

#### KEY TO INNOVATION AT VASCUTEK

#### JAPAN MATTERS FEBRUARY 7TH 2014





## VASCUTEK LTD: Background

- Manufacturer of synthetic vascular grafts
- In business since 1982
- Over 500 employees
- Turnover around £70 million
- No. 2 globally, No. 1 outside US (in grafts)
  - Located on single site at Inchinnan
  - Wholly owned by Terumo Corporation of Japan











#### ME

#### **Tim Ashton**

- Vice President, Innovation
- With company over 25 years
- Not an engineer
- Zoologist and former fish-farmer
- 40+ staff in R&D





#### What Do We Do?

- · Replacement arteries
- · From Heart to Leg
- Textile Polyester and ePTFE
- Implanted surgically and now by minimally invasive catheter techniques



#### TERUMO Surgical AAA Repair Aorto Hac aneurysm (open)





Sac plicated over graft **VASCUTEK** TERUMO



#### WARNING!

- Next few slides show surgical procedures
- · Look away now if you are squeamish





The abdomen has been opened through a long midline incision and good access is achieved by the aid of rail mounted metal retractors. The intestines are protected by moist saline soaked towels and the abdominal aortic aneurysm has been displayed showing the proximal ends of the aneurysm and both common iliac arteries.







The large intraluminal clot has been removed; the original lumen is displayed by the scissors. The thickened degenerate atheromatous tissue, which was the original aortic wall in the region of the neck, is displayed.





Both limbs of the graft are now functioning; haemostasis is completely secure. The sealed graft is not leaking any blood; it should be noted that the limbs of the graft have been deliberately kept very close together preventing any acute angulation at the site of the flow splitter.



#### ТЕRUMO Example – Bifurcate







## ENDOVASCULAR ANEURYSM REPAIR MINIMALLY INVASIVE





## Endovascular

- Aneurysm Repair
  The trend in recent years has been to less invasive approaches
- Grafts are introduced via the femoral arteries and secured in the aorta by stents
- · Less trauma for the patient and faster recovery
- 30-Day mortality for endovascular has been shown to be lower than for conventional surgical repair
- However, long-term durability is not yet established and regular follow-up is necessary











Guidewires removed after satisfactory check angiogram



#### TERUMO Example – Endovascular







#### Are We Innovative?

- · More than 60 patents granted
- · Queen's Awards to Industry
  - Technology 1988
  - Innovation 2001
- · Scottish Business Awards
  - Most Innovative Company 2012 & 2013
- · Scottish Enterprise Life Sciences Awards
  - Most Innovative Company 2010





#### **How Was This Achieved?**

 A historical perspective with some examples of innovative developments





## 1979 – Research & Development

Three groups worked together to develop a new vascular graft







## 1982 – Vascutek Ltd Founded

 Vascutek develop unique knitting machines capable of knitting to 60 needles per inch

 TriaxialTM and VP1200KTM grafts launched







## **Keys To Success**

- Building on existing platform
  - Knitting from Coats Patons
- · Bringing in external expertise
  - Strathclyde University & Glasgow Royal Infirmary
- · Differentiation, but not too much
  - Finer gauge knitting than competition
    - 60 needles per inch vs. 56





#### 1983 – Development of our gelatin sealant begins. Removes the need to seal the porous textile graft by soaking in the patient's blood

Removal in 14 days by simple hydrolysis

- No enzymatic mechanism required
- Antibiotic bonding option applies to all Vascutek sealed grafts
  - Now 37 publications to support this clinical application
  - CE Approval for the Rifampicin Bonding Process awarded in 2001







## **Keys To Success**

- Not the first on the market
  - Learn from others' mistakes
- Modest differentiation
  - Rapid resorbtion to promote healing
- · Use of gelatin
  - Cheap, bulk, pharma grade, easy to handle.
- Smart market introduction strategy
  - Small price premium led to widespread adoption



#### TERUMO Keys To Success

- Maximise the use of the technology
  - Apply sealant to a wide range of substrates
  - Use sealant as a matrix for drug delivery
    - · Antibiotic to prevent infection
    - · Heparin to prevent clotting
- Encourage publications
  - Engage with credible academic centres



#### **ТЕRUMO** 1999 – First ePTFE Grafts Launched





Gelatin sealed Ultrathin PTFE









Unsealed Ultrathin PTFE





## ePTFE

- · Microporous fluoropolymer like Goretex
- · Well established as a vascular graft material
- · Perceived as superior to polyester
- New to Vascutek







#### ePTFE

- Introduced as a technology transfer
- · Barriers to market entry
  - Very different manufacturing process
  - Two major competitors dominating market
  - Polyester and ePTFE traditionally handled by different companies





## **Keys To Success**

- · Choice of partners for technology transfer
  - Track record with this material
- · Differentiation
  - Gelatin coating to reduce suture hole bleeding





#### ePTFE

- One of the limitations of ePTFE is bleeding from the holes created by the needle when suturing into place
  - ePTFE is inelastic and the needle makes a hole bigger than the suture
  - Coating the graft with a thin layer of elastic gelatin reduces this problem







#### Without Gel







#### ePTFE with Pressurised Blood Before and after Gel Coating









#### ePTFE

- Reduced suture hole bleeding gave product differentiation and allowed penetration of an established market
- However, the technology is not trivial
  - ePTFE is hydrophobic (water repellent)
  - Gelatin is dissolved in water
  - How can the gelatin be made to adhere?





#### ePTFE Plasma Treatment

- Plasma treatment was used to overcome the hydrophobicity of the ePTFE surface
- No change to bulk properties





## Plasma "Fourth State Of Matter"

- · High energy state
  - Charged particles, ions, electrons, etc
    - **Overall neutrality**





#### Schematic of Plasma Surface Modification with Plasma Reactor





#### **TERUMO** View of Plasma Chamber and Controls







#### **Plasma Glow**







# Water Droplet on ePTFE before Plasma Treatment







#### Water Droplet on ePTFE after Plasma Treatment







#### **Keys To Success**

- Novel application of an established technology
- Collaboration with experts in the field (equipment manufacturers)





#### **Bio Valsalva**<sup>TM</sup> Porcine Aortic Valved Conduit

#### **The Biological Bentall**

- · Unique porcine aortic valved conduit
- Innovative self-sealing trilaminate graft material
- Pre-sewn device reduces procedure complexity and prevents valve-to-graft mismatch
  - Closely matches aortic root anatomy
  - Reduces patient risk potential for reduced bypass, cross-clamp and procedural time Enables treatment of vulnerable patient groups









#### BioValsalva

- · Opportunity
  - need for a ready to use conduit with a biological valve
- · Problem
  - Biological valves are stored in a solution that is not compatible wit the gelatin graft sealant
- · Solution
  - Use a sealant that is compatible with the storage solution





#### Triplex V 3 Layer Wall Design Cross section



Central elastomeric membrane





#### BioValsalva

- Inner and outer layers are existing Vascutek materials
- Middle layer is an elastomeric membrane developed and tested by Terumo Corporation.
- Key to success?
  - Intelligent combination of materials





#### 2005 - Anaconda

# Graft

#### Anaconda<sup>™</sup> AAA Stent Graft Receives CE Mark approval





## Anaconda

- Treats same disease (aneurysms) as established surgical grafts
- · Less invasive catheter based approach
- · IP acquired from Surgeon Inventor
- Novel, innovative design with nitinol ring stents and polyester fabric.
- Magnetic cannulation
- · Repositionable





#### Anaconda



- Guide wire with magnet for contralateral approach
- Flexible iliac legs with ring stents







Possibility to reposition the bifurcate body, adapting the endograft to the anatomy



#### fenestrated anaconda™

**FERUMO** 

Custom AAA Stent Graft System

- Supra-renal fixation and sealing
- Valleys in Anterior-Posterior orientation
- Vessel cradled in anterior valley
- Markers on left peak hook





#### **Fenestrated Anaconda**

- Based on Anaconda One-Lok platform
- Body lengthened by 15mm
- SMA cradled in anterior valley



![](_page_50_Picture_6.jpeg)

![](_page_50_Picture_7.jpeg)

![](_page_51_Picture_0.jpeg)

#### **Testing: Prototype Deployment**

![](_page_51_Picture_2.jpeg)

![](_page_51_Picture_3.jpeg)

![](_page_52_Picture_0.jpeg)

#### **Testing: Prototype Deployment**

![](_page_52_Picture_2.jpeg)

![](_page_52_Picture_3.jpeg)

- Test re-positioning in anatomy
- Check alignment of fenestrations
- Check ability to cannulate fenestrations
- Check for suitable clearance from SMA/celiac to proximal ring
- Check suitability of device landing zone in aorta

![](_page_52_Picture_9.jpeg)

![](_page_53_Picture_0.jpeg)

## Anaconda: Keys To Success

- Innovative design with unique features and capabilities
- Uses established materials Nitinol & polyester
- · Avoid "not invented here syndrome"
  - Not a Vascutek concept
- Build on platform
  - Fenestrated version

![](_page_53_Picture_8.jpeg)

![](_page_54_Picture_0.jpeg)

## Key To Innovation At Vascutek

- · Conclusions:
  - No single factor
  - Take small steps
  - Use existing materials& products in smart ways
  - Be receptive to external inputs
    - · Bring in expertise when required
  - Be creative
  - Be bold

![](_page_54_Picture_10.jpeg)