Histological evaluation of filter contents in mesh-covered vs standard nitinol stents during carotid stenting using the Paladin system

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Disclosure

Speaker name:

......Ivo Petrov..........................................................................

- I do not have any potential conflict of interest
Edward Diethrich and Donald Reid at the opening ceremony of City Clinic 12.12.2012
Endovascular experience after 5 years of work:

- 11,240 endovascular cases (“Head to toe”) in the cathlab and the hybrid OR including:
  - CTO and Left main Coronary interventions
  - EVAR/TEVAR
  - TAVR
  - Intracranial aneurysms stenting and coiling
  - CAS (920 CAS procedures)
  - Radial approach for complex peripheral cases
  - Complex venous interventions (including May-Thurner, CCSVI)
  - Renal denervation
## Improvement of the technique of CAS in the time:

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Contemporary</th>
<th>Effect on outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular access</td>
<td>Femoral</td>
<td>Femoral, radial, direct puncture</td>
<td>Applicable in all kind of vascular anatomy/pathology</td>
</tr>
<tr>
<td>Closure device</td>
<td>No</td>
<td>Yes</td>
<td>Early ambulation</td>
</tr>
<tr>
<td>French size</td>
<td>8-11</td>
<td>7..6..5..</td>
<td>Vascular complications reduction</td>
</tr>
<tr>
<td>Neuro Protection</td>
<td>No</td>
<td>Distal, proximal, combined</td>
<td>Improves complication rate/clinical outcomes</td>
</tr>
<tr>
<td>Dedicated stents</td>
<td>No or transferred from other</td>
<td>Dedicated: Nitinol, mesh, hybrid,</td>
<td>Improving early and late results. Reducing restenosis</td>
</tr>
<tr>
<td></td>
<td>vascular intervention territory</td>
<td>open cell, closed cell, membrane covered, tapered</td>
<td></td>
</tr>
</tbody>
</table>

**Initial**
- Femoral

**Contemporary**
- Femoral, radial, direct puncture
- Vascular complications reduction
- Improves complication rate/clinical outcomes
- Improving early and late results. Reducing restenosis
While CAS Results Are Steadily Improving

30 Day Death/Stroke/MI

- SAPPHIRE
- ARCHER
- SECURITY
- BEACH
- MAVERIC
- CABERNE
- CREATE
- EVA-3s
- SPACE
- EMPIRE
- EPIC 2008
- PROTECT
- ARMOUR
- CREST
- ROADSTE
- ACT / 2016

30 Day Death/Str...
Minor Stroke During CAS Remains An Unresolved Issue (the main reason for these small strokes is microembolization)
Hypothesis

• Significant portion of the risk of stroke during CAS occurs during post-dilation, due to plaque prolapse through the stent struts, resulting in a massive release of embolic particles

• Increasing the degree of protection during this phase would be clinically beneficial

• A novel catheter with a filter integrated distal to the balloon which could be adjusted to the size of each individual patient's anatomy would help capture micro-emboli and thereby reduce the risk of stroke

• Novel mesh covered stents have been developed with the purpose to limit the plaque protrusion and the degree of embolization during and after CAS.

Limitations of EPFs

- What is the ideal pore size?
  - Most filters have pore sizes less than 200 μm
    - Stroke victims have evidence of occluded arterioles ranging from 50 to 300 μm [38]
    - Small fragments (<100 μm) may cause late neuronal ischemia [39]
    - Calcified fragments cause greater levels of infarction than fibrous plaques [40]
PALADIN®
Carotid Post-Dilation Balloon with Integrated Embolic Protection (IEP)

Filter Chassis

Filter Membrane with 40-Micron Pore Size

Minimal Landing Zone

Angioplasty Balloon

Sheathless Design

First filter with ability to adjust size to suit patient anatomy
## Paladin® System Features

### Integrated Embolic Protection Device Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery System</td>
<td>5F (2.1 mm) Rapid Exchange</td>
</tr>
<tr>
<td>Guidewire compatibility</td>
<td>0.014”</td>
</tr>
<tr>
<td>Balloon Sizes</td>
<td>Diameter: 5.0 mm – 5.5 mm</td>
</tr>
<tr>
<td></td>
<td>Length: 20 mm – 30 mm</td>
</tr>
<tr>
<td>Filter membrane pore size</td>
<td>40 microns</td>
</tr>
<tr>
<td>Catheter length</td>
<td>140 cm</td>
</tr>
</tbody>
</table>
Paladin System Example

Images courtesy Ralf Langhoff, MD
Sankt Gertrauden Krankenhaus, Berlin, Germany

petrovivo@hotmail.com
### Comparative Results across MRI Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Paladin (n=30)</th>
<th>PROFI¹ Proximal group (n=31)</th>
<th>PROFI¹ Filter group (n=31)</th>
<th>ICSS² Filter group (n=37)</th>
<th>CARENET³ CGuard (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence of New Lesions</strong></td>
<td>36.7%</td>
<td>45%</td>
<td>87%</td>
<td>73%</td>
<td>48%</td>
</tr>
<tr>
<td><strong>Mean number of lesions per pt.</strong></td>
<td>0.50 ± 0.7</td>
<td>1.0 ± 1.4</td>
<td>3.6 ± 3.2</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Mean Lesion Volume (cm³)</strong></td>
<td>0.01</td>
<td>0.16</td>
<td>0.59</td>
<td>NA</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Total number of new ischemic lesions</strong></td>
<td>16</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>117</td>
</tr>
<tr>
<td><strong>Maximum lesion volume (cm³)</strong></td>
<td>0.158</td>
<td>0.84</td>
<td>2.4</td>
<td>NR</td>
<td>0.445</td>
</tr>
</tbody>
</table>


Comparison of MAE Across CAS Studies

30 Day Death/Stroke/MI

30 Day MAE
- Death
- Stroke
- MI

Paladin results

References available for individual study results
Prospective multi-center studies with >100 patients

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OCT and IVUS evidence: Significant plaque protrusion during and after implantation, even with closed cell design stent. It would have been deleterious for a patient with recent stroke and contralateral occlusion to allow additional embolization to both hemispheres. This was the reason to chose in this particular case a PET mesh covered stent thus avoiding intra and post procedural embolization.
## CGuard™ Carotid Embolic Prevention System Specifications

<table>
<thead>
<tr>
<th>Device Features</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent type</td>
<td>Nitinol Self-Expanding</td>
</tr>
<tr>
<td>MicroNet Aperture Size</td>
<td>150-180µ</td>
</tr>
<tr>
<td>Guidewire</td>
<td>0.014”</td>
</tr>
<tr>
<td>Foreshortening</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Sizes</td>
<td>Diameter( 6mm-10mm) x Length (20mm – 60mm)</td>
</tr>
<tr>
<td>Delivery System (OD)</td>
<td>6F (2.1mm)</td>
</tr>
</tbody>
</table>
C-Guard: Histopathology in Pig Carotid Artery

CARENET trial demonstrated the safety of the CGuard™ Technology with zero MACCE at 30 days
The procedural success was 100%

1 JACC, April 2012
2 Lancet, March 2010
PALADIN local Bulgarian registry. Patient Population (all comers)

• Study Population
  – Symptomatic subjects (history of ipsilateral TIA, stroke or amaurosis fugax within the past 6 months) with carotid stenosis ≥ 50% by angiography
  – Asymptomatic subjects with carotid stenosis ≥ 70% by angiography

• Primary Endpoints
  – Acute Technical success
  – 30 day (neurological death and stroke)
Histological substudy.

Carotid Stenting Procedure:

- CAS was performed in 13 patients using the novel C-Guard stent (Inspire MD, Tel Aviv, Israel) (n=5) and the closed cell nitinol XACT stent (n=8)
- Primary distal filter Spider was used in all 13 cases
- Pre-Dilation was at the discretion of the operator
- Paladin System (Contego Medical, Raleigh, NC, USA) was used for post-dilation
- All filters (13 pairs) were removed post-procedure, placed in formalin, and underwent histomorphometric analysis. Particles were categorized into three groups: 40-100µm, 101-200µm, and 201-400µm.
## Baseline Subject Characteristics

<table>
<thead>
<tr>
<th>Demographics (n=13)</th>
<th>N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65 ± 6.3</td>
</tr>
<tr>
<td>Male sex</td>
<td>10 (76)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>7 (54)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>7 (54)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>5 (38)</td>
</tr>
<tr>
<td>History of PCI/CABG</td>
<td>2 (15)</td>
</tr>
<tr>
<td>Hyperlipidemia requiring medication</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Hypertension requiring medication</td>
<td>7 (54)</td>
</tr>
<tr>
<td>History of peripheral vascular disease</td>
<td>3 (23)</td>
</tr>
<tr>
<td>History of previous contralateral CAS/CEA</td>
<td>2 (15)</td>
</tr>
<tr>
<td>Diabetes requiring medication</td>
<td>3 (23)</td>
</tr>
</tbody>
</table>
# In-hospital and 30 Day Clinical Results

<table>
<thead>
<tr>
<th></th>
<th>Discharge (n=13)</th>
<th>30 Days (n=13*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAE (death, stroke, MI)</td>
<td>0.0 % (0)</td>
<td>0.0 % (0)</td>
</tr>
<tr>
<td>All Death</td>
<td>0.0 % (0)</td>
<td>0.0 % (0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.0 % (0)</td>
<td>0.0 % (0)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0.0 % (0)</td>
<td>0.0 % (0)</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>0.0% (0)</td>
<td>0.0% (0)</td>
</tr>
</tbody>
</table>
Histological analysis of the filter contents revealed the presence of debris in 100% of the Paladin filters. The mean number of total particles in the Paladin filter among patients receiving the C-Guard stents vs Xact stents was 1379 vs 1260 respectively (p=NS). The mean number of 40-100μm particles in the Paladin filter among patients receiving the C-Guard stents vs Xact stents was 1310 vs 1164 respectively (p=NS).

The majority of particles captured were less than 100 microns.
• mean number of 40-100μm particles in the Paladin filter among patients receiving the C-Guard stents vs Xact stents was 1310 vs 1164 respectively (p=NS).
Case I (done with X-Act stent)

Gender: male, age 60y., symptomatic (history of stroke-contralateral hemisphere, recent TIA)

Concomitant disease:
- 2 vessel coronary disease
- Arterial hypertension II grade
- Dyslipidemia

Vascular access:
*Right femoral artery, Shuttle sheath 6F*

Target carotid artery: *RICA- 90% stenosis (note contralateral near occlusion “string sign”)*

*Primary distal protection system: Spider 5.0*

Implanted stent:
*Direct implantation Tapered X-Act 8-6/40mm.*

*Postdilatation:*
*Paladin 5.0/20 mm.*
LICA near occlusion (string sign). History of ipsilateral stroke.
RICA 90%. Ipsilateral TIA. Lesion crossing with .014 Whisper wire
Direct stenting X-Act 6-8/40mm
Paladin filter/balloon system positioning. Note head rotation can be helpful in some cases of excessive tortuosity.
Paladin filter opening and 5.0 mm balloon postdilation
Final result after stenting and both filters removal
Final intracranial in RAO projection
Final intracranial in AP cranial
Case II (done with C-Guard stent)

Gender: male, age 68y., symptomatic (history of minor left hemisphere stroke 2 months before)

Concomitant disease:
- Severe PAD with massive calcifications
- Arterial hypertension II grade
- Dyslipidemia

Vascular access:
*Right radial artery, Shuttle sheath 6F*

Target carotid artery: *LICA- subocclusive 99% stenosis (note right radial vascular approach for LICA/CAS in Bovine arch case)*

*Primary distal protection system:* Spider 5.0

Implanted stent:
*C-Guard 8/40mm after predilation.*

Postdilatation:
*Paladin 5.0/20 mm.*
LICA near occlusion in a patient with bovine arch
Predilatation after distal filter Spider insertion, Sprinter NC 3.0/15
Paladin insertion into the C-Guard and dilation
Conclusions

• Intraprocedural minor stroke remains an unresolved issue for CAS

• The Paladin (integrated balloon + small pores filter) is low profile RX system suitable both for femoral and radial vascular approach

• The use of the Paladin System for post-dilation during CAS was technically successful in all cases and resulted in no procedural strokes

• The majority of particles caught in the Paladin filter were <100 microns

• In this analysis, the total number of embolic particles, as well as particles between 40-100μm caught in the Paladin filter during post-dilation was not significantly different between the C-Guard mesh-covered stent and the X-ACT closed cell nitinol stent.
Histological evaluation of filter contents in mesh-covered vs standard nitinol stents during carotid stenting using the Paladin system

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