Morphology and morphometry of stented arteries

Stephen Greenwald
Institute of Cell and Molecular Science
Barts and the London School of Medicine and Dentistry
&
Interdisciplinary Research Centre in Biomedical Materials
Queen Mary University of London

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Outline

• Background
  – Occlusive vascular disease and its treatment by PCI and stenting

• Assessment of a novel compliance matching stent and comparison with a commercially available device
  – In vivo radiographic measurement in pig carotid and iliac arteries
  – Development of a micro CT method for stented vessel morphometry on excised arteries
Cardiovascular Disease statistics

- Heart and circulatory disease are the UK's biggest killers.
- In 2006, cardiovascular disease caused 40% of deaths in the UK, and killed over 245,000 people.
- Coronary arterial disease causes over 120,000 deaths a year in the UK: approximately one in four deaths in men and one in six deaths in women.
Revascularisation techniques

- Coronary Artery Bypass Graft (CABG)
- Percutaneous Coronary Intervention (PCI)
  - Angioplasty
  - Plus stenting (94%)
Balloon angioplasty
What is an intravascular stent?

- A small tubular mesh usually made of either stainless steel or Nitinol.
- Inserted into stenotic (blocked) arteries to keep the lumen patent. Normally during angioplasty.
- Used at various sites including the coronary, renal, carotid and femoral arteries.
- Non-arterial uses e.g. in bronchus, trachea, ureter, bile duct.
The concept of vascular stents is accredited to Charles Dotter in 1969, who implanted stainless steel coils in canine peripheral arteries.

- Not followed up in humans because of haemodynamically significant narrowing.

Not in clinical practice until 1980s.

Market leader is the Palmaz stent designed by Julio Palmaz in 1985.

- Initially, 18 grafts placed in canine vessels, with patency rates approaching 80% at 35 weeks.
Varied stent geometries
PCI activity to 2006 (UK)

Nombres de PCI dans certains pays Européens

Bernard De Bruyne, Aalst, Belgium

Par $10^6$ habitants
## Demographics

<table>
<thead>
<tr>
<th>Age (mean)</th>
<th>64.2 yrs</th>
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<tbody>
<tr>
<td>Diabetic</td>
<td>17.5%</td>
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<tr>
<td>Previous CABG</td>
<td>8.9%</td>
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### Ethnic Origin

<table>
<thead>
<tr>
<th>Ethnic Origin</th>
<th>Percentage</th>
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<tr>
<td>Caucasian</td>
<td>91.2%</td>
</tr>
<tr>
<td>Asian</td>
<td>7.5%</td>
</tr>
<tr>
<td>Black</td>
<td>1.1%</td>
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<tr>
<td>Oriental</td>
<td>0.2%</td>
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2006 data: Ludman

http://www.bcis.org.uk/resources/audit/audit_2006
Demographics - Age

Male: mean = 62.3
Female: mean = 67.4

http://www.bcis.org.uk/resources/audit/audit_2006
Procedures using Stents

% of Procedures

Year

'92  '93  '94  '95  '96  '97  '98  '99  '00  '01  '02  '03  '04  '05  '06

http://www.bcis.org.uk/resources/audit/audit_2006
The problem with stents.

Restenosis. (7 – 20%)
Rate depends on lesion type, length and severity
Factors Which Contribute to In-stent Restenosis (1)

- Thrombus/platelet/fibrin adherence to stent struts.
  - Anticoagulants
    - Heparin – systemically or coated on stent.
    - Inhibition of the GP IIb-IIIa receptor:
      - Prevents platelet aggregation.
  - Associated with raised incidence of MI.
- PTFE coated stents.
Factors Which Contribute to In-stent Restenosis (2)

- Metabolic disorder/smoking/atherogenic diet.
  - Life style changes
  - Restenosis rate double in insulin dependent diabetics.
Factors Which Contribute to In-stent Restenosis (3)

• Intimal hyperplasia due to wall injury from the stent
  – Brachytherapy:
    • Delivery: Radioactive stents, catheter radiation.
    • May cause necrosis.
  – Drug eluting stents
    • Anti-proliferative agents e.g. rapamycin (Sirolimus)
    • No improvement in outcome in insulin dependent diabetics when compared to bare metal stents
    • Impaired ‘healing’ → late thrombosis
Drug Eluting Stent cases
2006 data from 86 of 91 centres

Mean of % use by Centres

2002 2003 2004 2005 2006

% DES cases

http://www.bcis.org.uk/resources/audit/audit_2006
BMS and DES use PCI for Restenosis

2006 data: Ludman

http://www.bcis.org.uk/resources/audit/audit_2006
Factors Which Contribute to In-stent Restenosis (4)

- Mechanical factors
  - Stress concentration/bending at end of stent.
    - Raised hoop and bending stress sensed by vascular smooth muscle cells \(\rightarrow\) fibrosis/remodelling
  - Flow disturbance within stented region.
    - Time varying shear stress sensed by vascular endothelium
      \(\rightarrow\) release of vasoactive mediators in the short term and remodelling/intimal hyperplasia in the longer term
  - **Compliant-ended stent**
Compliant Ended Stent

- Rigid in the centre to provide recoil resistance
- Parabolic and cantilevered struts
  - gradual change in compliance and matching to native vessel
  - reduces stress concentration and bending
  - Less disturbed flow
Experimental assessment of compliant ended stent

Aims

- To compare the performance of the CES and SMART stents over 28 days on vessel and stent dimensions.
  - To compare the effect of 2 levels of stent stiffness
  - To compare the effect of stent oversize
Stents used in the Study

SMART stent
(Commercially available)

Compliant Ended Stent
Method

• 65 stents implanted in the iliac and carotid arteries of 17 Large White pigs
• Lumen diameter determined before and after implantation by angiography
  – Follow-up angiography on days 3, 7 and 28
  – At day 28 the arteries were pressure perfused and removed for histology and micro CT scanning
CES & Smart stents in common iliac arteries
Vessel dimensions

Graph showing the lumen diameter in millimeters along the position along the stent in millimeters.
Measurements

\[ \text{SOS} = \left( \frac{SD_{post} - LD_{pre}}{LD_{pre}} \right) \times 100 \]

\[ \text{LOS} = \left( \frac{LD_{post} - LD_{pre}}{LD_{pre}} \right) \times 100 \]

\[ \text{MH} = \left( \frac{SD_{post} - LD_{post}}{LD_{post}} \right) \times 100 \]

SD Stent diameter
LD Lumen diameter

SOS Stent Oversize
LOS Lumen Oversize
MH Migration/Hyperplasia
Changes in % lumen oversize with time

\[ LOS = \left( \frac{LD_{post} - LD_{pre}}{LD_{pre}} \right) \times 100 \]

Lumen tends to pre implant dimensions within 1 month
Changes in % stent oversize with time

\[ SOS = \frac{SD_{post} - LD_{pre}}{LD_{pre}} \times 100 \]

Stent diameter changes little up to 1 month after implantation.
Changes in stent migration or intimal hyperplasia with time

\[ MH = \frac{(SD_{post} - LD_{post})}{LD_{post}} \times 100 \]

CES induces less migration or intimal hyperplasia than Smart stent control.
6 week post implantation

Palmaz

CES
Limitations

• Limited resolution of in-vivo X-ray images
• Limited study duration
  – Part of a larger study with later endpoint
• Can not distinguish between stent migration and intimal hyperplasia
  – Histology in progress
• Difference in stiffness not yet quantified
• Response of carotids & iliacs different to that of coronaries
  – NIH develops more slowly
Conclusions

• Lumen diameter relative to immediate post implant diameter decreases with time
• Stent diameter changes little with time
• Degree of stent migration or intimal hyperplasia increases with time.
  – Effect is small in the compliant ended stent
Micro CT of excised vessels

- Vessels pressure fixed in situ (10% formol saline)
- Excised and immersed in oil based contrast medium
- Custom built Micro CT scanner (Dental Biophysics QMUL)
- Voxel size (30 x 30 x 30µm)
- Images processed on custom software developed under KS400 (Zeiss) image analysis system
Image processing

Original slice  Thresholded  Media/Adventita only

Stent struts  Ellipse fitted
Slice measurements

Intimal hyperplasia in vicinity of struts. Less wall movement?
3D rendering
3D rendering
3D reconstruction
Future work (collaboration?)

- More extensive experimental study
  - Effect of stent oversize and stiffness on intimal hyperplasia
  - Comparison of different stent types
- Modelling & measurement of interactions between blood/arterial wall/stent
  - Haemodynamics and solid mechanics
# Acknowledgements

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<thead>
<tr>
<th>Name</th>
<th>Role</th>
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<tbody>
<tr>
<td><strong>Joel Berry</strong></td>
<td>Engineer</td>
<td>Design of compliant ended stent</td>
</tr>
<tr>
<td>Department of Biomedical Engineering</td>
<td>Wake Forest University College Station, NC, USA</td>
<td></td>
</tr>
<tr>
<td><strong>James Moore Jr.</strong></td>
<td>Engineer</td>
<td>Design of compliant ended stent</td>
</tr>
<tr>
<td>Department of Biomedical Engineering</td>
<td>Texas A &amp; M University College Station, TX, USA</td>
<td></td>
</tr>
<tr>
<td><strong>Gemma Ryder</strong></td>
<td>PhD student</td>
<td>In vivo study</td>
</tr>
<tr>
<td>Institute of Cell and Molecular Science</td>
<td>Barts and the London School of Medicine and Dentistry London, UK</td>
<td></td>
</tr>
<tr>
<td><strong>Graham Davis</strong></td>
<td>Physicist</td>
<td>Micro CT</td>
</tr>
<tr>
<td>Department of Dental Biophysics</td>
<td>Queen Mary, University of London London, UK</td>
<td></td>
</tr>
<tr>
<td><strong>Luke Timmins</strong></td>
<td>PhD student</td>
<td>Image processing</td>
</tr>
<tr>
<td>Department of Biomedical Engineering</td>
<td>Texas A &amp; M University College Station, TX, USA</td>
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