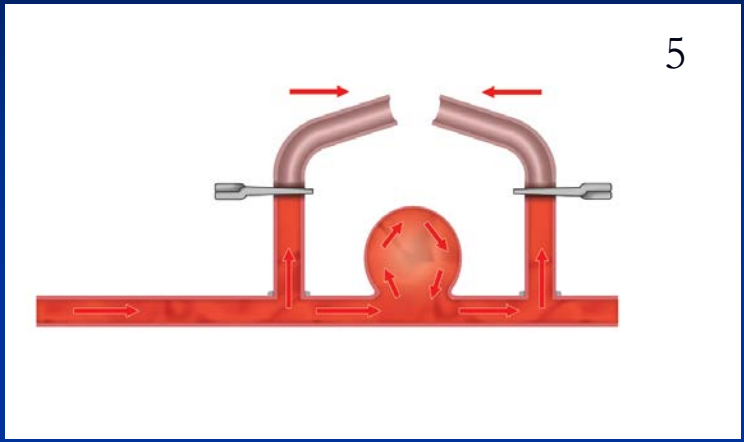


Step 3 – distal end of the Catheter is inserted into the donor graft through the open end of the graft



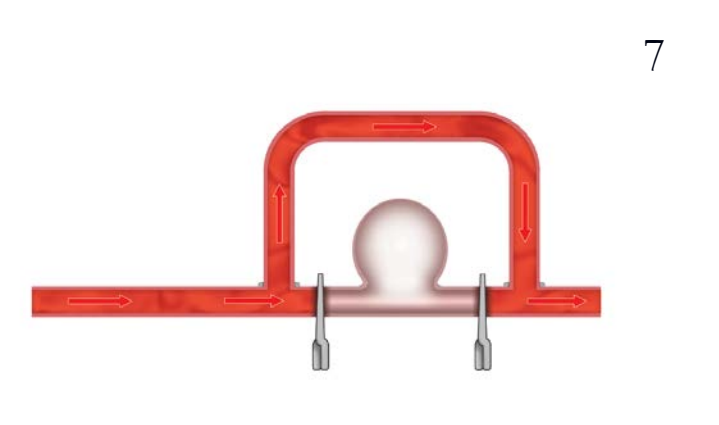
Step 4 –Laser and suction are applied for 2 minutes; circular flap of artery wall cut by the laser light is automatically retrieved by the catheter tip as the catheter is removed.

Device Description - Operating Steps



Step 5 –Retrograde blood flow through the donor graft can be stopped by temporarily occluding the donor graft.

Step 6 – The Elana technique is completed and the grafts are sutured together.



Step 7 -The aneurysm or tumor is blocked off.

Regulatory History

- IDE (G070052) approved:

  2007 for a non-randomized, prospective, single-arm, multicenter clinical trial

- HUD approved: September 26, 2003
- HDE approved : March 10, 2011

Pre-Market Clinical Data

Consists of the following data sets:

- IDE Study Data: Comprised 32 adult subjects and one (1) pediatric patient, a male aged 17 years.
- Retrospective European Data: Collected data from 7 centers in Europe; a total of 302 subjects (330 procedures) including four (4) pediatric subjects ages 10, 13, 18 and 18 years.
- Data on three (3) additional pediatric subjects from the Netherlands (collected between August, 2006 and March 2009) were provided. The subjects were aged 6, 14, and 17 years.

Data Sets were compared to historical literature of conventional extracranial to intracranial (EC-IC) bypass to a major intracranial artery.

Pre-Market Clinical Data

IDE Study

- Non-randomized, prospective, single-arm, multicenter clinical trial
- 7 U.S. study sites
- Data on 31 adult subjects and 1 pediatric subject (male, aged 17 yrs.) were submitted in HDE

Pre-Market Clinical Data

IDE Study

Key Inclusion Criteria

- Required a temporary (protective bypasses that are required during surgery only) or permanent bypass to be connected to one or more unoccluded intracranial vessel(s)
- Surgeon felt subject could not be safely treated otherwise, e.g., vessel failed balloon test occlusion, could not be sacrificed, or could not be treated with conventional means due to local anatomy or complexity
- Preoperative modified Rankin score (mRS) ≤ 3

Modified Rankin Scale (mRS)

- 0 - No symptoms
- 1 - No significant disability
- 2 - Slight disability
- 3 - Moderate disability
- 4 - Moderately severe disability
- 5 - Severe disability
- 6 - Dead.

Pre-Market Clinical Data

IDE Study

Study Endpoints

- Primary: flow through the bypass graft and no device-related adverse events
- Safety:
  - rate of mortality and non-fatal strokes at a 30 (+10/- 3) day follow-up period.
  - Neurological state and functional outcome using mRS at the 30 day follow-up visit
  - Safety of Elana was compared to historically-derived information from the literature.

Pre-Market Clinical Data

IDE Study

Table 1: IDE Study Patient Demographics

	N (%) (Total N = 32)
Sex:	
Male	11 (34%)
Female	21 (66%)
Age (in years):	
≤ 21	**1 (3%)**
22-35	3 (9%)
36-50	11 (34%)
51-65	13 (41%)
>65	4 (13%)
Surgical Indication:	
Aneurysm	29 (91%)
Tumor	2 (6%)
Ischemia	1 (3%)

Pre-Market Clinical Data

IDE Study

Table 2: IDE Study Effectiveness Results

Total Procedures:	33† Anterior: 32/33 (97%) Posterior: 1/33 (3%)
Bypass patent at end surgery:	31/33 (94%) Anterior: 30/32 (94%) Posterior: 1/1 (100%)
Bypass patent at 7 days post-op:	22/31 (71%) Anterior: 24/30 (73%) Posterior: 0/1 (0%)

† One of the 32 subjects had 2 Elana procedures

Pre-Market Clinical Data

IDE Study

Table 3: IDE Study Safety Results

Total Procedures:	33† Anterior: 32/33 (97%) Posterior: 1/33 (3%)
All moderate/severe adverse events:	15/33 (45%) Anterior: 14/32 (44%) Posterior: 1/1 (100%)
Mortality:	3/33 (9%) Anterior: 2/32 (6%) Posterior: 1/1 (100%)
Non fatal stroke with permanent deficits at 30 days:	5/33 (15%) Anterior: 5/33 (16%) Posterior: 0/1 (0%)

† One of the 32 subjects had 2 Elana procedures

Pre-Market Clinical Data

IDE Study

Adverse Event (AE) Definitions

Serious Adverse Event was defined as an event that led to death or led to a serious deterioration in the health of the patient that:

- Resulted in life-threatening illness or injury
- Resulted in permanent impairment of a body structure or a body function
- Required in-patient hospitalization or prolongation of existing hospitalization
- Resulted in medical or surgical intervention to arrest permanent impairment to body structure or a body function
- Led to fetal distress, fetal death or a congenital abnormality or birth defect

Pre-Market Clinical Data

IDE Study

Table 4: IDE Study Serious AEs

Serious Adverse Event	N
Non-fatal Stroke	5
• Aneurysm: Brainstem infarction/diffuse subarachnoid hemorrhage / thrombus of basilar aneurysm with compression of the ventral pons • Aneurysm: Intra-operative subarachnoid hemorrhage/large • Pseudoaneurysm of basilar artery/massive brain edema tumor: Stroke	3
Right SVG, wound dehiscence, infection → bacteremia, fever	1
Intracerebral hemorrhage under heparinization and hypertension	1
Dissection of left common carotid artery during angiogram	1
Left femoral and lower extremity DVT	1
Aneurysm bleeding	1
Increased brain swelling in the frontal lobe	1
Intracerebral hemorrhage and cerebral edema	1
Unable to complete bypass (due to aneurysm rupture)	1

Pre-Market Clinical Data

IDE Study

Table 5: IDE Study Pediatric Subject Results

Age	17
Sex	Male
Treated Condition	Anterior Aneurysm
Bypass patent at end surgery:	Yes
Bypass patent at 7 days post-op:	Yes
Post-op mRS:	1
Adverse Events	None

Note there was a "flap" (to be described further on) left behind that was manually retrieved with no adverse events

Pre-Market Clinical Data

Retrospective European Data

- Retrospectively collected on a total of 302 subjects (330 procedures) between 1993 and July 2006.
- Data analyzed included bypass patency, mortality and non-fatal stroke rates.
- Ninety-three per cent (93%) of the subjects were followed for more than 30 days.

Pre-Market Clinical Data

Retrospective European Data

Table 6: European Cohort Patient Demographics

	N (%) (Total N = 302)
Sex:	
Male	140 (46%)
Female	162 (54%)
Age (in years):	
< 18	**2 (0.6%)**
18-21	**2 (0.6%)**
22-50	117 (39%)
51-65	136 (45%)
>65	45 (15%)
Surgical Indication:	
Aneurysm	216 (72%)
Tumor	13 (4%)
Ischemia	72 (24%)
Other	1 (0.3%)

Pre-Market Clinical Data

Retrospective European Data

Table 7: European Cohort Study Effectiveness Results

Total procedures:	330 † Anterior: 307/330 (93%) Posterior: 23/330 (7%)
Bypass patent postoperatively:	255/330 (77%) Anterior: 235/307 (77%) Posterior: 20/23 (87%)

† Twenty-eight (28) of the 302 subjects had 2 Elana procedures.

Pre-Market Clinical Data

Retrospective European Data

Table 8: European Cohort Study Safety Results

Total Procedures:	330 Anterior: 307/330 (93%) Posterior: 23/330 (7%)
All moderate/severe adverse events:	52/330 (16%) Anterior: 38/307 (12%) Posterior: 14/23 (61%)
Mortality:	24/330 (7%) Anterior: 16/307 (5%) Posterior: 8/23 (21%)
Non fatal stroke:	17/330 (5%) Anterior: 12/307 (4%) Posterior: 5/23 (21%)

† Twenty-eight (28) of the 302 subjects had 2 Elana procedures.

Pre-Market Clinical Data

Retrospective European Data

Table 9: European Cohort Most Frequent Severe AEs

Adverse Event	N
Hemiparesis	26
Bypass occlusion	20
(Brain) Edema	13
High intracranial pressure	8
Brain infarction / stroke	8
Subdural/epidural hematoma	6
Hydrocephalus	5
Subarachnoid Hemorrhage	5
Aneurysm bleeding	4
Intracranial hemorrhage	4
Intracerebral hematoma	3

Pre-Market Clinical Data

Retrospective European Data

Table 10: European Cohort Pediatric Subject Results

Total Subjects:	4 (100%) All Anterior Aneurysms
Ages:	10, 13, 18, and 18
All moderate/severe adverse events:	0/4 (0%)
Mortality:	0/4 (0%)
Non fatal stroke:	0/4 (0%)
mRS 30 days post-op favorable:	4/4 (100%)

Pre-Market Clinical Data

Additional Pediatric Retrospective European Data¥

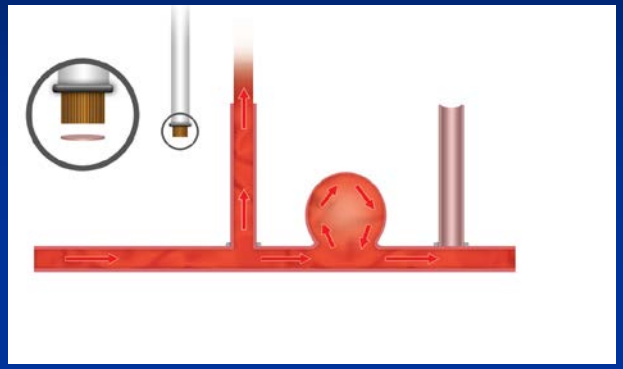
Table 11: Additional Pediatric Retrospective European Results

Total Subjects:	3 (100%) All Anterior Aneurysms
Ages:	6, 14, and 17
mRS 30 days post-op favorable:	3/3 (100%)
Bypass patent post-operatively:	3/3 (100%)
Adverse Events:	AE data unavailable

¥ Retrospective European Cohort was collected between 1993-July, 1996. Additional pediatric european data was collected between August, 2006 and March, 2006 in the Netherlands.

Pre-Market Clinical Data

"Flap" Retention



- Potential for the laser perforation not to be complete and result in a circular disk of tissue (or "flap") being retained on the artery wall.
- Potential risks: retained flap could embolize when it is not removed manually. In order to remove the flap, the artery must be occluded.

Pre-Market Clinical Data

"Flap" Retention – IDE Study

- Rate of "Flap" Retention: 22% (8/37 device uses in 33 procedures)
- Flap was manually retrieved in 5 subjects- average arterial occlusion time was 8 minutes (range 5 - 11 minutes).
  - 1 severe AE when "Flap" manually retrieved: a diffuse subarachnoid hemorrhage and thrombosis of basilar aneurysm with compression of the ventral pons
  - 1 pediatric subject had "Flap" retrieved with no AEs

Pre-Market Clinical Data

"Flap" Retention – IDE Study

- 3 cases in which "Flap" was NOT retrieved:
  - 1 SAE: aneurysm rupture during manipulation/inspection of distal anastomosis with subsequent stroke
  - 1 case where the "Flap" dissolved: anastomosis completed and arteriotomy was successful
  - 1 case: anastomosis and arteriotomy was abandoned

Pre-Market Clinical Data

"Flap" Retention - Retrospective European Cohort

- Rate of "Flap" Retention: 26% (96/375 device uses)
  - 1993-2003: Flap was not manually retrieved and bypass abandoned unless bypass flow of 50 ml/min
  - 2004-2006: "Flap" retrieval in 13% (9/68) of device uses
- In 1 case embolization of a retained flap could not be excluded but the subject improved markedly and was active walking (with aid), and talking but was still experiencing severe weakness of the right hand and arm.
- No pediatric subjects in the EU cohort had flap retention.

Pre-Market Clinical Data

Historical Data Comparison

- Historical literature data used to identify results of conventional EC-IC bypass operations to a major intracranial artery.
- Only the Mayo clinic experience (Regli et al., 1995) analyzes a large series over a long period of time with operations by several surgeons and includes the initial learning curve. It provides the most reliable comparison for mortality and non fatal stroke.
- The data within this article fall within the range of the average from all other literature articles.

Regli L, Piepgras DG, Hansen KK: Late patency of long saphenous vein bypass grafts to the anterior and posterior cerebral circulation. *J Neurosurg.* Nov;83(5):806-11, 1995.

Pre-Market Clinical Data

Historical Data Comparison

Table 14: Elana Arteriotomy System$_{HUD}$ versus Literature

Summary	IDE data	EU data	Literature (Regli et al., 1995)
Total procedures:	33	330	202
Bypass patent 0/7/30 days post-op:	**7 days**	**≥ 0 days**	**30 days**
	22/31 (71%)	255/330 (77%)	173/202 (86%)
Mortality:	3/33 (9%)	24/330 (7%)	30/201 (15%)
Non fatal stroke: with permanent deficits at 30 days	5/33 (15%)	17/330 (5%)	Estimated 18%

Safety and Probable Benefit

- The collective evidence of the prospective IDE study data and the retrospective European data, as compared to the available literature data, demonstrated a reasonable assurance of safety and probable benefit for the indicated patient population.
- The decision to approve use in pediatric subjects aged 13 and over was based on the following:
  - data on 8 pediatric subjects
  - the main limiting factor in device use is the recipient vessel size rather than patient age and by age 13 subjects should have approximately adult sized intracranial vessels
  - the vessel size must be large enough for Elana Ring attachment

Annual Distribution Number (ADN)

- Elana Arteriotomy System$_{HUD}$ was approved with ADN = 1000
- In 2012: 12 Elana Arteriotomy System$_{HUD}$ distributed in US which is < approved ADN of 1000

Elana Surgical Kit$_{HUD}$ Postmarket Update

Cara J. Krulewitch CNM PhD FACNM
Branch Chief, Division of Epidemiology
Center for Devices and Radiological Health

Objectives

- Summary of Medical Device Reports (MDRs)
- Background and update on status of the Post-Approval Study (PAS) condition of approval
- Review of literature

MDR Database Search

- The Manufacturer and User Facility Device Experience (MAUDE) database was searched up to August 8, 2012 to identify any Medical Device Reports (MDRs) associated with Elana device.
- Search criteria:
  - Manufacturer name with no begin date limitations
  - Brand name with no begin date limitations
- Based on these MAUDE searches, there are currently *no* MDRs within the MAUDE database associated with the Elana device

Background of PAS

- March 10, 2011
  - HDE Approval
  - PAS Protocol Approval
- Condition for PAS issued due to concerns
  - Flap retention
  - Real world use

PAS Study Overview

Study Element	Description
Study Design	All Comers Registry
Data Collection Points	Pre-Operatively During Surgery One Post-op follow-up > 25 days Modified Rankin Score (mRS) Mortality and non-fatal stroke
Primary Endpoint	Flap Retention
Sample Size	80 device uses Flap Retention Endpoint, 22% true rate not to exceed 38% 80% study power

PAS Status

- Based upon 12-month report and additional sponsor information
- Through July 30, 2012
- 8 sites, IRB approval at all sites
- 12 devices shipped, none used
- Expect 1st subject enrollment October, 2012

Literature Review-Methods

- PubMed search conducted March 11, 2011 to August 3, 2012
- Additional search in PubMed of "related citations"
- Seven articles
  - 2 Animal Studies
  - 2 Laboratory Studies
  - 3 Human Studies

Literature Review-Findings

- Two independent clinical studies and IDE study findings
- Pediatric use reported in age range (one study and IDE), number not specified in independent study
- Patency 85-94%
- Clinical improvement in 77-86% patients at 7 days
- 30-day mortality 6-12%
- One study reported 14% strokes

Postmarket Summary

- No MDRs
- PAS study pending
- Two pediatric uses reported in literature both in the outside the US (OUS) studies
  - One study, prior to FDA approval (besides IDE study)
- Literature studies report benefit of device with no unanticipated adverse events

Conclusion

- The device has not been used within the United States since HDE approval; therefore, FDA has not identified any new safety signals since that time.
- FDA concludes that the HDE device remains appropriately approved and labeled.
- FDA will continue routine surveillance including review:
  - MDRs
  - Mandated Post-Approval Study reports
  - Literature