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Australia and New Zealand Horizon Scanning Network

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TERRITORY GOVERNMENTS OF AUSTRALIA
AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology Prioritising Summary

Anal fistula plugs

**November 2008
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**Australian
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and Efficacy
Register
of New
Interventional
Procedures -
Surgical**



**Royal Australasian
College of Surgeons**

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This Horizon scanning prioritising summary was prepared by Miss Deanne Leopardi from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

PRIORITISING SUMMARY

REGISTER ID S000090

NAME OF TECHNOLOGY SURGISIS® AFP™ ANAL FISTULA PLUG

PURPOSE AND TARGET GROUP TO REINFORCE SOFT TISSUE FOR REPAIR IN PATIENTS WITH ANAL FISTULA

STAGE OF DEVELOPMENT (IN AUSTRALIA)

- | | |
|--|---|
| <input type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input checked="" type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | | |
|---|-------------|--------|
| <input checked="" type="checkbox"/> Yes | ARTG number | 153045 |
| <input type="checkbox"/> No | | |
| <input type="checkbox"/> Not applicable | | |

INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Belgium	✓		
Germany	✓		
Netherlands	✓		
United Kingdom	✓		
United States	✓		

IMPACT SUMMARY

Surgisis® AFP™ anal fistula plugs (Cook Biotech Incorporated, West Lafayette, IN) are used for reinforcing soft tissue, as an alternative to mucosal advancement flaps and fibrin glue, in the repair of anal fistulae. Fistula plug technology is in the experimental stage in Australia.

BACKGROUND

A fistula is an abnormal channel, or tract, connecting an organ, vessel or intestine with another structure (Cowles 2007). Fistulae can occur in many parts of the body, and may

be of congenital origin or occur as a result of trauma, surgery, infection or inflammation (Casadesus et al 2006). Various types of fistula include, blind or incomplete fistulae (one open end), complete fistulae (internal and external openings) and horseshoe fistulae (tract encircles the anus and opens externally at both ends) (Virtual Medical Centre 2008).

Anal fistulae occur between the internal anal canal and the exterior skin of the body, near the anus (Zagrodnik 2007). Park's classification describes four categories of anal fistula, based on the location and proximity of the fistula to the sphincter muscles (Zagrodnik 2007).

1. Intersphincteric, which account for 70% of all anal fistulae. The tract begins in the space between the internal and external sphincter muscles and opens adjacent to the anus.
2. Transsphincteric, which accounts for 25% of all anal fistulae. The tract begins in the space between the internal and external sphincter muscles, or in the space behind the anus, and crosses the external sphincter to open adjacent to the anus.
3. Suprasphincteric, which accounts for 5% of all anal fistulae. The tract begins in the space between the internal and external sphincter muscles and turns upward to a point above the puborectal muscle, where it crosses the muscle and extends downward between the puborectal and levator ani muscle to open adjacent to the anus.
4. Extrasphincteric, which are the least common (1% of all anal fistulae). The tract begins at the rectum or sigmoid colon and extends downward, passing through the levator ani muscle and opening around the anus.

Anal fistulae are almost always caused by previous anorectal abscess (Zagrodnik 2007). Approximately 26–37% of anorectal abscesses will result in the formation of a fistula (Nunoo-Mensah et al 2005). When the abscess is opened or ruptures the fistula is formed (Legall 2007). Ninety per cent of anorectal abscess is caused by an infection of the glands which empty into the anal canal; this is known as a cryptoglandular infection (Gordon 1992). Inflammatory bowel disease, in particular Crohn's disease, may also lead to anal fistula, with incidence of anal fistula in patients with Crohn's disease as high as 30–50% (Legall 2007). Trauma, diverticulitis, foreign body reactions, actinomycosis, *Chlamydia*, syphilis, tuberculosis, radiation exposure and human immunodeficiency virus (HIV) are also associated with the formation of anal fistulae (Legall 2007; Zagrodnik 2007). Approximately 30% of HIV patients develop abscess and anal fistula (Legall 2007). Very few patients with anal fistulae are asymptomatic; most patients experience recurrent malodorous perianal drainage, itching, recurrent abscesses, fever and perianal pain (Legall 2007).

The objective of anal fistula repair is to eliminate the primary fistula opening and any associated tracts and secondary openings, whilst maintaining faecal continence (Ellis 2007). Initial intervention for fistula treatment usually involves antibiotic therapy. Although antibiotics may occasionally be successful, the majority of patients with anal fistulae require more invasive treatment. There is no single universally successful technique for treating all manifestations of anal fistulae (Ellis 2007). Anal fistulae are classified as 'complex' if treatment of them is likely to interfere with the patient's

continence, when the tract involves more than 30–50% of the sphincter mechanism or when the patient has a history of pre-existing incontinence, Crohn's disease or local irradiation (Ellis 2007). 'Simple' fistulae are those with minimal sphincter involvement, and are generally easier to treat (Brauer et al 2003). The anatomy and aetiology of the fistula play a large role in determining the type of treatment which is suitable. Common interventions for repair include:

- Fistulotomy, or the laying-open technique, which is successful in 85–95% of simple (low) fistulae. This process involves dividing the subcutaneous tissue and internal sphincter muscles overlaying the fistula tract and removing any granulation tissue (Zagrodnik 2007). Small fistula can be treated under local anaesthesia in a doctor's office, whereas, larger more complex fistula are usually treated under general anaesthesia and in a hospital setting.
- Setons or single-stage (cutting) setons are useful for treating complex (high), recurrent or multiple fistulae. Setons, which can be made from a large silk suture, a silastic vessel marker or a rubber band, are threaded through the fistula tract and gradually tightened over 6–8 weeks. The seton gradually cuts through the sphincter muscles causing fibrosis, which essentially eradicates the tract (Zagrodnik 2007). Seton placement can be performed under local or general anaesthetic and may require a hospital stay.
- Fibrin glue is a solution of clotting factors (including fibrinogen and thrombin) which is injected into the fistula to form a clot within the tract and promote healing. This is an alternative treatment for complex high fistula (van Koperen et al 2008a).
- Mucosal advancement flap involves excising the primary opening of the fistula followed by mobilisation of the mucosa, submucosa and a small amount of muscle from the internal sphincter complex. A rectal flap (2–3 cm) is placed over the opening of the fistula with overlap to provide sufficient sealing of the opening. Granulation tissue is removed and the flap is sutured into place. This treatment is commonly used for high fistula, and occurs under general anaesthetic in a hospital setting (van Koperen et al 2008b).

Recently, the development of anal fistula plugs has provided an alternative method of fistula repair. Surgisis AFP anal fistula plugs are bioabsorbable xenografts made of lyophilized pig intestinal submucosa (Champagne et al 2006). The material is resistant to infection, produces no foreign body or giant cell reactions and is capable of becoming repopulated by the host cell tissue over a period of three to six months (Champagne et al 2006; O'Connor et al 2006). The plug is implanted into the fistula tract and sutured securely to the primary opening under general anaesthesia (Ky et al 2008).

CLINICAL NEED AND BURDEN OF DISEASE

Anal fistula is a common surgical condition, particularly in men. The overall prevalence of anal fistula is 8.6 cases per 100,000 individuals (Thekkinkattil et al 2008). The prevalence rate in men and women is 12.3 and 5.6 cases per 100,000, respectively (Zagrodnik 2007). Patients with anal fistulae not only suffer physically but emotionally, psychologically and socially (Casadesus et al 2006). Management of high anal fistulae is

particularly challenging, with fistulae recurrence rates as high as 54% and post-procedural incontinence rates as high as 35%.

DIFFUSION

The Surgisis anal fistula plug has been approved by both the Australian Therapeutic Goods Administration (TGA) and the US Food and Drug Administration (FDA). The FDA approved premarket notification [510(k)] for the device in March 2005 and the TGA approved it in 2008 (Centre for Devices and Radiological Health 2008; Medical Device Evaluation Committee 2008).

Clinical trials are mainly being conducted in the United States, with several isolated studies from Belgium, Germany, the Netherlands and United Kingdom. Although this technology is available in Australia, there have been no clinical trials produced using the device in an Australian population and there is little information available in regards to its stage of development.

COMPARATORS

Fistulotomy is the current 'gold standard' for treating anal fistulae (Ellis 2007). However, fistulotomy is the preferred treatment for simple (low) fistula, while fistula plugs are commonly used to treat complex (high) fistulae. Thus, it is more likely that mucosal advancement flaps and fibrin glue, which are also commonly used to treat complex fistulae, are the main comparators for anal fistula plugs.

Although seton placement is also used to treat high fistulae, the main purpose of this procedure is to control symptoms rather than heal the fistula like anal fistula plugs, advancement flaps and fibrin glue.

SAFETY AND EFFECTIVENESS ISSUES

A total of four studies were retrieved for inclusion in this summary. One non-randomised comparative study compared anal fistula plugs with mucosal advancement flaps (Ellis 2007) and another non-randomised comparative study compared anal fistula plugs with fibrin glue (Johnson et al 2006). The remaining two studies were prospective case series (Champagne et al 2006; Ky et al 2008).

In the prospective cohort study by Johnson et al (2006), patients with high anorectal fistulae were enrolled to receive treatment using anal fistula plugs (men n=11; women n=4) or fibrin glue (men n=8; women n=2). The mean age of patients in the anal fistula plug group was 45.4 ± 2.4 (standard error of the mean) years and 46.5 ± 3.3 years in the fibrin glue group. Patients with Crohn's disease or superficial fistulae (\leq low transsphincteric) were excluded. Six patients in each group had multiple fistula tracts (with multiple secondary openings); one patient in the plug group and two in the fibrin glue group had multiple primary openings also ($P > 0.05$). Twelve and eight patients in each group, respectively, had undergone one or more previous attempts at fistula closure. Successful fistula treatment was defined as closure of all secondary openings and the absence of drainage and abscess formation. Mean follow-up length (calculated for patients with successful closure) was similar between the groups, at 13.8 ± 3.1 weeks in the anal fistula plug group and 13.6 ± 0.9 weeks in the fibrin glue group.

Ellis (2007) conducted a retrospective analysis of prospectively collected data on patients with anal fistulae treated with fistula plugs or mucosal advancement flaps. A total of 18 patients (men n=12; women n=6) with a mean age of 32 years (range, 21–56 years) underwent anal fistula plug insertion and 95 patients (men n=43; women n=52) underwent mucosal flap advancement (mean age 42 years [range, 21–69 years]). Patients whose fistula was related to acute obstetrical trauma or radiation and patients with a history of Crohn's disease were excluded. In the patients receiving plug insertion 13 had transsphincteric fistulae and 5 had rectovaginal fistulae, compared with 51 and 44 patients receiving mucosal advancement flap repair, respectively. The treatment groups were comparable in regards to gender ratio, age and fistula anatomy ($P>0.05$). Median follow-up in the plug group was 6 months (range, 3–11 months) compared with 10 months (range, 6–22 months) in the mucosal advancement flap group.

Champagne et al (2006) recruited 46 patients (55 individual fistula tracts) with high cryptoglandular anorectal fistulae were enrolled during a two-year period to undergo repair using the anal plug technique. Patients with Crohn's disease or superficial (low transsphincteric or less) fistulae were excluded. Thirty-nine and seven patients had single or multiple tract fistulae, respectively. Long-term follow-up measured the success of the treatment and occurred at a median of 12 months (range, 6–24 months) after treatment (as calculated for fistulas that were successfully closed). Success criteria were defined as closure of all secondary openings, an absence of fistula drainage and an absence of abscess formation.

In the prospective case series study conducted by Ky et al (2008), 45 patients with anorectal fistulae were enrolled to receive a Surgisis anal fistula plug. The average age of the patients was 44.1 years (range, 22–71). Patients with low transsphincteric or superficial fistula tracts with minimal or no sphincter muscle involvement were excluded from the study. Patients had either simple (cryptoglandular, single tract; n=24 [54.6%]) or complex (rectovaginal, horseshoe, multiple tracts, in conjunction with Crohn's disease; n=20 [45.4%]) fistulae. The treatment was deemed to have failed if patients had an infected fistula tract, persistent drainage or a residual external opening. Median follow-up was 6.5 months (range 3–13 months).

Safety

As there were no safety data presented in any of the included studies, it is unclear whether any adverse events occurred.

Effectiveness

At final follow-up, Johnson et al (2006) reported significantly less patients with persistent drainage and/or patent secondary fistula openings in the plug group (13% (2/15) of patients), compared with the fibrin glue group (60% (6/10) of patients) ($P<0.05$). The median time to failure was four weeks in both groups.

Ellis (2007) reported fistula recurrence in 12% (2/18) of patients in the plug group compared with 32.6% (31/95) of patients in the mucosal advancement flap group. This difference was not significant. The two plug recurrences occurred at 28 days in one

patient with poorly managed diabetes and a horseshoe fistula and at 11 months in a patient with a rectovaginal fistula related to Crohn's disease. The median time to recurrence in the mucosal advancement flap group was 14 days (range, 7–42 days). Preoperative average pain scores (scoring system not specified) were 3.0 ± 1.0 in the plug group and 2.6 ± 0.8 in the mucosal advancement flap group. This increased in both groups to 3.8 ± 1.3 and 4.4 ± 2.7 , respectively, by the first or second postoperative day. By 7–10 days postoperative, pain score had decreased in the plug group (to 3.3 ± 1.1) but increased in the mucosal advancement flap group (5.8 ± 3.1).

Subset analyses were carried out between patients aged above and below 40 years, transsphincteric fistula compared with rectovaginal fistula and men compared with women. There was no significant difference seen between any of these groups (Ellis 2007).

In the study by Champagne et al (2006), there were no losses to follow-up. At the final follow-up (add time period here to remind reader), 83% (38/46) of patients had successful closure of all of their fistula tracts, which equated to 85% (47/55) of all fistula tracts. Patency persisted in 15% (8/55) of fistula tracts. There was no statistical correlation seen between multiple tracts and closure rates. Of the eight failures, seven occurred within 30 days of implantation of the plug and one patient developed recurrent fistula at nine months. Of the seven early failures, four plugs fell out of the fistula tract as a result of excessive activity or inadequate suturing. Extrusions occurred more frequently in shorter (superficial) tracts compared with longer (deeper) tracts. Two additional failures occurred in patients with horseshoe fistula tracts, in which the tract containing the plug was closed but the contralateral tract persisted. One patient experienced persistent drainage despite the plug remaining intact. In one female patient, a late recurrent abscess developed at the same site as the previously closed fistula tract; this was drained and a temporary seton was inserted. All of the nine patients with setons prior to surgery had multiple fistula tracts. There was no statistical correlation between the presence of setons and closure rate.

In the study by Ky et al (2008), one patient was lost to follow-up, which meant three month effectiveness outcomes were only available in 44 patients. There were early plug failures in 27.2% (12/44) of patients. By three months' follow-up an additional 11.4% (5/44) of patients had plug failures. A further 3 patients (6.8%) experienced recurrent drainage and fistula at 4, 11 and 12 months, despite documented closure at three months. The proportion of patients with healed fistula at approximately one month follow-up was 83.8% (31/37), which declined to 72.7% by the second month of follow-up, 62.4% by the third month of follow-up and 54.6% by one year. There were no incidences of incontinence to stool or flatus in the postoperative period.

Of the 24 patients with single fistulae, 70.8% (17) had successful closure compared with 35% (7/20) of patients with complex fistulae ($P=0.019$). Successful fistula closure occurred more frequently in patients who did not have Crohn's disease (66.7% [20/30]) compared with those who did (28.6% [4/14]) ($P=0.017$). There was also a significantly greater treatment success in patients with first-time plug placement (63.9% [23/26]) compared with patients receiving two subsequent plugs to replace an initial failed plug

(12.5% [1/8]) (P=0.011). There was no significant correlation between treatment success and the number of fistulae per patient or undergoing perianal drainage at the time of plug insertion (Ky et al 2008).

COST IMPACT

Thekkinkattil et al (2008) stated that the cost of a single plug was \$1000 (currency not specified), which is considerably greater than the cost of other anal fistula treatments in an Australian clinical setting (see Table 1 for details). Other authors have commented that the cost of the plug may deter some patients from using this treatment alternative (Christoforidis et al 2008).

However, it is important to note that the cost effectiveness of the plug may depend on its efficacy. That is, if a patient's fistula is successfully treated with the plug after one short procedure although the plug was more expensive than conventional therapies it may prove to be more cost effective than a cheaper conventional treatment with a lower success rate. This is because if the patient's fistula is not successfully treated after the initial intervention they may require drainage of their fistula tract, treatment for iatrogenic incontinence or further operations.

Table 1: Treatments for anal fistula listed on the Medicare Benefits Schedule (MBS) and their cost (MBS 2008)

Item number	Descriptor	Fee
32159	ANAL FISTULA, treatment of, by excision or by insertion of a Seton, or by a combination of both procedures, involving the lower half of the anal sphincter mechanism (Anaes.) (Assist.)	\$300.95
32162	ANAL FISTULA, treatment of, by excision or by insertion of a Seton, or by a combination of both procedures, involving the upper half of the anal sphincter mechanism (Anaes.) (Assist.)	\$437.05
32165	ANAL FISTULA, repair of, by mucosal flap advancement (Anaes.) (Assist.)	\$573.15
32166	ANAL FISTULA - readjustment of Seton (Anaes.)	\$186.20

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

One study was presented at the Surgisis® Consensus Committee, for which all of the participants received reimbursement for their expenses and an honorarium from Cook Medical Incorporated for dedicating their time. As well as this, in two other studies, one author (Dr D Armstrong) reported a patent-licensing agreement with the manufacturer of Surgisis® (Cook Surgical, Inc., Bloomington, IN). The same author reported the acceptance of royalties on sales of the Surgisis product in another included study.

A study protocol for a randomised controlled trial (RCT) was identified as relevant for this summary (van Koperen 2008b). The double-blinded RCT intends to compare fistula closure rate, continence, postoperative pain and quality of life following treatment of high anorectal fistulae of cryptoglandular origin using anal fistula plugs and mucosal

advancement flaps. The study appears to be of high methodological quality and would greatly add to and improve the current evidence base available for this comparison.

SUMMARY OF FINDINGS

From the included comparative studies anal fistula plugs appear to be more effective compared with mucosal advancement flaps and fibrin glue. However, additional high quality studies are required to support this.

Overall, the plugs appear to be more successful in patients with less anal sphincter involvement, or simple (low) fistulae and in the immediate postoperative follow-up, with inconsistent results for the long-term durability of the procedure. This may indicate a need to further refine the plug insertion technique, particularly the suturing stage as many late failures were due to extrusion of plugs that were insufficiently attached. Therefore, until the procedure's modality is optimised and appropriate selection criteria for patient selection are established it is difficult to reach a conclusion regarding the efficacy of anal fistula plugs. In particular, future studies should compare anal fistula plugs with the current standards of care, with emphasis on cost effectiveness and recurrence rate.

HEALTHPACT ACTION

Due to the lack of high quality comparative evidence available for anal fistula plugs and the largely variable success rates, the potential use of this procedure as a viable alternative remains unclear. Long-term studies are required; therefore it is recommended that anal fistula plugs are monitored for 24 months.

NUMBER OF STUDIES INCLUDED

Total number of studies	4
Level III-2 evidence studies	2
Level IV evidence studies	2

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SOURCES OF FURTHER INFORMATION

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SEARCH CRITERIA TO BE USED

Anal fistula*

Plug

Bioprosthetic OR bioprosthesis

“Surgisis”

PRIORITISING SUMMARY (UPDATE 2010)

NAME OF TECHNOLOGY

SURGISIS® AFP™ ANAL FISTULA PLUG

PURPOSE AND TARGET GROUP

TO REINFORCE SOFT TISSUE FOR REPAIR IN PATIENTS WITH ANAL FISTULA

2010 SAFETY AND EFFECTIVENESS ISSUES

Study descriptions

A total of four comparative studies were eligible for inclusion in this update (Ortiz et al 2009; Wang et al 2009; Christoforidis et al 2009; Adamina et al 2009), all of these studies compared outcomes of anal fistula plugs with those of endorectal advancement flaps for the treatment of complex (high) anal fistulas. One of the included studies was randomised (Ortiz et al 2009).

Ortiz et al (2009) randomly allocated consecutive patients, with high fistula *in ano* of cryptoglandular aetiology, from May 2007 to undergo repair with anal fistula plugs (n=16) or endorectal advancement flaps (n=16). The method of randomisation used in this study was a computer-generated table of random numbers. Patients were followed up at 2, 4, 8, 12, and 24 weeks and 1 year, in an outpatient clinic by an independent observer by means of an interview and physical examination (31 patients were available for follow-up at 1 year). Patients were well-matched at baseline in regards to demographic data and fistula characteristics. Recurrence was defined as the presence of an abscess arising in the same area as the original fistula, or obvious evidence of fistulation.

In the study by Wang et al (2009) patients who had undergone fistula plug placements (n=29) or mucosal advancement flap procedures (n=26) between 2001 and 2006 were identified and retrospectively reviewed. All included patients in both groups underwent treatment for transsphincteric cryptoglandular fistulas and were followed up postoperatively for a minimum of 3 months. The primary outcome measure in this study was complete fistula closure, defined as absence of drainage from the external opening of the repaired fistula.

Christoforidis et al (2009) retrospectively reviewed the electronic medical records of all patients treated for anal fistula. A total of 47 consecutive patients were treated with anal fistula plugs between January 2006 and April 2007, 37 of these were eligible for inclusion, and a total of 125 consecutive patients were treated with endorectal advancement flaps between April 1996 and April 2007, 43 eligible for inclusion. Patient characteristics were comparable at baseline in regards to age, duration of symptoms, and fistula characteristics. Mean follow-up duration was 14 months (range, 6-22 months) in the fistula plug group and 56 months (range, 6-136 months) in the advancement flap group. Failure of treatment was defined as the need for additional surgery, anal fistula plug extrusion, or persistence of drainage from a patent external opening.

Finally, Adamina et al (2009) compared consecutive patients with complex anal fistula of cryptoglandular origin who underwent anal fistula plug placement or endoanal advancement flap procedures by the same surgeon. A total of 12 patients treated between October 2006 and October 2007 were included in the anal fistula plug group and a total of 12 patients treated between July 1999 and October 2005 were included in the advancement flap group. These patients were followed up at a median of 28.1 weeks (range, 7.4-43.9 weeks) and 14.1 weeks (range, 2-160.7 weeks), respectively. Success was defined as the absence of drainage and fistula opening on physical examination and as the absence of abscess formation at any time during follow-up. Costing data was collected by an accountant who was blinded to the purpose of the study. All costs related to the surgical procedure and hospital stay were collated (reported in 2008 US dollars) and compared between the procedure types.

Safety

There was no safety data reported in the randomised controlled trial by Ortiz et al (2009), or the non-randomised comparative study by Wang et al (2009).

Christoforidis et al (2009) reported low complication rates in both the anal fistula plug group and the advancement flap group. Two patients in the advancement group required reoperation for bleeding on postoperative days 5 and 7, respectively. No serious complications occurred in the anal fistula plug group, and five patients suffered from pain and increased drainage postoperatively and were treated with antibiotics. Adamina et al (2009) reported no abscesses or complications in either the anal fistula plug group or the advancement flap group.

Effectiveness

Ortiz et al (2009) reported fistula recurrence at 1 year in 80% (12/15) of patients in the anal fistula plug group compared with 13% (2/16) of patients in the advancement flap group ($P<0.001$). Of the patients who underwent previous fistula surgery ($n=16$), 56% had recurring anal fistula, the majority of these patients (89%) underwent anal fistula plug placement as their secondary treatment. Of the 14 cases of fistula recurrence, seven healed, six were treated with advancement flap procedures, and one was treated with anal fistula placement. Specifically, in the anal fistula plug group: one patient was diagnosed with recurrence by abscess at the same site as the original fistula at 2 weeks follow-up, three patients were diagnosed with recurrence by plug extrusion at 2 weeks ($n=1$) or 4 weeks ($n=2$) follow-up, and persistent leakage around the plug was noted in eight patients. In the advancement group: two recurrences were diagnosed by the presence of abscess at the original fistula site, all of which were detected during the first 3 months follow-up.

In the study by Wang et al (2009) the median length of hospital stay was significantly shorter in patients following anal fistula plug placement (0 days; range, 0-2 days) compared with patients following advancement flap procedures (1 day; range, 0-3 days) ($P<0.001$). Complete fistula closure occurred at a significantly lower rate in the anal fistula plug group (34%) compared with the advancement flap group (62%) ($P=0.045$). The same was seen when five HIV positive patients (four of which had failed procedures) were excluded from analysis (35% versus 67%, $P=0.02$).

The study by Christoforidis et al (2009) reported healed fistula in 32% (12/37) of patients in the anal fistula plug group, which was significantly fewer than in the advancement flap group (27/43, 63%) (P=0.008). In a time to failure analysis, failure occurred less frequently following repair with an advancement flap. When patients in the anal fistula plug group who experienced early extrusion of their plug were excluded from analysis, the difference in healing rate between the groups was no longer significant (40% versus 63%; P=0.062). Recurrence following temporary healing, at greater than 6 months follow-up, occurred at a similar rate between the anal fistula plug group (20% of failures) and the advancement flap group (19% of failures). Four patients from the anal fistula plug group underwent secondary advancement flap procedures, of these two healed and two were unsuccessful, and one patient from the advancement flap group underwent successful secondary fistula plug placement.

The study by Christoforidis et al (2009) also assessed postoperative functional outcomes in patients undergoing treatment of their anal fistula through questionnaires. Fifty-eight percent (7/12 patients with healed fistula) and 85% (23/27 patients with healed fistula) of patients in the fistula plug group and advancement flap group, respectively, responded to this questionnaire. Findings from these questionnaires in regards to Cleveland Clinic Florida – Faecal Incontinence (CCF-FI) score are presented in Table 1.

Table 1: Functional outcomes in patients with healed fistula.

CCF-FI Score	Description of score	Treatment group	
		Anal fistula plug	Advancement flap
0-2	No continence disturbance or gas/liquid incontinence less than 1 time/month	6/7 (86%)	11/23 (48%)
3-4	Occasional gas incontinence with rare liquid stool incontinence	-	8/23 (35%)
7-12	Lifestyle alternations with frequent liquid stool and/or occasional solid stool incontinence	1/7 (14%)	4/23 (17%)

The final included study by Adamina et al (2009) reported a significantly shorter hospitalisation period in patients in the anal fistula plug group (median 1 day) compared with patients in the advancement flap group (median 2.5 days) (P=0.0002). At 6 months follow-up, 67% (8/12) of patients in the anal fistula plug group were healed, with an additional two failures occurring at 37 and 44 weeks follow-up, leading to an overall success rate of 50% (6/12). This was not significantly different to the overall success rate of the advancement flap procedure (33%; 4/12) (P=0.680).

COST IMPACT

Adamina et al (2009) reported the overall cost of the anal fistula plug procedure to be \$2,096.30 (95% confidence interval [CI], \$1,978.10-\$2,214.40). This was significantly less than the cost of the advancement flap procedure at \$3,690 (95% CI, \$3,306.50-\$4,073.50; t value 8.74, P<0.0001). A multiple regression analysis modelling the relationship between total cost and surgical therapy, while adjusting for the covariates age, sex, and length of stay, found that performing fistula plug surgery instead of advancement flap surgery saved on average \$824.90 (95% CI, \$132.60-\$1,517.30), when

adjusting for length of stay (plus \$444.30 for every additional hospital day; $t=2.3$, $P=0.033$), age, and sex. It is important to note that patient numbers in this study were small (12 patients per treatment group); therefore, caution is necessary when interpreting these results as the number of included patients may not have been sufficient to detect an actual significant difference in cost between anal fistula plugs and advancement flaps.

OTHER ISSUES

The study by Ortiz et al (2009) started recruiting patients in May 2007 and reported the discontinuation of inclusion of patients into the anal fistula plug group in October 2007 due to an ‘unusually high number of recurrences’.

Two of the authors in one of the included studies (Christoforidis et al 2009) received funding from Cook Medical Inc., the manufacturer of the anal fistula plug.

2010 SUMMARY OF FINDINGS

From the current evidence available, anal fistula plug placement in patients with complex (high) anal fistula of cryptoglandular origin does not appear to be associated with major complications. In terms of effectiveness, compared with the advancement flap procedure, fistula plug placement appears to be associated with a significantly higher recurrence rate, particularly in patient with previous failed fistula surgery. Complete fistula closure rate, as reported in two comparative studies, also appears to be significantly better (higher) following the advancement flap procedure (62-63%) compared with anal fistula plug placement (32-34%). In favour of plug placement to treat anal fistula, the duration of hospitalisation following the procedure was reported to be significantly reduced compared with the advancement flap procedure in two of the included studies. Also, one study reported functional (continence) outcomes following surgery, measured with a questionnaire, and found results to be improved with anal fistula plugs; however, only 7 patients in the anal fistula plug group responded to the questionnaire.

2010 HEALTHPACT ASSESSMENT

Based on the findings of this update and the unsubstantiated benefits of anal fistula plugs for the treatment of complex (high) anal fistula it is recommended that this procedure be noted and no further assessment by HealthPACT is necessary.

2010 INCLUDED STUDIES

Total number of studies	4
Level II intervention evidence	1
Level III-3 intervention evidence	3

2010 REFERENCES

Adamina M, Hoch JS, Burnstein MJ. To plug or not to plug: a cost-effectiveness analysis for complex anal fistula. *Surgery* 2009; 147(1): 72-78.

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