CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY
JANUARY 23-25 2014
MARRIOTT RIVE GAUCHE & CONFERENCE CENTER PARIS, FRANCE

US Experience with the INCRAFT AAA Stent Graft System: The INSPIRATION Trial

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For The INSPIRATION Pivotal Trial Investigators

www.cacvs.org

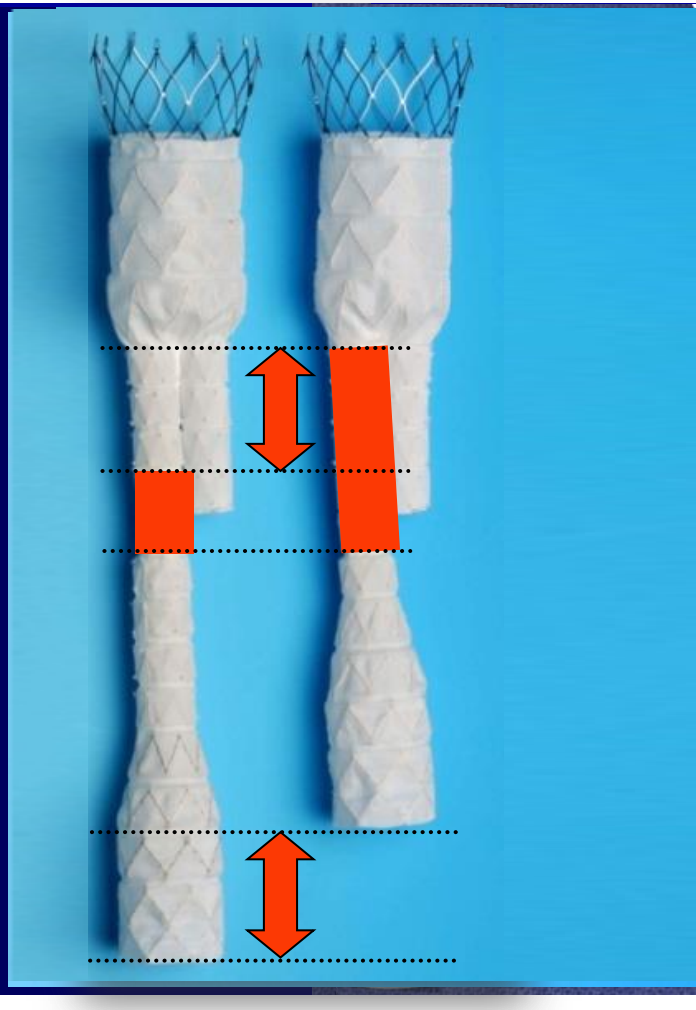
Disclosures

No Financial Interest
Uncompensated Consultant:

- *Cordis:* *Co-PI INSPIRATION Trial*
- *WL Gore:* *Scientific Advisory Board*
- *Medtronic:* *PI Endurant trial*

The INCRAFT ® Endoprosthesis

- Modular Trifab system
- Polyester graft fabric
- Electropolished Nitinol stents
- Active suprarenal fixation barbs
- Limbs are flexible with 2-3 cm **In-Situ length adjustment** that allows accurate distal landing.



Caution : Investigational Device / Limited by United States Law to Investigational Use
Not commercially available _ No Regulatory approval yet in US, Europe or Japan

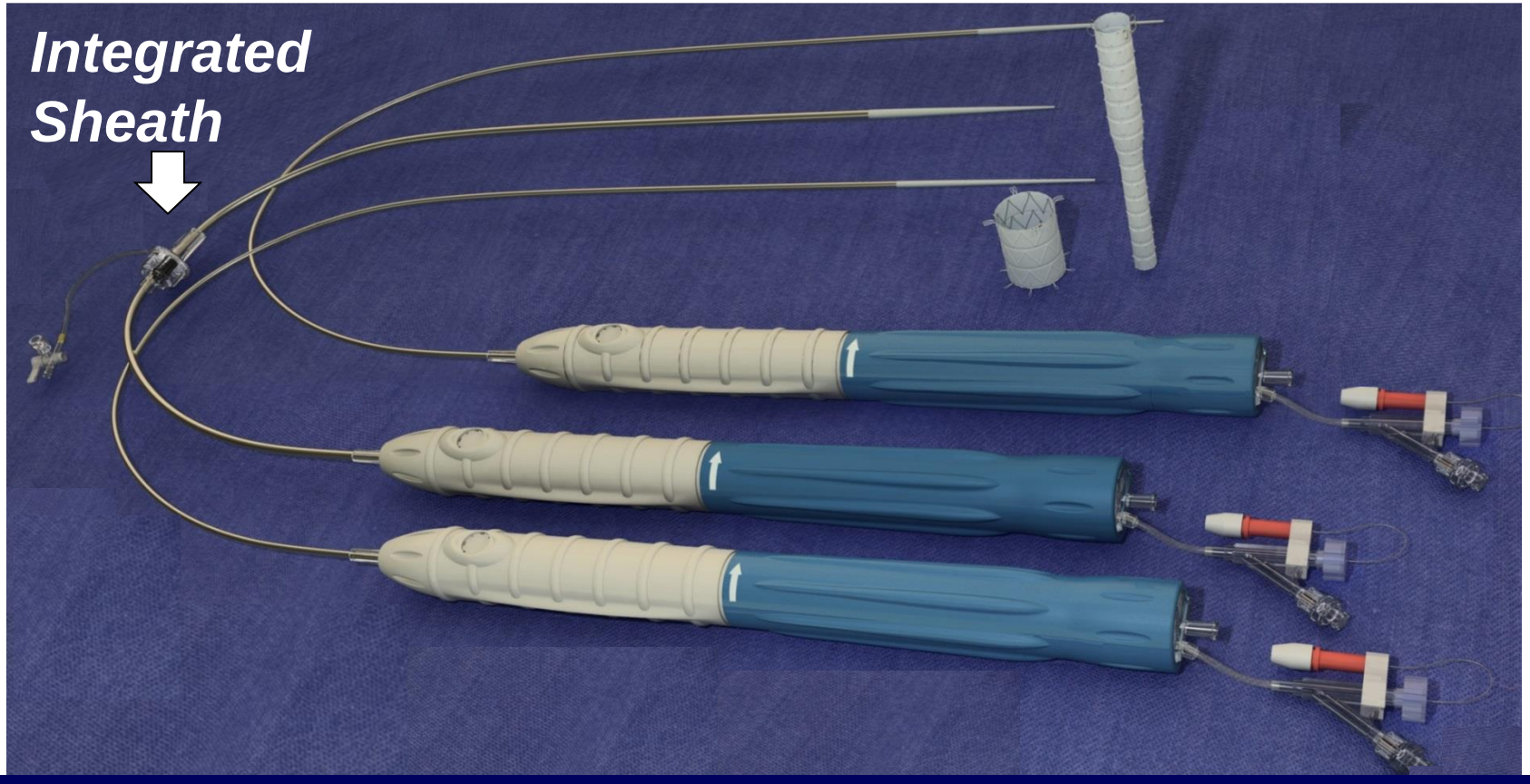
The INCRAFT ® Endoprosthesis

Modular Integrity In Vitro Testing

Fabric Crimps
Point Stiches

INCRAFT® Delivery System

Low Profile (14 Fr) and Flexible Delivery System with an Integrated Braided Sheath



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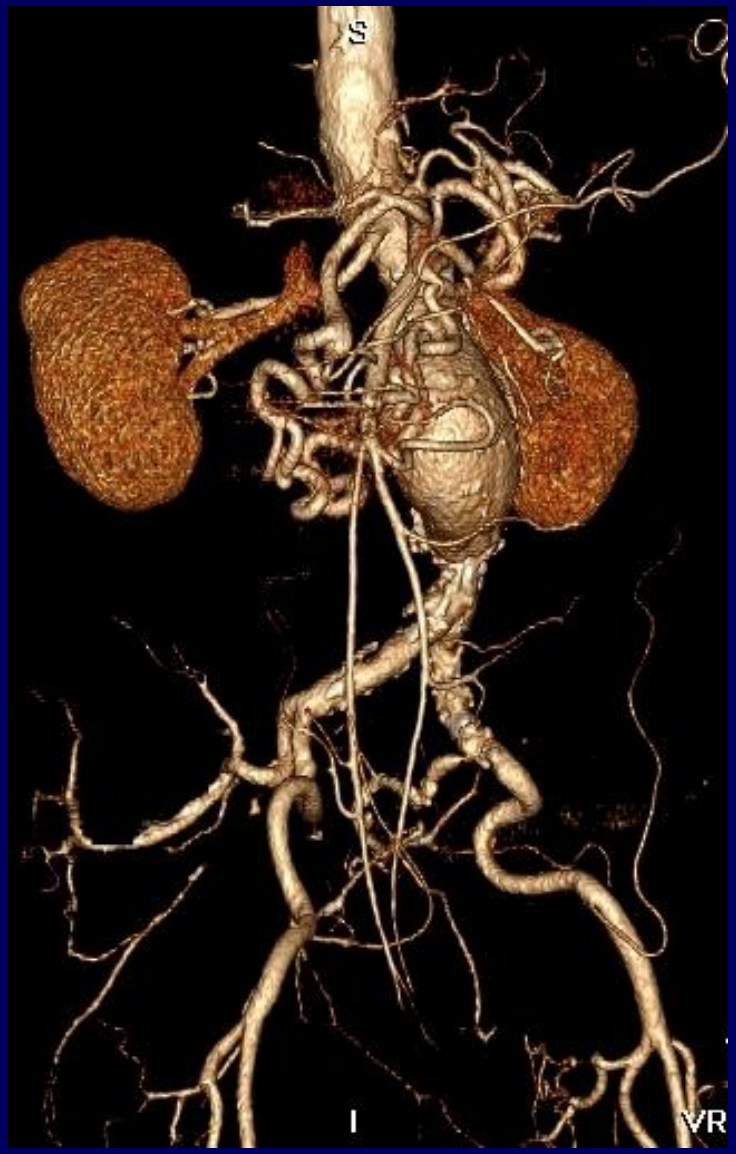
Potential Benefits of Lower Profile

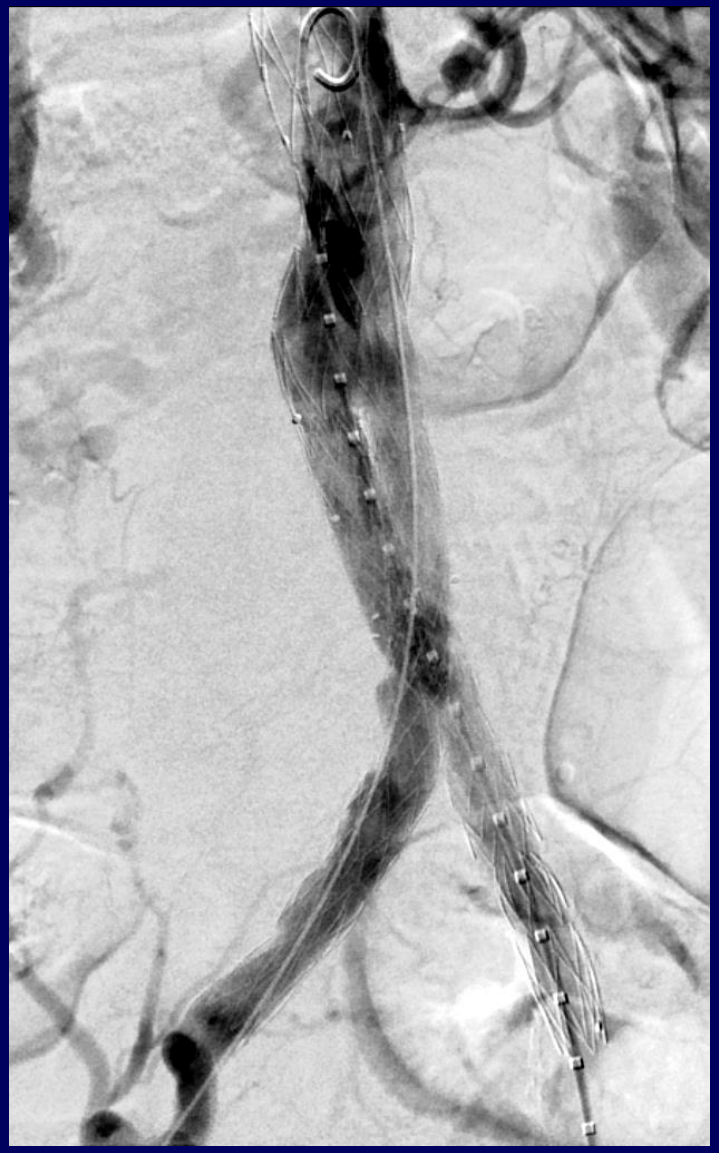
1. *Easier delivery*
2. *Navigates tortuous vessels better*
3. *Usable in smaller calcified iliac vessels*
4. *Less iliac injuries*
5. *More Applicable to women*
6. *Makes more patients candidates for EVAR*
7. *Safer and easier percutaneous access*

ND:Tortuous Iliacs



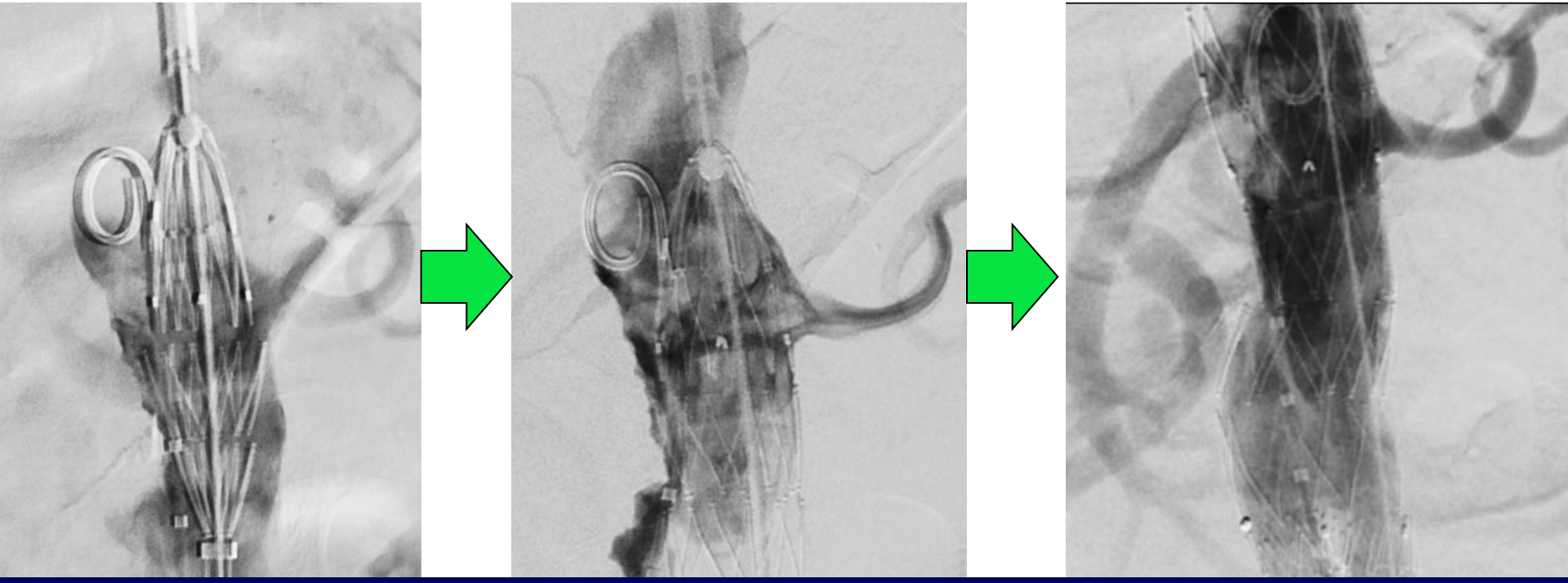
14 Fr

Easy Navigation



INCRAFT ® Deployment System

Allows for Slow, Deliberate, and Accurate Proximal Deployment



In Straight Necks

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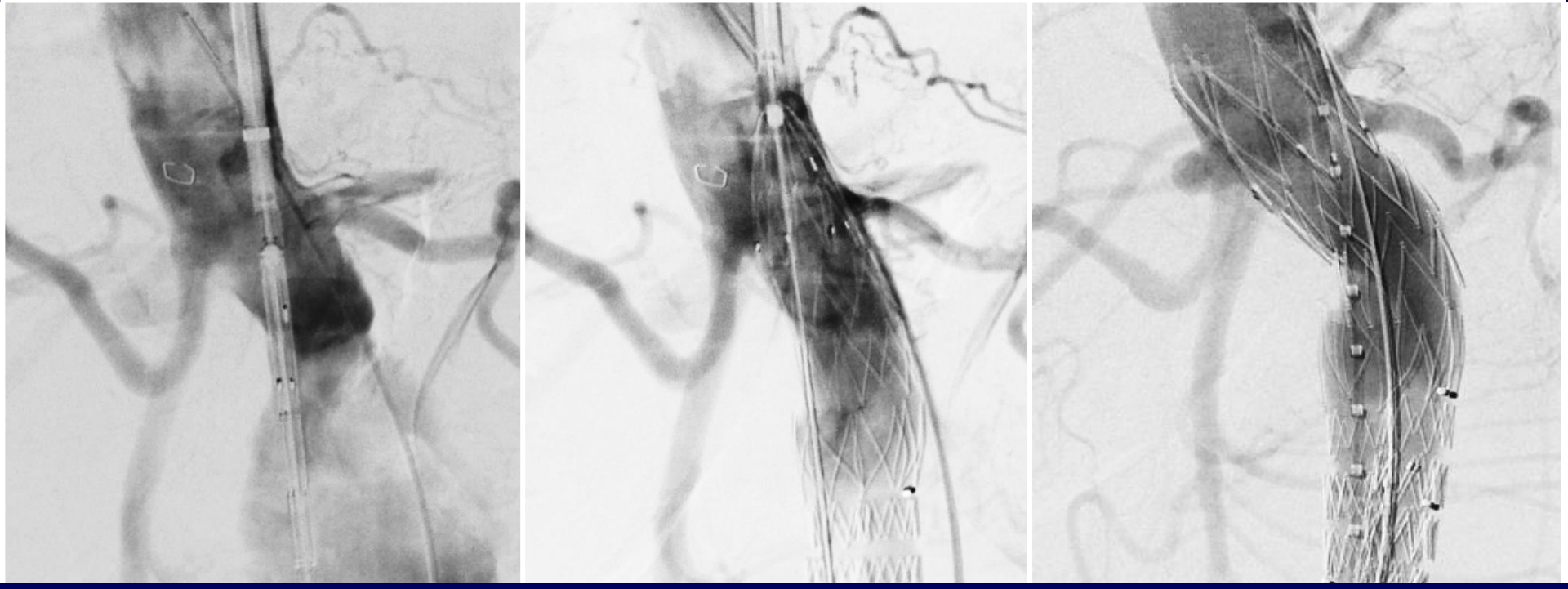
INCRAFT ® Deployment System

Allows for Slow, Deliberate, and Accurate Proximal Deployment



in somewhat Angulated Necks

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INCRAFT ® Deployment System

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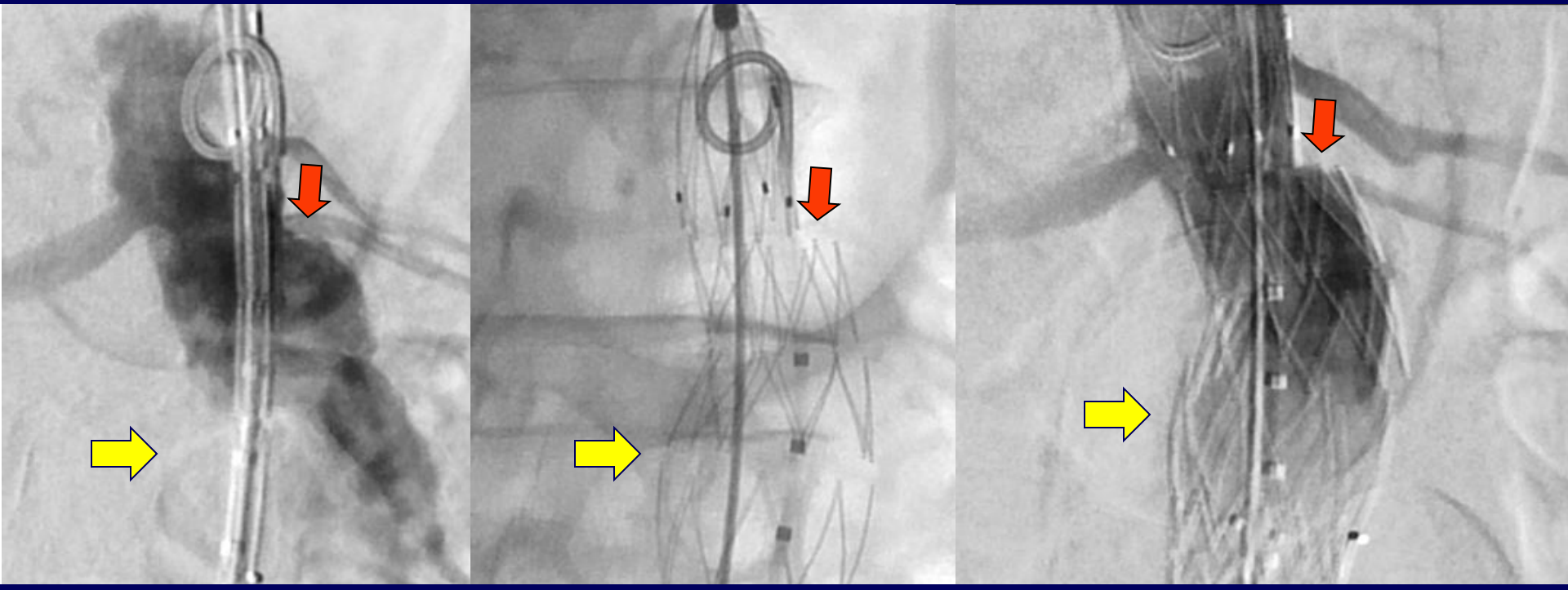

And in Uneven Necks

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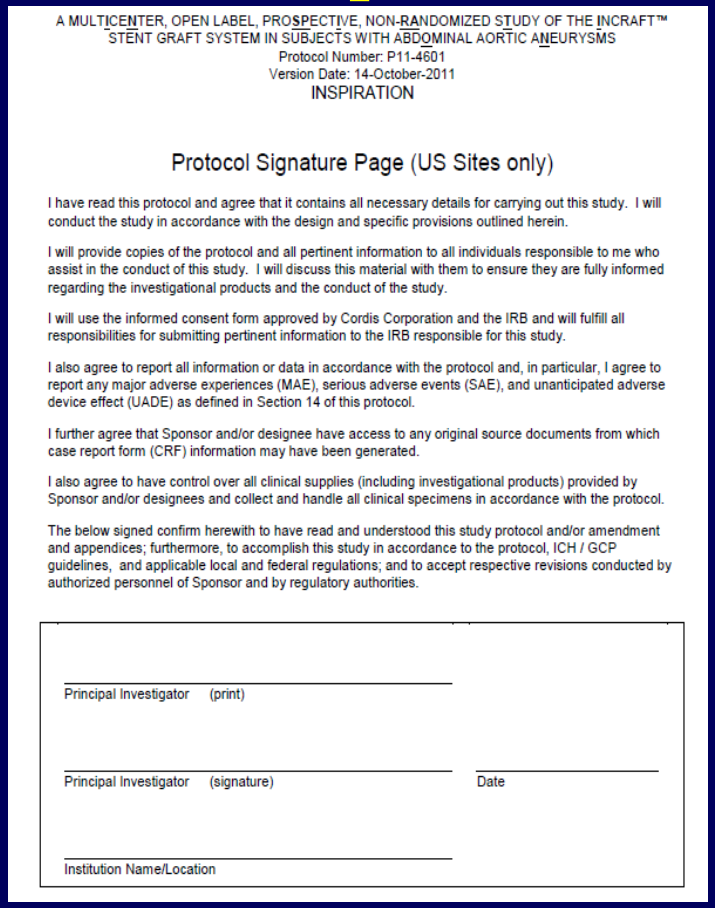
The INSPIRATION Regulatory Study

- **1st Study to run in Japan and US simultaneously and satisfies the requirements of both regulatory agencies**



A MULTICENTER, OPEN LABEL, PROSPECTIVE, NON-RANDOMIZED STUDY OF THE INCRAFT™ STENT GRAFT SYSTEM IN SUBJECTS WITH ABDOMINAL AORTIC ANEURYSMS
Protocol Number: P11-4601
Version Date: 14-October-2011
INSPIRATION

Protocol Signature Page (US Sites only)

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study in accordance with the design and specific provisions outlined herein.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the investigational products and the conduct of the study.

I will use the informed consent form approved by Cordis Corporation and the IRB and will fulfill all responsibilities for submitting pertinent information to the IRB responsible for this study.

I also agree to report all information or data in accordance with the protocol and, in particular, I agree to report any major adverse experiences (MAE), serious adverse events (SAE), and unanticipated adverse device effect (UADE) as defined in Section 14 of this protocol.

I further agree that Sponsor and/or designee have access to any original source documents from which case report form (CRF) information may have been generated.

I also agree to have control over all clinical supplies (including investigational products) provided by Sponsor and/or designees and collect and handle all clinical specimens in accordance with the protocol.

The below signed confirm herewith to have read and understood this study protocol and/or amendment and appendices; furthermore, to accomplish this study in accordance to the protocol, ICH / GCP guidelines, and applicable local and federal regulations; and to accept respective revisions conducted by authorized personnel of Sponsor and by regulatory authorities.

Principal Investigator (print)

Principal Investigator (signature) Date

Institution Name/Location

Michel Makaroun Co-PI

治験実施計画に対する合意書

Protocol Signature Page (Japan Sites Only)

下記の治験実施計画書及び症例報告書の内容並びに下記治験実施計画書を遵守して本治験を実施することに合意いたします。

I agree with the protocol and the case report forms indicated below, and agree to conduct the study in accordance with the design and specific provisions outlined in the protocol.

治験機器名 Study Device Name	(コード名： Device Code)					
治験課題名 Protocol Title						
(治験実施計画書番号) Protocol #						
治験実施計画書 Protocol	作成日： Version Date	年 Year	月 Month	日 Date		
症例報告書 Case Report Form	版番号： Version #	版	作成日： Version Date	年 Year	月 Month	日 Date

治験担当部門長 Clinical Research Director

所属： ジョンソン・エンド・ジョンソン株式会社 Johnson & Johnson K.K.
Title

氏名：
Print Name

署名： 日付：
Signature Date

治験責任医師 Principal Investigator

治験責任医師及び試験実施医療機関の長は、治験に関するモニタリング、監査、IRB及び規制当局の調査の際に、原資料を含むすべての治験関連記録を求められた場合には、これに供しなければならない。
The Principal Investigator and study sites must provide direct access to all the study related records such as the source documents for monitoring and auditing, as well as IRB review, and inspections by the regulatory authorities

医療機関・診療科：
Institution Name

氏名・職名：
Name & Title

記名捺印又は署名： 日付：
Print Name & Seal/Signature Date

Tak Ohki Co-PI

The INSPIRATION Regulatory Study

- **Enrolment: July 2012 to Aug 2013**
- **190 patients:**
  - **134 from US**
  - **56 from Japan**
- **32 sites**
  - **27 US**
  - **5 Japan**
- **All Imaging reviewed by a Core Lab (M2S)**
- **Clinical Events Committee (CEC) with 3 Independent members adjudicates all untoward events**
- **Control: Lifeline Registry Open Surgical Group**

The INSPIRATION Regulatory Study

Selected Inclusion Criteria

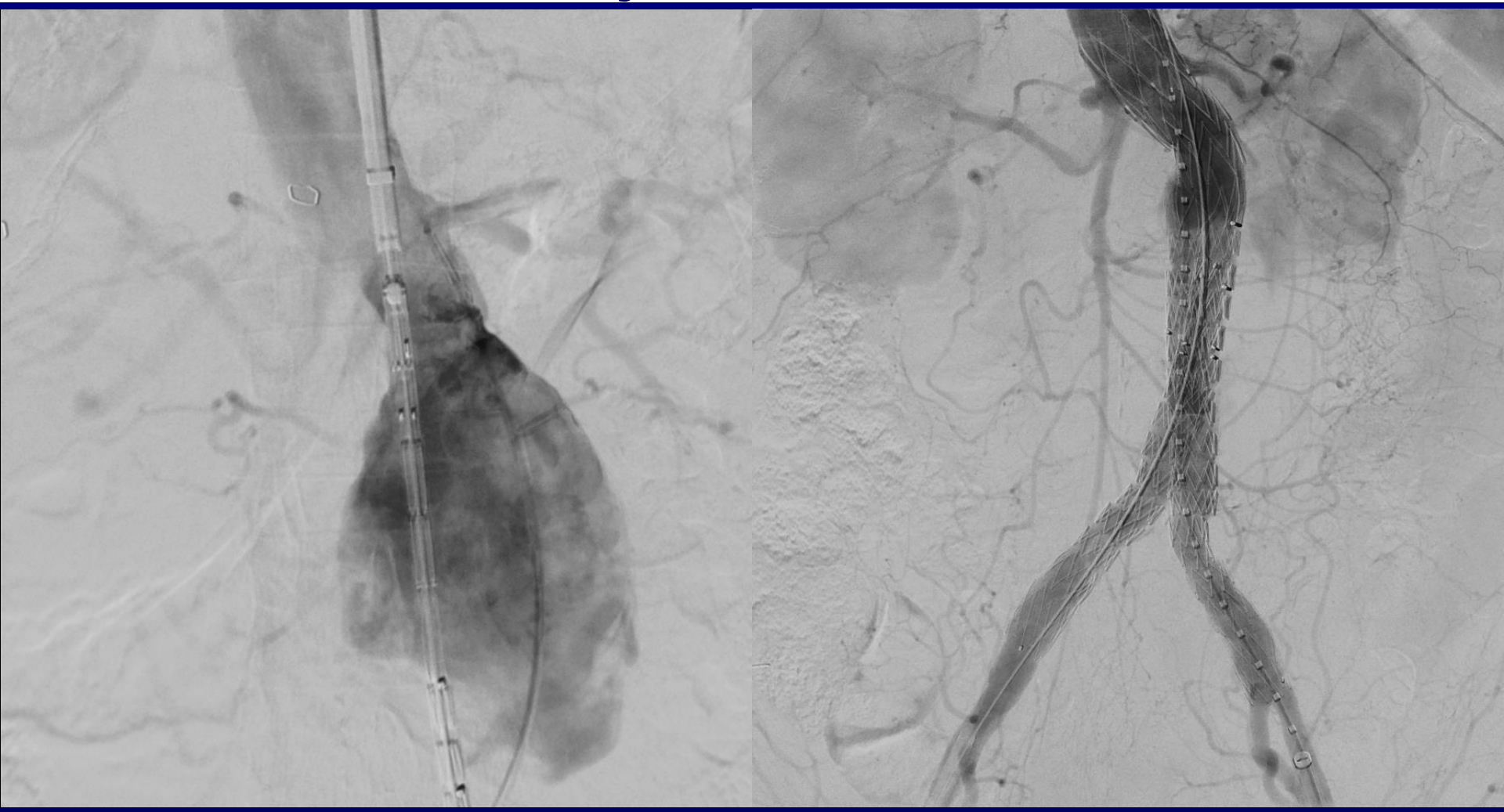
- AAA ≥ 5 cm
- Neck length ≥ 10 mm
- Neck angulation ≤ 60 degrees
- Iliac Fixation length ≥ 15 mm
- Iliac access ≥ 5 mm

Primary Endpoints

- Safety Endpoint: MAE rate @ 30 days
- Effectiveness Endpoint: Composite of Technical and Clinical Success of AAA Rx @ 1 year

Illustrative cases

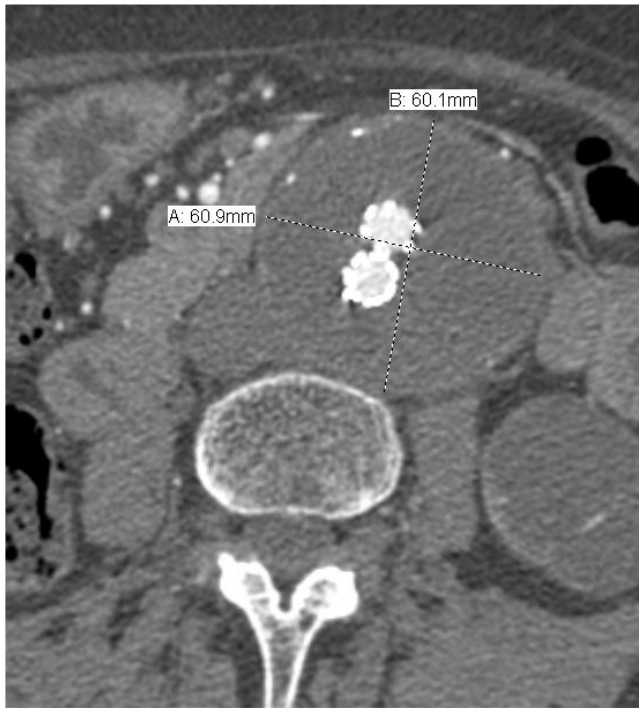
ES / 72 year old woman

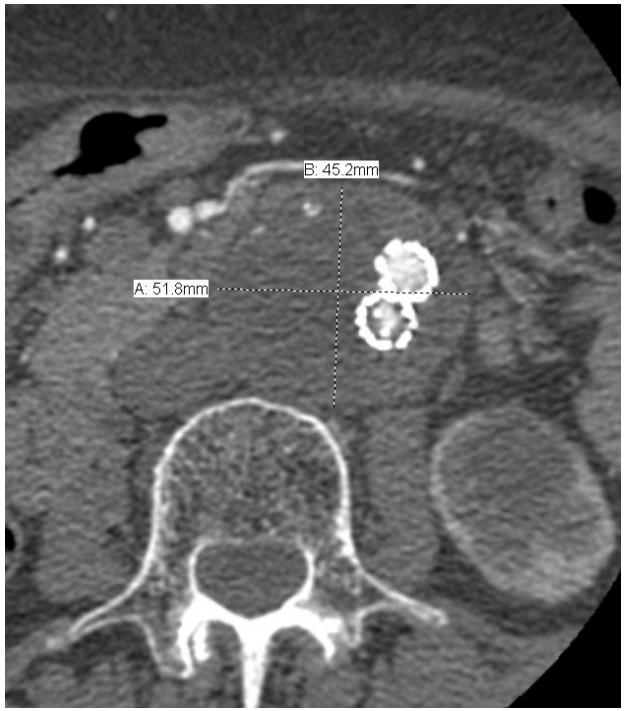


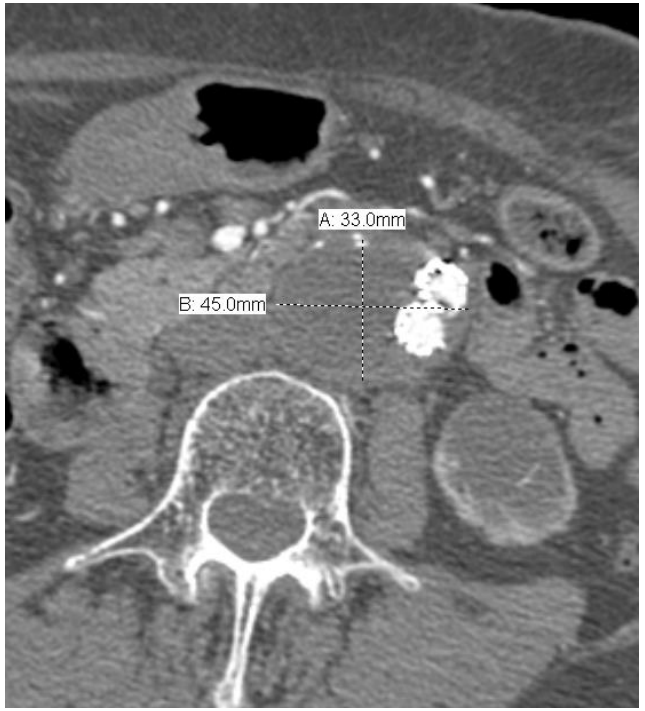
ES: First patient enrolled at UPMC, Pittsburgh

Illustrative cases

ES / 72 year old woman







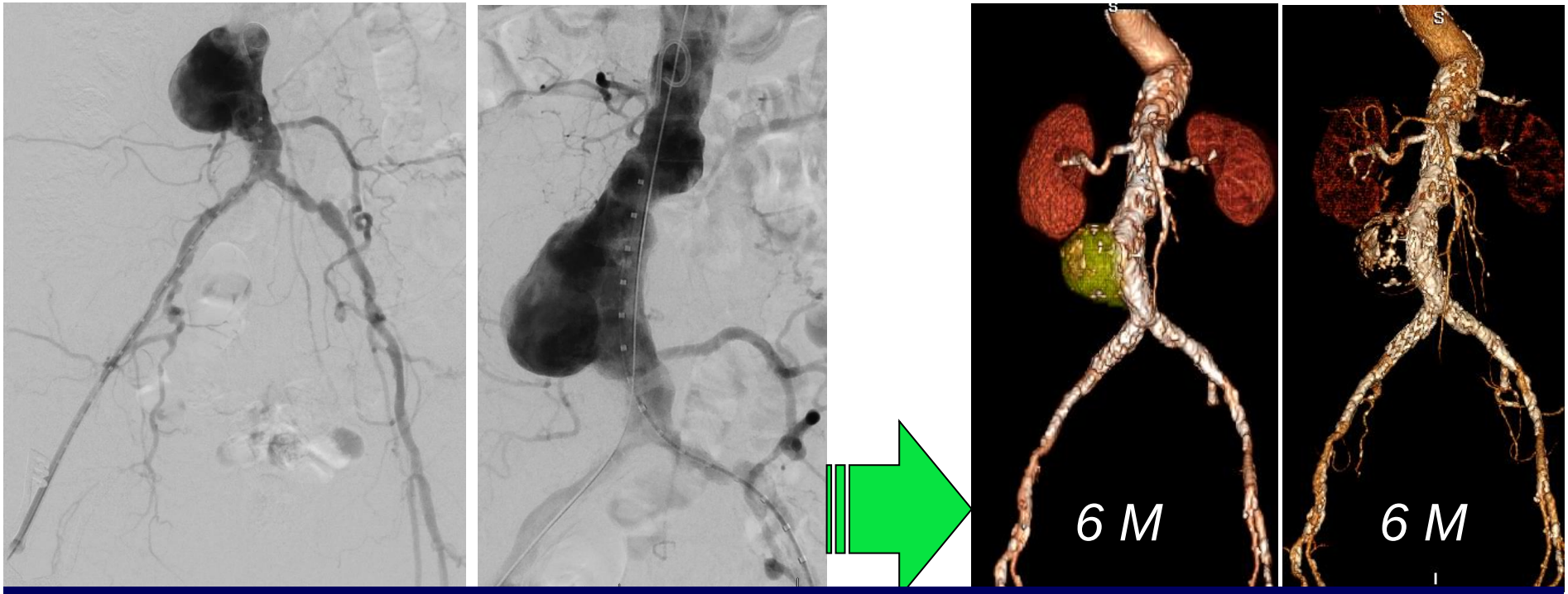
1 month
60 x 61 mm
No endoleaks

6 months
45 x 52 mm

1 year
33 x 45 mm

Illustrative cases

GR / 79 year old woman



With >50% of patients with iliac access < 7 mm

No iliac ruptures or significant injuries reported

The INSPIRATION Regulatory Study

Demographics

Age	Mean (years) ± SD	73.8 ± 8.0
Gender	Male	90% (171/190)
Co-Morbidities	Coronary Artery Disease	40.5%
	History of MI	18.4%
	Hypertension	77.9%
	Peripheral Arterial Disease	14.7%
	Diabetes Mellitus	25.3%
	COPD	26.8%
	Renal Insufficiency (cr ≥1.5mg/dL)	5.3%
	Current Smokers	20%

The INSPIRATION Regulatory Study

Procedure		
AAA Size (mm)	Mean ± SD	54.9 ± 6.9
Local Anesthesia	%	41%
Totally Percutaneous	%	63%
Duration (min)	Mean ± SD	103.2 ± 42.7
Blood loss > 500 ml	%	5.8%
Successful Deployment		100% (190/190)
Repositioning in 1 patient / Inadvertent coverage of 1 internal iliac in 1 patient		

***Preliminary results. Final outcomes being audited.*

The INSPIRATION Regulatory Study

30 Day Results**

- **Mortality** **0.5% (1/190)**
- **Major Adverse Event (MAE)** **3.1% (6/190)**
  - Myocardial Infarction 0.5% (1/190)
  - Renal Failure 0.0% (0/190)
  - Respiratory Failure 0.0% (0/190)
  - Stroke 0.5% (1/190)
  - Bowel Ischemia 0.0% (0/190)
  - Procedural Blood Loss $\geq$ 1000cc 2.1% (4/190)
- **No Limb occlusions in the first 30 days**

***Preliminary results. Final outcomes being audited.*

The INSPIRATION Regulatory Study

Imaging Follow-up

- Schedule: 1, 6 and 12 months. Yearly thereafter.
  - CT with and without contrast
  - 4 views Abdominal X-rays
- All imaging reviewed by Core lab
- Patients with elevated Cr had non contrast CT with ultrasound duplex or MRA

The INSPIRATION Regulatory Study

Imaging: *Endoleaks during Follow-up (site Reported)*

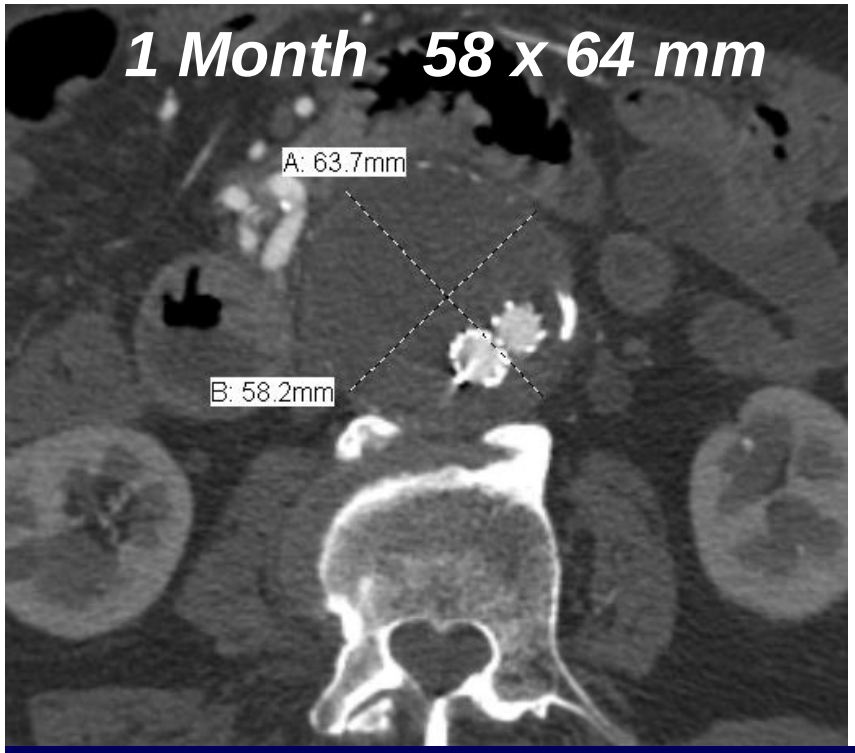
Endoleaks	1 Month	6 Months	1 year
	N=189	N=157	N=67
Type I	0.0% (0)	0.0% (0)	2.9% (2)
Type II	27.5% (52)	21.0% (33)	13.4% (9)
Type III	0.0% (0)	0.0% (0)	0.0% (0)
Indeterminate	0.0% (0)	0.0% (0)	0.0% (0)
ANY endoleak	27.5% (52)	21.0% (33)	16.3% (11)

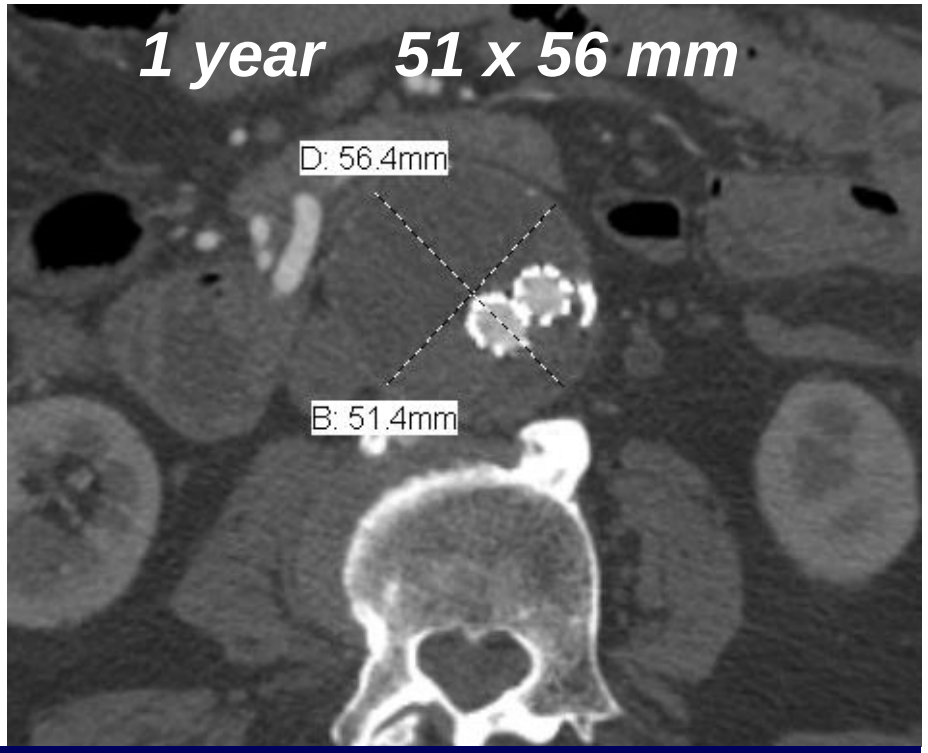
***Preliminary results. Final outcomes being audited.*

The INSPIRATION Regulatory Study

Imaging: *Size Changes*

Size Changes ≥ 5mm considered significant





NC second patient enrolled at UPMC, Pittsburgh

The INSPIRATION Regulatory Study

Imaging: Size Changes (Core Lab)

	6 Month	1 Year
	N=116	N=37
≥ 5mm diameter Decrease	24% (28)	38% (14)
≥ 5 mm diameter Increase	0% (0)	0% (0)
No Change	76% (88)	62% (23)

***Preliminary results. Final outcomes being audited.*

The INSPIRATION Regulatory Study

Follow-up after 30 days

- **No Fractures**
- **No Migration**
- **No Ruptures**
- **No aneurysm Related Mortality**
- **Two Conversions to Open Repair, one for "embolization to Popliteal artery at 6 months"**
- **7 Limb Thromboses associated with anatomic restrictive factors**

***Preliminary results. Final outcomes being audited.*

The INSPIRATION Regulatory Study

Follow-up after 30 days

- **14 Re-Interventions in 13 patients**
  - **6 Open including 2 Explantations**
  - **8 Endovascular**
  - **1 for Endoleak**
  - **Rest for Limb Thrombosis or Stenosis of Native Arteries or graft limb**

***Preliminary results. Final outcomes being audited.*

The INNOVATION EU Regulatory Study

Study Design

- FIH, multi-center prospective, open label, non-randomized investigation of INCRAFT in subjects with AAA.
- 60 patients have been included in 6 German and Italian centers

Objective

- To assess the technical success and safety of the Cordis INCRAFT™ Stent Graft System in subjects with AAA

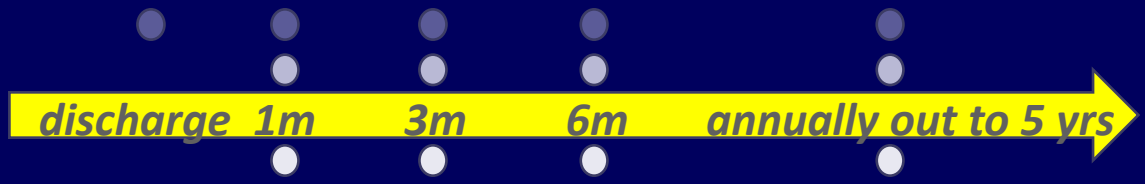
Primary Endpoints

- Successful deployment at desired location and absence of Endoleaks (I, III or IV) post-procedure
- Absence of Endoleaks and device or procedure related major adverse events (MAE) at 30 days

Follow- up

AE assessment
CT scan and X-ray

QOL questionnaire



The INNOVATION EU Regulatory Study

Investigators	Study Sites	Patients
Prof. D. Scheinert A. Schmidt	Leipzig, Germany	10
Prof. G.Torsello	Münster, Germany	17
Prof J. Brunkwall	Köln, Germany	4
Prof. G. Coppi	Modena, Italy	7
Prof. C. Pratesi	Firenze, Italy	14
Prof. R. Chiesa	Milano, Italy	8
	Total	60

The INNOVATION EU Regulatory Study

	Operative	30 days (58/60)	1 Year (56/60)
Successful deployment	98.3%	NA	NA
Freedom from Endoleak			
Type I	98.3%*	96.6%†	100%
Type III	100%	100%	100%
Type IV	93.3%	100%	NA
Stent Graft Patency	100%	100%	100%
Freedom from Migrations	NA	100%	100%
Freedom from Fracture	NA	100%	100%
Freedom from Sac Enlargement	NA	100%	100%
Freedom from MAE	100%	100%	98.2%‡

The INSPIRATION Regulatory Study

Summary and Conclusions

- The Incraft ® is a low profile device that allows In-Situ limb length adjustments and safe use in patients with small external iliac arteries
- The INSPIRATION trial is the first regulatory device trial conducted simultaneously in the US and Japan
- Early Results so far are encouraging !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