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Horizon Scanning Report

Artificial Cervical Disc Replacement (update) January 2006

ASERNIP-S

Australian Safety and Efficacy Register of New Interventional Procedures - Surgical

Royal Australasian College of Surgeons

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This Horizon scanning report was prepared by staff from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

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Background

Background to the Condition

Discectomy and arthrodesis with or without compression has been used for many years to treat significant radicular pain and symptomatic spinal spondylosis (Trayelis 2002). This surgical approach, however well developed, is not without its limitations. In addition, the success of artificial prostheses for hip and knee joints has prompted further investigation into comparable intervertebral disc replacement alternatives. Both lumbar and cervical disc replacement systems have been proposed. Several lumbar disc models are currently available. Cervical disc prostheses have had a slower period of development which can be attributed to the more complex biomechanical considerations posed by the cervical spine.

Patients suitable for cervical disc replacement are those where conservative management has failed and surgical intervention is indicated for their chronic symptoms resulting from cervical disc herniation, disc degenerative disease or spondylosis. Current surgical treatment involves discectomy and/or decompression and fusion. Therapeutic modalities include medication, chiropractic, physical therapy and intradiscal electrothermal therapy (IDET) (Blumenthal *et al.* 2002).

Disadvantages of discectomy, decompression and fusion include:

- loss of cervical mobility or hypermobility
- risk of increased load and degeneration of adjacent spinal levels
- increased incidence of postoperative interscapular pain
- reliance on postoperative immobilisation such as a cervical collar or internal plate and screws, or both
- donor site complications from bone grafting performed for fusion procedures
- possible disease transmission from donor bone grafts for fusion procedures.

The main advantage of cervical disc replacement is that it attempts to re-create a more anatomical functional spinal unit to replace a symptomatic disc without the need for spinal fusion so more anatomic motion can be preserved.

Description of the Technology

This report covers only cervical disc technologies including:

- The Bristol (Cummins) Disc
  A 'ball and socket' device constructed of stainless steel.
  Other modifications on this basic design have been known as the Frenchay or Prestife™ or Prestige™ cervical disc system (Medtronic Sofamor Danek, Tennessee, USA). These later models have been re-designed with a 'sleeker profile' and instrumentation that allows for easier implantation.

- The Bryan® cervical disc system (Medtronic Sofamor Danek, Tennessee, USA)
  A composite artificial disc with a low friction, wear resistant elastic nucleus placed between two anatomically shaped titanium end-plates.

- The Porous Coated Motion (PCM) cervical disc (Cervitech, Rockaway, New Jersey, USA)
  An artificial cervical disc with large, anatomically designed cobalt chrome endplates, shaped to maximise loading in the more dense lateral vertebral surfaces, and a porous ingrowth material (two ultra-thin layers of titanium with electrochemically coated Calcium Phosphate).

Another cervical disc prosthesis design that is under clinical investigation is the PRODISC® (Synthes-Stratec Spine Solutions, New York, USA) which is currently undergoing multi-centre clinical trial work in the US. More information about this trial can be found at (http://www.spineuniverse.com/print.php/article2436.html), accessed March 24 2004). A number of other designs have also been developed by Weber, Patil, Lesoin, Kehr, Ibo and Pierotto, Cauthen, Buhler and Ramadan and Medizadeh (Szpalski *et al.* 2002).

The Procedure

Advances in joint reconstruction and biomaterials have revolutionised the treatment of all types of degenerative joint disease. Following the success of total joint arthroplasties for the hip or knee joints, attention has more recently focused on the successful development of intervertebral disc prostheses. Prostheses developed to replace lumbar intervertebral discs have been attempted first; more than 40 years ago Alfred Nachemson implanted stainless steel balls to replace lumbar intervertebral disc spaces in over 100 patients (Nachemson 1992). Since then several lumbar disc prostheses have been developed such as the Link SB Charité, the Acromed Acroflex, and PRODISC®.

The cervical spine is a more complex biomechanical construct, necessitating a longer period of development to produce suitable artificial discs. Recent advances in both biomechanical knowledge of the cervical spine and the long-term use of biomaterials have assisted the development of several cervical disc replacement systems. There are many issues to consider in the design and use of an artificial joint in the spine. Proper intervertebral spacing needs to be maintained to provide stability whilst allowing for natural joint motion. The artificial disc must also emulate the ability of a functional spinal unit to provide shock absorption. Also, the prosthesis must be designed so that it can be implanted and worn safely, as there is potential for injury to major vascular and neural structures during device placement, unanticipated device displacement or fracture and wear debris. Additionally, the ideal device would allow safe revision (Guyer & Ohnmeiss 2003; Hallab *et al.* 2003). As the expected treatment population includes older patients with degenerative disc disease, as well as relatively younger patients with cervical disc injury due to trauma, the artificial disc itself must have a life expectancy over a time frame of 50 years (Hallab *et al.* 2003).

Intended Purpose

The current purpose is to replace a cervical intervertebral disc where surgically indicated for patients with cervical disc herniation or cervical disc degenerative disease or spondylosis.

Clinical Need and Burden of Disease

The target group consists of two main sub-groups:

- younger, otherwise healthy patients with cervical disc injury due to trauma
- older patients with cervical degenerative disc disease.

In the USA, cervical degenerative disc disease accounts for 36% of all disc disease and is a condition more common in women with an incidence peak in persons aged 45 to 50 years of age. Prevalence studies of cervical radiculopathies demonstrate that two age peaks exist; at 20 to 30 years and 60 to 70 years (Windsor & Nieves 2002). The vertebra C7 is the most common nerve root involved (Kramer 1981). In Australia, from July 2004 to June 2005, there were 4775 requested Medicare services processed for cervical discectomy (without fusion), cervical decompression including fusion, discectomy (including fusion or bone grafting), spinal bone graft and spinal fusion (Medicare Benefits Schedule item numbers 40333, 40335, 48639, 48640, 48642, 48645, 48648, 48651, 48654, 48657, 48660, 48663, 48666, 48669, 48672 and 48675) by the Health Insurance Commission (Medicare Australia) for the private health care sector.

Stage of Development

The rate of diffusion of cervical disc replacement technology into Australia has been relatively slow. At the time of report writing, only one cervical disc replacement system had obtained TGA approval in Australia (product ID 162167, Orthopaedic Internal Fixation Systems, Spinal) sponsored by Medtronic Sofamor Danek Aust Pty Ltd (ARTG Number 40374). It is still under clinical investigation in Australia with results available through both a published case report and small case series, and an unpublished case series. These have been included in this report.

Treatment Alternatives

Existing Comparators

The current surgical treatment is discectomy and/or decompression and fusion. While it is an effective surgical strategy to minimise radiculopathy and chronic pain, there are several disadvantages which have been outlined above such as increased adjacent disc degeneration, altered mechanics because of surgical fusion and risk of donor bone graft site complications.

In relation to the current surgical treatment, overall success rates in reducing radicular pain following discectomy have been reported in the literature as being between 48% and 89% (Crawshaw *et al.* 1984; Hanley *et al.* 1989; Nordby 1985).

Re-operation rates following discectomy and fusion for adjacent level disease is reported to be 3% per year (Hilibrand *et al.* 1997). At 10 years follow-up, 25% of all patients exhibit symptoms of adjacent level disease (Hilibrand *et al.* 1999). Clinical series have demonstrated excellent to good clinical outcomes in 80% to 90% of patients (Clements *et al.* 1992). Successful fusion (or arthrodesis) has been demonstrated in 92% to 96% of patients after single-level discectomy (Edwards *et al.* 2003). Numerous studies have reported a range in pseudoarthrodesis rates of 2% to 20% after single-level uninstrumented anterior cervical discectomy and fusion using structural allografts to be the same as that obtained from autografts. However for multilevel discectomy and fusion, the incidence of non-union is higher with allografts. The later introduction of cervical plating has led to an improvement in this rate of successful fusion (Edwards *et al.* 2003).

With increased degeneration of spinal units adjacent to a fused unit, as well as an increase in longitudinal strain, further medical or surgical interventions are often warranted for patients due to an artificially accelerated rate of degeneration (Pickett *et al.* 2003) in the adjacent disc levels. It is possible that a cervical disc replacement may solve the problem of adjacent level disease because of more anatomic cervical biomechanics from disc replacement rather than disc removal and fusion.

It is not yet clear whether cervical disc replacement would be more efficient or require fewer resources than cervical discectomy and/or fusion. Both procedures require operative intervention but there may possibly be a minimised requirement for postoperative bracing or orthoses with the cervical disc replacement option.

Clinical Outcomes

A total of 13 studies were located; one randomised controlled trial (RCT) with preliminary results, 10 case series and two case reports. The RCT by Porchet *et al.* (2004) trialled the Prestige II™ disc and the case series by Wigfield *et al.* (2002), Pimenta *et al.* (2004) and Robertson *et al.* (2004) examined the Frenchay artificial cervical joint, the porous coated motion (PCM) prosthesis and the Prestige I™ cervical disc respectively. The remaining nine studies used the Bryan® cervical disc.

Effectiveness

Clinical Outcomes

Patient satisfaction in regards to clinical outcomes was not reported in the RCT by Porchet *et al.* (2004). However, a majority of patients across seven case series had excellent, good or fair clinical outcomes.

At six months follow-up, two case series (Goffin *et al.* 2002, Pimenta *et al.* 2004) reported excellent, good or fair outcomes in 87% (52/60) and 100% (52/52) of their patients, respectively. Goffin *et al.* (2003) reported excellent, good or fair outcomes in 90% (83/92) of patients who received single-level cervical disc replacement and 82% (28/34) of patients who received bi-level disc replacement. Sekhon (2003) noted that all seven patients in their small case series exhibited excellent to fair clinical outcomes at a mean 6.3 months follow-up. There appears to be some overlap of patients with a case series of 12 patients by Sears *et al.* (unpublished). Sears *et al.* (unpublished) reported excellent to fair subjective patient outcomes in 92% (11/12) of patients, and a worse procedural outcome reported by one patient.

Excellent, good or fair outcomes were reported in 87% (40/46; Bryan *et al.* 2002), 90% (27/30; Goffin *et al.* 2002) and 100% (52/52; Pimenta *et al.* 2004) of patients at one-year follow-up. The same positive outcomes were reported in 85% (76/89) of single-level patients and 96% (25/26) of bi-level patients at one-year follow-up (Goffin *et al.* 2003). A high percentage of bi-level patients in the study by Anderson *et al.* (2004) also reported excellent, good or fair outcomes (29/30, 97%).

In patients with two years of follow-up, 89% (8/9, Bryan *et al.* 2002; 65/73 single-level patients, Anderson *et al.* 2004) and 90% (44/49 single-level patients, Goffin *et al.* 2003) of patients had excellent, good or fair outcomes.

A poor outcome was reported in a minority of patients across five case series, ranging from 0% to 18% at six months follow-up, 0% to 15% at one-year follow-up and 10% to 11% at two years follow-up (Bryan *et al.* 2002, Goffin *et al.* 2002, Goffin *et al.* 2003, Anderson *et al.* 2004, Pimenta *et al,* 2004).

Hospital Stay

Goffin *et al.* (2002) reported an average hospital stay of 3.6 days. This remained the same in their later series (2003) with an average length of stay of 3.5 days for single level replacement patients and 3.6 days for bi-level patients. Pimenta *et al.* (2004) reported a mean hospital stay of 1 day for the implantation of 81 cervical discs in 52 patients.

Radiculopathy

In terms of radiculopathy, Goffin *et al.* (2002) reported scores of excellent, good to fair for 89% (47/53) of patients at six months, with 72% (38/53) of patients reporting excellent outcomes. At one year, 89% (24/27) of the scores were excellent, good or fair with most patients (78%) in the 'excellent' result category.

Sears *et al.* (unpublished) reported recurrent radiculopathy at 19 months postprocedure for one out of twelve patients (8%) undergoing the procedure.

Myelopathy

No postoperative cases of myelopathy were reported in the patients who underwent anterior cervical discectomy and arthroplasty with the Prestige II™ disc. Of the 28 control patients who underwent anterior cervical discectomy and fusion in the RCT by Porchet *et al.* (2004), two of the 19 reported adverse events involved secondary

myelopathy requiring additional adjacent-level surgery. The symptoms resolved in one case but were permanent in the other.

Goffin *et al.* (2002) reported 72% (5/7) of patients had scores of excellent, good or fair for this particular parameter. Goffin *et al.* (2003) reported that 1/26 (4%) patient developed recurrent myelopathy one year post-operatively.

Range of Motion

Porchet *et al.* (2004) reported no statistically significant differences between cervical disc and controls in adjacent-level motions in the limited sample of patients analysed at 12 months.

Motion was preserved in all 14 cases in the study by Pickett *et al.* (2004); however, there were no significant differences seen in range of motion between the postoperative and preoperative measures. A later study by Pickett *et al.* (2005) reported similar results in 20 patients, where range of motion remained similar post-operation. However, cervical saggital motion from C2-C7 was shown to have increased significantly (mean 8.9º, p=0.027) at 24 months. This increase of 8.9º was distributed over all spinal levels. Further kinematic analysis did not reveal and changes in the centre of rotation, translation and disc distraction post-surgery.

Goffin *et al.* (2002) reported that 93% (53/57) of patients demonstrated a flexion/extension range of motion ≥ 2 degrees at 6 months. By one year, the number of patients with a range of motion of ≥ 2 degrees had dropped slightly to 88% (21/24).

Goffin *et al.* (2003) reported that 97% (86/89) of patients demonstrated a flexion/extension range of motion ≥ 2 degrees at 6 months, 88% (79/90) at one year and 94% (43/46) at 2 years for the single-level patients. For the bi-level patients, 99% (72/73) had a range of motion ≥ 2 degrees at 6 months and 86% (42/49) at one year.

Bryan *et al.* (2002) reported at one year follow-up that 87% (38/44) of all patients had a range of motion ≥ 2 degrees.

For patients who received one-level disc replacement in the case series by Anderson *et al.* (2004), range of motion ≥ 2 degrees was present in 89% (65/73) of patients at one year and two-year follow-up (mean range of motion was 8 degrees). Patients who received bi-level disc replacements reported motion ≥ 2 degrees at both artificial disc levels in 83% (25/30) of patients at one year follow-up, with a mean range of motion of 8 degrees (Anderson *et al.* 2004).

Robertson *et al.* (2004) reported a mean angulation of motion of 4.9 degrees at 36 months follow-up and 5.7 degrees at 48 months follow-up, compared with a mean preoperative angulation of motion of 7.5 degrees.

The study by Wigfield *et al.* (2002), examining the Frenchay device, found that all 15 patients in their series demonstrated flexion/extension ranges of motion of 3 to 15 degrees at two years.

Quality of Life Results

Patients who received the Prestige II™ disc showed improvement similar to the control patients at all postoperative intervals in both the physical and mental component categories (Porchet *et al.* 2004). Both treatment groups in this RCT also showed an improvement in patient assessment questionnaires (i.e. Neck Disability Index (NDI), Visual Analogue Scale (VAS) for arm and neck pain) at all postoperative intervals. The improvement in NDI and VAS for arm pain scores between the two treatment groups showed no difference.

The SF-36 scores from the 14 patients in the Pickett *et al.* (2004) case series demonstrated significant improvements in the areas of physical function (p=0.002), physical role (p=0.017), body pain (p=0.008), vitality (p=0.002), and emotional role (p=0.0004), in the 6- to 24-month follow-up evaluations. Mean NDI scores decreased significantly from the preoperative score of 20.1 to 11.1 at 3 months (p=0.038 vs preoperative score) and 7.4 at 12 months (p=0.006 vs preoperative score) (Pickett *et al.* 2004). However, 1/14 (77%) patient with substantial preoperative and postoperative global cervical kyphosis reported severe axial neck pain and continued to have an NDI score of 30, indicating severe disability, in the 6- to 24-month follow-up evaluations.

Results from the SF-36 questionnaire distribution to patients at 6 months and one year by Bryan (2002) and Goffin *et al.* (2002, 2003) indicate that at one year, all patients had met or exceeded the American population mean for the 'physical' component and 'mental' component dimensions of the questionnaire. Goffin *et al.* (2003) reported SF-36 average scores in the single-level group of 45.3 at 6 months postoperatively, 46.9 at one year and 46.6 at two years for the 'physical' component dimension compared to an average score of 36.1 prior to operation (patient numbers not provided). The 'mental' component dimension of the SF-36 also improved before and after operation; from 41.0 preoperatively to 52.2 at 6 months, 50.0 at one year and 52.9 at two years postoperatively (patient numbers not provided). Similar improvements in SF-36 scores were also observed in Anderson *et al.* (2004) and Robertson *et al.* (2004).

The bi-level group showed similar improvements before and after operation on both 'physical' and 'mental' dimensions (Goffin *et al.* 2003). Whether these preoperative and postoperative results were statistically significant was not reported.

In the Frenchay cervical joint case series, Wigfield *et al.* (2002) reported an improvement in patient assessment questionnaires (i.e. European Myelopathy Score, Neck Disability Index, SF-36, visual analogue scale for neck and upper limb pain) in "all aspects of patient function and quality of life".

Device Stability/Migration/Failure

There were no device-related failures during the follow-up period (at least 12 months follow-up) for patients who were randomised to receive the Prestige II™ disc and no subsidence of any of the devices into the vertebral body bone (Porchet *et al.* 2004). However, 1/17 (6%) patient reported cervical pain and posterior cervical rigidity five weeks postprocedure due to a malposition of the Prestige II™ disc. The joint was removed and the patient underwent a fusion with an anterior cervical cage and follow-up evaluations indicate a good clinical condition.

Goffin *et al.* (2002, 2003) reported no device instability or subsidence in any patients in their series. However, only 57 of their 97 (59%) patients had postoperative radiographic assessment and two patients had either a confirmed or suspected anterior/posterior device migration. Goffin *et al.* (2003) reported implant migration for only one patient.

Bryan *et al.* (2002) found no cases of device instability, subsidence or failure in their case series. One patient had an anterior/posterior device migration but this patient may indeed be the same patient reported with this problem in Goffin *et al.* (2002).

Anderson *et al.* (2004) also reported no evidence of subsidence for both the one-level and two-level groups. One of the 73 (1%) one-level patients had temporary anterior migration of the device (3 mm) and 1/30 (3%) bi-level patient had temporary posterior migration of the device (< 3 mm). Both cases of device migration were associated with a partially milled cavity.

Pimenta *et al.* (2004) reported a 4 mm anterior displacement of the PCM prosthesis in 1/52 (2%) patient.

The small Frenchay cervical disc case series reported by Wigfield *et al.* (2002), found no evidence of joint dislocation. However, two screws broke midshaft after 6 months in one patient and there was some evidence of stress shielding of the anterior vertebral border. None of the Bryan® case series reported on stress shielding so no data are available for comparison.

Safety

Complications

There was no significant difference in the frequency of adverse events reported in patients who were randomised to receive the Prestige II™ disc versus control patients (who received anterior cervical discectomy and fusion) (Porchet *et al.* 2004). Of the 27 patients receiving the Prestige II™ disc, 17 adverse events were reported. These include 3 (18%) permanent adverse events (pancreatitis – 1, continuous neck pain -1, continuous shoulder pain -1) and 14 transient adverse events including neck pain, recurrent palsy on the right side requiring logopaedic treatment and dysphagia. The control group (n=28) reported 19 adverse events and also cases of intermittent neck and arm pain and continuous neck pain and procedure-related complications involving a graft that was too small, a contaminated graft and a haematoma at the graft site that required revision.

Bryan *et al.* (2002) reported that one patient developed temporary dysphonia (1/55, 1.8%) after insertion of a Bryan® cervical disc. Anderson *et al.* (2004) reported complications including cerebrospinal fluid leak in one patient (1/103, 1%) and oesophageal injury in another (1/103, 1%). Transient unilateral vocal cord paralysis occurred in 1/14 (7%) patient but this resolved by six weeks (Pickett *et al.* 2004). There was also one case (1/52, 2%) of heterotopic ossification which occurred in the ninth month of follow-up (Pimenta *et al.* 2004). Leung *et al.* (2005) reported that 16/90 patients (17.8%) that received the Bryan® cervical disc developed heterotopic ossification within 12 months. Ten patients (11%) were revealed to have no movement of their cervical disc, and of these, four had grade 3-4 heterotopic ossification.

The small cases series of 15 patients examining the new Frenchay cervical disc (Wigfield *et al.* 2002) reported no postoperative wounds or periprosthetic infections. However, 1/15 (7%) patient experienced torrential venous bleeding perioperatively, 2/15 (13%) patients experienced transient hoarseness, 4/15 (27%) patients suffered neck pain on full extension postoperatively, 2/15 (13%) patients reported recurrent brachialgia and 2/15 (13%) patients developed a progression of their myelopathy.

The study of 12 patients by Sears *et al.* (unpublished) reported no intraoperative complications. However there were some early and late postoperative complications. In the early postoperative period all 12 (100%) patients developed dysphagia, which resolved in all patients; 1/12 (8%) patient had arm and leg (ipsilateral) pain and sensory loss; 1/12 (8%) patient had kyphotic shells; and 1/12 (8%) patient developed a urinary tract infection. In the late postoperative period 1/12 (8%) patient had complex regional pain syndrome; 1/12 (8%) patient developed recurrent radiculopathy at 19 months postprocedure; and 1/12 (8%) patient had 'clicking', which was reported to not be related to the prosthesis.

Reoperation

Goffin *et al.* (2002, 2003) report re-operation rates for both single-level and bi-level patient groups. In the single-level series, three patients (3%) required re-operation; one patient (0.97%) to implant another cervical disc replacement due to radiculopathy caused by a disc herniation. After this re-operation, the patient experienced severe dysphonia. A second patient complained of left shoulder pain 26 hours after the first operation. Re-operation revealed a prevertebral haematoma which resolved following this second surgical intervention. One patient of 60 (2%) had their first cervical disc replacement performed at the wrong level. This was corrected at second operation after which the patient temporarily experienced dysphonia.

In the bi-level series, 4 patients of 43 (9%) required re-operation for evacuation of a prevertebral haematoma, an epidural haematoma, repair of a pharyngeal tear and for anterior decompression respectively.

Four of the 103 (4%) patients from the Anderson *et al.* (2004) case series required evacuation of haematomas and 3/103 (3%) patients required revision decompression due to incomplete removal of neural compression.

Results for the Frenchay cervical joint by Wigfield *et al* (2002) indicate that 1/15 (7%) patient required surgical removal of their joint at one year. Two other patients (15%) required further surgical intervention: one patient underwent a foraminotomy for recurrent brachialgia and pain whilst another underwent a decompression laminectomy at two cervical levels below the prosthesis and fusion at the prosthetic level.

Potential Cost Impact

Cost Analysis

There is a lack of evidence on the cost-effectiveness of artificial cervical disc replacement. No cost data are presently available for Australia.

Ethical Considerations

Informed Consent

Australian patients are currently being enrolled into a case series investigating the Bryan® cervical disc system. Data available from this trial have been outlined in this report. Patients in this trial undergo a consent process.

Access Issues

No potential issues have been identified, however it appears that artificial cervical disc replacement is only available through a clinical study setting.

Training and Accreditation

Training

It is expected that artificial cervical disc replacement should ideally be performed by surgeons experienced in this specialised surgery.

Clinical Guidelines

No clinical guidelines could be found for artificial cervical disc replacement.

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

A Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, a Horizon Scanning Report is a 'state of play' assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of artificial cervical disc replacements, its present and potential use in the Australian public health system, and future implications for the use of this technology.

Search Strategy Used for Report

A systematic search of Ovid MEDLINE® In-Process and other non-indexed citations, Ovid, MEDLINE®, EMBASE, Current Contents, PubMed, Cochrane Library and Science and Citation Index was conducted, from the inception of the databases until November 2004. The York Centre for Reviews and Dissemination, Clinicaltrials.gov, National Research Register, SIGLE, relevant online journals and the Internet were also searched in November 2004. Searches were conducted without language restrictions.

Search terms used: artificial disk or artificial disc, cervical disk replacement or cervical disc replacement, prosthetic disc or prosthetic disk, prosthesis disc or prosthesis disk, invertebral disc replacement or invertebral disk replacement.

Availability and Level of Evidence

Articles were obtained on the bases of the abstract containing safety and efficacy data on artificial cervical disc replacements in the form of randomised controlled trials (RCTs), other controlled or comparative studies, case series and case reports. Conference abstracts and manufacturer's information were included if they contained relevant safety and efficacy data. Foreign language papers were included if they contained safety and efficacy data and were considered to add substantively to the English language evidence

base. In the case of duplicate publications, the latest, most complete study was included, except when different outcomes were reported. Papers were rejected for reporting no clinical outcomes, or being review articles without data or involving techniques other than artificial cervical disc replacement. Data for this procedure report were extracted from all identified studies. These studies appear in bold in the reference list.

List of Studies Found

Total number of studies:	13
Systematic reviews	0
RCTs	1
Non-randomised comparative studies	0
Case series	10
Case reports	2

Sources of Further Information

There is currently one clinical trial underway in Australia, which is investigating the Bryan® cervical disc system. Medtronic is currently also sponsoring multicentre clinical trials of the Bryan® and Prestige™ cervical discs across the USA (http://www.medtronic.com/newsroom/news_20030716a.html). The trials are expected to enrol approximately 1,100 patients at 50 clinical sites, and aim to evaluate the safety and effectiveness of the artificial discs and compare outcomes of patients who receive an artificial disc with those who have standard cervical fusion.

Impact Summary

Joint replacement has become a successful surgical treatment modality in other orthopaedic applications. It would be beneficial if the positive effects observed with total hip or knee arthroplasty could be extended to cervical spine degenerative disorders because of the magnitude of the disorder and the debilitating nature of degenerative disc disease. The biomechanical considerations required for the design of a suitable cervical disc prosthesis have necessitated a slower period of development than for other prostheses. At this stage of development, cervical disc replacement is showing some early promise. Further clinical investigation is needed and is already underway.

Conclusions

This report outlines the current research findings of two types of cervical disc replacement systems: the Bryan® disc and the Bristol (Cummins) or Frenchay cervical discs. Only preliminary findings of an RCT comparing the Prestige II™ disc to anterior

cervical discectomy and fusion with iliac crest autograft have been published. Therefore, only this and a few case series have been published which provide some preliminary findings upon which to base some conclusions. Both cervical prostheses report comparable clinical outcomes to those reported for the current standard surgical treatment. Adequate postoperative range of motion appears to be preserved for the majority of patients. Early quality of life outcome results also appear promising with both single-level and bi-level groups experiencing an improvement postoperatively.

Several complications have been reported and the preliminary RCT findings report a similar frequency of adverse events between the Prestige II™ disc and control group. However, it is difficult at this early stage to compare complication rates to standard treatment. The Frenchay cervical disc reported one instance of device failure. There have also been some cases of device migration.

The studies thus far provide follow-up results up to an average of 2 years, which although commendable may not be sufficient for cervical arthroplasties. No studies have been conducted using the Bryan®, Bristol of Frenchay discs to determine if these discs restore load bearing and buffering functions of the spine. In addition to this, the ability of these artificial cervical discs to preserve adjacent levels has not been extensively investigated at the time of writing.

Joint arthroplasty has proven to be a successful treatment for several joints, including the hip and knee. The effort to translate the success of peripheral joint arthroplasty to the spine has been considerable, and there is evidence that these artificial discs are capable of restoring range of motion to the disc in the short term. However, the limitations of current studies should be taken to consideration and further long-term research would be required to address the concerns such as heterotopic ossification.

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Appendix A: Table of Key Efficacy and Safety Findings

Bryan® Cervical Disc

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Bryan 2002, Belgium, UK, France, Germany, Sweden, France and Italy (May be overlap of patients with Goffin 2002 and 2003.) 97 patients implanted; results for 59 patients. Single level DDD. Follow-up: 6 weeks, 3 months, 6 months, 1 year and 2 years. *Inclusion criteria:* Patients with disc herniation or spondylosis, with radiculopathy and/or myelopathy that had not responded to conservative treatment. *Exclusion criteria:* Previous cervical spine surgery involving any other device, axial neck pain as the solitary symptom, significant cervical anatomical deformity or clinical instability and active infection.	*Clinical success results:* Follow-up / Sample size / Clinical Success n(%) / Excellent n(%) / Good n(%) / Fair n(%) / Poor n(%) 1 yr / 46 / 40(87.0) / 32 (69.6) / 2(4.3) / 6(13.0) / 6(13.0) 2 yr / 9 / 8(88.9) / 7(77.8) / - / 1(11.1) / 1(11.1) Table adapted from Bryan 2002 At 1 yr follow-up, 3/49 (6.1%) had incomplete scores and weren't included in analysis in paper. Clinical success (rated as excellent, good, fair) was rated 87% (40/46). At 2 yr follow-up, 3/10 (30%) had incomplete scores and weren't included in analysis in paper. Clinical success was rated at 88.9% (8/9). No device failures or device explants. *Radiographic results:* Follow-up data for 43/49 (87.8%) at 1 yr; 10/10 (100%) at 2 yr. *Device position:* No subsidence reported. Anterior and/or posterior device migration was detected in 1/59 patient (1.7%). *Range of motion (ROM):* At 1 yr follow-up: 38/44 (86.4%) patients had motion ≥2°, 4/44 (9.1%) measured 1°, 1/44 (2.3%) results not interpretable. The ROM at 1 yr averages at just over 8° [5]. At 2 yrs averages at just over 11°[5]. Motion observed in all patients, no evidence of spondylotic bridging. *Quality of Life:* At 1 yr PCS scores were just under US mean (47), at 2 yr PCS and MCS scores met or exceeded US mean.	1/55 (1.8%) patient had temporary dysphonia. 1/55 (1.8%) patient reported pain at 3 mo follow-up, resolved by foraminotomy. 1/55 (1.8%) patient reported pain in the right shoulder, right arm and in the sternum region, approx 6 mo postoperatively. Not due to neural compression. 1/55 (1.8%) patient reported on unresolved non-specific shoulder pain and left axial pain. 1/55 (1.8%) surgical intervention at the target space occurred approximately 26 hrs after surgery, revealing a prevertebral haematoma. After intervention the patient responded well.	Patient's assessment is based on relief of preoperative symptoms using the Cervical Spine Research Society (CSRS) and SF-36 patient questionnaires, and relief of objective neurological signs as assessed by the physician. Results were scored according to a modified Odom's Criteria. Excellent: improvement in most (at least 80%) of the preoperative signs and symptoms, with little deterioration (not more than 10%). Good: Improvement in some (at least 70%) of the preoperative signs and symptoms, with some deterioration (not more than 15%). Fair: Improvement in half (at least 50%) of the preoperative signs and symptoms, or significant deterioration (not more than 20%). Poor: Improvement in few (less than 50%) of the preoperative signs and symptoms, or significant deterioration (more than 20%). 55 patients rather than 59 (4 lost to follow-up). Results only for 59 (55 or less) patients although 97 were implanted. Device position: 2 mm detection threshold All PCS/MCS scores are norm based with the general population mean equal to 50 and the SD 10.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Goffin *et al*. 2002 **(May be overlap of patients with Bryan 2002.)** European multicentre trial. 97 patients implanted. Age range: 26-79 yrs Follow up: 6 months (n=60), 1 year (n=30 of those followed up at 6 mo) *Inclusion criteria:* Patients with single-level degenerative disc disease of the cervical spine, (disc herniation or spondylosis, with radiculopathy and/or myelopathy, which had not responded to conservative treatment). *Exclusion criteria:* Previous cervical spine surgery involving any other device, axial pain as the solitary symptom, significant cervical anatomic deformity or clinical instability and active infection. Prospective study. Approved by ethics committee. * values averaged to 1 SD. *Continued over…*	Average length of surgery: 126[52]* min Hospital stay: mean 3.6{2.2}d, range 1-10d. Cervical collar not required. No device failures or explanations were reported. *Six months:* Scores were excellent, good or fair for 52/60 patients (86.6%). Excellent scores were reported for 41/60 patients (68.3%), good 5/60 (8.3%), fair 6/60 (10%) and poor 5/60 (8.3%). 3/60 patients (5%) missed follow-up or had incomplete patient and/or surgeon forms. For radiculopathy, scores were excellent, good or fair for 47/53 patients (88.7%). Excellent scores were reported for 38/53 (71.7%), good 4/53 (7.5%), fair 5/53 (9.4%) and poor 4/53 (7.5%). 2/53 patients (3.8%) missed follow-up or had incomplete patient and/or surgeon forms. For myelopathy, scores were excellent, good or fair for 5/7 patients (71.4%). Excellent scores were reported for 3/7 (42.8%), good 1/7 (14.3%), fair 1/7 (14.3%) and poor 1/7 (14.3%). 1/7 patient (14.3%) missed follow-up or had incomplete patient and/or surgeon forms. *One year:* Scores were excellent, good or fair for 27/30 patients (90%). Excellent scores were reported for 24/30 patients (80%), good 1/30 (3.3%), fair 2/30 (6.7%) and poor 3/30 (10%). For radiculopathy, scores were excellent, good or fair for 24/27 patients (88.9%). Excellent scores were reported for 21/27 (77.8%), good 1/27 (3.7%), fair 2/27 (7.4%) and poor 2/27 (11%)*.	In 1/60 patients (1.7%) the wrong level was initially operated on, reoperation at the correct level resulted in temporary dysphonia. After 3 mo follow-up, pain as a result of insufficient far lateral decompression in the first operation as well as long-term preoperative pain was reported by 1/60 patient (1.7%). A posterior foraminotomy was performed without placement of device. Six months postoperatively, 1/60 patients (1.7%) reported pain in right shoulder, right arm and the sternum region; this was not due to neural compression. 1/60 patients (1.7%) reported unresolved non-specific shoulder pain on the left side. One surgical intervention at the target space occurred approximately 26 hrs after surgery, revealing a prevertebral haematoma. After intervention the patient responded well.	Patients underwent implantation with the Bryan® prosthesis after a standard anterior cervical discectomy. Levels implanted: C4-C5, C5-C6, C6-C7 Patients at 1 yr follow-up (n=30) were also part of group assessed at 6 months (n=60). Preoperative data only available for 37 patients. Results were scored and according to modified Odom's criteria and categorised as follows: Excellent: improvement in most (at least 80%) of the preoperative signs and symptoms, with little deterioration (not more than 10%). Good: Improvement in some (at least 70%) of the preoperative signs and symptoms, with some deterioration (not more than 15%). Fair: Improvement in half (at least 50%) of the preoperative signs and symptoms, or significant deterioration (not more than 20%). Poor: Improvement in few (less than 50%) of the preoperative signs and symptoms, or significant deterioration (more than 20%). Operating times are reported after subtracting the first two operations for each investigator. Clinical results based on relief of preoperative symptoms (as assessed by the patient) and relief of neurologic signs (as assessed by the surgeon) for follow-up visits.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Goffin *et al*. 2002	For myelopathy, scores were excellent for 3/3 patients (100%). From baseline assessment, 15/30 (50%) of the patients demonstrated improvement in all preoperative abnormal findings, 9/30 (30%) had one or two findings that remained unchanged, 3/30 (10%) had deterioration in one finding, 3/30 (10%) had deterioration in more than one finding. *Device position:* Radiographic follow-up data obtained for 57/60 patients (95%) at 6 mo and 24/30 (80%) at 1 yr. Lateral radiographs at each follow-up showed device instability did not occur in any patient. Subsidence was not reported in any patient. Anterior and/or posterior device migration was detected in 1/60 patient (1.7%) and suspected in 1/60 patient (1.7%). Migration >3 mm was not observed in any patient. *Range of motion:* At 6 mo 53/57 patients (93%) demonstrated flexion-extension range of motion ≥ 2 degrees. 4/57 patients' (7%) radiographs were uninterpretable. The range of motion at 6 mo averaged <9{4} degrees. Motion was observed in all patients, with no evidence of spondylotic bridging. At 1 yr, 21/24 patients (87.5%), flexion-extension range of motion ≥ 2 degrees was reported. 2/24 patients (8.3%) measured 1 degree.		Cobb angles for flexion-extension of the function spine unit demonstrated motion of the device in flexion-extension. Flexion-extension range of motion ≥ 2 degrees is considered motion, 1 degree is considered fused. SF-36 Physical Component Summary and Mental Component Summary scores use US population means to establish normalised scores, with the general population mean equal to 50 and the SD 10. 6 patients 6/60 (10%) lost to follow-up or had incomplete patient and/or surgeon forms.

Continued over…

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Goffin *et al*. 2002	The range of motion at 1 yr averaged >9{6} degrees. No evidence of spondylotic bridging. *Quality-of-life results:* SF-36 Health survey results for patients at 6 mo and 1 yr. At 12 mo after implantation, patients met or exceeded the US population mean for Physical Component Summary and Mental Component Summary scores.		

*There is a discrepancy for the data reported for 'poor' 2/27 is 7.4%, 3/27 is 11%.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Goffin *et al*. 2003 **Update on Goffin *et al*. 2002. May be overlap of patients. (May also be overlap of patients with Bryan 2002.)** European multicentre trial. 146 patients. 103 single level; 43 bi-level Age range: single level age 26-79yrs; bi-level 28-62yrs Follow up: 100/103 patients (single level) reached their 12 mo follow-up and 51/103 reached their 24 mo follow-up. 29/43 patients (bi-level) reached their 12 mo follow-up and 1/43 reached their 24 mo follow-up. *Inclusion criteria:* Patients with degenerative disc disease of the cervical spine at single level and two adjacent levels, (disc herniation or spondylosis, with radiculopathy and/or myelopathy, which had not responded to conservative treatment). *Continued over…*	Operative times for single level surgery average 125{51} min, bi-level surgery 158{53}min (recorded as skin to skin). Hospital stay average 3.5{2.2}d for single level, 3.6 {6.2}d for bi-level. No restrictive postoperative management was needed. *Summary of clinical results for single-level study:* Followup (mo) / No. of patients / Excellent n (%) / Good n n (%) / Fair n(%) / Poor n(%) 6 / 92 / 66(71.7) / 6 (6.5) / 11 (11.9) / 9 (9.7) 12 / 89 / 62 (69.6) / 7 (7.9) / 7 (7.9) / 13 (14.6) 24 / 49 / 32 (65.3) / 2 (4.1) / 10 (20.4) / 5 (10.2) Table adapted from Goffin *et al.* 2003 At 6 mo follow-up 83/92 (90.2%) patients were classified as excellent, good, or fair, at 1 yr follow-up 76/89 (85.3%) and at 2 yr follow-up 44/49 (89.8%). 1/103 (0.97%) required a second device implant on an adjacent level 21 mo after initial surgery due to radiculopathy caused by disc herniation. After reoperation, severe dysphonia was reported.	*Single level study:* 3/103 (2.9%) reinterventions at the treatment level (evacuation of a prevertebral haematoma, posterior foraminotomy, posterior decompression). 1/103 patient (0.97%) was operated on at the wrong level, resulting in pain which was corrected by reoperation, which resulted in temporary dysphonia. 1/103 patient (0.97%) reported in pain in the right shoulder, arm and sternum region approximately 6 mo after surgery; this was not due to neural compression. 1/103 patient (0.97%) reported unresolved non-specific shoulder pain on the left side. *Bi-level study:* 4/43 reinterventions (9.3%) at treatment level were required (evacuation of a prevertebral haematoma, evacuation of an epidural haematoma, repair of pharyngeal tear/oesophageal wound, anterior decompression). 1/43 patient (2.3%) experienced cerebral spinal fluid leak while decompressing posteriorly.	The primary endpoint is classification based on relief of each preoperative symptom as assessed by the patient using the Cervical Spine Research Society questionnaire. Results were scored according to Odom's Criteria. Excellent: improvement in most (at least 80%) of the preoperative signs and symptoms, with little deterioration (not more than 10%). Good: Improvement in some (at least 70%) of the preoperative signs and symptoms, with some deterioration (not more than 15%). Fair: Improvement in half (at least 50%) of the preoperative signs and symptoms, or significant deterioration (not more than 20%). Poor: Improvement in few (less than 50%) of the preoperative signs and symptoms, or significant deterioration (more than 20%). Operating times are reported after subtracting the first two operations for each investigator. Clinical results based on relief of preoperative symptoms (as assessed by the patient) and relief of neurologic signs (as assessed by the surgeon) for follow-up visits.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Goffin *et al*. 2003 *Exclusion criteria:* Previous cervical spine surgery involving any other device, axial pain as the solitary symptom, significant cervical anatomic Deformity, clinical instability or active infection. Prospective study. Approved by ethics committee.	*Summary of clinical results for bi-level study:* Followup (mo) / No. of patients / Excellent n(%) / Good n(%) / Fair n(%) / Poor n(%) 6 / 34 / 18 (52.9) / 6 (17.6) / 4 (11.8) / 6 (17.6) 12 / 26 / 20(76.9) / 1 (3.8) / 4 (15.4) / 1 (3.8) Table adapted from Goffin *et al.* 2003 At 6 mo follow-up 28/34 (82.3%) patients were classified as excellent, good, or fair and at 1 yr follow-up 25/26 (96.1%). 1/26 patient (3.8%) presented with discrete signs and symptoms of recurrent myelopathy at 1 yr follow-up. No device failures or device explants in either study. Subsidence of the device into the end plates has not been observed in any patients. Migration >3.5 mm not reported. *Device position in single level study:* Radiographic follow-up data obtained for 89/103 patients (86.4%) at 6 mo, 90/103 (87.3%) patients at 1 yr and 46/103 (44.7%) at 2 yrs. Temporary anterior/posterior device migration was detected in 1/103 (0.97%) patient and suspected in 1/103 (0.97%). *Average range of motion:* Follow-up (mo) / No. of patients / ROM≥ 2° n (%) / ROM < 2° / Average [SD] (degrees) 6 / 89 / 86(96.6) / 3 / 8.3[4.5] 12 / 90 / 79(87.8) / 11 / 7.9[5.3] 24 / 46 / 43 (93.5) / 3 / 9.0 [4.9] Table adapted from Goffin *et al.* 2003		SF-36 Physical Component Summary and Mental Component Summary scores use US population means to establish normalised scores, with the general population mean equal to 50 and the SD 10 (from previous paper).

Continued over…

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Goffin *et al*. 2003	At 1 yr and 2 yr follow-up 79/90 (87.8%) and 43/46 (93.5%) of patients, respectively had motion ≥ 2°. *Device position in bi- level study:* Radiographic follow-up data obtained for 38/43 patients (88.4%) at 6 mo and 26/43 (60.5%) at 1 yr. Migration detected in 1/43 patient (2.3%). *Average range of motion:* Follow-up (mo) / No. of patients / ROM≥ 2° n (%) / ROM ‹ 2° / Average [SD] (degrees) 6 / 73 / 72(98.6) / 1 / 7.3[4.1] 12 / 49 / 42(85.7) / 7 / 7.4[5.1] Table adapted from Goffin *et al.* 2003 At 1yr follow-up 42/49 (85.7%) of patients had motion ≥ 2°. *Average Quality of Life results:* *Single Level (n= not reported)* / *Bi-level n= not reported)* Follow-up (mo) / PCS / MCS / PCS / MCS Before operation / 36.1[6.4} / 41.0[12.1] / 37.4[7.2] / 35.5[10.5] 6 / 45.3[10.3] / 52.2[10.5] / 44.1[9.2] / 44.7[12.9] 12 / 46.9[10.1] / 50.0[12.4] / 47.0[10.7] / 46.1[12.5] 24 / 46.6[109] / 52.9[10.6] / No data / No data Adapted from Goffin *et al*., 2003 Follow-up CT scans were obtained from some patients in single-level study at 2 yr follow-up, anterolateral paravertebral ossification was observed in some cases. (reported that results will be published later)		

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Sears *et al*. unpublished, Australia **(May be overlap of patients with Sekhon 2003.)** 12 patients. Mean age 44.8 years (range 27-59) 9 single level; 3 bi-level Follow-up: mean 21.9 months (range 19.7 - 24.1) Symptom duration: mean 18.3 months (range 3-39) Indications: Radiculopathy 9/12 (75%) Myelopathy 1/12 (8.3%) Myeloradiculopathy 1/12 (8.3%) Neck pain 1/12 (8.3%) *Inclusion & exclusion criteria:* Not stated	*Subjective patient assessment:* 6/12 (50%) excellent procedural outcome 3/12 (25%) good procedural outcome 2/12 (16.7%) fair procedural outcome 1/12 (8.3%) worse procedural outcome 9/12 (75%) patients reported the procedure worthwhile 1/12 (8.3%) patients reported to be unsure if the procedure was worthwhile 2/12 (16.7%) patients reported the procedure to not be worthwhile 10/12 (83.3%) patients reported they would repeat the operation under similar circumstances 2/12 (16.7%) patients reported they would not repeat the operation under similar circumstances	*Complications:* No intraoperative complications were reported. Early postoperative: 1/12 (8.3%) arm & leg pain/sensory loss (ipsilateral) 1/12 (8.3%) kyphotic shells 12/12 (100%) dysphagia, which resolved in all patients 1/12 (8.3%) urinary tract infection Late postoperative: 1/12 (8.3%) complex regional pain syndrome 1/12 (8.3%) recurrent radiculopathy at 19 months 1/12 (8.3%) clicking, reported to not be prosthesis related	Six males and six female patients. Subjective patient comments were used to evaluate procedure efficacy. The study period was reported as 25 July 2001 to 16 October 2001. There appears to be overlap of patients (& study periods) with Sekhon (2003), with a reported study period from July 2001 to November 2002. The study by Sekhon (2003) reports on less patients (i.e. 7), but has a longer study period of 16 months. Sekhon (2003) also reported no intraoperative or postoperative complications. One patient (1/7 (14.3%)) was reported to have intermittent left arm pain, but they reported an improvement from preoperative state.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Sekhon 2004, Australia (May be overlap of patients with Sears *et al.* unpublished.) 7 patients Follow-up: mean 6.3 months (range 1-17) *Inclusion criteria:* Spondylotic disease or acute disc herniation. *Exclusion criteria:* Kyphotic deformity, severe multilevel spondylotic disc degeneration, spinal cord injury with possible instability, and pure radiculopathy secondary to posterolateral disc protrusion or foraminal stenosis. Prospective study.	No collar needed postoperatively. All patients (7/7; 100%) discharged within 48-72 hrs postoperatively and returned to work within 2-4 wks after surgery. Immediate improvement in all patients in preoperative symptoms. No losses to follow-up. Pt no / Follow-up (mo) / Postop neck symptoms[a,b] / Postop arm symptoms[a,c] / Postop deformity / Postop ONDI[d] / Odom criteria 1 / 17 / 0 / 0 / Loss of lordosis / 2 / Excellent 2 / 14 / 2 / 2 / Loss of lordosis / 8 / Good 3 / 6 / 0 / 0 / Loss of lordosis / 16 / Excellent 4 / 3 / 0 / 0 / Loss of lordosis / 0 / Excellent 5 / 2 / 0 / 0 / Nil / 2 / Excellent 6 / 1 / 1 / 0 / Nil / 10 / Good 7 / 1 / 0 / 0 / Nil / 0 / Excellent Adapted from Sekhon 2003 [a]0=nil symptoms; 1=mild symptoms;2=moderate symptoms;3=severe symptoms. [b] when compared with preoperative values, statistically significant difference, P<0.01 [c] when compared with preoperative values, statistically significant difference, P<0.01 [d] when compared with preoperative values, statistically significant difference, P<0.0001 All patients postop Nurick grade I, when compared with preoperative values, statistically significant difference, P<0.05 Improvement in arm and neck symptoms, ONDI score and Nurick grade. (Preop results reported in paper). No patient had persistent weakness. Out of 6 patients suffering with loss of lordosis, 2 (33.3%) had cervical lordosis restored. All patients demonstrated a good range of cervical motion at final postop assessment. Odoms criteria: 100% (7/7) had good or excellent outcome.	No complications reported in the intraoperative or postoperative period. There were no reported deaths. 1/7 patient (14.3%) had intermittent left arm pain, but reported improvement from preoperatively; no residual neural compression was found. At 14 mo follow-up, persistence of neck and shoulder discomfort of a lesser degree postoperatively, but could return to work.	All surgeries performed by 1 surgeon. Independent radiologist assessed imaging. Assessment of surgical outcome was based on Odom's criteria. Excellent: All preoperative symptoms relieved, able to carry out daily occupations without impairment. Good: Minimum persistence of preoperative symptoms, able to carry out daily occupations without significant interference. Fair: Relief of some preoperative symptoms, but whose physical activities were significantly limited. Poor: Symptoms and signs unchanged or worse. The surgical and postop Nurick grade, ONDI scores and arm and neck symptom scores were compared using two sample t tests paired for means, A P value of <0.05 was regarded as significant. All scores were expressed as means ± SEM.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Report			
Pickett 2003, Canada 2 patients Single level cervical disc herniation Follow-up: one day postoperatively, three weeks, three months and 6 months *Inclusion criteria:* Patients with cervical disc herniation with C6 radiculopathy refractive to conservative management. *Exclusion criteria:* Not reported Prospective study.	*Clinical success results:* Both patients experienced immediate relief from their radicular pain post operatively. Post operative mobilisation was 'rapid'. No external mobilisation was used. At 9 months postoperative, both patients had an 'excellent' resolution of their symptoms. *Radiographic results:* Radiographs taken at postoperative day 1 and three weeks postop while flexion/extension radiographs were performed at 3 and 6 months postoperatively. Neutral cervical radiographs one postoperative day 1 and three weeks postoperative revealed that disc height had been restored, spinal alignment was restored. *Device position:* Prostheses had maintained their original position *Range of motion (ROM):* Not reported	Not reported	Authors report that a major potential complication may be associated with the insertion of this prosthesis, due to the technique of preparing vertebral endplates. This involves drilling without direct supervision. Despite the involvement of calibrated tools and a secured reference frame in disc space drilling, there is a risk of vertebral artery or spinal cord injury. The authors recommend careful analysis of preoperative computed tomography to determine the appropriate size of the prosthesis, and to assess any anatomical abnormalities, including the position of the vertebral arteries. Intraoperative fluoroscopy is also recommended to confirm accurate alignment, reference points and drilling margins.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Report			
Sekhon 2003, Australia 48 yr old patient Follow-up 11 mo Presented with myeloradiculopathy with 2 level spinal cord compression.	No complications. Total operating time 3h 15 min. No cervical collar needed. 'Pain had settled and numbness improved'. Flexion-extension range of motion was normal. Patient discharged after 48h. Follow-up at 6 wks: no pain, paraesthesia and normal neck motion (Nurick Grade 0), back at work 2 wks postop with no adverse events. At 11 mo follow-up, no complications, good motion, adequate cord decompression. Artefact associated with titanium shells of the implant was evident after scan. No evidence of ectopic calcification and osteophyte formation.	Blood loss minimal.	

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Pickett *et. al.* 2005, Canada 20 patients Follow-up: 6,12 and 24 mo. Static and dynamic radiographs completed at each visit. *Inclusion criteria:* Patients with cervical spondylosis at 1 or 2 levels, presenting with radiculopathy and/or myelopathy. Patients should have underwent anterior cervical discectomy. Prospective study.	24 discs implanted in 20 patients (4 patients had 2 level implantations) *Radiological evidence of motion preservation* **Mean postoperative sagittal range of motion** Preoperatively (n=20) 8.89º Early Postop 8.04º Late Postop 8.92º **Overall cervical sagittal motion (C2-C7)** Preoperatively (n=20) 47.2º Late Postop 56.1º This increase in mobility (mean 8.9º) was distributed over all spinal levels. **Horizontal translation** Preoperatively (C5-C6) 1.5mm Preoperatively (C6-C7) 0.7mm Late postop (C5-C6) 1.5mm Late postop (C6-C7) 1.1mm Anterior and posterior disc distraction or compression did not change significantly following the procedure. COR values did not change significantly at the operated level or at any other spinal level during early or late follow-up.	Not reported	Radiographs were conducted by several experienced radiographers at a distance of 72 inches. The general increase in overall cervical motion (mean 8.9º) at adjacent levels occurred over time and the reason for this was uncertain. The authors speculate that this was due to relief in neck pain after the procedure. All patients involved in this study were symptomatic before the procedure and hence preoperative parameters are not 'normal'. Therefore the non-significant changes in pre and post-operative radiographs cannot be interpreted as a retainment to 'normal' function. Small patient numbers may have contributed to the lack of significance observed in this study.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Leung *et al*. (2005), England, Belgium, France, Germany, Sweden, Italy 90 patients Follow-up: 12 months *Inclusion criteria:* Patient data was obtained from the Bryan Disc study conducted by the European Consortium. Patient inclusion criteria for this study consisted of disc herniation or spondylosis, with radiculopathy and /or myelopathy, that had not responded to conservative treatment. *Exclusion criteria:* Patients with previous cervical spine surgery involving the use of any other device, axial neck pain as the solitary symptom, significant cervical anatomic deformity or radiographic signs of instability (translational instability of more than 2 mm, angular motion more than 11° more than either adjacent level), and active infection. Observational study	Sixteen (17.8%) patients experienced heterotopic ossification (HO) Six (6.7%) patients experienced grade 3 and 4 HO Ten (11%) patients had movement of artificial discs of less than 2° on flexion and extension cervical x-rays at 12 months. Four of these patients had Grade 3 or 4 HO. Aging (p=0.023; odds ratio-1.10, 95% CI=1.01-1.19)and being a male ($\chi 2=4.1$; p=0.0407) were determined to be associated with the development of HO. The presence of Grade 3 or 4 HO was associated with loss of cervical disc movement at 12 months ($\chi 2=20.1$; $p<0.0001$). 89.9% of patients (80/89) had favourable outcomes (Odom;s criteria).	Not reported	Although 16 patients (17.8%) had HO at 12 months, 10 patients (11%) showed no movement of the artificial discs (only 4 of these had grade 3-4 HO). It was not reported if all of the 10 patients with no movement of the artificial cervical disc had HO. This study indicated that 11% of patients who underwent cervical disc replacement may lose the advantage of preserving segmental movement (as compared to fusion) at 1 year post-surgery. This study has limited power due to the small sample size.

Prestige II

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Randomised controlled trial			
Porchet et al. (2004), Switzerland, USA. 55 patients (27 Prestige II, 28 controls) Follow-up: 6 weeks, 3, 6, 12, and 24 months post-surgery. *Intervention* Anterior cervical diskectomy and arthroplasty with Prestige II versus anterior cervical diskectomy and fusion with iliac crest graft. *Inclusion criteria* Patients must have cervical DDD defined as intractable radiculopathy or myelopathy caused by nauroradiologically documented disc herniation or osteophyte formation, patients with single level disease in C4-5 to C6-7, unresponsive to non-operative treatment for approximately 6 weeks, or the presence of pregressive symptoms or signs of nerve root compression while nonoperative management continued, >18 years old and preoperative NDI scores >30. *Exclusion criteria* Patients with previous surgical treatment of the cervical spine, osteopenia, osteoporosis, osteomalacia and cancer.	37 patients were evaluated at 12 months and 9 patients were evaluated at 24 months. *Radiographic outcomes* Motion analysis revealed maintenance of motion in the Prestige II group while there was no significant motion in the control group. Mean angulation of motion segment Prestige II / control Preoperatively: 5.9º / 6.3º 3 mo postoperatively: 6.5º / 1.6º 12 mo postoperatively: 5.9º / 1.1º No statistically significant differences were reported in adjacent-level motions at 12 months. *Neck Disability Index (NDI)* At all postoperative intervals, the NDI for both treatment groups improved from preoperative scores. The improvement in the treatment groups were statistically equivalent ($p<0.05$) up to the 24 month follow-up interval. *Neck pain frequency and intensity* Postoperative neck pain scores improved for both treatment groups compared to preoperative scores ($p<0.05$). Statistical equivalence was not shown between treatment groups. *Arm pain frequency and intensity* Mean arm pain score improved after surgery in both treatment groups at all follow-up intervals. Both treatment groups were statistically equivalent at all	*Prestige II patients* 17 adverse events were reported in the Prestige II group. One patient suffered from malposition of the device (grade 2), the artificial disc was removed at 4 months post-implant and the patient underwent fusion with an anterior cervical cage. 14 events were not permanent and resolved with treatment after 3 months. One patient suffered pancreatitis (not related to procedure) (grade 3). One patient experienced continuous neck pain while another suffered continuous shoulder pain (grade 2). No evidence of neurocompression was located. No device related failures were identified and artificial discs maintained their position with no incidence of joint dislocation. There were no subsidence of artificial discs into the VB bone. *Control patients* 19 adverse events were reported. 3 events were directly related to the procedure, one graft was too small, another graft was contaminated and the third patient had hematoma at the graft harvest site thus requiring revision. 15 adverse events were resolved after a mean period of three months (11 intermittent neck and arm pain). Two grade 3 events, both involved secondary myelopathy requiring additional adjacent level surgery. One case was resolved.	Severity of adverse events was assessed according to WHO recommendations. Grade 1: noticeable to patient but does not interfere with routine activity Grade 2: interferes with routine activity but responds to symptomatic therapy or rest Grade 3: significantly limits patient's ability to perform routine activities despite symptomatic therapy. All follow-up evaluations were performed by one clinician who was directly involved in the surgery. Method of randomisation was not described.

	follow-up time points up to 24 months ($p<0.05$). *General health (SF-36)* Physical component scores and mental component scores for both treatment groups improved after surgery. The difference in scores between both groups was not significant.	Three patients with continuous neck pain were considered permanently affected and required symptomatic treatment.

Frenchay Cervical Disc

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case Series			
Wigfield *et al*. 2002, UK and USA 15 patients Follow-up: 6 wks, 3, 6, 12 and 24 mo. Assessment and questionnaires completed at each visit. 9/15 (60%) had previous surgical fusions. *Inclusion criteria:* Patients with radiculopathy or myelopathy with evidence of compression by osteophytes or herniated disc material in the presence of an adjacent surgical or congenital cervical fusion. Also, patients with radiological evidence of asymptomatic disc degeneration adjacent to the symptomatic disc undergoing surgery. Prospective study.	No drains used. No cervical collars needed. Patient's mobile 1 day postoperation and discharged within 48h. Mean operative time 143{48}min No postoperative wound or periprosthetic infections were reported. *Radiological evidence of motion preservation:* *Mean angular movement for the motion segment undergoing joint insertion:* Mean angulation of motion segment Preoperatively (n=15) 7.5º (range 1-15º;[4.6º] 24 mo postoperatively (n=14) 6.5º (range 3-12º;[3.8º] Table adapted from Wigfield *et al*., 2002 In all cases flexion and extension was demonstrated, at 2 yrs this was between 3° and 15°, with mean motion of 6.5°. Translation in an anteroposterior direction of up to 2 mm was achieved. *Radiological evidence of device stability:* No evidence of joint dislocation. 2/60 (3.3%) screws inserted broke midshaft after 6 mo in one patient. No subsidence of device was reported. Evidence of stress shielding of the anterior vertebral border and vertebral endplate junction after 12 mo. All locking screws functioned well. No corticocancellous screws backed out. *Results from assessment questionnaires:* Improvement in all aspects of patient function and quality of life. Employment status improved among patients.	Mean blood loss 316 ml (median 50{662} ml). 1/15 (6.7%) patient had torrential venous bleeding. Transient hoarseness was noted in 2/15 (13.3%) patients, which resolved at 3 and 6 mo. 4/15 (26.7%) experienced neck pain on full extension. One patient had the joint removed, a fusion was performed, but pain was not alleviated. One patient reported neck pain after a car crash and the other after two screws in the lower component of the joint broke at 6 mo with pain developing 18 mo later. 2/15 (13.3%) patients had recurrent brachialgia; pain resolved spontaneously in 12 mo in one patient the other required a foraminotomy at an adjacent level for removal of osteophytes (present before surgery). 2/15 (13.3%) patients had progression of myelopathy. One of these patients underwent a decompression laminectomy at 2 cervical levels below the artificial joint and fusion at the affected area. Joint motion at the level above was preserved.	Redesigned the Cummins joint – called it the Frenchay joint. Preoperatively patients completed SF-36 PCS (short form-36 physical component score), SF-36 MCS (short form-36 mental component score), Neck Disability Index (NDI), the European Myelopathy Score (EMS) and a visual analogue scale (VAS) relating to both neck and upper limb pain. Two surgeons performed operations. The degrees of motion were calculated using an Oxford Cobbometer accurate to 1°. No statistically significant changes were detected due to small patient numbers.

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Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments

Case Series

Pimenta et al. 2002, USA

52 patients

Follow-up: 1 wk, 1 mo, 3 mo, 6 mo, 9 mo, 12 mo.

Inclusion criteria
Patients 20 to 70 years old, degenerative disc disease with radicular or medullary complression.

Exclusion criteria
Metabolic and bone diseases, patients in terminal phase of chronic disease, patients with pyrogenic infection or active granulomatosis, patients with neoplastic or traumatic diseases of the cervical column, biomechanical instability of traumatic origin.

Visual Analog Scale (VAS)

Follow-up	Score
Preoperative	85
1 week	54
1 month	23
3 months	25
6 months	22
9 months	27
1 year	20

NDI scale results

Follow-up	Score
Preoperative	45
1 week	17
1 month	17
3 months	16
6 months	15
9 months	20
1 year	15

Treatment intensity gradient test

Follow-up	Score
Preoperative	11.6
1 week	8
1 month	5.8
3 months	2.6
6 months	4.7
9 months	3.8
1 year	3.5

A marked decrease in pain intensity (VAS scores), percentage of disability (NDI scores) and the number of analgesic medications and rehabilitative medicine treatment (treatment intensity gradient test) was noted at 1 year follow-up compared to preoperative scores.

There was one case of prosthesis displacement (4mm anterior displacement) 3 months after the procedure. However, no clinical symptoms were evident.

One patient developed Grade 1 heterotopic ossification at 9 months follow-up.

At 1 year follow-up, 100% of patients rated the results of the surgery as fair, good or excellent. A consistent 90% of patients reported their results as good or excellent since the 1 month follow-up.

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments

Case Series

Robertson & Metcalf et al. 2004, USA

17 patients

Observational study of patients treated with Prestige I discs

Follow-up: 36 months and 48 months post-surgery.

Radiographic analysis

		Sagittal plane rotation (º)		Translation (mm)	
Eval time	No. of patients	Mean	Range	Mean	Range
Preop	13	7.5	1-15	1.5	0-3
6 mo	15	6.4	0-15	0.8	0-2
12 mo	15	5.9	1-10	1.1	1-2
24 mo	14	6.5	1-15	0.9	0-2
36 mo	11	4.9	0-10	1.2	0-2
48 mo	12	5.7	0-12	0.83	0-2

* Eval = evaluation

Percentage improvements of self-administered assessment questionnaires (14 patients)

Questionnaire	Preop score	4 yr Postop score	% improvement
VAS			
Arm pain	10.2	4.5	55.9
Neck pain	10.5	6.0	42.9
NDI score	43.3	30.1	30.5
SF-36			
PCS	32.2	35.9	11.5
MCS	44.1	50.0	13.4
EMS	14.4	14.8	2.8

* EMS = European Myelopathy Scale; MCS = Mental component Score; NDI = Neck Disability Index; PCS =

Adverse events
No adverse events were reported and there was no development of symptomatic or radiological disc disease.

Physical Component Score.