Off-the shelf scaffolds: the future of urethroplasty

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INTRODUCTION: Actual surgical procedures using existing autologous tissues for the treatment of congenital malformations or injuries of the urethra are associated with post-operative stenosis and fistula. Tissue engineered collagen tubes could be a promising alternative for this reconstructive surgery to overcome current post-operative complications. In our previous work, we could demonstrate the spontaneous regrowth of urothelium and ingrowth of smooth muscle cells after implantation of high-density collagen gel tubes1 in a rabbit model. Other groups claim that autologous cell therapies are the path of the future2. However, such solutions are associated with high costs, regulatory issues and added patient discomfort. If an off-the shelf solution could show a good regenerative potential, it would have a great chance of broad translation into clinics.

METHODS: We have developed two manufacturing procedures resulting in two acellular collagen tubes with enhanced mechanical properties, allowing better handling of the graft as compared to our previous collagen gel tubes1. The tubes were used as urethral grafts in New Zealand white rabbits and sutured between the native prostatic and the very distal urethra following subtotal excision of more than 80% of the total urethral length. No catheter was placed postoperatively. This procedure was applied in 40 male rabbits (20 rabbits/scaffold) in two different transplantation centers. At 1, 3, 6, and 9 months the animals were macroscopically evaluated and contrast voiding cysto-urethrography was performed. After sacrifice histological examination was done.

RESULTS:

This multi-centric study revealed from the contrast voiding cysto-urethrography that one of the produced acellular collagen tube had a 40% failure rate, while the other had a 10% failure rate, steadily decreasing during the learning curve (Table 1). Furthermore, spontaneous urothelial coverage of the grafts and time-dependent smooth muscle cell migration could be observed in all grafts.

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>No Complication</th>
<th>Fistula</th>
<th>Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scaffold 1</td>
<td>60%</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Scaffold 2</td>
<td>90%</td>
<td>10%</td>
<td>0%</td>
</tr>
</tbody>
</table>

DISCUSSION & CONCLUSIONS: Results obtained in this rabbit study show the promise of off-the shelf tubular collagen scaffolds from a surgical and regenerative perspective. Therefore, we will invest into further optimization and regulatory compliance of such scaffolds to turn them into a clinical product for future urethroplasty surgeries.


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