

# Considered Judgement Form

*This form is a checklist of issues that may be considered by the Purchasing Guidance Advisory Group when making purchasing recommendations.*

**Meeting date:** 20 February 2008

**Topic:** Evidence based review: Intervertebral Disc Replacements – Cervical Total Disc Replacement

## **Background and purpose:**

In recent years total disc replacement (TDR) has emerged as a viable alternative to spinal fusion for Degenerative disc disease (DDD) in the lumbar spine and DDD/neuropathy in the cervical spine. The benefits over and above the “gold standard” of spinal fusion are potentially to preserve range of motion and prevent the degeneration of the nearby vertebral segments, a sequelae of spinal fusion.

A brief report prepared by ACC in 2002 reviewed the evidence for cervical and lumbar intervertebral disc replacements. Firm conclusions relating to the clinical effectiveness of spinal disc replacement were difficult to make. There was some evidence (from poor quality studies) that lumbar disc replacement may be beneficial in patients with degenerative disc disease aged between 36 and 55 years. No studies were found relating to cervical TDR.

In addition to revisiting this brief, this 2007 report also reviewed the literature with respect to the indications and contraindications for intervertebral TDR and has reported on any new TDR and related technologies.

Currently ACC funds TDR on a case-by-case basis via a formal application process for both cervical and lumbar TDR, under the proviso that patients are part of a formal clinical trial and are informed the treatment is innovative.

This 2007 EBH review has been peer reviewed by two spinal surgeons who currently perform TDR surgery.

## **Effectiveness, Volume of Evidence, Applicability /Generalisability and Consistency**

### **Safety and Efficacy**

#### **The MSAC Report**

A pivotal Health Technology Assessment (HTA) by The Medical Services Advisory Committee Australia, (July 2006) was identified that reported on the safety and efficacy of both lumbar and cervical TDR. This report was of high quality, therefore enabling literature after this date only to be reviewed (i.e. January 2006 (literature search completion date) to August 2007).

Since the MSAC report, three randomised controlled trials, three non-randomised comparative studies and 12 case series were identified from literature. These primarily involved the Bryan cervical TDR (9 case series, two non-randomised comparative trials). Due to the paucity of literature implanting cervical TDR, the MSAC report concluded that public funding should not be supported for cervical TDR.

## ***Safety***

### ***The Prestige ST FDA IDE trial***

This RCT implanted TDR in 276 patients and compared outcomes fusion with the Atlantis Cervical Plate and cortical ring allograft spacer fusion (n=265, single-level, C3-7). Published results are only available at this stage for approximately half of the study cohort. This was a non-inferiority trial (FDA recommended 10% threshold).

Adverse events data were reported for 223 TDR and 198 control subjects at 24 months. Note that efficacy results are for 137 and 148 subjects respectively.

There was no significant difference with respect to overall rates of adverse events (>1) or serious adverse events between the two groups (TDR=6.2%, fusion=4.2%\*). Three deaths occurred in the control group over this period, all due to myocardial infarction.

Peri-operative adverse events included dysphonia, dysphagia and haematoma (TDR=17, 7.6%; control=11, 5.5%\*). Re-operation for Adjacent level disease (ALD) was necessary in three TDR cases and 9 controls (p=0.0492). One case of subsidence was reported in the TDR group at three months.

No revision surgeries were required in the TDR group, however, five were required in the control group (1.9%; p=0.0277). Supplemental fixation was necessary in the control group only (n=8, 4.5%; p=0.0031). Removal of the implant was necessary in five TDR patients and 9 fusion patients (p=0.2870). Revision of four of the five TDR patients was due to persistent post-operative radicular pain.

### ***Other Trials***

One non-randomised comparative trial reported results for ALD (74 TDR subjects were compared with 158 subjects who underwent Affinity cervical cage fusion). The incidence of ALD between the two groups was significantly different in favour of the TDR group at 24 months (p=0.018). The incidence of new symptomatic ALD in the fusion group was 13.9% and 1.3% in the TDR group. One further study compared single- and multiple-level TDR (Porous Coated Motion TDR) in 140 TDR subjects. Three single-level and two multi-level cases required re-operation or suffered serious adverse events (no statistical comparison reported). One case of heterotopic ossification (HO) (level IV) was noted in the single-level group. It is unknown at what period these adverse events post-op were identified.

Case series provided some additional safety data (n=12). One study reported five cases (n=11) of subsidence at six months following TDR. Two papers reported HO following cervical TDR. One case series implanting the Pro-Disc-C reported 30 TDR (/77) with HO (Grade II) at 12 months post-op with range of motion (ROM) restricted in a further eight. It was reported that HO did not interfere with function. A further paper reported that of the 16% of the patients identified suffering from HO in their sample (n=89), 6.9% of these were Grade III or IV. The presence of HO correlated with a loss of motion at 12 months (p<0.0001).

## ***Efficacy***

### ***The Prestige ST FDA IDE trial***

Two-year results were available for 137 TDR patients and 148 control patients. Overall success in the TDR group at 24 months post-op was 79.3% and in the control group was 67.8%. This was statistically in favour of the TDR patients ( $p < 0.0001$  – non-inferiority). Overall patient “success” was defined as  $\geq 15\%$  improvement in the Neck Disability Index score (NDI), maintenance or improvement of neurological status, no device-related or other serious adverse events and maintenance of the functional spinal unit (as evidenced by post-operative motion and absence of bony bridging). Secondary clinical outcomes at 24 months included NDI scores (all mean outcomes) (TDR=19.3, fusion=22.4 (/50);  $p=0.827$ ), SF-36 (physical scores TDR=13.1, fusion=11.8 (/100);  $p=0.174$ ), post-operative maintenance or improvement in neurological status (TDR=92.8%, fusion=84.3%, statistically significant\*) and return to work figures results (pre-op TDR=66% working, fusion=63%; post-op TDR=75.4%, fusion=74.7%\*).

This study was graded as “1-“ as per the SIGN grading as there was a lack of information with respect to blinding, randomisation and concealment allocation.

### ***Other Trials***

The remaining two randomised controlled trials added little to the body of evidence for safety and efficacy of cervical TDR as they reported small samples, reported single-site results for multi-centre trials and were both poorly reported. One of these studies involved the Bryan cervical TDR.

### ***Summary of Safety and Efficacy for Cervical TDR***

Since the publication of the MSAC report, there is now some evidence for the safety and efficacy of cervical TDR from one RCT. The results are, however, limited to approximately half of the study cohort at 24 month follow-up.

### ***Indications/Contraindications for Cervical TDR***

The literature reviewed regarding indications/contraindications presented primarily indirect evidence, coming from enrolment criteria for clinical trials assessing safety and efficacy. Contraindications and indications appear largely consistent across the literature. There is no evidence to support TDR at more than one vertebral level in the cervical spine is safe and efficacious. The current ACC protocol accepts applications for one- or two-level disease.

Clinical trials acknowledge the need for long-term data to be collected to ensure long-term safety and efficacy.

### ***New technologies***

Other Cervical TDR types were identified from the literature searching. Only one clinical trial (case series,  $n=53$ ) implanting the Porous Coated Motion TDR has thus far been published.

**Note** also that a recent ACC report (2006) has identified that patient data provided to the National Joint Register by surgeons performing TDR is incomplete for both cervical and lumbar cases.

\* = no statistic reported

### ***Cost***

Comment on any economic costs associated with this service, product or procedure

No direct cost effectiveness literature was identified for this review.

ACC currently funds TDR in the cervical and spine for ACC covered conditions on a case-by-case basis provided the patient is part of a formal clinical trial and understands the treatment is innovative. Between 2002 and May 2007 ACC funded 45 Total Disc replacements in the cervical spine. Total core and non-core cases combined indicate in general a significant increase each year since funding was approved. The 2006 total cost for cervical TDR, procedure and implant, was \$549,920.65 (excluding GST). Cases from 2002-7 have also increased annually from two in 2002 to 23 in 2006 (data unavailable for 2003).

### ***Clinical impact***

Comment on the clinical impact e.g. size of population, magnitude of effect, relative benefit over other management options, resource implications, balance of risk and benefit.

TDR is purported as better than the current “gold-standard” of spinal fusion for DDD in the lumbar spine and DDD/neuropathy in the cervical spine. The clinical impact of this technology is unknown as there is no known New Zealand data on the need for such interventions. The need for cervical TDR in future is likely, however, to be less of an issue than lumbar TDR due to the different indications for cervical TDR.

### ***Equity, Maori Health, Pacific Health, Acceptability***

Comment on the extent to which the service, product or procedure reduces disparities in health status (equity of access, resources, health outcome), is consistent with the treaty of Waitangi and encourages Maori/ Pacific participation in providing and using service, product and procedures, and is consistent with values and expectations of New Zealanders.

No issues identified.

### ***Possible Purchasing Options***

List the possible purchasing options.

### ***Cervical TDR***

***1. Purchase on a case-by-case basis with appropriate follow-up and comprehensive outcome reporting to the National Joint Register.***

***2. Do not purchase.***

### ***Evidence Statement***

***Summarise the advisory group's synthesis of evidence relating to this service, product or procedure, taking the above factors into account, and indicate the evidence level that applies.***

- For the surgical treatment of persistent cervical myelopathy/radiculopathy, compared with spinal fusion, the evidence from one medium-large sized randomised controlled trial implanting the Prestige ST cervical TDR:
- Supports the **safety** of single-level cervical TDR (C3-7) at two years post-operatively.  
Note: Implants were predominantly implanted at C5/6 and C6/7
- Indicates the twelve month-effectiveness of single-level cervical TDR (C3-7) with respect to disability as measured by the Neck Disability Index, general health physical scores (SF-36), pain and range of motion. There is currently low quality evidence for longer-term safety and efficacy from two case series (Prestige ST) only with three- and four-year follow-up respectively. These two studies indicate positive pain and disability outcomes, however, 10/15 patients in one case series suffered serious adverse events.
- There is currently insufficient evidence to assess the safety and efficacy of implanting cervical TDR of double- or greater-level. There are a small number of

low quality studies reporting conflicting results.

- Low quality data has indicated (one non-randomised comparative study and two case series) that the incidence of adjacent level degeneration may be mitigated at 24 month follow-up and that Heterotopic Ossification (HO) occurred at 12 months post-operatively (Bryan TDR and ProDisc-C). The case series evidence, however, was conflicting with respect to the patient impact of HO.
- Safety and efficacy statements can only be made for the Prestige ST. Results may not be generalisable to other TDR types.

### ***Purchasing Recommendations***

What recommendation(s) does the advisory group draw from this evidence?

- That ACC continue to purchase cervical intervertebral disc replacement on a case-by-case basis according to the revised (2008) ACC cervical approval protocol with outcome reporting to an appropriate joint register.