

Tissue engineered collagen based tubular scaffolds for urethral regeneration. A novel technology for the surgical treatment of VSD (Variation of Sex Development) patients with severe hypospadias.

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Introduction

Actual surgical procedures for the treatment of patients with VSD (Variation of Sex Development), in particular severe hypospadias, are associated with frequent post-operative complications. Tissue engineered collagen tubes are a promising alternative.

Methods:

We elaborated a new, two layered, collagen based tube that can be sutured. Mechanical testing proved a better resistance of those collagen tubes compared to our previous single layered technique. These tubes were used as urethral grafts in a rabbit model and sutured after a subtotal excision of the urethra. The graft was anastomosed between the prostatic urethra and the very distal native urethra. This subtotal urethral replacement (more than 80% of the total length) was done in 20 male New Zealand white rabbits, in Lausanne (Switzerland) and Kuala Lumpur (Malaysia). The constructs were all acellular, potentially off-the-shelf and no catheter was placed postoperatively.

1) Neutralized liquid collagen is poured into mold for tubes

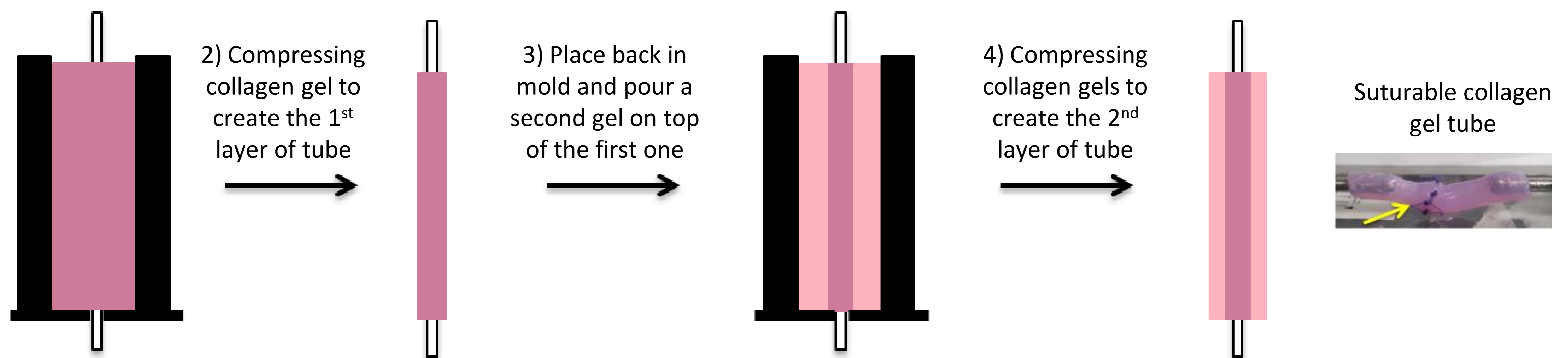


Figure 1 Double layered, double compressed collagen tube construction

Results:

- ✓ The animals were evaluated at 1, 3, 6, and 9 months by contrast voiding cysto-urethrography, histological examination and immunohistochemistry staining.
- ✓ All rabbits survived the surgical implantation.
- ✓ This multicentric study revealed spontaneous regrowth of urothelial cells (UC) and smooth muscle cells (SMC) in all grafts at 9 months and reduced severe postoperative complications.
- ✓ Stenosis (20%) and fistulae (20%) could be potentially overcome by leaving the urinary catheter after surgery.

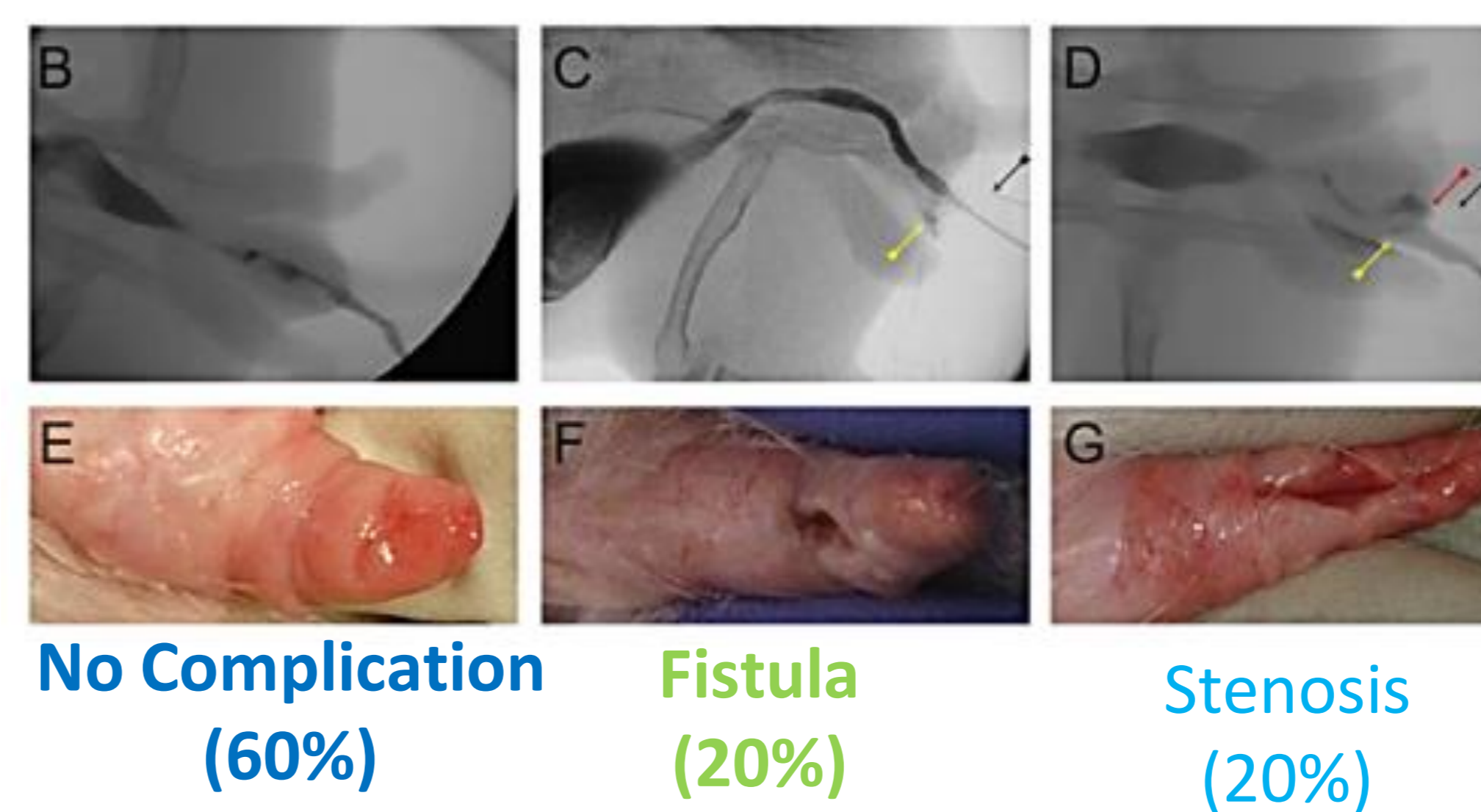


Figure 2 Contrast Voiding Cysto-Urethrography to confirm macroscopic evaluation.

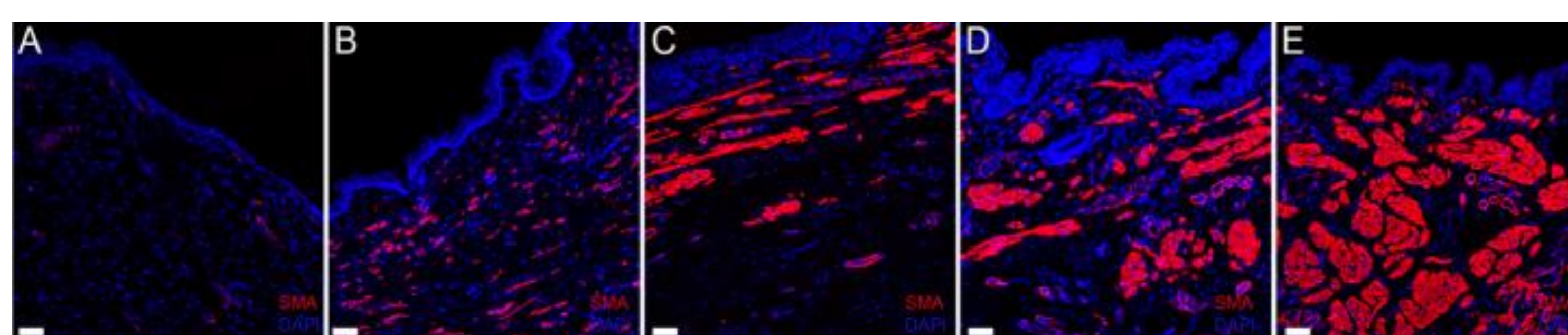


Figure 4: Immunohistochemistry staining showing Smooth muscle cells repopulating the graft at 9 month. D: operated urethra at 9 months. E: Normal urethra.

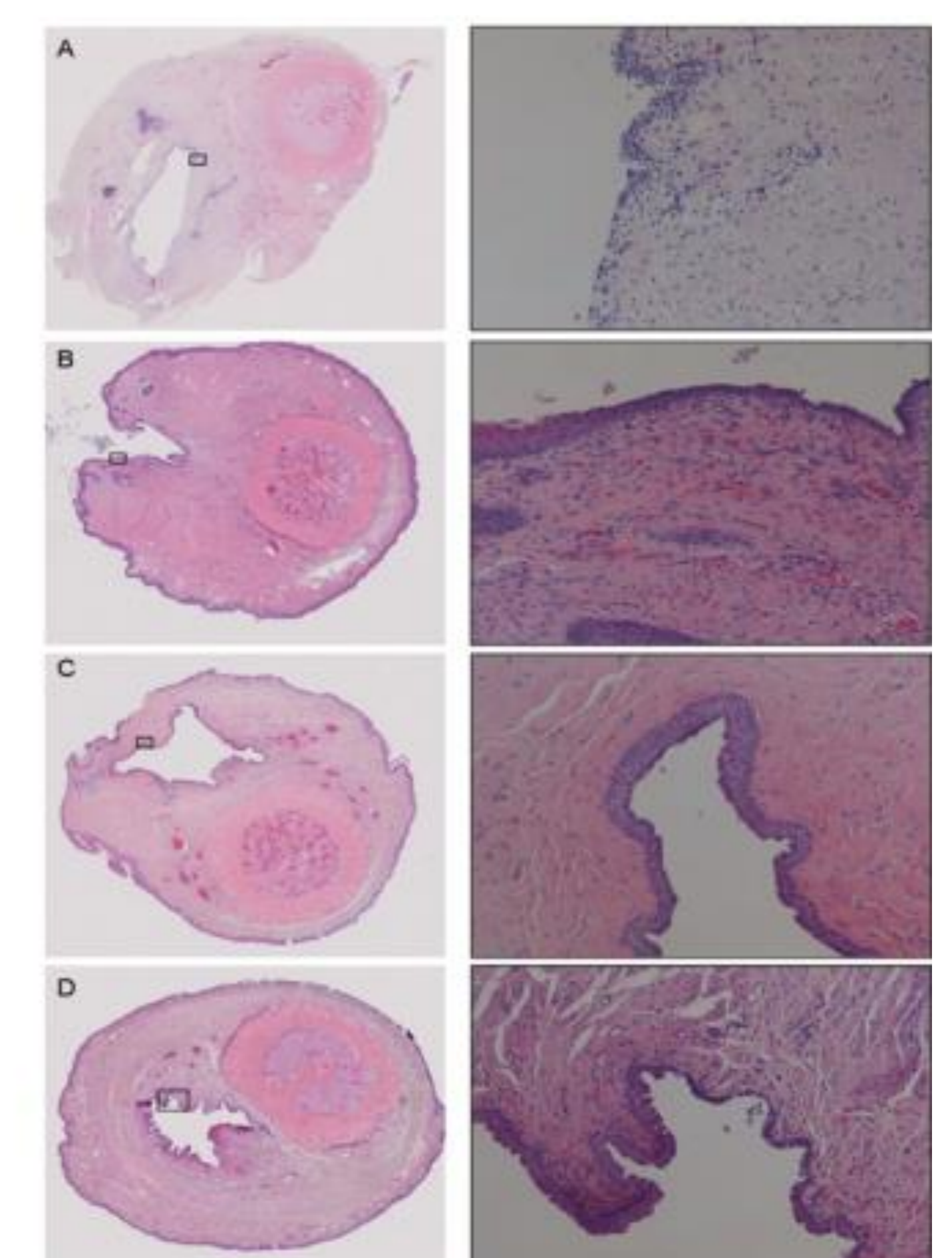


Figure 3 Histologic evaluation at 1,3,6 and 9 months. Gradual regeneration is observed with time. D: regeneration at 9 months.

Conclusion:

Those novel compressed collagen gel tubes are easy to handle, can be sutured and therefore are suitable for clinical applications. This may be an alternative to the existing surgical treatment of severe hypospadias.