NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of injectable bulking agents for faecal incontinence

Faecal incontinence is when a person loses the ability to control their bowel movements. The procedure involves injecting a material into the muscles around the anus (anal sphincter) with the aim of bulking the sides of the sphincter. Different materials are available to provide the extra strength, and these are called bulking agents.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in May 2006

Procedure name

- Injectable bulking agents for faecal incontinence
- Implantable bulking agents for faecal incontinence

Specialty societies

- Association of Coloproctology of Great Britain and Ireland
- British Society of Urogynaecology

Description

Summary of the condition

Faecal incontinence occurs when a person loses control of their bowel and is unable to retain faeces in the rectum. Faecal incontinence can be caused by a wide variety of conditions that affect either the anatomy or function of the anal sphincter. Perineal injury during vaginal delivery is a common cause of faecal incontinence in women. It can also be caused by neurological disorders, such

as spinal injury and multiple sclerosis. In some patients faecal incontinence may occur as the result of surgical correction of congenital anorectal conditions, such as anorectal atresia or Hirschprung's disease, or the result of other anorectal surgery.

Faecal incontinence is associated with a high level of physical and social disability. The patients may have to wear incontinence pads to manage the condition.

Current treatment and alternatives

Typically, first-line treatment for faecal incontinence is conservative, such as antidiarrhoeal medication and pelvic floor muscle training (including biofeedback therapy). In patients for whom conservative treatments have been unsuccessful, surgical alternatives include tightening the sphincter (overlapping sphincteroplasty), sacral nerve stimulation, creation of a new sphincter from other suitable muscles (for example, dynamic graciloplasty), implantation of an artificial sphincter or the creation of a permanent colostomy.

What the procedure involves

The role of bulking agents is to augment the anal sphincter wall and increase the anal pressure. Several millilitres of bulking agent are injected into the submucosa just above the dentate line. The procedure is usually performed under local anaesthetic. The injections may be undertaken either via a proctoscope or with simple manual anal dilatation, either directly or via a trans-sphincteric route. More than one injection may be given.

Several bulking agents are currently available, including collagen, silicone particles, carbon beads and autologous fat, which is harvested prior to the procedure from sites such as the abdomen. The agent should be nonimmunogenic and biocompatible to reduce inflammatory response. The particles should be large enough to prevent migration away from the site of injection and durable enough to maintain the effect over time.

Efficacy

According to the Specialist Advisers, important efficacy outcomes for this procedure include improvement in faecal leakage, improvement in quality of life, long-term maintenance of improvement, and necessity and frequency of repeat injections.

The evidence on this procedure is based on seven case-series studies, totalling 158 patients with a mean follow-up ranging from 6 to 28.5 months. The case series reported on a range of different bulking agents, as well as techniques.

Continence grading
In the largest case series of 82 patients, significant improvement in continence scores was reported at 6 months follow-up ($p < 0.001$), with a subset of patients maintaining this improvement at 12 months follow-up

(n = 42) [1]. Similar results were reported in a case series of 18 patients; this study found a significant improvement in continence grading at 12 months (p = 0.0002) [2]. The authors noted that the improvement in continence scores was directly related to the number of sites injected, with improvement significantly higher in patients who had two or more sites injected. In another case series (n = 10) 60% of patients (n = 6) reported improvement at 6 weeks following the procedure; however, at 6 months only 30% of patients (n = 3) still reported some improvement [3].

Frequency of repeat procedure
In four of the seven case series studies it was reported that a number of patients (n = 13/52) had one or two repeat injections. These were typically patients who had not reported benefit following the first injection. In the majority of patients improvement was reported following the repeat procedure.

Quality of life and patient satisfaction
Two studies reported on quality of life and of patient satisfaction following the procedure. In the study (n = 18) [2] with longer follow-up improvement was reported in patient satisfaction (p = 0.053) and in all quality-of-life scales at 12 months. In the second study of 82 patients [1], quality-of-life domains were improved at a median follow-up of 6 months.

The Specialist Advisers commented that there was lack of good quality data assessing the efficacy of this procedure. In particular, the advisers noted that there was uncertainty as to the duration of any possible effects and the necessity of repeat injections to maintain this effect.

Safety

The evidence in relation to safety relates to seven case series studies.

Few complications were reported in the studies. The most commonly reported complication was pain at the anal injection sites. In the largest case series [1] 7% (6/82) of patients reported some pain following the procedure. In a smaller case series, half of the patients (5/10) experienced pain or minor ulceration at the injection site or in the anal canal; however, after a change in technique no further complications were reported [3]. Other complications included leakage of the bulking agent (1/10) [3] and, in a different study, passing of the bulking agent (2/18) [2].

The Specialist Advisers listed infection, pain and leakage along the injection track as the main complications reported following the procedure. Migration and rectovaginal fistula were also noted as possible complications.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to injectable bulking agents for faecal incontinence. Searches were conducted via the following databases, covering the period from their commencement to

3rd April 2006, an updated search was then conduction on the 3rd July 2006. MEDLINE, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (table 1)Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with faecal incontinence.
Intervention/test	Injectable/implantable bulking agents.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy. Key efficacy outcomes included: • improvement in faecal leakage • improvement in quality of life • long-term maintenance of improvement • necessity and frequency of repeat injections. Key safety outcomes included: • pain • infection • leakage • migration.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on seven case series studies.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Existing reviews on this procedure

An Australian horizon scanning report on injectable silicone biomaterial implants was published in December 2005. This report covers a number of

indications including faecal incontinence. Only those studies reporting on silicone as a bulking agent were included, and all three of these studies have been included in this overview (either in the main table or in appendix A).

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

Related indication

Artificial anal sphincter implantation. *NICE Interventional procedures guidance* no. 66 (2004). Available from: www.nice.org.uk/IPG066

Sacral nerve stimulation for faecal incontinence. *NICE Interventional procedures guidance* no. 99 (2004). Available from: www.nice.org.uk/IPG099

Stimulated graciloplasty for faecal incontinence. *NICE Interventional procedures guidance* no. 159 (2006). Available from: www.nice.org.uk/IPG159

Related procedure

Intramural urethral bulking procedures for stress urinary incontinence in women (2005). *NICE Interventional procedures guidance* no. 138. Available from: www.nice.org.uk/IPG138

Technology appraisals

None relevant

Clinical guidelines

- Faecal incontinence: the management of faecal incontinence. *NICE clinical guideline*. (Publication expected June 2007.) Consultation on draft of guideline with stakeholders is expected Autumn 06 − Winter 07.

  See www.nice.org.uk/page.aspx?o=207033 for further information.

Public health

None relevant

Table 2 Summary of key efficacy and safety findings on injectable bulking agents for faecal incontinence

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Tjandra (2004) [1]

Case series

Australia

Study period

n = 82

Population: 64 females, 8 males. Median age: 66 years, range 34−89 years. 21 (26%) patients had previous sphincter repair. 27 patients had prior anorectal surgery.

Indications: Patients with severe faecal incontinence for solid or liquid stool caused by internal sphincter dysfunction. Previous treatment with bulking or constipating agents and physiotherapy had failed in all patients.

Technique: Patients were randomised to have injection with or without transanal ultrasound guidance. Bulking agent: PTP implants (silicone). Four injection sites of 2.5 ml of implants were used.

Median follow-up: 6 months (range 1−12 months)</td>
<td>
Wexner Continence Score and VAS n = 42 (guided by ultrasound – group A)
<table>
<tr><th></th><th>Baseline</th><th>6 months</th><th>12 months</th></tr>
<tr><td>Patients (n)</td><td>42</td><td>30</td><td>10</td></tr>
<tr><td>Wexner</td><td>14.5 (10−20)</td><td>5 (2−13)</td><td>3 (1−12)</td></tr>
<tr><td>VAS</td><td>4 (1−8)</td><td>9 (6−10)</td><td>10 (9−10)</td></tr>
</table>
Wexner Continence Score and VAS n = 40 (guided by palpitation – group B)
<table>
<tr><th></th><th>Baseline</th><th>6 months</th><th>12 months</th></tr>
<tr><td>Patients (n)</td><td>40</td><td>21</td><td>5</td></tr>
<tr><td>Wexner</td><td>14.5 (11−20)</td><td>8 (2−12)</td><td>11 (2−12) p = 0.05</td></tr>
<tr><td>VAS</td><td>4 (1−7)</td><td>9 (1-10)</td><td>4 (2−10) p = 0.07</td></tr>
</table>
Authors note that for both groups the p values for almost all values of the Wexner and VAS scores during follow-up were p < 0.001.

Quality of life and SF-12 n = 42 (guided by ultrasound – group A)
<table>
<tr><th></th><th>Baseline</th><th>6 months</th></tr>
<tr><td>Patients (n)</td><td>42</td><td>42</td></tr>
<tr><td>QOL – lifestyle</td><td>2.9 ± 0.94</td><td>3.7 ± 0.44</td></tr>
<tr><td>Coping</td><td>2.2 ± 0.92</td><td>3.2 ± 0.66</td></tr>
<tr><td>Depression</td><td>3.1 ± 0.76</td><td>3.9 ± 0.52</td></tr>
<tr><td>Embarrassment</td><td>2.2 ± 0.96</td><td>3.4 ± 0.53</td></tr>
</table>
</td>
<td>Complications:

Authors note that allergy was not a problem in any of the patients.

There were no instances or infection, erosion of implants or fistulation. Constipation was not encountered.

Seven patients experienced some pain:
-Six patients noted minor discomfort at anal injection sites, which was resolved with analgesia.
- 1 patient had the injections in a more superficial place than intended, causing discomfort.</td>
<td>Randomised controlled trial comparing injection with or without ultrasound; however, for the purpose of this review it is treated as a case-series study.

Authors note that during follow-up the use of bulking agent or antidiarrhoeal medications was not monitored or controlled.

Authors present results separately for those undergoing ultrasound and those undergoing palpation.

Outcomes:
Wexner score: 0 – perfect continence; 20 – complete continence (never, 0; rarely, <1/month; sometimes, <1/week, ≥1/month; usually, <1/day, ≥1/week; always, ≥1/day; 0, perfect; 20, complete incontinence).

Visual Analog scale (1–10, 10 being the best).

Authors note that the results may diminish over time.

Authors note that their technique differed to that described by the St. Marks group. Implants were injected into the intersphincteric</td>
</tr>
</table>

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale

Study details	Key efficacy findings	Key safety findings	Comments
Disclosure of interest: not reported			space through the anal skin.

SF-12 physical	47.1 ± 1.61	50.6 ± 8.3 p = 0.003
SF-12 mental	47.5 ± 1.44	52.3 ± 7.4 p = 0.004

Authors note that the p values for all QOL values of during follow-up were p < 0.001

Quality of life and SF-12 n = 40 guided by palpitation – group B

	Baseline	6 months
Patients (n)	40	31
QOL – lifestyle	2.9 ± 0.88	3.1 ± 0.83 p = 0.01
Coping	2.4 ± 0.94	2.7 ± 0.94 p = 0.009
Depression	2.9 ± 0.79	3.1 ± 0.82 p = 0.01
Embarrassment	2.2 ± 0.88	2.7 ± 0.91 p < 0.001
SF-12 physical	43.7 ± 1.62	43.7 ± 9.9
SF-12 mental	44.3 ± 1.71	45.2 ± 9.7

Anorectal manometry

	Group A	Group B
Maximum resting pressure (mm Hg) Baseline	23 ± 9.7 (10−51)	27 ± 8.7 (10−47)
Maximum resting pressure (mm Hg) 6 months	38 ± 12.4 (21−62) p < 0.01	35 ± 6.5 (25−55)
Maximum squeeze pressure (mm Hg) Baseline	106 ± 22.3 (65−151)	112 ± 25.1 (71−171)
Maximum squeeze pressure (mm Hg) 6 months	116 ± 21.7 (89−178)	121 ± 21.2 (92−172)

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Malouf (2001) [3] Case series UK Study period: not stated **n = 10** Population: 6 females, 4 males. Median age: 64 years, range 41−80 years. Patients had a weak (6) or disrupted (4) IAS. Indications: Patients with passive faecal incontinence to solid or liquid stool. Patients had failed previous treatment with antidiarrhoeal agents. Technique: Ultrasound was used to identify injection site. Bulking agent: silicone. One to multiple injection sites with a volume between 5 and 11.5 ml. Protocol was changed after six patients to a trans-sphincteric injection to reduce infection and leakage. **Follow-up: 6 months** Disclosure of interest: Not reported	**Self-reported improvement** At 6 weeks: 3 patients (30%) were greatly improved 3 patients (30%) were asymptomatic 1 patient (10%) showed no lasting effect after one session; however, after a second injection, reported improvement 3 patients (30%) showed no improvement after the treatment. At 6 months: 2 patients (20%) had sustained marked improvement 1 patient (10%) sustained slight improvement 7 patients (70%) reported no relief of symptoms Authors note that all 3 patients who showed improvement had a weak IAS. **Anal manometry** There was no significant change in either the maximum resting pressure. Baseline: Median: 54 (range 28−95) 6 weeks: Median: 40 (range 30−86) p = 0.83 6 months: Median 60 (range 35−127) p = 0.66 **Endoanal ultrasound** Correct placement in 9/10 patients (leakage in 1 patient)	**Complications:** 1 patient had leakage of the bulking agent out of the injection site. 5 of the first 6 patients had pain or ulceration over the injection site or in the anal canal. This pain was severe, and the infection required up to 10 weeks of the antibiotic therapy. Authors note that all patients ultimately healed with resolution of pain. Following a change in protocol there were no more complications.	Small study. Authors describe it as a pilot study. Clinical assessment, anal manometry, endoanal ultrasound and completion of a 2-week bowel diary were undertaken before and 6 weeks after the injection. *Complete improvement* – no leakage of solid or liquid stool *Marked improvement* – minimal leakage of liquid stool and judged by the patient as >75% improvement *Minor improvement* – leakage of liquid stool and judged by the patient as a 20−50% improvement *Nil improvement* – leakage or liquid and at times solid stool and judged by the patient as <20% improvement. **Patients were precluded from taking antidiarrhoeal agents during the diary assessment periods.** Patients who were not continent to solid or liquid stool at 6 weeks were offered a second injection section. Authors note that poor results in the first 6 patients led them to consider the sites of injection.

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Davis (2003) [2] Case series UK Study period: December 1999 to April 2002 **n = 18** Population: 9 females, 9 males. Mean age: 60 years, range 31−87 years. 17 had a IAS defect (17). 7 females also had disrupted EAS. Indications: All patients presented with persistent faecal leakage/soiling greater than one per week for at least 6 months. All patients had previously tried a range of conservative options (dietary, antidiarrhoeal medication). Technique: Proctoscope and ultrasound was used to guide the needle. Bulking agent: carbon coated beads injected in 1−4 sites. Mean volume injected: 1.28 ml. **Mean follow-up: 28.5 months (11−40 months)** Disclosure of interest: Authors acknowledge Carbon Medical Technologies for their support.	**Anorectal physiology** Authors note that anorectal physiological parameters apart from the maximum tolerable rectal volume at 12 months (p = 0.036) showed no significant improvement. **Cleveland Clinic continence grading scale** Baseline 11.89 12 months 8.07, p = 0.0002 Authors note that the improvement in continence scores was directly related to the number of sites injected. The improvement was significantly higher in patients who had two or more sites injected p=0.034. **Satisfaction (VAS)** Patient satisfaction was improved at 12 months p = 0.053 **Quality of life (Rockwood)** All four subscales showed improvement between the baseline and 12 months (lifestyle p = 0.006, coping p = 0.008, depression p = 0.024 and embarrassment p = 0.059) scores.	**Complications:** ▪ 2 patients reported mild anal discomfort 2−3 days post procedure that resolved without treatment ▪ 1 patient reported worsening of longstanding purities ani] for 5 days post procedure ▪ 2 patients reported the passage of bulking agent during the first few days post procedure.	Cleveland Clinic scoring system (0 = no incontinence to 20 = complete continence). This scale relates severity of incontinence to five variables including gas, liquid and solid incontinence, pad usage and lifestyle. Patients VAS (0 = not satisfied to 10 = complete satisfaction). 2 patients exited the study at 6 months perceiving no improvement. 1 other patient had to withdraw due to unrelated surgery – an analysis was undertaken including these patients. No comment is made as to whether patients were precluded from taking antidiarrhoeal agents during the follow-up period. Authors make a statement about the relationship between continence grade and number of sites injected; however, specific information on sites injected is not reported in the study.

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Kumar (1998) [4] Case series UK Study period **n = 17** Population: 12 females, 5 males. Mean age: 53 years, range 42−76 years. 9 patients had idiopathic faecal incontinence secondary to weakness of the IAS. Indications: All patients were incontinent to flatus and liquid stool. All patients had failed conservative treatment and had a surgically incorrectable problem. Technique: All patients were given an allergy test to the agent prior to treatment. Proctoscopy was used for injections. Bulking agent: collagen injected in 1−3 sites. Maximum volume injected: 2 ml. **Mean follow-up: 8 months (range 4−12 months)** Disclosure of interest: Authors acknowledge BARD for supplying bulking agent.	Self-reported improvement. 11 patients (65%) showed marked symptomatic improvement (no reports of leaked liquid stool or reported soiling). 1 patient (6%) reported symptomatic improvement (frequency of incontinence episodes improved). 2 patients (12%) reported minimal improvement. 3 patients (18%) reported no improvement, but 1 had a repeat injection and showed improvement. 3 patients had required repeat injections. **Anorectal physiology** Authors note that mean resting pressures were low before the operation and remained low after the operation. There was a trend towards an increase in resting pressures; the differences were not significant.	**Complications:** Authors note that all patients tolerated injection without any ill-effects.	Limited information. Clinical outcome was measured at an interview with the patient on follow-up visits at 1 and 6 months. No comment is made whether patients were precluded from taking antidiarrhoeal agents during the follow-up period. Authors note that physiological measurements do not necessarily correlate with symptoms, and low resting and squeeze pressures are fully compatible with normal continence.

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Shafik (1993) [5] Case series Egypt Study period: not stated **n = 11** Population: 5 females, 6 males. Mean age: 53 years, range 29−58 years. Developed after internal sphincterotomy for chronic anal fissure in 7 patients and was idiopathic in 4 patients. Mean rectal pressure was within a normal range; however, rectal neck pressure was significantly reduced. Indications: Patients with partial faecal incontinence who were refractory to conservative measures. Patients had experienced incontinence to flatus and fluid stools for 4−11 years. Technique: Patients did not have any anaesthesia. A protoscope was used. Two injection sites; 5 ml of polytetrafluoroethylene was given. **Mean follow-up: 22 months (range 18−24 months)** Disclosure of interest: not stated	**Resistance to flatus grading and/or fluid stools** Authors note that in the first 2 weeks all patients were scored as grade 1. At 12 months: 5 (46%) patients were grade 1 4 (36%) patients were grade 2 2 (18%) patients as grade 3 or failures. **The rectal neck pressure** The rectal neck pressure of the 2 patients with score 3 did not show significant change from pre-procedure values. The rectal neck pressure of the remaining 9 patients (grade 1 or grade 2) showed a significant increase ($p < 0.01$ and $p < 0.005$, respectively). The two grade 3, and three grade 2 patients were reinjected 13 months after the initial procedure. These patients were followed for an additional 4−8 months. 4 patients upgraded, with one patient remaining grade 2.	**Complications:** Authors note that no complications were encountered during injection or the time of follow-up. However, the authors note that mild pain occurred on the first post-injection data in some patients.	No comment is made whether patients were precluded from taking antidiarrhoeal medication during the follow-up period. Outcomes: patients were questioned every month. The rectal neck pressure was measured every 3 months. Resistance to flatus and/or fluid stools was scored into 3 grades (unclear if a validated measure). Score 1 – completely continent to 20 bouts Score 2 – continent to more than 10 but less than 20 bouts Score 3 – continent to less than 10 bouts of the 20 bouts or no improvement. Authors note that prior to the procedure all patients were scored as grade 3.

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale

Study details	Key efficacy findings	Key safety findings	Comments
Shafik (1995) [6] Case series Egypt Study period **n = 14** Population: 9 females and 5 males Mean age: not stated, range 36−62 years. 6 patients had idiopathic faecal incontinence. Mean rectal pressure was within a normal range; however, rectal neck pressure was significantly reduced. Indications: Patients with partial faecal incontinence who were refractory to conservative measures. Patients had experienced incontinence to flatus and fluid stools. Technique: Autologous fat was used in this procedure and harvested from the abdominal wall. 15−20 ml of fat were injected into 2 sites. **Mean follow-up: 6 months** Disclosure of interest: not stated	**Continence grading:** Authors note that in the immediately postinjection period all patients were scored as grade 1. At 6 months: 3 (21%) patients were grade 1 7 (50%) patients were grade 2 4 (29%) patients as grade 3 or failures. Grade 3 patients: Two patients were injected and after the second injection were graded as continent. The remaining two patients became continent after another two injections at a further follow-up of 6−8 months. Digital rectal examination showed that after a few months submucosal fat spread along most of the rectal neck length.	**Complications:** Authors note that no complications were encountered during injection or the time of follow-up. However, the authors note that mild pain occurred on the first post-injection data in some patients.	No comment is made whether patients were precluded from taking antidiarrhoeal agents during the follow-up period. Timing of outcomes assessment: patients were questioned every month. The rectal neck pressure was measured every 2 months. Continence scoring (unclear if a validated measure). Score 1 – completely continent with rectal neck pressure higher than pre-procedure. Score 2 – continent to fluid stools but not to flatus with occasional pad soiling. Initial rectal neck pressure was higher but reduced. Score 3 – no improvement. Authors note that the best results were obtained when the harvested fat was washed many times to rid it of contained debris. At the start of the study this was not done.

Abbreviations used: EAS, external anal sphincter; IAS, internal anal sphincter; VAS, Visual Analogue Scale

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Feretis (2001) [7]

Case series

Greece

Study period

n = 6

Population: 2 females, 4 males. Mean age: 43 years, range 29−60 years. Patients had incontinence for a mean of 124.6 (range 60−240) months. The cause of incontinence was a sequel of surgery (4) and obstetric injury (2).

Indications: Patients with severe faecal incontinence as estimated using the modified symptom severity score, with at least one previous attempt of surgical repair.

Technique: Microballoons made of silicone were implanted (3−5 balloons were usually implanted). Proctoscope was used.

Mean follow-up: 8.6 months (range 7−12 months)

Disclosure of interest: not reported</td>
<td>Outcomes measured: incontinence score, rest pressure, squeeze pressure

<table>
<tr><th></th><th>Baseline</th><th>At follow-up</th></tr>
<tr><td>Incontinence score
p = 0.0027</td><td>Mean: 16
Range 14−18</td><td>Mean: 5
Range 4−7</td></tr>
<tr><td>Rest pressure (mm Hg)
p = 0.752</td><td>Mean: 50
Range 18−80</td><td>Mean: 53
Range 30−76</td></tr>
<tr><td>Squeeze pressure (mm Hg)
p = 0.34</td><td>Mean: 103.3
Range 55−170</td><td>Mean: 98.6
Range 60−150</td></tr>
</table>
</td>
<td>Complications:
Authors note

- no adverse effects documented during implantation except one from one case of self-limited bleeding.

- post-implantation pain was minimal and no patient required analgesia.

- no post-implantation complications occurred during follow-up.

However, in one patient one balloon was lost (unclear where/how) and in a second patient an obstacle to defaecation was reported (two balloons were deliberately burst, resolving the problem).</td>
<td>Recruitment: authors note that patients were consecutive.

Incontinence was assessed by using a modification of the Browning-Parks scoring system (0 = complete continence to 20 = complete incontinence).

Authors note that there was no correlation between post-implantation anal pressures and clinical outcome.

No comment is made whether patients were precluded from taking antidiarrhoeal agents during the follow-up period.</td>
</tr>
</table>

Validity and generalisability of the studies

- The evidence for this procedure is based on a number of small case series studies.
- Among the studies there was substantial variation in terms of the procedure − for example, the injection route used, the number of sites injected, the volume of bulking agent injected and the type of bulking agent used.
- It has been reported that some of the bulking agents are no longer used for this procedure for example autologous fat.
- Patient characteristics also differed in the studies, with some patients having a weak or disrupted sphincter. In one study only the patients with a weak internal sphincter benefited from this procedure [3].
- Many of the studies did not use validated outcome measures and few studies reported on patient-focused outcomes such as quality of life or satisfaction.
- It should also be noted that physiological measurements do not necessarily correlate with symptoms and that low measurements may also indicate normal continence. Therefore the usefulness of these outcomes is unclear.
- It many of the studies it was also unclear whether antidiarrhoeal medication was used following the treatment; the use of such medication as in the study by Tjandra [1] would have an influence on efficacy outcomes.
- There is a lack of long-term data on this procedure. This is particularly important given that there is some suggestion that benefits diminish with time.

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Mr Edward Kiff, Mr Peter Sagar, Mr Phil Toozs-Hobson, Ms Carolynne Vaizey, Mr Jag Varma

- The alternative to this procedure would be an overlapping sphincter repair. This is a more complex procedure which carries risks of scarring, pain and worsening of incontinence.
- Bulking agents have been used in other areas of surgery and therefore their safety profile had already been established.
- Several different bulking agents have been used with different techniques of injection.
- There is a lack of long-term data on this procedure.
- Many patients will need repeat injections.
- There are also some uncertainties regarding which patients are most likely to benefit from this procedure.

Issues for consideration by IPAC

- IPAC has assessed the same procedure for stress urinary incontinence (see appendix B). Relatively more evidence was available for this indication.
- There is currently a randomised controlled trial under way in Norway: 'A randomised controlled clinical trial of biofeedback and anal injections as first treatment of faecal incontinence.' The expected completion date is December 2011.
- One of the authors of the included studies[1] also stated that a randomised controlled trial was to be undertaken in Australia. However, at the time of writing no further details have obtained.

References

1. Tjandra JJ, Lim JF, Hiscock R et al. (2004) Injectable silicone biomaterial for fecal incontinence caused by internal anal sphincter dysfunction is effective. *Diseases of the Colon and Rectum* 47: 2138−46.
2. Davis K, Kumar D, Poloniecki J (2003) Preliminary evaluation of an injectable anal sphincter bulking agent (Durasphere) in the management of faecal incontinence. *Alimentary Pharmacology and Therapeutics* 18: 237−43.
3. Malouf AJ, Vaizey CJ, Norton CS et al. (2001) Internal anal sphincter augmentation for fecal incontinence using injectable silicone biomaterial. *Diseases of the Colon and Rectum* 44: 595−600.
4. Kumar D, Benson MJ, Bland JE (1998) Glutaraldehyde cross-linked collagen in the treatment of faecal incontinence. *British Journal of Surgery* 85: 978−9.
5. Shafik A (1993) Polytetrafluoroethylene injection for the treatment of partial fecal incontinence. *International Surgery* 78: 159−61.
6. Shafik A (1995) Perianal injection of autologous fat for treatment of sphincteric incontinence. *Diseases of the Colon and Rectum* 38: 583−7.
7. Feretis C, Benakis P, Dailianas A et al. (2001) Implantation of mircoballons in the management of fecal incontinence. *Diseases of the Colon and Rectum* 44: 1605−9.

Appendix A: Additional papers on injectable bulking agents for faecal incontinence not included in summary table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Chan MKY, Tjandra JJ (2006) Injectable silicone biomaterial (PTQ) to treat fecal incontinence after hemorrhoidectomy. *Diseases of the Colon and Rectum* 49: 433−9.	n = 7 Follow-up 12 months	Continence score improved for up to 12 months.	Larger series included in the main data extraction table.
Bernardi C, Favetta U, Pescatori M (1998) Autologous fat injection for treatment of fecal incontinence: manometric and echographic assessment. *Plastic and Reconstructive Surgery* 102: 1626−8.	n = 1	Authors state this is a report of a patient successfully treated with autologous fat.	Case report
Kenefick NJ, Vaizey CJ, Malouf AJ et al. (2002) Injectable silicone biomaterial for faecal incontinence due to internal anal sphincter dysfunction. *Gut* 51: 225−8.	n = 6 Median follow-up 18 months	At follow-up 5/6 patients had marked symptom improvement. There were no complications.	Comment made by one of the authors (Vaizey) that this paper may be withdrawn or need a major erratum due to data collection flaws.

Appendix B: Related NICE guidance for injectable bulking agents for faecal incontinence

Guidance programme	Recommendation
Interventional procedures	**IPG 66 Artificial anal sphincter implantation** 1.1 Current evidence on the safety and efficacy of artificial anal sphincter implantation does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake artificial anal sphincter implantation should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. Use of the Institute's *Information for the Public* is recommended. • Audit and review clinical outcomes of all patients having artificial anal sphincter implantation. 1.3 Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. The Institute may review the procedure upon publication of further evidence. 1.4 It is recommended that this procedure is carried out only in units with a specialist interest in faecal incontinence. **IPG 99 Sacral nerve stimulation for faecal incontinence** 1.1 Current evidence on the safety and efficacy

Guidance programme	Recommendation
	of sacral nerve stimulation for faecal incontinence appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 The procedure should only be performed in specialist units by clinicians with a particular interest in the assessment and treatment of faecal incontinence. **IPG 138 Intramural urethral bulking procedures for stress urinary incontinence in women** 1.1 Current evidence on the safety and short-term efficacy of intramural urethral bulking procedure for stress urinary incontinence is adequate to support the use of these procedures provided that normal arrangements are in place for clinical governance and for audit or research. 1.2 Clinicians should ensure that patients understand that the benefits of the procedures diminish in the long term and provide them with clear written information. In addition, use of the Institute's Information for the public is recommended. 1.3 Further publication of longer-term efficacy outcomes will be useful. Clinicians should submit data to the British Association of Urological Surgeons registry (available from www.baus.org.uk), or the British Society of Urogynaecologists registry (for further information contact BSUG@rcog.org.uk). **IPG 159 Stimulated graciloplasty for faecal incontinence** 1.1 Current evidence on the safety and efficacy of

Guidance programme	Recommendation
	stimulated graciloplasty for faecal incontinence is limited, but appears sufficient to support the use of this procedure for carefully selected patients in whom other treatments have failed or are contraindicated, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 This procedure should be performed only in specialist units by clinicians with specific training and experience in the assessment and treatment of faecal incontinence.
Technology appraisals	None relevant
Clinical guidelines	Faecal incontinence: the management of faecal incontinence. (Publication expected June 2007.)
Public health	None relevant

Appendix C: Literature search for Injection of biocompatible material to the internal anal sphincter for faecal incontinence

Database	Date searched	Version searched
Cochrane Library	03.05.06	Issue 2: 2006
CRD databases	"	–
Embase	"	1980 – week 17 2006
Medline	"	1966 – April week 3 2006
Premedline	"	2nd May 2006
CINAHL	"	1982 – April week 3 2006
British Library Inside Conferences	"	–
NRR	"	Issue 2: 2006
Controlled Trials Registry	"	–

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

Search strategy used in Medline

1 Fecal Incontinence/
2 ((fec$ or faec$ or anus or anal) adj3 incontinen$).tw.
3 Anal Canal/ab, su, in [Abnormalities, Surgery, Injuries]
4 internal anal sphincter$.tw.
5 IAS.tw.
6 or/1-5
7 exp biocompatible materials/
8 biocompat$.tw.
9 biomaterial$.tw.
10 (inject$ adj3 bulk$).tw.
11 or/7-10
12 silicon$.tw.
13 silicones/
14 polydimethylsiloxane.tw.
15 polyvinylpyrrolidone.tw.
16 povidone.tw.
17 pyrolytic.tw.
18 hydroxyapatite.tw.
19 dextranomer.tw.
20 dextran.tw.
21 polyacrylamide hydrogel.tw.
22 Stem Cells/
23 stem cell$.tw.
24 collagen.tw.
25 (autologous adj3 fat).tw.
26 polytetrafluoroethylene.tw.
27 or/12-26
28 (polytef or contigen or macroplastique or bioplastique or PTQ or durasphere or coaptite or zuidex or permacol or bulkamid).tw.
29 27 or 28

30 6 and 11
31 6 and 29
32 30 or 31
33 animal/
34 human/
35 33 not 34
36 32 not 35