Peri-urethral Injections

13

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Abbreviations

PBA Peri-urethral bulking agent
SUI Stress urinary incontinence

Introduction

Urinary incontinence is a common and distressing problem with an overall prevalence of 15 % that rises steadily in later life [46]. Given the aging population, it is likely that the estimated 103,000 surgical procedures currently performed annually for the treatment of stress urinary incontinence (SUI) in the USA will increase [47, 62]. Several minimally invasive surgical options have been developed over the last several decades in an attempt to provide a safe and efficacious method for the surgical treatment of SUI. One such minimally invasive treatment is the injection of peri-urethral bulking agents (PBA). This chapter discusses the history of PBA, indications and contraindications for their use, injection techniques, success, and complication data for the currently available peri-urethral bulking procedures.

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Mechanism of Action

Urethral coaptation at rest is provided by the urethral mucosa, submucosal vascular cushions, and smooth muscle elements. Submucosal bulking agents are believed to act by creating artificial urethral cushions that can improve urethral coaptation, resulting in urinary continence [31]. In a small study investigating the mechanism of action of bulking agents, Klarskov et al. injected 15 subjects with polyacrylamide gel and measured change in opening urethral pressure by urethral pressure reflexometry [30] 100 days postinjection. He noted that patients who exhibited improvement in their stress incontinence symptoms had significantly higher squeezing opening pressure than the group without an effect. From this data, he concluded that certain agents may increase the strength of the sphincter by providing a central filler that increases the length of muscle fibers and the power of the urethral sphincter.

Ideal Bulking Agent

Many experts who perform urethral bulking believe that the ideal urethral bulking agent is one that is non-immunogenic and biocompatible, creating minimal inflammatory and fibrotic response. The bulking agent's particle size needs to be a sufficient size to prevent migration from the injection site. Migration is thought to occur due to macrophage phagocytosis of

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particles smaller than 80 μm; an agent that is >110 μm avoids macrophage phagocytosis and migration [42, 55]. Ideally, one should also utilize a low pressure injection system to prevent vascular introduction of the bulking agent.

History

Since 1938, a variety of materials have been injected into and around the urethra to treat SUI. Murless was the first to discuss the use of the sclerosing agent sodium morrhuate into the anterior vaginal wall and around the urethra [45]. In 1955, Quackels used paraffin wax in the perineum [51]. In 1973, Berg described injecting polytetrafluoroethylene paste (Poltef™), produced by the pyrolysis of Teflon™, into the urethral sphincter [8]. This was further popularized by Politano in 1974, and these treatments initially showed promise as simple, minimally invasive treatments for SUI [50]. The paucity of long-term outcome data for polytetrafluoroethylene and the reports of adverse events associated with local extrusion and distant particle migration to the liver, lung, and spleen minimized the support for and popularity of the procedure [42]. Gonzales de Garibay et al. described the use of autologous fat as a PBA in 1989 [19]. Although economical and readily available, subsequent studies have shown that there can be issues with injecting the agent into the correct location, rare complications with pulmonary fat embolus, and the long-term outcomes of fat as a PBA are poor [36].

Peri-urethral injections of cross-linked bovine collagen came to prominence in the 1990s after the successful use of collagen for cosmetic surgery and the treatment of vesicoureteric reflux were described [24]. Since the 1990s, use of glutaraldehyde cross-linked (GAX) bovine collagen (marketed as Contigen, C.R. Bard, Inc., Covington, GA) as a PBA gained universal acceptance. Immediate and delayed hypersensitivity to cross-linked bovine collagen necessitated skin testing several weeks prior to injection. Although considered to have a relatively low risk profile, more serious complications, such as osteitis pubis, arthralgias, and pulmonary embolism (resulting from intravascular injection), have been reported. The manufacturing of collagen by its parent company, however, ceased in 2011, and it is no longer available as a bulking agent. When compared with retropubic colposuspension, pubovaginal sling, and synthetic midurethral sling, urethral bulking with collagen has had less long-term success [1, 13, 52]. This has prompted the search for and development of newer agents.

Another synthetic agent, ethylene vinyl alcohol copolymer (marketed initially as Uryx and then later as Tegress, CR Bard, Covington, Georgia), was initially FDA approved in 2004 and found to have better long-term success than collagen in trials for FDA approval. This product, however, was found to be associated with high rates of urethral and vaginal extrusion and, consequently, was discontinued in 2007 [17, 28]. Another agent that had been used for pediatric vesicoureteral reflux, a combination of hydrophilic dextran polymer in a non-animal stabilized hyaluronic acid vehicle (Ziudex™) underwent initial FDA trials in the USA in 2003 and 2006, but was not FDA approved due to the high incidence (10–15 %) of pseudo-abscess [39, 40].

The PBA that are currently available in the USA for the treatment of SUI are carbon-coated zirconium oxide beads suspended in a water-based gel (Durasphere EXP®, Coloplast, Inc., Minneapolis, MN), calcium hydroxylapatite (Coaptite®, Boston Scientific Corp., Natick, MA), and silicon microimplants (Macroplastique®, Uroplasty, Inc., Minnetonka, MN), and were FDA approved for use in peri-urethral bulking in 1999, 2005, and 2006, respectively. Other agents that are still being studied for use as PBA are autologous cartilage [6, 7], human collagen [61], autologous primary myoblasts [54], and autologous muscle-derived stem cells [11].

Currently Used Bulking Agents: Success and Complications

Although the production of cross-linked bovine collagen was discontinued in 2011, most

comparative studies of newer bulking agents use bovine collagen as the control bulking agent. The 2012 Cochrane Review on urethral injection therapy for SUI in women identified 14 trials including 2004 women that met inclusion for analysis [29]. The included trials were small, moderate quality, with limited long-term follow-up data and found to be unsuitable for meta-analysis. Their conclusions stated that currently available evidence remains insufficient to guide practice. The summary of the Cochrane Review follows.

One randomized trial compared peri-urethral injection (Macroplastique) agents to home-based pelvic floor exercises. At 3 months of follow-up, the group receiving the peri-urethral injections showed greater subjective "cure" or "marked improvement" 62.5 % versus 19 %, $p = .002$) [60]. The two trials comparing injectable agents with surgical interventions [Macroplastique versus pubovaginal sling [41]; collagen versus open Burch, open sling, open bladder neck suspension [13] found significantly better objective cure in the surgical groups.

Finally, only three trials included in the Cochrane Review compared routes of bulking agent injection [33, 40, 53]. The trial by Lightner looked at midurethral versus proximal urethral injection but utilized different bulking agents at each site; therefore, a comparison of outcomes was confounded by this variable [40]. Schulz et al. compared peri-urethral and transurethral methods of collagen injection and noted that both methods had similar subjective and objective outcomes at 1, 3, 6, and 12 months, but showed a higher rate of early postprocedural urinary retention in the peri-urethral injection group (30 % versus 5 %, $p < .05$) [53]. Kuhn et al. [33] found that midurethral and bladder neck injection seems to result in similar postprocedural continence levels.

The eight trials included in the Cochrane Review that compared different agents had wide confidence intervals. Overall, the currently available bulking agents were not shown to be more or less efficacious than collagen [29]. The efficacy and complication outcomes of pertinent trials included in the Cochrane Review are discussed in the sections that follow.

Carbon Beads (Durasphere, Durasphere EXP)

Durasphere, pyrolytic carbon-coated zirconium oxide beads, is suspended in an absorbable 2.8 % glycan polysaccharide carrier gel. Prior to its use in urethral bulking, this material had been used in several medical devices, such as replacement heart valves [4]. This material is radio-opaque and can be identified in radiographs and appears as dense as cortical bone on CT [49, 10]. On MRI, it appears hypodense on T1 and T2 weighted images and fails to enhance after gadolinium [10]. The initial carbon bead product (Durasphere) was found to be difficult to inject due to a large particle size of 200–550 μm, which resulted in injection needle obstruction. Consequently, a newer version of the product was developed, utilizing particles of 95–200 μm (Durasphere EXP®, Coloplast, Inc., Minneapolis, MN). Durasphere EXP is the only form of Durasphere available in the USA market and is the only currently available bulking material that is FDA approved for either transurethral or peri-urethral injection. Additionally, this is the only available bulking material that is not contraindicated for patients with a "fragile urethra," due to past radiation or past urethral surgery.

In a multicenter, double-blind randomized controlled trial of transurethral bladder neck injection of Durasphere compared with bovine collagen for treatment of intrinsic sphincter deficiency (aLPP <90 cm H_2O), Lightner et al. [38] found the two materials to be equivalent with respect to postprocedure continence grade and pad weight testing, with 66.1 % (76/115) in the Durasphere group and 65.8 % (79/120) in the bovine collagen group, reporting improvement in one or more Stamey continence grades ($p = 1.00$) (Table 13.1). A smaller volume of Durasphere was needed to obtain comparable clinical results (4.83 mL versus 6.23 mL, $p < .001$). Side effects of the agents were similar, but there was a higher incidence of postprocedure urinary urgency and acute retention in the Durasphere group (24.7 % and 16.9 %, respectively) compared with the bovine collagen

Table 13.1 Success outcomes for bulking agents from randomized controlled trials (RCT)[a]

Agent (author)	RCT design (*N*)	Follow-up (years)	Volume injected (mL)[b]	Dry/improved[c]	Subjects requiring multiple treatments
Durasphere [38]	Multicenter				
	Agent (176)	1	Agent: 4.83****	–/66 %	35 %
	Control (188)		Control: 6.23****	–/66 %	36 %
Durasphere [3]	Agent (25)	2.6	Agent: 4.5	40 %/80 %	
	Control (21)	2.8	Control: 4.2	14 %/62 %	
Coaptite [43]	Multicenter				
	Agent (131)	1	Agent: 2.15****	39 %/63.4 %	62 %†
	Control (100)		Control: 3.39****	37 %/57 %	74 %†
Macroplastique [20]	Multicenter				
	Agent (122)	1	Agent: 4.6	37 %†/62 %****	52 %
	Control (125)		Control: 4.6	25 %†/48 %****	58 %

[a]Comparison in all trials was transurethral bovine collagen
[b]Volume injected: mean volume of bulking agent injected at initial bulking treatment session
[c]Dry: Stamey grade 0 [4 level scale, with range from 0 = continent-dry to 3 = total incontinence regardless of activity [57]]
Improved: improvement of ≥1 Stamey Urinary Incontinence Scale grade
$^{****}p < .001$ $^{\dagger}p < .05$

group (11.9 % and 3.4 %, respectively, $p = .001$). At 12 months of follow-up, urinary urgency resolved in a greater proportion of the Durasphere subjects (90 %) compared with the bovine collagen subjects (65 %, $p = .021$). Retention in all subjects resolved in 7 days following the procedure.

In a randomized, controlled, double-blind trial comparing Durasphere to bovine collagen, Andersen [3] found there was no difference in the percentage of patients with an improvement of one or more Stamey Continence Grades between the Durasphere group (80 %) and the bovine collagen group (61.9 %, $p = .205$) at an average of 2.6 and 2.8 years of follow-up, respectively (Table 13.1). At this long-term follow-up, 40 % (10/25) of the Durasphere subjects and 14.3 % (3/21) of the bovine collagen subjects reported that they were dry ($p = .099$). Complications rates were not reported in this trial.

Although Lighter et al. reported on radiologic stability of Durasphere, with no evidence of spread beyond local confines of the pelvis at 1- and 2-year follow-up [38], there have been reports of local migration into areas lateral to the urethra and along regional lymphatic chains [49]. Foreign body reactions with associated urethral prolapse and delayed presentation of a pseudoabscess 5 years postprocedure have been reported [9].

Calcium Hydroxylapatite (Coaptite)

Coaptite is composed of spherical calcium hydroxylapatite particles, ranging from 75 to 125 mm in diameter, in a carboxymethylcellulose gel carrier [16, 43]. The gel carrier degrades over several months, and the patient's fibroblasts infiltrate amongst the particles. Calcium hydroxylapatite is a constituent of human bone and teeth and has been used for 25 years in dental and orthopedic procedures [44]. It is radiopaque and can be easily identified with plain film radiography and ultrasound after injection [16]. Calcium hydroxylapatite is neither immunogenic nor inflammatory and remains pliable after injection into soft tissues, lending itself to use in augmentation of the vocal cords and facial structures [5, 37]. Initial studies of its endoscopic use in the treatment of vesicoureteral reflux in pediatric subjects have shown it to be both durable and efficacious [44].

In a multicenter, prospective, randomized, single-blind trial of 296 women with SUI

secondary to intrinsic sphincter deficiency, subjective improvement in urinary incontinence symptoms, as graded by the Stamey Urinary Incontinence Scale, were similar at 12-month follow-up for patients who received Coaptite compared to those who received bovine collagen (63.4 % versus 57 %, respectively, $p = 0.34$) ([43], Table 13.1). The cure rate (Stamey grade 0) at 12 months was also similar for both groups (39 % for Coaptite versus 37 % for Contigen, $p = 0.34$). A greater number of patients receiving Coaptite injections required only one injection over the first 6 months of the study (38.0 % versus 26.1 %, $p = 0.034$); however, most subjects required two to three injections in either group. There was no difference in the percentage of patients with transient urinary retention (41 % Coaptite versus 33 % bovine collagen), and there was less postprocedural urge incontinence in the Coaptite group (5.7 % versus 12 %, $p < .05$). There was one vaginal wall erosion in the Coaptite group, and one patient with dissection of the Coaptite beneath the trigonal mucosa, resulting in difficulty with visualization of one ureteral orifice cystoscopically. This patient, however, had no abnormal lab or radiographic abnormalities and had no urinary incontinence.

Serious adverse events related to Coaptite are rare. Palma et al. reported on a patient presenting with a 3 cm urethral prolapse containing macrophages surrounding the Coaptite particles 3 months after initial peri-urethral bulking with a total of 2.5 mL of Coaptite [48]. Coaptite has also been used in the pediatric population for vesicoureteral reflux and has been found to be quite safe in multicenter prospective trials [44].

Silicone (Macroplastique)

Macroplastique, a hydrogel-suspended cross-linked polydimethyl-siloxane elastomer, has been approved by the FDA as a urethral bulking agent since 2006 for the treatment of SUI secondary to intrinsic sphincter deficiency [37]. This bulking agent is composed of relatively large silicone particles measuring 100 μm to 450 μm in diameter (mean diameter approximately 180 μm) suspended in a non-silicone carrier gel that is excreted unchanged in the urine [16, 25, 56]. The silicone particles quickly become encapsulated in fibrin with minimal inflammation [16, 26]. Studies of this material in rat and canine models show that Macroplastique is not readily phagocytized by macrophages, and fibroblasts do not readily adhere to Macroplastique [56].

In a multicenter, randomized, controlled trial comparing transurethral Macroplastique to bovine collagen for treatment of intrinsic sphincter deficiency, a greater proportion 61.5 % (75/122) of the patients receiving Macroplastique had an improvement of at least one Stamey Grade compared with 48 % (60/125) receiving bovine collagen ($p < .001$) at 12-month follow-up [20]. Additionally, a greater proportion of the patients receiving Macroplastique were dry (Stamey grade 0) compared with those receiving bovine collagen (36.9 % versus 24.8 %, $p < .05$). The total number of subjects who underwent two treatments in the 12-month follow-up was the same for both groups (Macroplastique 52.5 % and bovine collagen 58.4 %, $p = .35$), and the treatment volumes were not significantly different between the Macroplastique and bovine collagen groups. Additionally, Incontinence Quality of Life scores (I-QOL) improved in a similar magnitude from baseline between the Macroplastique and bovine collagen groups. Overall, adverse effects were similar between the two treatment groups (59 % and 54.5 %) with urinary tract infection (23.8 % versus 24.8 %), dysuria (9 % versus 8 %), urgency (9 % versus 7.2 %), frequency (8.2 % versus 9.6 %), and urinary retention (6.6 % versus 3.2 %) being the most frequently reported in the Macroplastique and bovine collagen groups, respectively. Only one serious adverse event (pyelonephritis) was reported in the bovine collagen group.

Ghoniem et al. reported 2-year follow-up data on the above cohort of patients who had received Macroplastique [21]. Of the 67 patients included in this 2-year follow-up, 67 % were dry (Stamey grade 0). Of the 38 patients who were dry at 12 months, 33 (87 %) of these remained dry at

2 years. Overall and subscale I-QOL scores at 24 months were also improved significantly over baseline for the 2-year follow-up group ($p < .001$). The conclusions from this ancillary study are limited, as they only followed the Macroplastique patients for the additional 1 year, and only reported on 55 % (67/122) of the original Macroplastique cohort.

Bulking Procedure

Patient Characteristics, Indications, and Contraindications

In general, most patients are thought to be ideal candidates for urethral bulking if they have SUI associated with intrinsic sphincter deficiency, defined as a valsalva leak point pressure (VLPP) <60 cm H_2O or maximum urethral closure pressure <20–25 cm H_2O, with at least 150 mL bladder fill, and an immobile urethra. There is evidence, however, that bulking agents are effective in cases of SUI associated with higher VLPP or in cases where SUI occurs with bladder neck hypermobility [6, 7, 58]. Currently, Medicare requires a LPP $\leq$ 100 cm H_2O for procedural coverage. Other patients for whom bulking agents are considered are those who are medically compromised and cannot undergo a midurethral sling or have failed a prior surgery for stress incontinence [18, 32, 35]. In general, patients who are not considered to be optimal candidates for urethral bulking are those with urinary tract infections, urethral diverticula, poor urethral blood supply, high baseline post void residual urine volumes, severe detrusor overactivity, and reduced bladder capacity (<250 mL).

Necessary Equipment

The exact equipment required for a bulking procedure varies according to which agent you are utilizing for the procedure. In general, one needs a sterile prep solution for the vagina and peri-urethral tissues, 2 % lidocaine hydrochloride jelly (Uro-jet), 1 % lidocaine for peri-urethral blockade (if desired), sterile water, irrigation tubing with stopcock, camera, light cord, and cystoscopy tower. The type and size of endoscope utilized for peri-urethral bulking varies according to the bulking product.

Procedural Overview

The patient has a urinalysis upon arrival on the day of the procedure to assure there is no underlying urinary tract infection, and the procedure is cancelled if urinalysis suggests an existing urinary tract infection. According to the 2013 American Urological Association (AUA) Guidelines for urologic surgery antimicrobial prophylaxis, a prophylactic antibiotic (either a fluoroquinolone or trimethoprim-sulfamethoxazole) is given (http://www.auanet.org/common/pdf/education/clinical-guidance/Antimicrobial-Prophylaxis-PocketTable.pdf) [2]. Alternative antimicrobials include an aminoglycoside with ampicillin, first or second generation cephalosporin, or amoxicillin/clavulanate.

After informed consent and procedural time out are performed, the patient is placed in the dorsal lithotomy position, and betadine is used to perform a sterile preparation of the peri-urethral region and perineum. Local anesthetic, typically one 2 % lidocaine Uro-jet, is administered to the urethral lumen. Onset of anesthesia is typically 3–5 min. Additionally, a peri-urethral blockade with injectable local anesthetic, such as 1 % lidocaine, can be preformed. If this is done, injection at 3–4 o'clock and 8–9 o'clock is recommended, with approximately 4 mL of lidocaine used on each side [12].

Using a 30° operative cystoscope (lens degree can vary), the bulking agent is injected into the submucosa at two or more sites at the same level of the proximal urethra. Bulking agents can be injected just distal to the bladder neck or at the midurethra, although there is little data to support either approach. The efficacy of midurethral and bladder neck placement of urethral bulking agents has been compared in a small ($N = 30$), randomized study utilizing

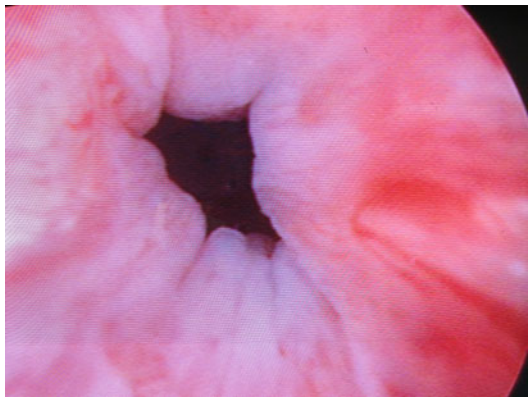

Fig. 13.1 Urethra prior to urethral bulking (Image courtesy of Drs. Mark Walters and Cecile Unger)

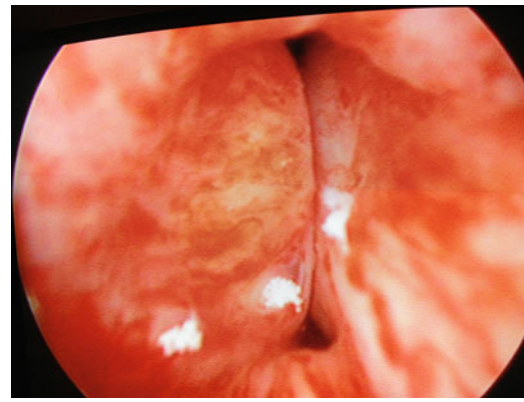

Fig. 13.2 Urethral coaptation after urethral bulking (Image courtesy of Drs. Mark Walters and Cecile Unger)

transurethral collagen [33]. At 10 months postoperatively, patients' satisfaction on a visual analog scale did not significantly differ, and the proportion with negative cough stress tests did not differ between the bladder neck and midurethral groups (60 % versus 66 %, respectively). Bulking agents can also be injected periurethrally through the perineum, while viewing the bulking effect simultaneously with a cystoscope. The procedure for peri-urethral injections is discussed in the Procedural section for Durasphere EXP below. Most clinicians, however, seem to feel more comfortable with transurethral injections.

After the clinician has delivered what is perceived to be an adequate volume of the bulking material so that the urethral lumen coapts (Figs. 13.1 and 13.2), the patient is asked to cough. If transurethral urine loss is witnessed, additional bulking material may be administered. Once the bulking procedure is finished, the patient is asked to void. If she cannot void spontaneously, intermittent self-catheterization with a small diameter (8–12 French) catheter is taught. Clinicians may also prefer to teach intermittent self-catheterization prior to the procedure. Patients are typically given home-going instructions and precautions by the nursing staff and treating physician. Follow-up is typically arranged at 1–3 months, and patients are encouraged to call with any concerns.

Tips and Tricks for Specific Bulking Agents

Each urethral bulking agent and injection system has its own unique features and challenges. Please refer to Table 13.2 for a summary of currently available bulking agents and their corresponding supplies. The following text summarizes instructions pertinent to each specific agent.

Durasphere (Durasphere EXP® Office Procedure Guide) [15]

Transurethral Injection

Preparation

- Hold needle by its wings, and align the arrow on the 1 mL syringe tip with the dark bar located on the needle hub
- Turn the syringe to connect the needle to the hub
- Move the hand on the syringe back to finish tightening the syringe to the needle with a 360° rotation, until the arrow is aligned with the dark bar located on the needle
- Prime the needle

Needle Placement

- Chose a position between 4 and 8 o'clock
- At the level of the midurethra, position the needle bevel toward the urethral lumen
- Puncture the tissue at a 45° angle, do not insert past the needle bevel

Table 13.2 Currently FDA-approved agents for peri-urethral bulking

Bulking agent (FDA approval)	Trade name (manufacturer)	Gauge needle	Syringe for agent	Injection locations (typical total volume)
Glutaraldehyde cross-linked bovine collagen (1993)	Contigen™ (Bard, Inc.)[a]	22–23 g	2.5 mL	(2.5–5 mL)
Pyrolytic carbon coated graphite beads (carbon) (1999)	Durasphere EXP™ (Coloplast, Inc.)	Transurethral 18/20 g 15 in. Peri-urethral 18/20 g 1.5 in.	Transurethral 1.0 mL Peri-urethral 3.0 mL	Between 4 o'clock 8 o'clock At 3 and 9 o'clock (2–4 mL)
Calcium hydroxylapatite (CaHA) (2005)	Coaptite™ (Boston Scientific)	21 g[b]	1.0 mL	4 o'clock 8 o'clock (2–4 mL)
Polydimethylsiloxane particles (silicone) (2006)	Macroplastique™ (Uroplasty)	18/20 g	2.5 mL	6 o'clock 2 o'clock[c] 10 o'clock[c] (5.5 mL)

[a]Production of Contigen ceased in 2011
[b]End injection and Sidekick needle available
[c]May deliver 1.25 mL rather than 2.5 mL at these locations

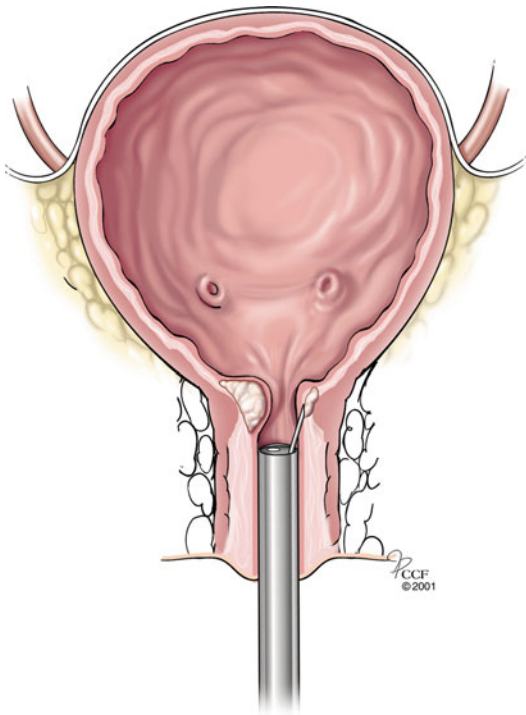

Fig. 13.3 Transurethral injection of bulking agent

- Re-angle the scope to an orientation parallel to the urethra (Fig. 13.3)
- Tunnel the needle toward the bladder neck for 1–2 cm, using needle markings as a guide

Injection

- Use consistent, moderate thumb pressure on the plunger to inject evenly
- The submucosa should distend toward the urethral lumen
- You can also rotate the orientation of the needle bevel superiorly and inferiorly, to facilitate flow of the agent
- Choose an opposing site for the second injection, and repeat the above procedures until the bladder neck coapts
- Most procedures will require 4 or more 1 mL syringes of the bulking agent

Peri-urethral Injection

Preparation

- Attach the 1.5 in., bent pencil point tip needle to a 3 mL syringe filled with sterile saline
- The needle has a 15° bend to facilitate submucosal injection between the lamina propria and the muscularis

Needle Placement

- Insert the 30° cystoscope into the urethra, with the scope lens oriented toward the side of the urethra where the injection is planned
- Note the two peri-urethral dimples at 3 and 9 o'clock
- Position the needle tip at the dimple with the needle hub parallel to the scope. The proximal

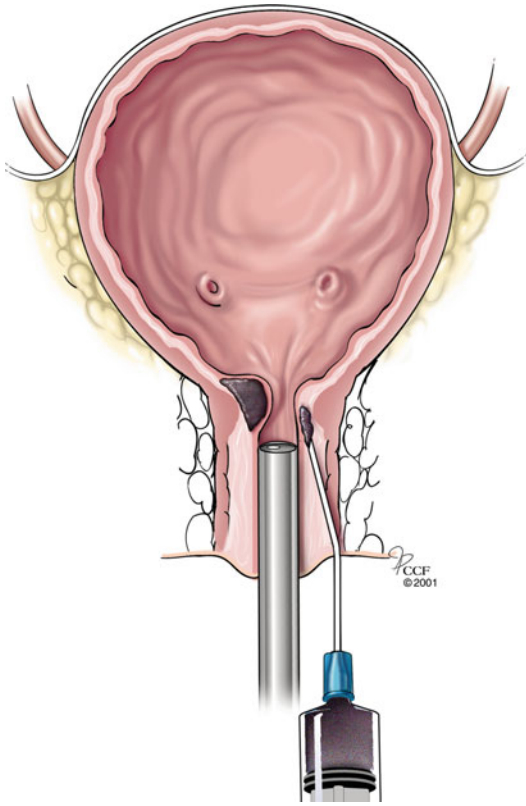

Fig. 13.4 Peri-urethral injection of bulking agent

Fig. 13.5 Sidekick needle used for Coaptite (Images courtesy of Boston Scientific Corporation. Opinions expressed are those of the author alone and not Boston Scientific)

Fig. 13.6 End injection needle used for Coaptite (Images courtesy of Boston Scientific Corporation. Opinions expressed are those of the author alone and not Boston Scientific)

half of the needle will be angled away from the scope
- Penetrate the tissue and continue to advance the needle approximately 3 cm, keeping the needle hub parallel with the scope. Once advanced, the needle tip should be in the proximal urethra (Fig. 13.4)
- Verify needle tip placement in the submucosal plane gently wiggling the distal hub of the needle while looking through the cystoscope
- To assure correct needle placement, hydrodissect by injecting some fluid into the site. Temporary bulking of the tissue should occur if the needle is in the correct location. If no bulking occurs, reposition the needle more superficially

Injection
- Attach the 3 mL syringe containing the bulking agent to the needle
- Inject with slow, consistent pressure while observing the bulking effect
- If circumferential distribution of the material is occurring, keep injecting until complete coaptation is achieved
- If the product is not flowing circumferentially, continue to inject into the site until the bulge has crossed the urethral midline, then reposition the needle on the opposite side and continue the injection protocol, as above
- Most procedures require at least 4 mL of bulking agent

Coaptite (Coaptite® Injectable Implant Procedure Guide) [14]

Preparation
- Choose either the Sidekick (Fig. 13.5) or End injection (Fig. 13.6) needle

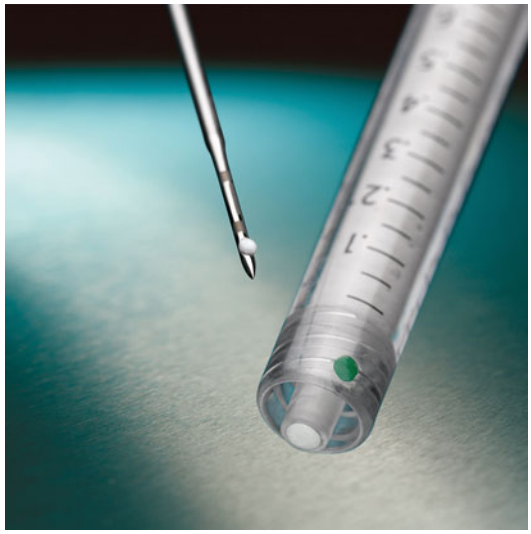

Fig. 13.7 Coaptite needle is attached to the injection syringe by aligning the green dot and securing it with 1.5 turns (Images courtesy of Boston Scientific Corporation. Opinions expressed are those of the author alone and not Boston Scientific)

- When connecting 1 mL syringe to needle, make sure that you line up the green dot on the syringe to the green circular hole on the needle hub (Fig. 13.7)
- Then, turn syringe to screw it onto needle hub (about one-and-a-half times) (Fig. 13.7)
- It should feel tight, you will probably hear a click or two, and you will see one of the green dots now through the circular hole on the needle hub
- When priming, the bulking agent should flow easily
- After priming, insert primed needle into the scope

Needle Placement
- At the midurethra, insert needle at 4 o'clock position into tissue at a 45° angle with the open bevel facing toward the urethral lumen until you get to the first black marking
- Adjust needle parallel to urethral lumen and advance needle somewhere between the first and second black marking, approximately 1 cm toward bladder neck

Injection
- Slowly inject
- If you feel resistance, resist pushing through it, as the aqueous carrier will only be placed
- Pull back on needle and/or rotate needle slightly to adjust placement where the bulking material flows easily (Fig. 13.3)
- After injection to a particular site is concluded, slowly remove needle part way
- When you start to see the first black marking coming out of the injection site, pause for a few seconds (~10) before removing it completely
- This will help limit any extravasation
- Repeat injection a 8 o'clock position

Macroplastique (Macroplastique® Procedure Guide) [63]

Preparation
- Slide adapter over syringe (Fig. 13.8)
- Lock adapter onto administration device (Fig. 13.9)
- Remove plastic cap from syringe containing product
- Attach winged needle hub and turn 2–2.5 times to tighten needle onto syringe (Figs. 13.10 and 13.11)
- Remove plastic needle sheath
- Prime needle by squeezing lever of administration device (Fig. 13.12)
- When product flows from needle tip, depress release mechanism to stop flow

Needle Placement
- Use the black needle hash marks to guide the depth of the needle prior to releasing the bulking agent.
- Tilt the scope at a 30–40° angle in relation to the urethral lumen to advance the needle into the tissue to level of the first mark on the needle at the 6 o'clock position on the urethra.
- Once the first mark is passed, reduce the needle angle to close to 0° to the urethral lumen and advance the needle to the second hash mark.
- The bulking agent should then be released in the midurethra.

Fig. 13.8 Sliding metal adapter over syringe containing Macroplastique (Images courtesy of ©Uroplasty, Inc. All rights reserved)

Fig. 13.9 Locking adapter onto administration device for Macroplastique (Images courtesy of ©Uroplasty, Inc. All rights reserved)

- If the patient has a short urethra, the site will be just passing the first hash mark on the needle.
- The black arrows on the needle indicate needle bevel and orientation. The needle bevel should face toward the urethral lumen when injecting.

Injection

- Allow 1.5 min to release the entire 2.5 mL syringe at the 6 o'clock position, and use a slow, consistent injecting technique.
- If you do not see an immediate bleb, you are likely too deep and need to pull needle back slightly.
- Once the agent is injected, wait 30 s before withdrawing the needle.
- If you see product extruding at the incision site, you are either injecting too quickly or you didn't tunnel the needle far enough into the tissue.
- The administration device rotates 360° for precise placement.
- Typically administer 1.25 mL of the agent at 10 and 2 o'clock after injecting at the 6 o'clock position.

Short- and Long-Term Complications

Most complications related to urethral bulking agents are urinary tract infections (10–25 %), transient urinary retention (3–40 %), dysuria (8–10 %), urinary urgency (7–11 %), and localized pain [20, 38, 43]. Rates specific to each agent are discussed in the above sections. More rare localized complications, such as urethral erosions [27, 28], sterile abscess [9, 59], urethral abscess [23], urethral prolapse [22, 48], and urethral diverticulum [34], have been reported. In addition, complications due to distant particle migration, such as pulmonary embolus [59] and deposition in local and distant lymph nodes and organs [49], have been reported. Bovine collagen causes a systemic immunogenic response in 2–5 % of patients.

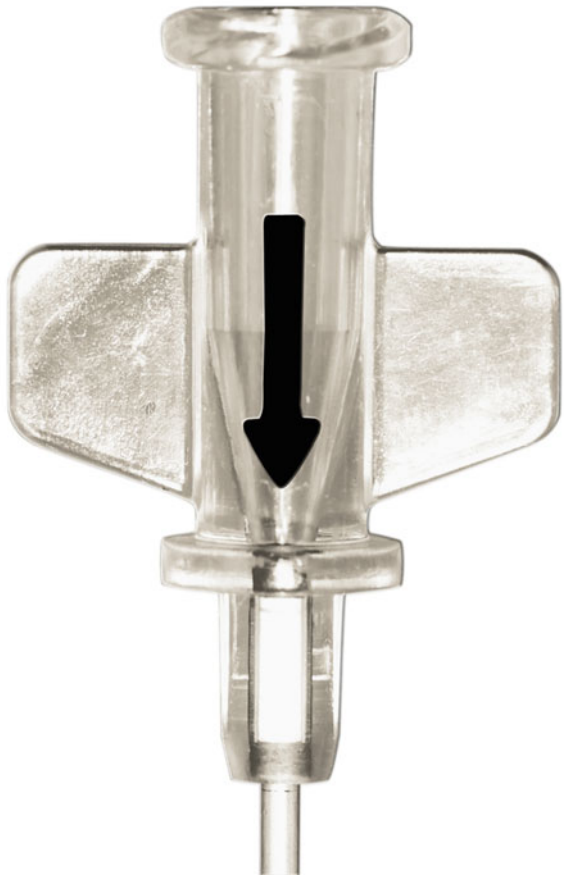

Fig. 13.10 Use of wings to attach needle to syringe containing Macroplastique (Images courtesy of ©Uroplasty, Inc. All rights reserved)

Fig. 13.11 Attaching winged needle hub and syringe of Macroplastique (Images courtesy of ©Uroplasty, Inc. All rights reserved)

Fig. 13.12 Priming needle by squeezing the level of the administration device (Images courtesy of ©Uroplasty, Inc. All rights reserved)

Conclusions

Despite their variable short- and long-term success rates, PBA are a viable treatment option for SUI. Although many agents have not stood the test of time, prospective, randomized trials of the three currently available bulking agents in the USA offer hopeful data concerning improvement in continence at 1–2 years. Overall, these agents are well tolerated in women of various ages, varying comorbid conditions, and varying histories of past continence surgeries.

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