Biodegradable stent

The PLLA biodegradable stent as a drug delivery platform

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Biodegradable stent

Drug Loading into the Stent

• Coating a stent with a polymer containing drug
• Making a stent from a polymer incorporated by drug
• Coating a polymer stent incorporated by drug with a polymer containing drug
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Stent incorporated by Tranilast

IGAKI-TAMAI® STENT

Tranilast stent

Decrease of Radial Force: < 10%

(Comparison with IGAKI-TAMAI STENT, uniaxial compression)

Tranilast content: 184 µg/stent
IGAKI-TAMAI knitted-type PLLA stent coated with tyrosine kinase inhibitor (ST638) in porcine coronary arteries

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*IGAKI-TAMAI knitted-type PLLA stent coated with tyrosine kinase inhibitor (ST638) in porcine coronary arteries*


Control (3 weeks) ST638 (3 weeks)
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Angiographic Stenosis at 3 Weeks

![Graph showing stenosis comparison between Control and ST638](image)

- Control: 47% stenosis
- ST638: 25% stenosis

*P < 0.05*
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Intima / Media Ratio at 3 Weeks

![Graph showing Intima/ Media Ratio comparison between Control and ST638 with p<0.05](image)

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**IGAKI-TAMAI Coil-type PLLA Stent**

Material: PLLA  
(poly-l-lactic acid) monofilament,  
molecular mass: 183kD

Design: zigzag helical coil  
self-expanding ability (+)

Thickness: 0.17mm (0.007inch)  
Length: 12mm

Surface area: 24%

Deployment: thermal balloon  
expandable covered sheath system

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History of Studies

1. Knitted-type PGA stent in dog coronary artery: 1993
2. Knitted-type PGA stent in pig coronary artery: 1994
4. Coil-type PLLA stent in pig coronary artery: 1997
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Tranilast-eluting PLLA stent

Tranilast: 50µg, 450µg per stent
Coating thickness: 10 ~ 20 µm
(0.0004 ~ 0.0007 inch)
### Biodegradable stent

In vitro Content ratio of Tranilast $450 \, \mu g$ in a stent immersed in 37 °C Phospate—Buffered Saline (PBS)

<table>
<thead>
<tr>
<th>Time (Day)</th>
<th>Content ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>0.25</td>
<td>60.8</td>
</tr>
<tr>
<td>0.50</td>
<td>44.4</td>
</tr>
<tr>
<td>1</td>
<td>28.0</td>
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<tr>
<td>2</td>
<td>11.0</td>
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<tr>
<td>3</td>
<td>5.3</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>1.4</td>
</tr>
<tr>
<td>10</td>
<td>0.9</td>
</tr>
<tr>
<td>14</td>
<td>0.7</td>
</tr>
<tr>
<td>21</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Biodegradable stent

Residual Tranilast Amount (in vivo)

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Histopathologic Examination at 4 weeks

- Tranilast-eluting PLLA stent
  - T-50: tranilast 50 μg/stent 18 stents
  - T-450: tranilast 450 μg/stent 14 stents

- Sirolimus-analogue-eluting PLLA stent
  - A-9: biolimus A-9* 150 μg/stent 8 stents

- Non-drug-eluting PLLA stent
  - Control 13 stents

(* Biosensors)

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# Biodegradable stent

## Values for Vessel Injury Score*

<table>
<thead>
<tr>
<th>Score</th>
<th>Description of Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Internal elastic lamina intact; endothelium typically denuded; media compressed but not lacerated</td>
</tr>
<tr>
<td>1</td>
<td>Internal elastic lamina lacerated; media typically compressed but not lacerated</td>
</tr>
<tr>
<td>2</td>
<td>Internal elastic lamina lacerated; media visibly lacerated; external elastic lamina intact but compressed</td>
</tr>
<tr>
<td>3</td>
<td>External elastic lamina lacerated; typically large lacerations of media extending through the external elastic lamina; coil wires sometimes residing in adventitia</td>
</tr>
</tbody>
</table>

\[
\text{Mean injury score}^* = \frac{\text{Sum of weighs for each wire}}{\text{Number of coil wires present}}
\]

*Schwartz et al. JACC 1992;19:267-74*
Biodegradable stent

• **Inflammation Score**

  Score 0: no inflammation at each stent strut site

  Score 1: mild inflammation at each stent strut site

  Score 2: moderate inflammation at each stent strut site

  Score 3: severe inflammation at each stent strut site

• **Neointimal thickness**

• **%Neointimal area** = \( \frac{\text{stent area} - \text{lumen area}}{\text{stent area}} \)
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Drug-eluting Biodegradable Stent

Pig at 4 weeks, LCX, HE, x5

T-50

Injury Score = 0.9

Control

Injury Score = 0.8

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Drug-eluting Biodegradable Stent

Pig at 4 weeks, LAD, HE, x5

Injury Score = 2.2

T-50

Injury Score = 2.3

Control

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**Drug-eluting Biodegradable Stent**

**Pig RCA (T-450)**

Injury Score = 0.2

H.E.

E.V.G.

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Drug-eluting Biodegradable Stent

Pig LCX (T-450)

Injury Score = 1.4

H.E.

E.V.G.

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Drug-eluting Biodegradable Stent

Pig LCX (T-450)

Injury Score = 1.9

H.E.

E.V.G.

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Drug-eluting Biodegradable Stent

Pig coronary artery (A-9)

Injury Score = 0.2

H.E.  E.V.G.

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Drug-eluting Biodegradable Stent

Pig coronary artery (A-9)

Injury Score = 0.5

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**Biodegradable stent**

**Drug-eluting Biodegradable Stent**

**Pig coronary artery (A-9)**

Injury Score = 1.0

H.E.  

E.V.G.  

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A-9

T-50

T-450

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A-9

T-50

T-450

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Injury Score

- Control
- T-50
- T-450
- A-9

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Control  T-50  T-450  A-9

Neointimal Thickness

p=0.054

p=0.042

0.76

0.52  0.57  0.39

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Inflammation Score

Control
T-50
T-450
A-9

$p=0.018$

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% Neointimal area

- Control
- T-50
- T-450
- A-9

n.s.
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High-injured Group (Injury Score > 1.0)

<table>
<thead>
<tr>
<th>Injury Score</th>
<th>Control</th>
<th>T-50</th>
<th>T-450</th>
<th>Exclude A-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>n.s.</td>
</tr>
<tr>
<td>1.5</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>n.s.</td>
</tr>
<tr>
<td>1.6</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Control: 8
T-50: 8
T-450: 8
Exclude A-9: 1

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Biodegradable stent

High-injured Group (Injury Score > 1.0)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>T-50</th>
<th>T-450</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neointimal Thickness</td>
<td>1.06</td>
<td>0.65</td>
<td>0.72</td>
</tr>
</tbody>
</table>

p = 0.016

p = 0.029

Control: 8
T-50: 8
T-450: 8
Exclude A-9: 1

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**High-injured Group** (Injury Score > 1.0)

- **Control**: 8
- **T-50**: 8
- **T-450**: 8

Exclude A-9: 1

**Inflammation Score**

- Control: 2.4
- T-50: 1.6
- T-450: 2.2

*p = 0.002 for Control vs. T-50*

*p = 0.049 for Control vs. T-450*
Biodegradable stent

High-injured Group (Injury Score > 1.0)

$p = 0.019$

% Neointimal area

Control: 8
T-50: 8
T-450: 8
Exclude A-9: 1

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Conclusions

• Tranilast-eluting PLLA stents reduced neointimal hyperplasia in pig coronary arteries.
• T-50 revealed less inflammation surrounding the stent struts than T-450 and A-9.
• T-50 tranilast-eluting PLLA stent is most promising as a new drug-eluting biodegradable stent.