Bulking agents for the treatment of urinary incontinence

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Stress urinary incontinence is a highly prevalent disorder in women and also concerns men after prostatectomy. Minimally invasive endoscopic treatment rely on the injection of bulking agents under the urethral mucosa (Fig. 1) to improve urethral closure pressure, hence continence. Among various treatment assessed, the clinical gold standard, collagen, still suffers from short-lasting efficiency implying repeated injections. Migration and occasionally granuloma formation still limit the use of microparticles (PTFE, silicon).

In a first phase, we performed a formulation screening through ex vivo cystoscopic injections in pig urethra\(^2\). Selection criteria were:

- Ability to form a tissue augmentation (bulk) comparable to collagen
- Preservation of mucosal tissues
- Syringeability through a cystoscope
- Elasticity comparable to urethral tissues

Figure 1: Endoscopic injection of a urethral bulking agent beneath the mucosal layer.

The goal of this project is to design non-degradable or slowly biodegradable bulking agents. In this view, we propose different strategies:\(^1\):

(I) In situ precipitating formulations based on preformed polymers dissolved in water-miscible organic vehicles that form an implant upon injection, either a hydrophobic foam (Ia) or a hydrophilic gel (Ib).

(II) Suspensions of biocompatible microspheres in hydrogels.

Bulking agents based on the precipitation of polylactic acid (Ia) or hydrophilic polyurethane (Ib) combined ease of injection and rapid in situ formation of a mechanically competent elastic implant. Microsphere suspensions (II) also lead to bulking effect, although with much weaker mechanical properties.

Subsequent \textit{in vivo} testing by pig vesical endoscopic injection revealed, after a 9 months period, an excellent integration of all the implants with preserved mucosal layer and absence of inflammation (Fig. 2). In contrast, no collagen bulk could be retrieved after 9 months.

Figure 2: Histological sections of vesical implant of (left, Ia) polylactic acid and (right, II) acrylic microspheres 9 month after pig implantation.

These novel injectable urethral bulking agents based on preformed, in situ precipitable polymers or biocompatible microspheres could produce the long-term tissue augmentation required for a permanent correction of urinary stress incontinence. Further work will aim at confirming \textit{in vivo} the effectiveness of these materials.

References

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