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Australia and New Zealand Horizon Scanning Network
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Horizon Scanning Technology Prioritising Summaries

Sonablate® 500 System for prostate cancer

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ASERNIP-S
Australian Safety and Efficacy Register of New Interventional Procedures - Surgical

Royal Australasian College of Surgeons

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

Name of Technology:

Sonablate® 500 System (Focus Surgery Inc., Indiana, USA).

Purpose and Target Group:

The Sonablate 500 System is indicated for the treatment of localised prostate cancer.

Stage of Development (in Australia):

- ☐ Experimental
- ☐ Investigational
- ☑ Nearly established
- ☐ Established
- ☐ Established but changed indication or modification of technique
- ☐ Should be taken out of use
- ☐ Not yet emerged in Australia

An Australian Register of Therapeutic Goods (ARTG) number was not located for the Sonablate 500 system on the ARTG website. However, Focus-Surgery stated on their website that the system has received TGA approved in August 2005.

International Utilisation:

COUNTRY	LEVEL OF USE		
	Trials underway	Limited use	Widely diffused
Europe		✓	

Impact Summary:

Background

Prostate cancer is the most common noncutaneous malignancy among males and is a significant cause of mortality worldwide. The severity of prostate cancer, patient age, staging, Gleason score and serum prostate-specific antigen (PSA) often dictates the type of treatment. Non-surgical therapy for prostate cancer includes watchful waiting (regular examinations, PSA monitoring and digital rectal examination), androgen ablation, external beam radiation therapy (often used in combination with androgen ablation), brachytherapy and transperineal cryotherapy (necrosis using low temperatures) (Theodorescu & Krupski 2005).

Radical prostatectomy (removal of the prostate and seminal vesicles) is currently the standard surgical treatment for patients with organ-confined prostate cancer. There are three variations to this surgical approach, radical retropubic prostatectomy (open/laparoscopic and can be performed with robotic assistance), radical perineal prostatectomy (less discomfort, faster recovery, requires specialised instruments possibly higher fecal incontinence rates) and nonrobotic laparoscopic prostatectomy (steep learning curve, relatively new) (Theodorescu & Krupski 2005). However, despite excellent survival rates of 5 to 10 years, radical prostatectomy is associated with a range of complications and morbidity, such as blood loss with transfusion related complications, erectile dysfunction in 30% to 70% of patients and stress incontinence in 10% of patients (Uchida *et al.* 2006). In addition to this, surgical interventions are not commonly considered for patients whose life expectancy is less than 10 years. Due to these complications, alternative treatments which are less invasive were developed. Among these are the previously mentioned brachytherapy, laparoscopic radical prostatectomy and cryotherapy, as well as three dimensional conformal radiotherapy and intensity-modulated external beam radiotherapy. In addition to these, a new form of treatment utilising high-intensity focused ultrasound (HIFU) has been developed. This technique utilises ultrasound technology to noninvasively induce complete coagulative necrosis of the tumour thus completely circumventing the complications associated with invasive surgery (Uchida *et al.* 2006). HIFU was initially developed to treat benign prostate hyperplasia, but has evolved to be used as a method of killing prostate cancer cells. The procedure utilises a transrectal ultrasound that is highly focused into a small area, creating intense heat of 80 to 100ºC. The non-ionising characteristics of ultrasound means that the tissue in the entry and exit path of the HIFU beam is not injured.

The Sonablate 500 is the latest version of the Sonablate system, which utilises HIFU to treat localised prostate cancer. The development of Sonablate began in the late 1980s and since then the system has undergone several reiterations, the Sonablate 1 (1992), Sonablate 200 (1995) and finally the current Sonablate 500 (2001). The system consists of a main console, ultrasound transrectal probe (HIFU and imaging), a pump/cooling unit (Sonachill™) and a probe arm (Focus-Surgery 2006).

Clinical Need and Burden of Disease

According to the American Cancer Society, 220,900 new cases of prostate cancer were diagnosed in 2003 and 28,900 men will die from prostate cancer. Between 1989 and 1992, the incidence of prostate cancer increased dramatically, this was attributed to the development of a more advanced screening technique which involved measuring PSA levels (Theodorescu & Krupski 2005).

In Australia, prostate cancer is the most commonly diagnosed cancer in Australian men and is the second leading cause of cancer death in Australian men. An estimated 61,000

Australian men are currently diagnosed with prostate cancer. Statistics in 2001 revealed that 11,191 new cases were diagnosed while 2718 men died from the disease (Cancer Council Australia 2005).

Estimated Speed, Geographic and Practitioner Use, Patterns of Diffusion in the Health System

The Therapeutic Goods Administration (TGA) gave full marketing approval for the Sonablate 500 in August 2005 and is currently being distributed by Meditron. At the time of writing, the extent of use of Sonablate in Australia is not known.

The Sonablate 500 is not cleared for marketing in the United States. In Europe the system received the CE mark for European distribution in 2001 and has been utilised to treat patients in the United Kingdom, Germany, Italy and other European countries (Focus-Surgery 2006). Other countries which have utilised Sonablate 500 include Canada, Japan, China, Mexico and the Dominican Republic (eMaxHealth 2005).

Existing Comparators

- Radical prostatectomy
- Radiation therapy (Brachytherapy)
- Hormone therapy (Androgen ablation)
- Ablatherm HIFU system (EDAP, Lyon, France)

Estimated Cost Impact

The cost of the Sonablate 500 system was not revealed in our searches. The relevant types of surgery as well as their Medicare Benefits Schedule item numbers, reimbursement fee and number of claims are summarized in the table below.

Category	**Item Number**	**Benefit**	**Number of Claims** (July 2004-June 2005)
Radiation oncology treatment, single photon energy linear accelerator (1 field), prostate	15218	$51.65	46
Radiation oncology treatment, single photon energy linear accelerator (2 or more fields), prostate	15233	Fee of #15218 + $32.80 for each field in excess	11,846
Radiation oncology treatment, dual photon energy linear accelerator (1 field), prostate	15248	$51.65	94
Radiation oncology treatment, dual photon energy linear accelerator (2 or more fields), prostate	15263	Fee of #15248 + $32.80 for each field in excess	117,380
Radioactive seed implantation using transrectal ultrasound guidance	15338	$809.70	305
Radiation source localisation using a simulator or x-ray machine or CT for brachytherapy	15513	$265.40	298
Brachytherapy planning, radiation dosimetry for I125 seed implantation	15539	$542.90	335
Initiation of management of anaesthesia for transurethral resection of prostate	20914	$120.05	10,486
Open prostatectomy	37200	$879.60	145
Prostate, transurethral radio-frequency needle ablation of, with or without cystoscopy and with or without urethroscopy, in patients with moderate to severe lower urinary tract symptoms who are not medically fit for transurethral resection of the prostate (that is, prostatectomy using diathermy or cold punch) and including services to which item 36854, 37203, 37206, 37207, 37208, 37303, 37321 or 37324 applies	37201	$717.40	74
Prostate, transurethral radio-frequency needle ablation of, with or without cystoscopy and with or without urethroscopy, in patients with moderate to severe lower urinary tract symptoms who are not medically fit for transurethral resection of the prostate (that is prostatectomy using diathermy or cold punch) and including services to which item 36854, 37303, 37321 or 37324 applies, continuation of, within 10 days of the procedure described by item 37203,37207, 37201 which had to be discontinued for medical reasons	37202	$360.05	-1

Prostate, endoscopic non-contact (side firing) visual laser ablation, with or without cystoscopy and with or without urethroscopy	37207	$749.90	168
PROSTATE, endoscopic non-contact (side firing) visual laser ablation, with or without cystoscopy and with or without urethroscopy, and including services to which items 36854, 37203, 37321 or 37324 applies, continuation of, within 10 days of the procedure described by items 37201, 37203, 37207 or which had to be discontinued for medical reasons	37208	$360.05	0
PROSTATE, and/or SEMINAL VESICLE/AMPULLA OF VAS, unilateral or bilateral, total excision of, not being a service associated with a service to which item number 37210 or 37211 applies	37209	$1,117.45	154
PROSTATECTOMY, radical, involving total excision of the prostate, sparing of nerves around the bladder and bladder neck reconstruction, not being a service associated with a service to which item 35551, 36502 or 37375 applies	37210	$1,379.05	1,267
PROSTATECTOMY, radical, involving total excision of the prostate, sparing of nerves around the bladder and bladder neck reconstruction, ***with pelvic lymphadenectomy***, not being a service associated with a service to which item 35551, 36502 or 37375 applies	37211	$1,674.90	2,523
PROSTATE, radioactive seed implantation of, urological component, using transrectal ultrasound guidance, for localised prostatic malignancy at clinical stages T1 (clinically inapparent tumour not palpable or visible by imaging) or T2 (tumour confined within prostate), with a Gleason score of less than or equal to 6 and a prostate specific antigen (PSA) of less than or equal to 10ng/ml at the time of diagnosis. The procedure must be performed by a urologist at an approved site in association with a radiation oncologist, and be associated with a service to which item 55603 applies.	37220	$903.70	329

Efficacy and Safety Issues

List of Studies Found

Total number of studies	3
Case series studies	3

The studies included in this summary are highlighted in bold in the reference list.

Safety and efficacy data from three case series studies have been selected for inclusion in this summary. These studies were the only studies retrieved which utilised the Sonablate 500 system; an abstract by Uchida *et al.* (2005) involving 237 patients was not included as a substantial proportion of patients were treated with the Sonablate 200 system.

Efficacy

The latest case series by Uchida *et al.* (2006) investigated the safety and efficacy of the Sonablate 500 system in 63 patients with stage T1c-2bN0M0 localised prostate cancer. The prostate was treated in one (50 patients) or two (13 patients) HIFU sessions, resulting in a total of 76 procedures in 63 patients. Median operative duration was 149 (range: 55 to 356) minutes while median hospitalisation time was 4 (range: 2 to 20) days. Prostate gland size was reported to have decreased from an initial volume of 28.6 ml to 14.5 ml post-treatment ($p<0.001$) within a mean of 6.5 (3 to 23) months. Mean PSA nadir levels were 1.38 ± 2.55 (median: 0.5) ng/ml. Uchida *et al.* (2006) reported that 47/63 (75%) patients were biochemically disease free during the follow-up period. When patients were analysed based on their PSA levels before treatment of <10, 10.01 to 20 and >20 ng/ml, the three year biochemical disease free survival (DFS) rates were 82%, 62% and 20% respectively ($p<0.001$). PSA nadir was achieved 4 to 8 weeks after treatment with 3-year biochemical DFS rates for patients with PSA nadir of <0.2 (20 patients), 0.21 to 1.0 (25 patients), and >1 (18 patients) being 100%, 72% and 21% (log-rank test, $p<0.001$) respectively. Prostate biopsies at 6 months post-procedure revealed that 55/63 (87%) patients were cancer-free.

The multicentre case series study by Uchida *et al.* (2005) treated 72 consecutive prostate cancer patients with the Sonablate 500 system. It is important to note that there may be possible patient overlap to Uchida *et al.* (2006). Median operative duration was 169 (range: 65 to 485 minutes) minutes while median duration of hopitalisation was 5 (2 to 55) days. Prostate size was reduced from a pre-treatment volume of 24.2 ml to 14.0 ml post-treatment in 45 patients ($p < 0.01$). Biopsies conducted 6 months after treatment revealed that 49/72 (68%) patients were cancer free. A total of 60 patients were included in the biochemical DFS rates analysis with a median follow-up duration of 14 (2 to 24 months) months. Biochemical DFS rates in all patients at 1 and 2 years post-treatment were 78% and 76% respectively. For patients with stage T1c, T2a and T2b cancer, the biochemical DFS rates at 2 years were 89%, 67% and 40% respectively ($p = 0.0817$). Meanwhile, DFS rates for patients with Gleason scores 2 to 4, 5 to 7 and 8 to 10 at two years were 88%, 72% and 80% respectively. Patients

with PSA levels less than 10 mg/ml and those with PSA levels 10 to 20 ng/ml achieved biochemical DFS rates of 75% and 78% respectively (p = 0.6152). No statistically significant difference was noted in I-PSS (International prostate symptom score, rates urinary symptoms), Q-max (urinary flow rate) and the FACT quality of life analysis (Uchida *et al.* 2005).

The United States' experience with the Sonablate 500 system was outlined in a brief abstract which involved patients with localised primary (T1/T2) and recurrent prostate cancer (Gardner *et al.* 2004). Mean treatment time was 183 minutes (range 67 to 516 minutes). Patients with recurrent prostate cancer (n=3) were cancer-free after treatment based on biopsy results, while a PSA nadir of <0.5 ng/ml was maintained over 18 months. In patients with localised primary cancer (T1/T2), 8/20 (40%) underwent a second session of HIFU treatment, no further details on this group was provided (Gardner *et al.* 2004). This FDA approved clinical trial is currently ongoing.

Safety

All patients in the Uchida *et al.* (2006) study reported urinary symptoms (e.g. frequency, difficulty and urgency in urination) during the first two months after HIFU treatment. Urinary catheters were removed 1-2 days after treatment but were reinserted in patients who could not urinate spontaneously, the median catheterisation period after HIFU was 14 days (range 0-31 days). Urethral stricture was identified in 15/63 (24%) patients, 2/63 (3%) patients complained of retrograde ejaculation and 2/63 (3%) developed epididymitis. There was one case (2%) of prolonged urinary retention (treated with TURP), one case (2%) of grade 1 transient incontinence for one month, and one case (2%) of recto-urethral fistula. A total of 8/34 (24%) patients who were sexually active experienced erectile dysfunction after treatment, compared to the 30% to 70% rate in radical prostatectomy patients (Uchida *et al.* 2006). From this group two patients requested treatment and were provided with sildenafil citrate, both patients recovered (Uchida *et al.* 2006).

Uchida *et al.* (2005) reported that 13/72 (18%) patients developed urethral structure, 6/72 (8%) patients experienced epididymitis and 4/72 (6%) patients developed prostatitis. Erectile dysfunction was reported in 12/31 (39%) patients who were sexually active. One case of nephrotic syndrome, transient urinary incontinence, transit stooly incontinenece, balanoposthitis and retrograde ejaculation was reported (Uchida *et al.* 2005).

In the US study, there were two cases of gross hematuria and three cases of urinary tract infection (Gardner *et al.* 2004). No details regarding erectile dysfunction were presented.

Ethical Issues

No issues were identified from the retrieved material.

Cultural or Religious Considerations

No issues were identified from the retrieved material.

Other Issues

No issues were identified from the retrieved material.

Recommendation:

The available evidence indicates that the Sonablate 500 system is capable of successfully treating patients with localised prostate cancer with minimal complications and lower rates of erectile dysfunction (20 to 40%) compared to radical prostatectomy (30% to 70%) (Uchida *et al.* 2005, Uchida *et al.* 2006). However, the amount of studies conducted is few and no comparative studies with radical prostatectomy were located at the time of writing. Based on the limited evidence available, it is recommended that the Sonablate 500 system should be monitored for 12 months for any new evidence.

☐ Horizon Scanning Report	☐ Full Health Technology Assessment
☑ Monitor	☐ Archive

Note: Monitor until randomised controlled trial is published.

References:

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Search Criteria:

A search of MEDLINE, PubMed and Cochrane Library, Current Controlled Trials metaRegister, UK National Research Register, International Network for Agencies for Health Technology Assessments, relevant online journals and the Internet was conducted in February 2006.

Search terms used were: 'Sonablate', 'HIFU', 'High Intensity Focused Ultrasound' and 'ultrasound prostate treatment'.

This Horizon Scanning Prioritising Summary was prepared by Mr. Irving Lee from the NET-S Project, ASERNIP-S for the Health Policy Advisory Committee on Technology (Health PACT), on behalf of the Medical Services Advisory Committee (MSAC) and the Australian Health Ministers' Advisory Council (AHMAC).