



Medical Services Advisory Committee

Public Summary Document

Application No. 1143 – Radiofrequency Ablation for the treatment of Barrett’s Oesophagus

Applicant: Device Technologies Australia Pty Ltd

Date of MSAC consideration: 51st MSAC meeting, 2 December 2010

1. Purpose of Application

On 13 October 2009, Device Technologies Australia Pty Ltd requested that MSAC undertake an assessment of Radiofrequency Ablation (RFA) for the treatment of dysplastic Barrett’s Oesophagus (BO).

MSAC noted that BO with low-grade dysplasia (LGD) is treated differently to BO with high-grade dysplasia (HGD), due to the different rates of progression to oesophageal cancer. MSAC considered the strength of the evidence in relation to RFA in the treatment of BO separately for LGD and HGD.

2. Current arrangements for public reimbursement

RFA is generally provided as a day procedure performed under conscious sedation in an outpatient setting by a gastroenterologist or surgeon trained in the procedure. RFA for the treatment of BO is not currently listed on the MBS.

The fee for MBS item 30479 was considered by MSAC to accurately reflect the time and expertise required to perform RFA and was therefore used in the economic evaluation of the procedure. At the time of this appraisal, this item attracted a fee of \$458.05. The existing descriptor for MBS item 30479 is: *ENDOSCOPY with LASER THERAPY or ARGON PLASMA COAGULATION, for the treatment of neoplasia, benign vascular lesions, strictures of the gastrointestinal tract, tumorous overgrowth through or over oesophageal stents, peptic ulcers, angiodysplasia, gastric antral vascular ectasia (GAVE) or post-polypectomy bleeding, 1 or more of.*

The applicant proposed a fee of \$1,330 for this procedure based on the fee for the MBS item for double-balloon enteroscopy. No MBS descriptor was proposed for this procedure.

The comparators for RFA for BO with LGD are conservative therapy (acid suppression and surveillance) and argon plasma coagulation (APC). The comparators for RFA for BO with HGD are APC, endoscopic mucosal resection (EMR) and oesophagectomy.

The primary MBS item for conservative therapy is 30473, which has a fee of \$170.40. The item descriptor is:

OESOPHAGOSCOPY (not being a service to which item 41816 or 41822 applies), GASTROSCOPY, DUODENOSCOPY or PANENDOSCOPY (1 or more such procedures), with or without biopsy, not being a service associated with a service to which item 30476 or 30478 applies

The primary MBS item for oesophagectomy is 30535, which has a fee of \$1,632.35. The item descriptor is:

OESOPHAGECTOMY with gastric reconstruction by abdominal mobilisation and thoracotomy

MSAC noted that neither APC nor EMR are currently funded on the MBS for the treatment of BO.

3. Background

Barrett's Oesophagus with Dysplasia is a condition resulting in a metaplastic change to the lining of the oesophagus, such that the normal squamous epithelium is replaced by columnar epithelium. The disorder seems to be a complication of chronic gastro-oesophageal reflux disease (GORD), although asymptomatic individuals might also be affected, and it is a risk factor for the development of oesophageal adenocarcinoma, a cancer with rapidly increasing incidence in developed societies.

Although the natural history of the disease is not fully understood, the biggest risk factors for progression to cancer are the length of time with abnormal mucosa and the degree of dysplasia. Expert pathologists can differentiate between low grade dysplasia (LGD) and high grade dysplasia (HGD). HGD is generally accepted as a precursor to oesophageal cancer which carries a poor prognosis, but not all patients with LGD progress to HGD.

The purpose of Radiofrequency Ablation (RFA) is to thermally destroy dysplastic mucosa, allowing for re-epithelialisation with healthy squamous epithelium. Initially, a sizing balloon is used to measure the diameter of the oesophagus whilst the patient is under conscious sedation. An appropriately sized radiofrequency balloon catheter is then introduced over a guidewire in a side-by-side manner with an endoscope. The catheter's balloon is then inflated and radiofrequency energy applied, circumferentially ablating the epithelium of the oesophagus to less than one millimetre. The ablated epithelium is then removed by the clinician using irrigation, suction and light pressure. Once dysplasia has progressed to adenocarcinoma, invading to deep layers (lamina propria or beyond), oesophagectomy is the treatment of choice to ensure no potentially malignant cells remain in any cell layer.

MSAC considered that in a typical year of RFA treatment, the following MBS items would be claimed (if RFA was publicly funded):

- 30479/new item – RFA (x3)
- 30473 – Oesophagoscopy
- 20740 – Anaesthesia (x4)

MSAC agreed that the accurate diagnosis of dysplastic Barrett's Oesophagus is an important and difficult step in the treatment algorithm, and noted expert advice that two experienced pathologists should confer on the final grading. MSAC considered that the choice of treatment should be overseen by a multi-disciplinary team and, if considered appropriate for the patient, RFA should be performed by an appropriately trained specialist gastroenterologist or surgeon.

RFA requires similar time and expertise to endoscopic laser therapy or APC, which are listed on the MBS under item 30479. The inclusion of RFA for BO with either LGD or HGD on the MBS would require amendment of MBS item 30479 or the creation of a new item.

In a clinical setting, RFA for LGD and HGD is undertaken once dysplastic BO has been confirmed by pathology testing.

MSAC noted expert advice that two experienced pathologists should confer on the final grading of BO. MSAC agreed that professional bodies should be involved in developing standards for both the diagnostic process as well as for the conduct of the procedure.

4. Clinical need

MSAC noted that both LGD and HGD BO can be treated with currently funded services. It noted that oesophagectomy is the only treatment currently funded for HGD, which is an invasive procedure with 30-50% morbidity and around 2% mortality in the Australian setting.

MSAC noted that once dysplasia has progressed to adenocarcinoma, invading to deep layers (lamina propria or beyond), then RFA is not indicated. Rather, an oesophagectomy is the treatment of choice to ensure no potentially malignant cells remain in any cell layer.

MSAC noted that an estimated 100 patients per year are diagnosed with HGD in Australia, with an average age at diagnosis of 60. Approximately 300 patients per year are diagnosed with LGD.

MSAC also noted that there are limited data available regarding the prevalence of Barrett's Oesophagus in Australia. However, there has been an increase in the frequency of diagnosis of Barrett's Oesophagus from 2.9 to 18.9 per 1000 endoscopies between 1992 and 2002, although these data do not specify the severity of disease or level of dysplasia.

5. Comparator

MSAC noted that BO would be diagnosed during an endoscopy. Following diagnosis of BO, the patient would receive multiple endoscopic biopsies which would then be graded by experienced pathologists. A confirmed diagnosis of dysplasia would result in treatment being undertaken depending on the grading of the dysplasia; RFA would be one option for treatment.

Listing of RFA on the MBS would result in some instances of RFA being used instead of conservative therapy or APC in the case of diagnosed LGD; or oesophagectomy, APC or EMR in the case of diagnosed HGD. MSAC therefore agreed that conservative therapy and APC were the appropriate comparators for LGD BO; and that oesophagectomy, APC and EMR were the appropriate comparators for HGD.

Photodynamic therapy is another ablative technique used internationally to treat dysplastic BO. The technique employs photosensitising agents which are ingested by the patient. MSAC did not consider photodynamic therapy as a comparator because it is not used in Australia, as exposure to light (particularly sunlight) can cause serious adverse reactions for many days following treatment.

6. Scientific basis of comparison

The primary source of evidence for MSAC's advice was an assessment report produced by contracted evaluators. The assessment report comprised of a scientific literature review that was informed by an advisory panel of clinical experts and a consumer representative who ensured that the assessment considered relevant consumer issues and appropriately reflected the Australian setting.

The findings of one randomised control trial (RCT), five case series, two health technology assessments, three sets of guidelines and four reviews (including two Cochrane reviews) were included in the assessment report.

Five of the six available studies, including one RCT, met the inclusion criteria for assessment of safety. MSAC noted that these limited data were not comparative, which prevented a direct comparison of the safety of RFA with other available treatments.

Six studies, including one RCT, met the inclusion criteria for the assessment of effectiveness. MSAC noted that the limited studies showed only short-term data, with a maximum of 24 months follow-up. MSAC further noted that a lack of comparative data prevented the clinical effectiveness of RFA being directly compared to other available treatments.

7. Safety

MSAC noted that the literature reported few major complications following multiple treatment sessions. Most adverse events reported were minor and resolved without intervention.

MSAC agreed that the limited evidence suggests that RFA is safe for the treatment of Barrett’s Oesophagus with dysplasia and/or early intra-mucosal cancer (IMC). However, lack of comparative data prevented the safety of RFA being directly compared to other treatments available for patients with LGD, HGD and intra-mucosal carcinoma (IMC). As a result, conclusions cannot be drawn as to whether RFA is safer than surveillance or APC in patients with LGD. In addition, limitations in the literature also prevented the comparison of the safety of RFA to APC, EMR or oesophagectomy for patients with HGD and IMC. However, MSAC accepted that RFA had lower morbidity and mortality than oesophagectomy.

8. Clinical effectiveness

MSAC noted that the RCT reported the following eradication of intestinal metaplasia and dysplasia following RFA for LGD:

	RFA	Control	p value
CR-IM %	81	4	<0.001
CR-D %	90	23	<0.001

* CR-IM: complete eradication of intestinal metaplasia

* CR-D: complete eradication of dysplasia

MSAC noted that the RCT reported the following eradication of intestinal metaplasia following RFA for HGD:

	RFA	Control	p value
CR-IM %	74	0	<0.001

* CR-IM: complete eradication of intestinal metaplasia

MSAC also noted that the incidence of subsquamous intestinal metaplasia was lower in the RFA group than the control group for LGD and HGD.

In the non-RCT studies, complete eradication of intestinal metaplasia was reported in 54-79% of cases, and complete eradication of dysplasia was reported in 80-100% of cases.

The limited literature suggests RFA is effective for achieving histological eradication of intestinal metaplasia and dysplasia at a mucosal level. Lack of comparative data prevented the clinical effectiveness of RFA being directly compared to other available treatments. As a result, MSAC could not conclude whether RFA is as effective or more effective than surveillance or APC in patients with LGD. Similarly, MSAC was unable to conclude whether RFA is less or more effective than APC, EMR or oesophagectomy in patients with HGD.

MSAC found the length of follow-up studies, ranging from 11-24 months in the included studies, was insufficient to determine long-term success in cancer prevention.

MSAC noted the exact incidence of BO with dysplasia in Australia is uncertain. It also noted a lack of evidence on the rate of progression of LGD to HGD.

9. Economic evaluation

There was sufficient evidence to conduct a full cost-effectiveness analysis of RFA for the treatment of LGD. A decision analytic model was developed, which provides a framework for decision making under conditions of uncertainty. The economic evaluation estimated the incremental cost-effectiveness of RFA compared to surveillance.

MSAC noted there was insufficient comparative data available to conduct a cost-effectiveness analysis on RFA for HGD, therefore a cost analysis was conducted to compare the different costs associated with the procedure and its comparators.

MSAC found that replacing surveillance with RFA for LGD would yield an additional benefit of 0.129 QALYs at an additional cost of \$10,175. This resulted in an incremental cost-effectiveness ratio (ICER) for RFA compared with surveillance of \$78,975 per QALY.

The main drivers of the cost-effectiveness result are the probability of eradication of low grade dysplasia after treatment with RFA, the probability of progressing to cancer from low grade dysplasia, and the cost of RFA.

In the sensitivity analysis, if the frequency of surveillance is reduced after eradication of low grade or high grade dysplasia, the resulting ICER is \$71,075.

MSAC found that for HGD, based on an estimated prevalence of 100 cases, if direct replacement of RFA occurred for oesophagectomy, the overall cost savings would be \$1,259,446. If RFA was used to treat 100 patients instead of EMR or APC, there would be a total additional cost of \$778,146 or \$606,155 respectively. This cost analysis assumed that RFA, EMR, APC and oesophagectomy have equivalent effectiveness, with no account for reduction in quality of life with oesophagectomy.

MSAC noted that the average co-payments for one year of RFA treatment would be \$487 for both LGD and HGD. They also noted that the patient would be liable for the disposable catheters used in each RFA procedure which would cost the patient \$6,339 in the first year.

MSAC noted that all MBS items for RFA, EMR and APC are performed in the outpatient setting. Therefore any out of pocket cost associated with these items will contribute towards the Extended Medicare Safety Net (EMSN). The total out of pocket costs for these items is below the \$1,126 threshold (\$562.90 for concession card holders). Consequently, out of pocket contribution procedures relating to BO are unlikely to impact upon the EMSN.

MSAC noted that the ICER of RFA for LGD was sensitive to the probability of eradication of LGD after treatment with RFA, the rate of progression from LGD to HGD and/or cancer, and the cost of RFA. MSAC noted that the ICER was likely to remain very high but uncertain in any sensitivity analyses involving these parameters.

When reviewing the economic implications of RFA for HGD, MSAC noted that if the rate of RFA treatment failure leading to oesophagectomy were to be considered, there may be a reduction in the relative cost-effectiveness of RFA for HGD. Conversely, MSAC also noted the assessment report did not attempt to quantify the cost of mortality associated with oesophagectomy, which is likely to positively affect the relative cost-effectiveness of RFA.

10. Financial/budgetary impacts

MSAC noted estimates that approximately 100 patients per year are diagnosed with high grade dysplasia (HGD) in Australia, with an average age at diagnosis of 60. Approximately 300 patients per year are diagnosed with LGD.

MSAC noted that based on an estimated incidence of 299 cases of BO with LGD per year, RFA for LGD would incur a cost of \$489,433 per annum to the MBS. Based on an estimated incidence of 100 cases of BO with HGD per year, RFA for HGD would cost the MBS \$163,690 per annum.

11. Other significant factors

For BO with HGD, MSAC noted that oesophagectomy is a highly morbid procedure compared with RFA and that RFA is cost saving compared with oesophagectomy. However, MSAC was not able to determine the number of patients who would fail RFA and ultimately be recommended to have oesophagectomy.

MSAC noted that RFA is more costly than APC and EMR but that there was no comparative clinical effectiveness data for these procedures. It noted that a Cochrane review concluded that RFA appeared to be the most successful therapy to date for patients with HGD in BO after comparing the different interventions (except oesophagectomy). MSAC also noted that the RFA catheters are not able to be included on the Prosthesis List, and thus may be a cost that would be borne by the patient.

MSAC suggested that relevant professional groups should develop some form of accreditation for this procedure.

12. Summary of consideration and rationale for MSAC's advice

MSAC reconsidered the strength of the evidence relating to the safety, effectiveness and cost-effectiveness of radiofrequency ablation (RFA) for the treatment of Barrett's Oesophagus with either low grade dysplasia (LGD) or high grade dysplasia (HGD). MSAC noted that there are limited data available regarding the prevalence of Barrett's Oesophagus in Australia. However, there has been an increase in the frequency of diagnosis of Barrett's Oesophagus from 2.9 to 18.9 per 1000 endoscopies between 1992 and 2002, although these data do not specify the severity of disease or level of dysplasia. MSAC noted estimates that approximately 100 patients per year are diagnosed with high grade dysplasia (HGD) in Australia, with an average age at diagnosis of 60. Approximately 300 patients per year are diagnosed with LGD. The natural history of BO is poorly understood however HGD is generally accepted as a precursor to oesophageal cancer. The skills of expert pathologists are needed to differentiate between low grade dysplasia (LGD) and high grade dysplasia (HGD).

MSAC separately considered the strength of the evidence in relation to radiofrequency ablation (RFA) in the treatment of Barrett's Oesophagus with either LGD or HGD. RFA is generally provided as a day procedure performed under conscious sedation in an outpatient setting by a gastroenterologist or surgeon trained in the procedure.

For LGD, RFA was compared with current conservative therapy (acid suppression and surveillance) and APC. For HGD, RFA was compared with oesophagectomy or alternative endoscopic therapies (including Endoscopic Mucosal Resection (EMR) and Argon Plasma Coagulation (APC)). MSAC found that the evidence base for this assessment was very poor, with one randomised controlled trial (RCT) applicable to the Australian setting, and the length of follow up in the included studies insufficient to determine the long term success rate of RFA.

MSAC agreed that the limited evidence suggests that RFA is safe for the treatment of Barrett's Oesophagus with dysplasia and/or early intra-mucosal cancer (IMC). However, lack of comparative data prevented the safety of RFA being directly compared to other treatments available for patients with LGD, HGD and IMC. As a result, conclusions cannot be drawn as to whether RFA is safer than surveillance or APC in patients with LGD. In addition, limitations in the literature also prevented the comparison of the safety of RFA to APC, EMR or oesophagectomy for patients with HGD and IMC. However MSAC accepted that RFA had a lower morbidity and mortality than oesophagectomy and thus would be more desirable than an oesophagectomy

The limited literature suggests RFA is effective for achieving histological eradication of intestinal metaplasia (IM) and dysplasia at a mucosal level. Lack of comparative data prevented the clinical effectiveness of RFA being directly compared to other available treatments.

When reviewing the economic implications of RFA for LGD, MSAC took note of the low progression rate from LGD to HGD and/or cancer. For LGD, replacing surveillance with RFA would yield an additional cost of \$10,175 per patient, giving an incremental cost-effectiveness ratio (ICER) for RFA compared to surveillance of \$78,975 per quality adjusted life year (QALY) gained. MSAC concluded that this ICER was sensitive to the probability of eradication of LGD after treatment with RFA, the rate of progression from LGD to HGD and/or cancer, and the cost of RFA. MSAC noted that the ICER was likely to remain very high but uncertain in any sensitivity analyses involving these parameters.

When reviewing the economic implications of RFA for HGD MSAC noted that if the rate of RFA treatment failure leading to oesophagectomy were to be considered, there may be a reduction in the relative cost-effectiveness of RFA for HGD. Conversely, MSAC also noted the assessment report did not attempt to quantify the cost of mortality associated with oesophagectomy, which is likely to positively affect the relative cost-effectiveness of RFA. Taking these uncertainties into account, MSAC concluded that RFA for HGD was likely to have a cost advantage over oesophagectomy.

MSAC was unable to determine the cost-effectiveness of RFA for HGD due to limitations of the data. Costing showed that RFA is likely to be less expensive than oesophagectomy, but more expensive than APC and EMR. Furthermore, due to the cost of the disposable catheters, there may be access and equity issues for uninsured patients with low socioeconomic status, who therefore may be more likely to choose other forms of treatment of HGD due to the lower cost to the patient. However, the assessment report did note that the method of treatment for HGD can vary depending on clinical presentation and treatment methods are not always interchangeable.

MSAC noted that oesophagectomy is an invasive procedure with morbidity of approximately 30-50% and mortality of 2% in Australian centres. MSAC also noted that oesophagectomy is currently funded through the MBS, but EMR and APC for Barrett's Oesophagus are not reimbursed.

MSAC also agreed that the accurate diagnosis of dysplastic Barrett's Oesophagus is an important and complex step in the treatment algorithm, and noted expert advice that two experienced pathologists should confer on the final grading. The choice of treatment should be overseen by a multi-disciplinary team and, if considered appropriate for the patient, RFA should be performed by an appropriately trained specialist gastroenterologist or surgeon. MSAC agreed that both the clinical effectiveness and economic benefit of RFA depend upon the accuracy of the diagnosis of HGD, and noted that professional bodies should be involved in developing standards for both the diagnostic process as well as for the conduct of the procedure.

MSAC agreed that, at least in the short term, RFA is safe and effective for LGD, but it is not cost-effective. MSAC further noted that LGD may regress following conservative treatment for gastro-oesophageal reflux disease (GORD), and does not necessarily progress to HGD or cancer. MSAC therefore did not support public funding for RFA for Barrett's Oesophagus with LGD.

For HGD, MSAC took into account that the only other comparative procedure reimbursed on the MBS, oesophagectomy, is an invasive procedure with significant morbidity and mortality rates compared to RFA. As RFA for HGD appears to be safe and clinically effective, and cost saving compared with oesophagectomy, MSAC supports public funding for RFA for Barrett's Oesophagus with HGD.

13. MSAC's advice to the Minister

On the basis of its high cost and uncertainty of clinical benefit due to uncertainty of progression rate from Barrett's Oesophagus with low grade dysplasia (LGD) to oesophageal cancer, MSAC does not support public funding for radiofrequency ablation (RFA) in the treatment of Barrett's Oesophagus with LGD.

Based on a better safety profile and lower cost than oesophagectomy, but noting lack of evidence of comparative clinical effectiveness, MSAC supports public funding for RFA for Barrett's Oesophagus with high grade dysplasia (HGD). MSAC advises that the diagnosis of HGD should be confirmed by two expert pathologists with experience in upper gastrointestinal pathology, that treatment options for patients with HGD should be reviewed by an appropriate multi-disciplinary team, and that RFA should be performed (where indicated) by an appropriately qualified specialist gastroenterologist or surgeon who has received specific training in the procedure.

14. Context for Decision

This advice was made under the MSAC Terms of Reference.

“MSAC is to:

Advise the Minister for Health and Ageing on medical services including those that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:

- the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
- whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
- the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;

- the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
- other matters related to the public funding of health services referred by the Minister.

Advise the Australian Health Minister's Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to such sub-committees.”

15. Linkages to Other Documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.

The MSAC Assessment Report is available at www.msac.gov.au/internet/msac/publishing.nsf/Content/app1143-1.