Anal Injectable and Implantable Bulking Agents for Faecal Incontinence

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Faecal Incontinence

- Can have an adverse effect on quality of life
- Can cause severe social restriction
- Is a stigmatising condition
- Significant cost to the NHS

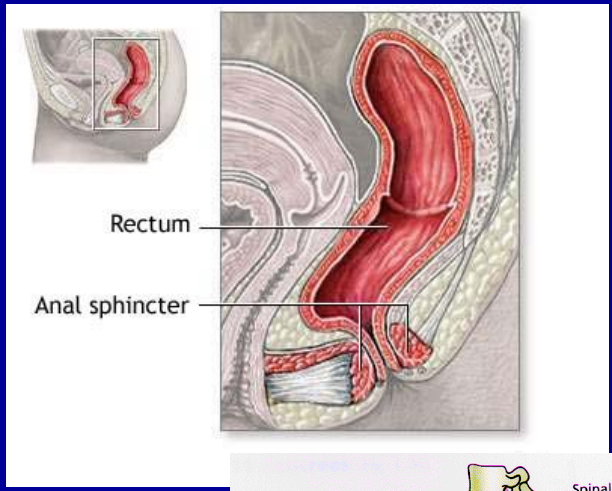
Factors affecting Continence

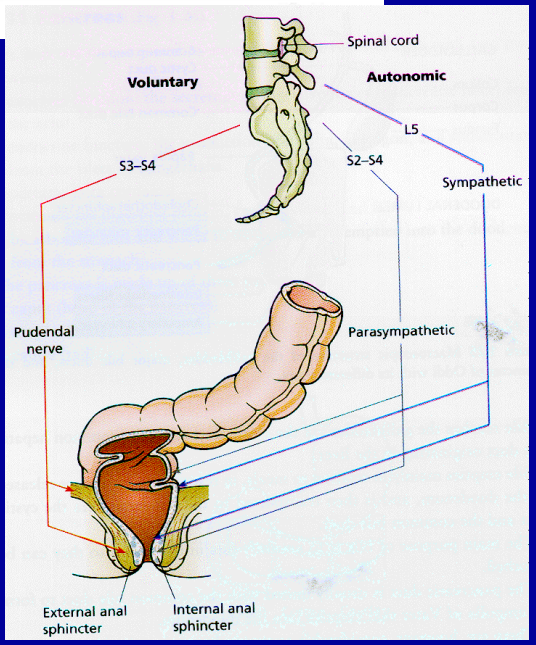
Continence depends on a number of inter-related factors:

- Cognitive ability and physical mobility
- Sphincter muscles (IAS, EAS, Puborectalis)
- Innervation (somatic and autonomic)
- Anorectal sensation – sampling reflex (RAIR)
- Rectal reservoir – capacity and compliance
- Normal stool volume and consistency

Any impairment of these elements may result in faecal incontinence

Classic 'barrier-centric' theory vs 'rectal-centric' theory proposed by Knowles





Surgical Treatment

- Only if conservative measures (eg. physiotherapy, anal plugs, irrigation, biofeedback) fail

- Spectrum of interventions – from the simple to the very complex

Surgical Options

1. Restoration and improvement of residual sphincter function
a. Correcting a defective EAS- Sphincteroplasty
b. Correcting a defective pelvic floor- Levatorplasty, Postanal repair, Total PFR
c. Correction of Anorectal Deformities
d. Sacral Nerve Stimulation (SNS)
e. Posterior Tibial Nerve Stimulation (PTNS)

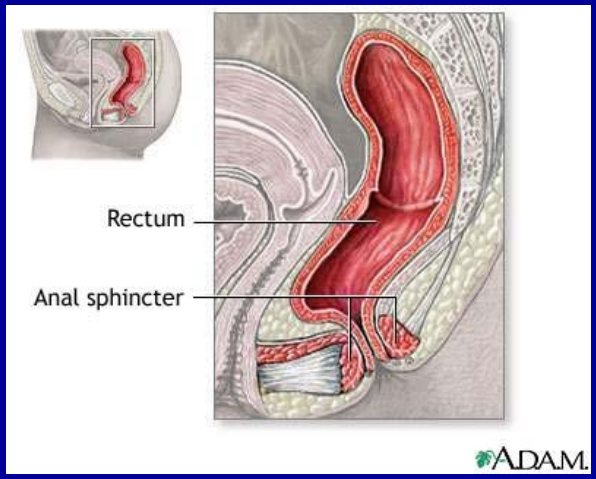
2. Increasing the outlet resistance of the anal sphincter
a. Augmentation of the anal sphincter and anal cushions – Anal bulking agents
b. Anal submucosal fibrosis- SECCA
c. Anal encirclement- Tiersch procedure
d. Non-dynamic graciloplasty

3. Dynamic sphincter replacement - Dynamic graciloplasty, Artificial anal sphincter
4. Antegrade continence enema (ACE)
5. Faecal diversion – Colostomy. Ileostomy

Anal bulking agents

- Emerged as a treatment for F.I. following the success of bulking agents for urinary stress incontinence (bladder neck augmentation and increase in urethral resistance)

- Aim of intervention is to prevent F.I. by
  Closing the anal canal or
  Increasing the pressure
  within the anal sphincter



Ideal characteristics of a bulking agent

Biocompatible

Non-migratory

Non-allergenic

Non-carcinogenic

Easy to inject

Produces durable results

(Vaizey et al, BJS 2005)

Initial studies: Phase 1

- First described in 1993 by Shafik (Int.Surg.1993;78:159-61) : Injection of PTFE (Polytef/Teflon) paste in 11 patients, 7 of whom has incontinence following a lateral internal sphincterotomy for anal fissure.

- Same author used abdominal wall fat, as a submucosal injection in 15 patients (Dis Colon Rectum1995; 98:583-7).

- One case report by Pescatori et al. using buttock fat (PlastReconSurg 1998)

Results of initial studies

- Good short term results
- Poor medium and long-term results
- Re-injection necessary to maintain efficacy

? Resorbtion or migration of injected material

- Safety issues:
  - Teflon could potentially cause granuloma formation and sarcomas
  - Autologous fat has been implicated in fatal fat embolism and stroke

2nd phase of anal injectibles

- Use of similar materials to those used in urology
- Improvements in techniques
- Variations in practice

Variations in practice – What, How and When?

- Type of material
- Site of implantation
- Route of injection
- Freehand or ultrasound-guided
- Local or general anaesthesia
- Clinical indications

Injectable materials used from 2000 onwards

- Silicone biomaterial (PTQ, Bioplastique). At least 21 studies with more than 600 patients
- Carbon-coated zirconium beads (Durasphere). 7 studies, 187 patients
- Calcium hydroxyl apatite microspheres (Coaptite). 1 study, 10 patients
- Hyaluronic acid (NASHADx,Solesta, Zuidex). 5 studies, 192 pts
- Glutaraldehyde cross-linked collagen (Contigen). 2 studies, 90 patients
- Polyacrilamide hydrogel (Bulkamid). 1 study, 5 patients
- Porcine dermal collagen (Permacol). 5 studies, 172 patients
- Ethylene vinyl alcohol co-polymer (Enteryx). 1 study, 21 patients
- Expandable silicone microballoons. 1 study 6 patients

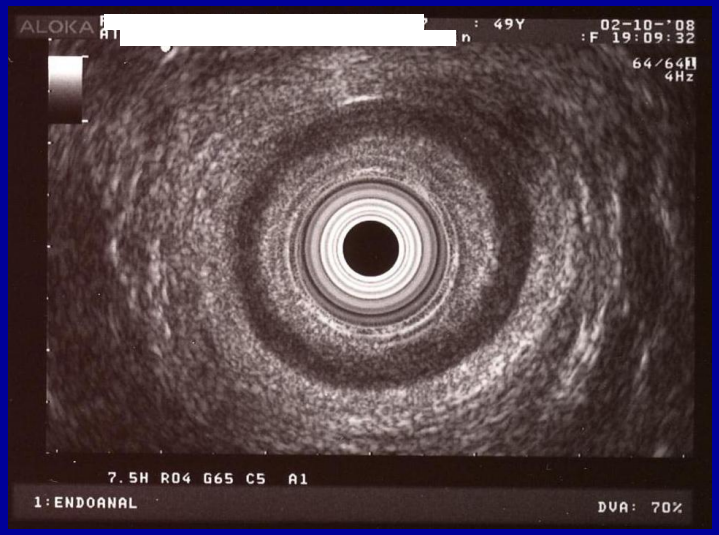
Clinical Indications

- Failure of conservative management
- Structurally intact but weak IAS

  Primary idiopathic degeneration

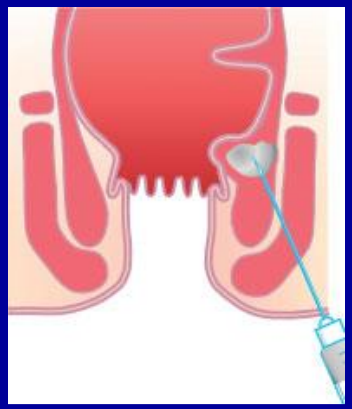
  Secondary to tissue disorders such as scleroderma
- IAS damage (childbirth, haemorrhoidectomy, anal stretch, sphincterotomy)

- Defect in EAS

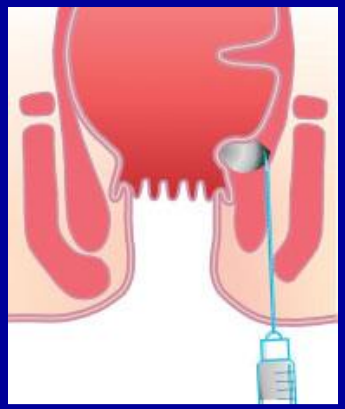


Injection sites and routes

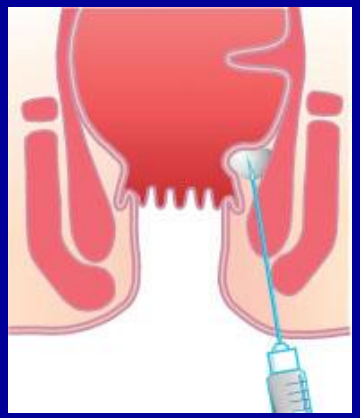
(Hussain et al, BJS 2011)



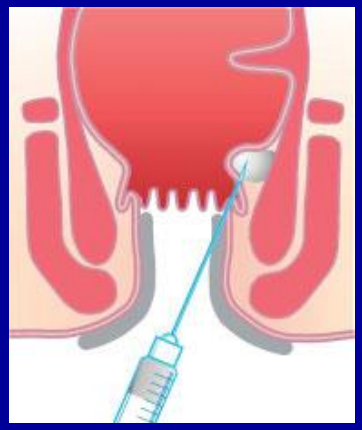
Transsphincteric injection into IAS



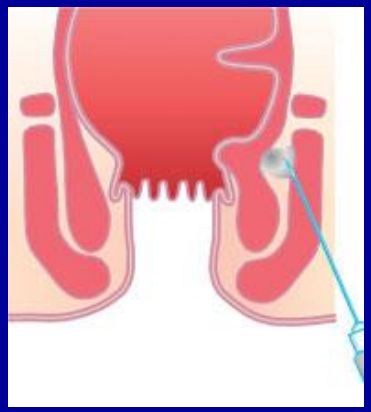
Intersphincteric injection into IAS



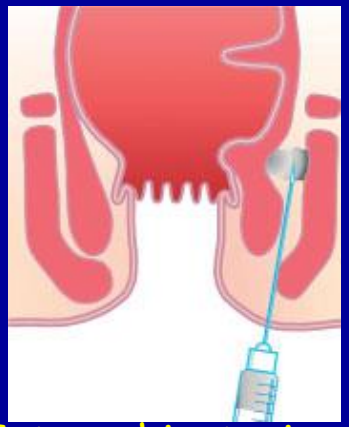
Submucosal site, intersphincteric route



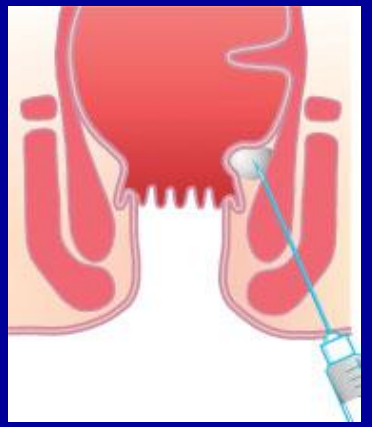
Submucosal site, transanal route



Intersphincteric site, trans-sphincteric route



Intersphincteric site, intersphincteric route



Submucosal site, trans-sphincteric route

Results

- Mainly case series. 6 RCT. Small numbers
- Follow up for the majority of studies was less than a median of 3 years ? Long term durability
- Majority (97%) of patients were only followed up once or twice
- Overall **complication rate** 13.5%:

  Pain, leakage of injected material, infection

  2 reported cases of local giant cell foreign body reaction after injection of silicone

  Durasphere has been associated with skin rashes and arthritis
- Overall **improvement in continence** 56%
- Complete continence in 13.4%

Comparative studies

- PTQ (silicone) vs Saline (Siproudhis et al, 2007).
  Small numbers. Similar improvement in continence 23% vs 27%. No long-term results.

- Hyaluronic acid vs sham injection (Graf et al 2011)
  Improved continence with hyaluronic acid up to 9 months. More adverse events (pain, infection, rectal and prostate abscess)
  Hyaluronic acid vs sham injection (Graf et al 2014)
  3 year follow up. 'Significant improvement in majority'

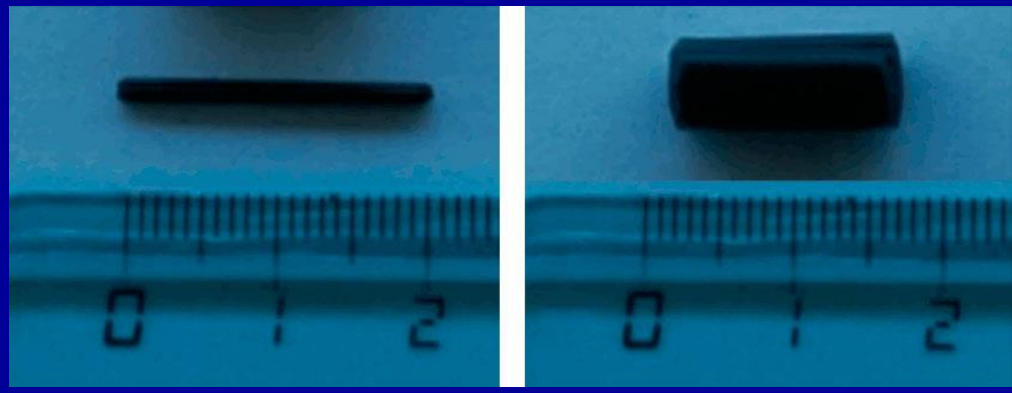
- PTQ vs Durasphere (carbon-coated beads) (Maeda et al, 2008)
  Better continence scores with PTQ. Safer.

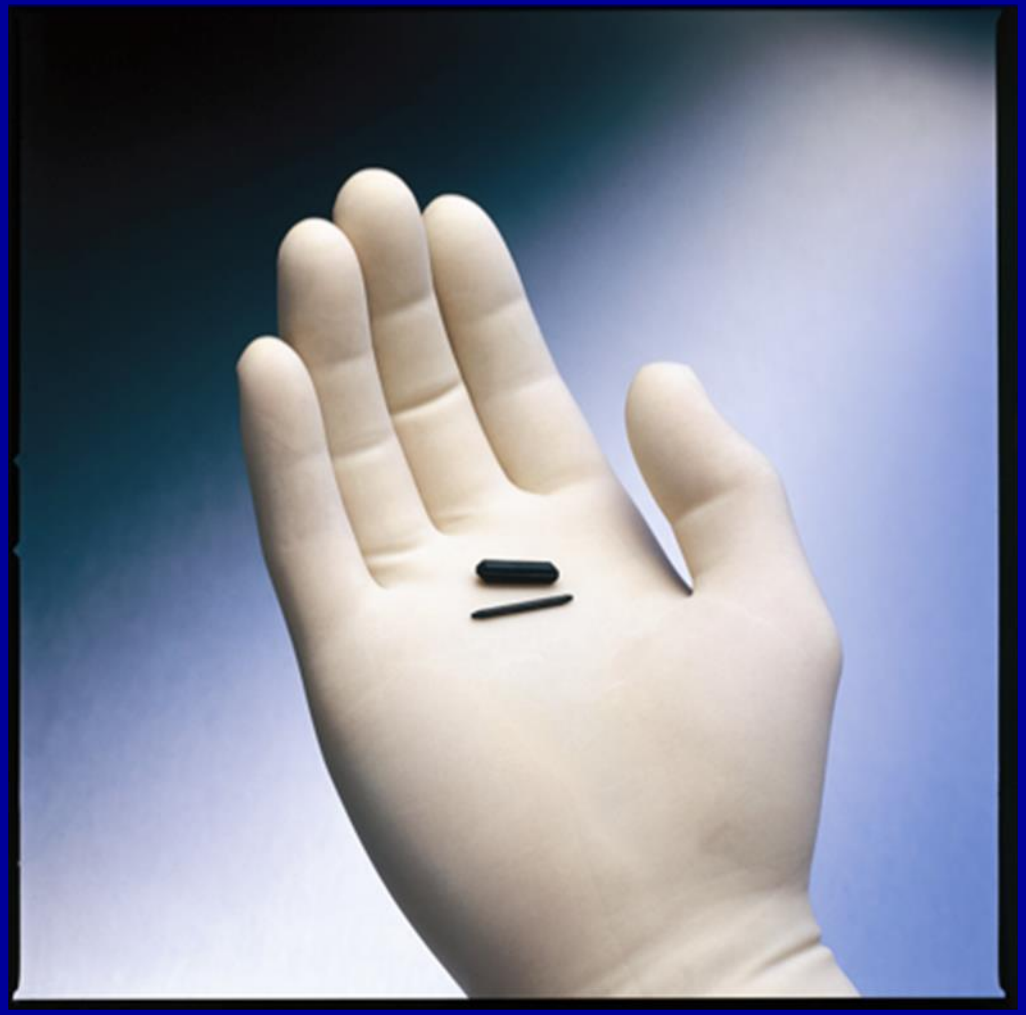
- Bulkamid (Polyacrilamide) vs Permacol (Porcine collagen) (Tjandra et al, 2009)
  Trial was too small to detect a difference
  Improvement in scores with both agents
  Continence scores maintained at 6 months with Bulkamid but deteriorated back to baseline with Permacol

- Ultrasound guided injection of PTQ vs digital guidance (Tjandra et al, 2004)
  Short-term benefits from US guidance

3rd phase of anal bulking agents

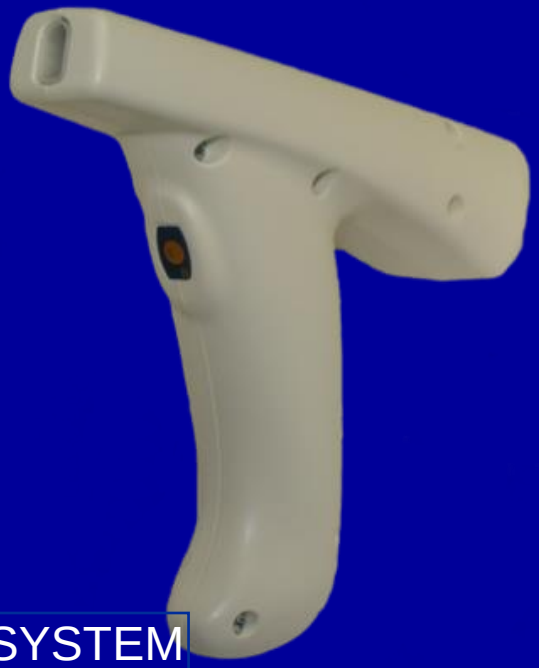
- THD Gatekeeper (Polyacrylonitrile, Hyexpan)
- Inert, non-allergenic, non-degradable material
- Implanted into the intersphincteric space as thin solid cylinders (length 21mm, diam. 1.2mm)
- Hydrophilic material.
- Becomes thicker (7mm), shorter (17mm) and softer on contact with tissue
- Volume increases from 70mm^3 to 500mm^3



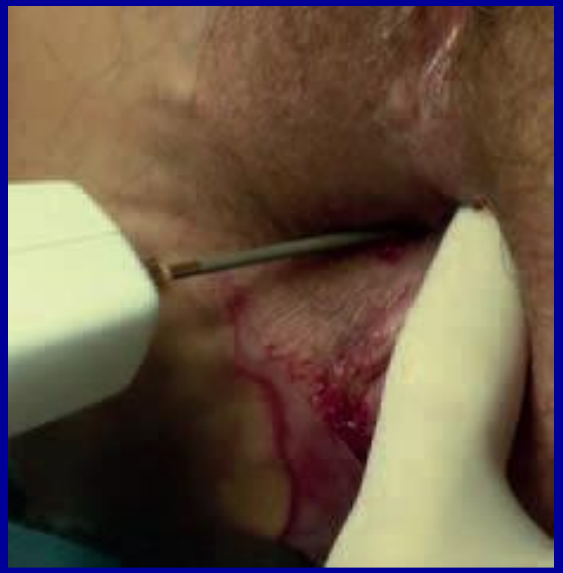


THD Gatekeeper

DISPENSER



DELIVERY SYSTEM



- Implantation of bulking agent between IAS and EAS

Results

- First reported experience (Ratto et al, BJS, 2011)
- 14 patients
- 8 had idiopathic FI, 4 had IAS defect, 2 has combined IAS and EAS defect
- Median FU 12 months (5-48)
- Clinically significant improvement in continence in 13 patients
- Sustained significant improvement in Wexner and Vaizey scores and SF36 and FIQL quality of life scores
- No improvement in resting or squeeze pressures.
- No reported complications

Results

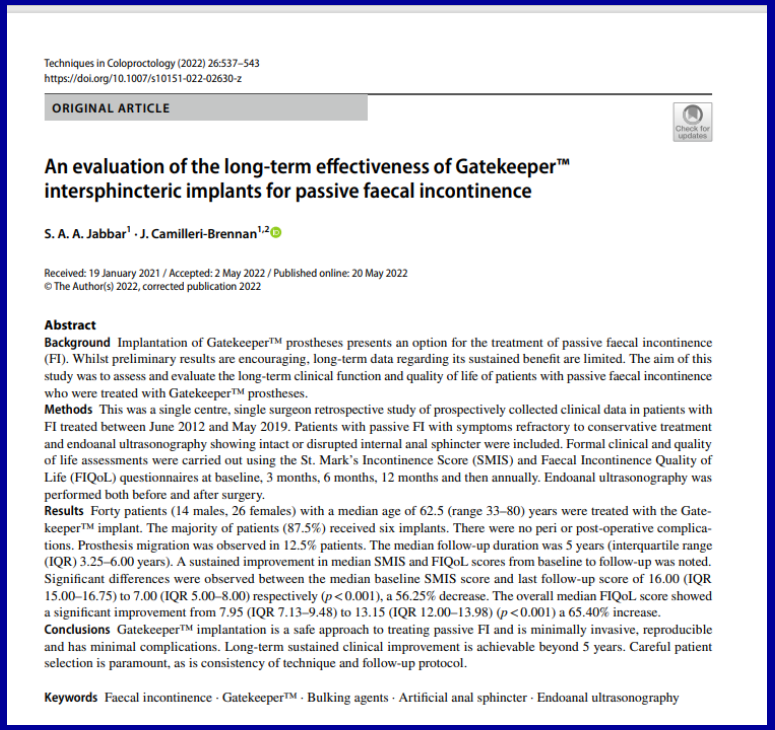
- Comparative retrospective study (Parello et al, Tech Coloproctol, 2012)
- Gatekeeper vs. Sacral nerve stimulation
- 7 vs 6 patients
- Median follow up 18 months vs 20 months
- Sustained improvement in Wexner continence scores with both modalities

Initial Forth Valley Royal experience

- 9 patients from June 2012 to December 2013
- 6 female, 3 male
- Full 2 year follow up data on first 3 patients
- 2 patients had 1 year follow up
- All presented with passive FI.
- 6 had idiopathic FI, 1 post anal stretch, 2 post haemorrhoidectomy
- All failed conservative management for > 1 year
- Significant sustained improvement in median Vaizey scores at 6, 12 and 24 months (16 vs 4, $p<0.01$)
- Improvement in Rockwood FIQOL scores across all 4 domains

(Zino S, Camilleri-Brennan J. Prospective analysis of the treatment of passive faecal incontinence with a new anal bulking agent. Tripartite Meeting, Birmingham, 2014)

Long term results



Techniques in Coloproctology (2022) 26:537–543
https://doi.org/10.1007/s10151-022-02630-z

ORIGINAL ARTICLE

An evaluation of the long-term effectiveness of Gatekeeper™ intersphincteric implants for passive faecal incontinence

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Received: 19 January 2021 / Accepted: 2 May 2022 / Published online: 20 May 2022

Abstract

Background Implantation of Gatekeeper™ prostheses presents an option for the treatment of passive faecal incontinence (FI). Whilst preliminary results are encouraging, long-term data regarding its sustained benefit are limited. The aim of this study was to assess and evaluate the long-term clinical function and quality of life of patients with passive faecal incontinence who were treated with Gatekeeper™ prostheses.

Methods This was a single centre, single surgeon retrospective study of prospectively collected clinical data in patients with FI treated between June 2012 and May 2019. Patients with passive FI with symptoms refractory to conservative treatment and endoanal ultrasonography showing intact or disrupted internal anal sphincter were included. Formal clinical and quality of life assessments were carried out using the St. Mark's Incontinence Score (SMIS) and Faecal Incontinence Quality of Life (FIQoL) questionnaires at baseline, 3 months, 6 months, 12 months and then annually. Endoanal ultrasonography was performed both before and after surgery.

Results Forty patients (14 males, 26 females) with a median age of 62.5 (range 33–80) years were treated with the Gatekeeper™ implant. The majority of patients (87.5%) received six implants. There were no peri or post-operative complications. Prosthesis migration was observed in 12.5% patients. The median follow-up duration was 5 years (interquartile range (IQR) 3.25–6.00 years). A sustained improvement in median SMIS and FIQoL scores from baseline to follow-up was noted. Significant differences were observed between the median baseline SMIS score and last follow-up score of 16.00 (IQR 15.00–16.75) to 7.00 (IQR 5.00–8.00) respectively ($p < 0.001$), a 56.25% decrease. The overall median FIQoL score showed a significant improvement from 7.95 (IQR 7.13–9.48) to 13.15 (IQR 12.00–13.98) ($p < 0.001$) a 65.40% increase.

Conclusions Gatekeeper™ implantation is a safe approach to treating passive FI and is minimally invasive, reproducible and has minimal complications. Long-term sustained clinical improvement is achievable beyond 5 years. Careful patient selection is paramount, as is consistency of technique and follow-up protocol.

Keywords Faecal incontinence · Gatekeeper™ · Bulking agents · Artificial anal sphincter · Endoanal ultrasonography

- 5 year + follow up
- 40 patients studied between 2012 and 2019
- Sustained clinical improvement in continence is maintained beyond 5 years in the majority of patients

Sphinkeeper

- Ten modified prostheses, which are longer and larger than those of the Gatekeeper, were implanted using the same technique. This results in a very high final volume of implanted material (8650 mm^3, approximately 480 % increase in size of the native sphincter), surrounding the anal canal and playing the role of an "additional" sphincter.
- Ratto's hypothesis is that 'the large volume Sphinkeeper implants, placed between EAS and IAS (pushing the EAS outwards and the IAS inwards), may increase the muscle fibers' length and therefore increase their contractility'.

- To date, literature on the Sphinkeeper is scarce. Largest sample to date had 45 patients with 1 year FU
- These short-term studies showed promising results with a significant decline in episodes of incontinence

THD Gatekeeper and Sphinkeeper

Clinical and Technical considerations

Indications

- **Passive faecal incontinence**
- Structurally intact but weak IAS. This would be due to either primary idiopathic degeneration of the IAS, or degeneration secondary to tissue disorders such as scleroderma
- IAS damage (childbirth, haemorrhoidectomy, anal stretch, sphincterotomy)
- Where conservative measures or injection of other bulking agents such as PTQ or Permacol have failed.

Contraindications

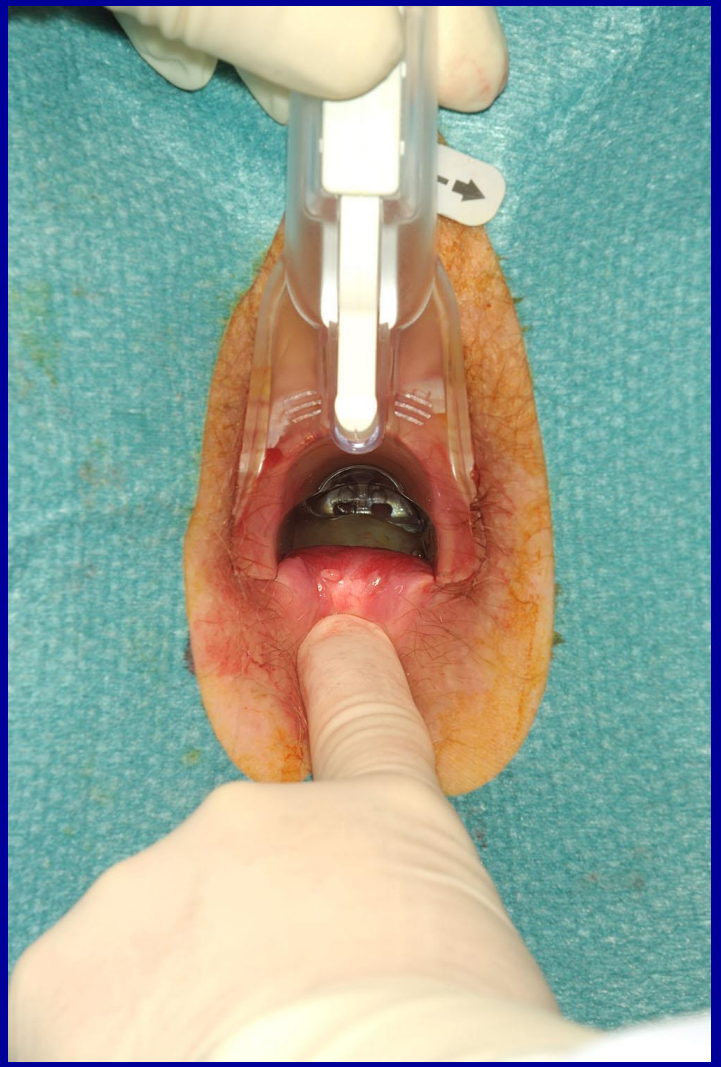
- Perianal sepsis
- Inflammatory bowel diseases with anorectal involvement (Crohn's disease, ulcerative colitis)
- Anal cancer
- Rectal or colon cancer undergoing active treatment;
- Rectal bleeding of unknown or undiagnosed origin;
- Rectal prolapse
- Uncontrolled blood coagulation disorders
- Pelvic radiotherapy
- Immunosuppression
- Pregnancy or planned pregnancy in the next 12 months.

Procedure

- Day case.
- Regional or general anesthesia.
- IV antibiotics are given at induction. Our patients receive Gentamicin 1.5 mg/kg and Metronidazole 500mg IV.
- Lithotomy position.
- A strict sterile technique is used.

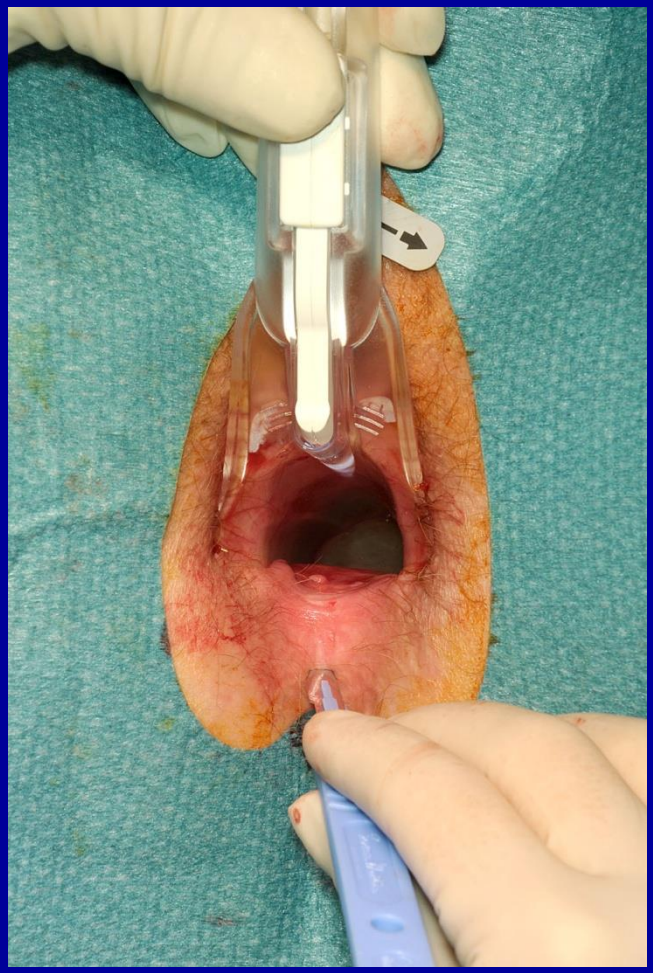
Procedure

- The IAS and intersphincteric groove are identified by the placement of an anal retractor (eg. Eisenhammer or Mini-light proctoscope)



Procedure

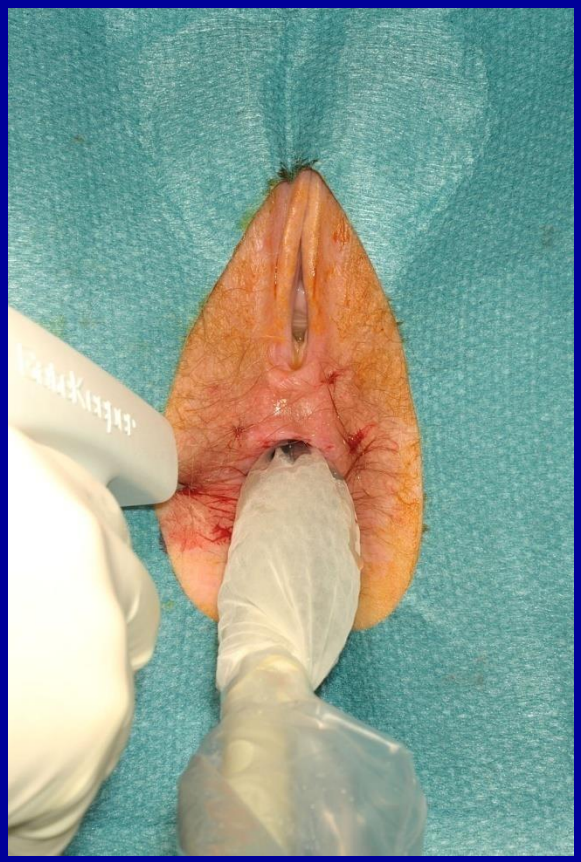
- A 2mm incision is made in the perianal skin, 2 cm from the anal verge

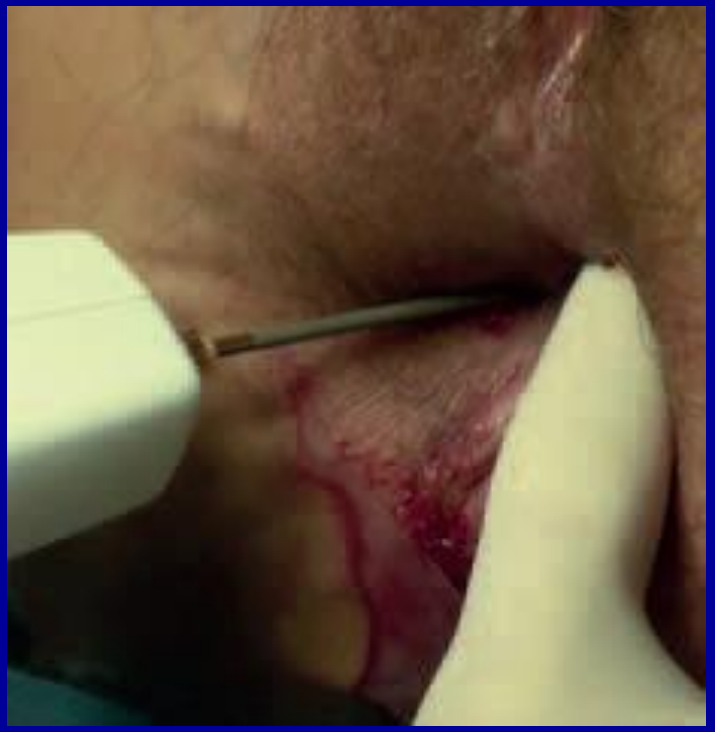


Procedure

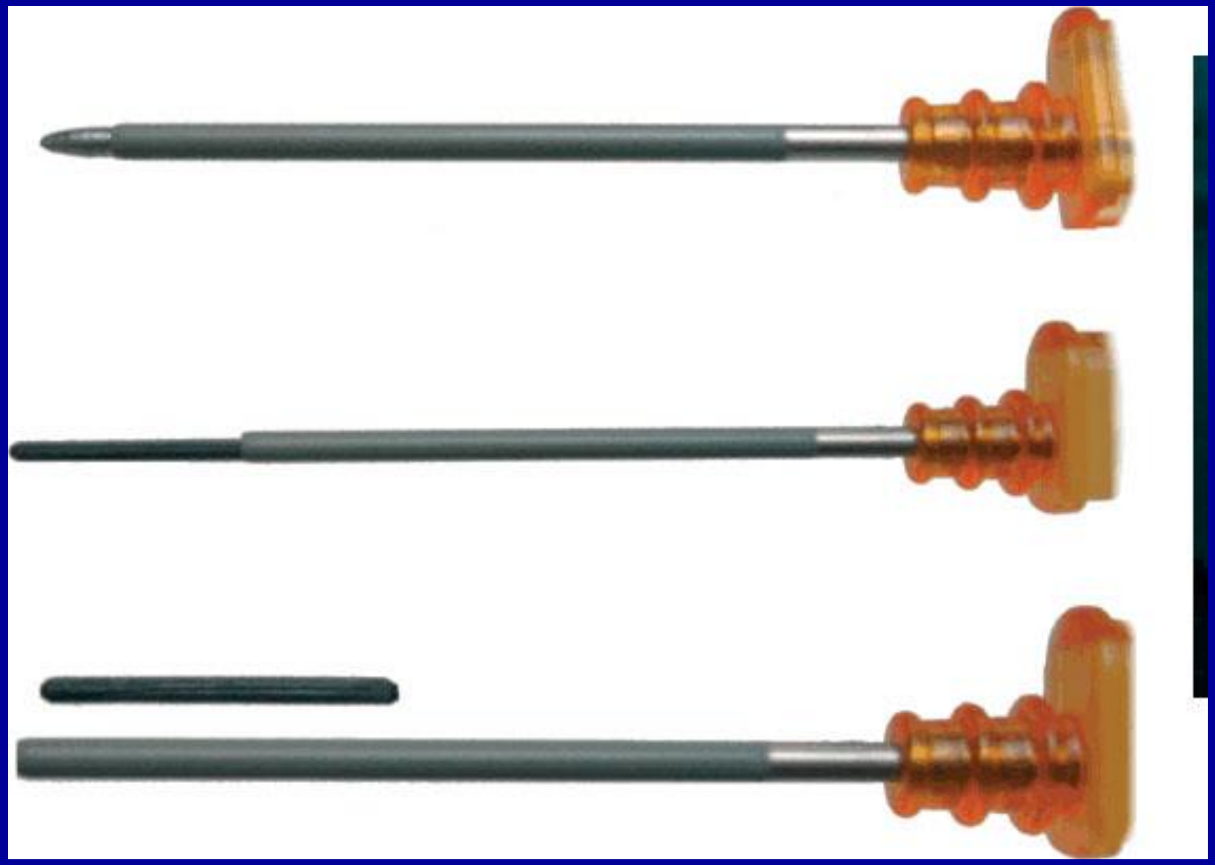
- Attach the dispenser to the delivery system
- Prime the delivery system
- Needle is inserted through the incision and tunneled to the intersphincteric margin and introduced into the intersphincteric space.
- The needle is then positioned so that the tip would lie just beyond the dentate line.

Implantation: Freehand vs US-guided



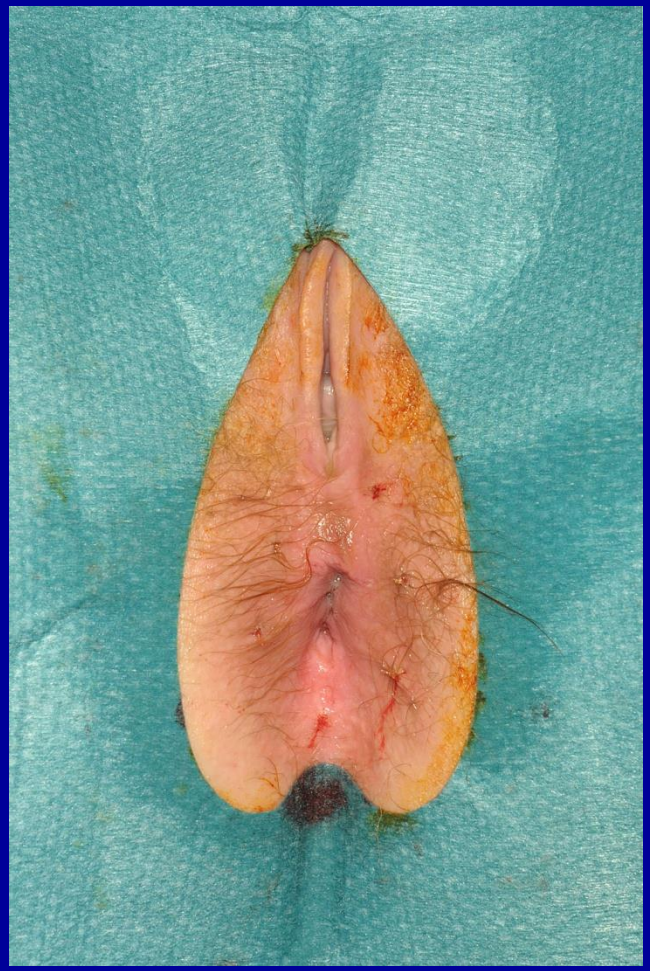


- When the needle is identified in the correct position, by direct vision and palpation and/or by endoanal ultrasound, the prosthesis is released into the intersphincteric space



Procedure

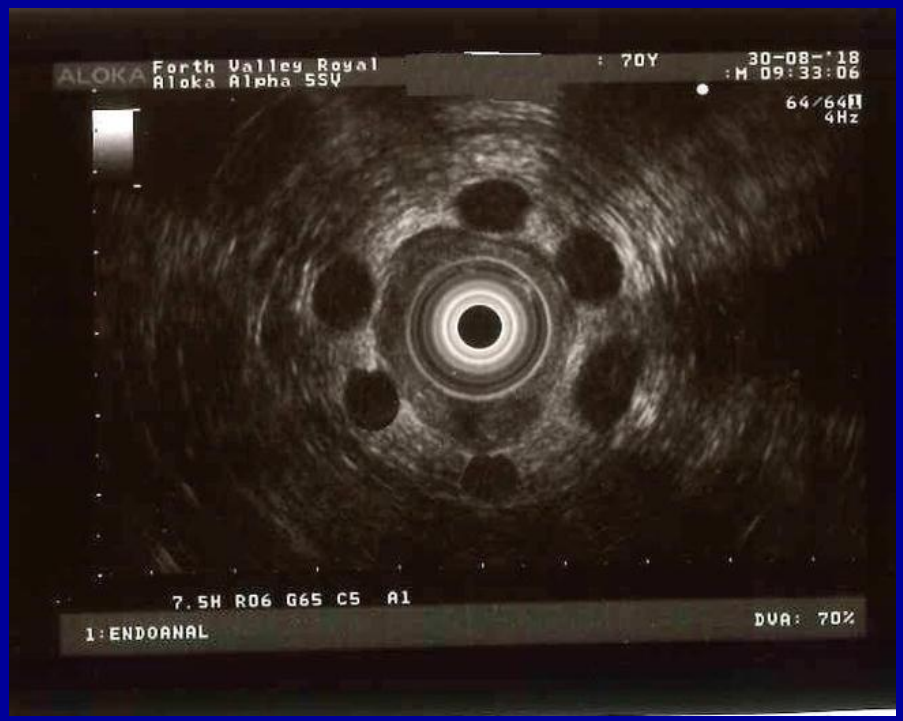
- The steps may be repeated to insert between four to six prostheses, equidistant from each other.
- The wounds are closed with a single absorbable suture

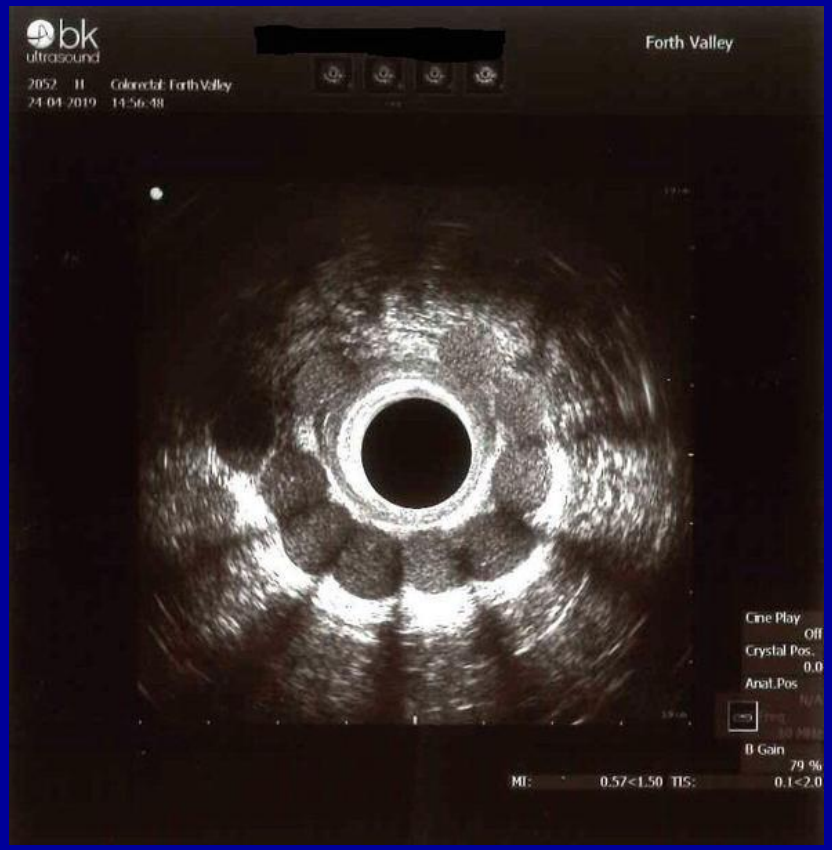


Postop Follow up

- The procedure takes about 30 to 40 minutes to complete.
- Oral metronidazole 400mg tds is prescribed for 5 days postoperatively.
- Oral laxatives such as lactulose are prescribed to minimize the risk of constipation.
- Patients are advised to avoid any anal trauma as well as anal intercourse for at least 72 h after implant insertion.
- The patients are followed up after 6 weeks and 3 monthly thereafter (questionnaire at each visit, USScan at 6 weeks and 1 year)

Endoanal USScan Images of Gatekeeper and Sphinkeeper





Conclusion

- Successful management of sphincter dysfunction depends on correct diagnosis and careful patient selection
- More research required in this field
- Results of Gatekeeper and Sphinkeeper are promising
- Fit the criteria for the ‘ideal’ bulking agent
- Overcome most limitations of other bulking agents
- Scope for RCTs?
- Will anal bulking agents replace more invasive surgical procedures?

Thank you!