



**Australian Government**

**Department of Health and Ageing**



Australia and New Zealand Horizon Scanning Network

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AN INITIATIVE OF THE NATIONAL, STATE AND  
TERRITORY GOVERNMENTS OF AUSTRALIA  
AND THE GOVERNMENT OF NEW ZEALAND

# **Horizon Scanning Technology Prioritising Summary**

## **Extracorporeal shock wave therapy for the treatment of angina**

**September 2010**





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# PRIORITISING SUMMARY

**REGISTER ID:** 000483

**NAME OF TECHNOLOGY:** EXTRACORPOREAL SHOCK WAVE THERAPY FOR TREATMENT OF ANGINA

**PURPOSE AND TARGET GROUP:** PATIENTS WITH PERSISTENT ANGINA DUE TO ISCHAEMIC HEART DISEASE

## STAGE OF DEVELOPMENT (IN AUSTRALIA):

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

## AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

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

## INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
USA	✓		
Japan	✓		
Germany	✓		
India		✓	
Canada		✓	
Russia		✓	

## IMPACT SUMMARY

Medispec Ltd provides Cardiospec™ which incorporates extracorporeal shock wave myocardial revascularisation (ESMR) technology with the aim of relieving chronic pain and improving quality of life for patients with severe ischaemic heart disease. The technology could be made available through existing infrastructure for patients who experience persistent angina for whom surgical treatment options have been exhausted.

## BACKGROUND

Ischaemic heart disease is the result of narrowing coronary arteries which supply blood to the muscle of the heart, or myocardium (Ito et al 2009). Atherosclerotic changes associated with lifestyle and other factors<sup>1</sup> contribute to this narrowing and decrease in blood flow, which in turn causes an imbalance between the supply and demand for oxygen to the myocardium. Myocardial ischaemia can cause temporary chest pain and reduced tolerance for physical exertion ('angina pectoris'), permanent damage to the heart muscle (acute infarction), lethal arrhythmia and sudden cardiac death. Prognosis and quality of life for patients who have severe ischaemia/coronary artery disease and who are not indicated for surgery are poor. Often surgical options will have been exhausted, and alternative forms of effective treatment are lacking. Extracorporeal shock wave therapy (SWT), the generic term for ESMR™ technology, is emerging as a prospect for this application. SWT, which was first introduced 20 years ago as a fragmentising treatment for kidney stones, has been adapted as a non-invasive therapy for ischaemic heart patients (Ito et al 2009). The ESMR™ technology produces acoustic shock waves via a generator, supported against the patient's chest by a water cushion. The generator produces an underwater spark at high-voltage (Figure 1), resulting in a high-amplitude pulse delivered to the appropriate area of the heart, as determined by ultrasound imaging (echocardiography) which locates and defines the extent of ischaemia. Several treatment sessions are required to obtain optimal results. No anaesthesia is necessary during the procedure.

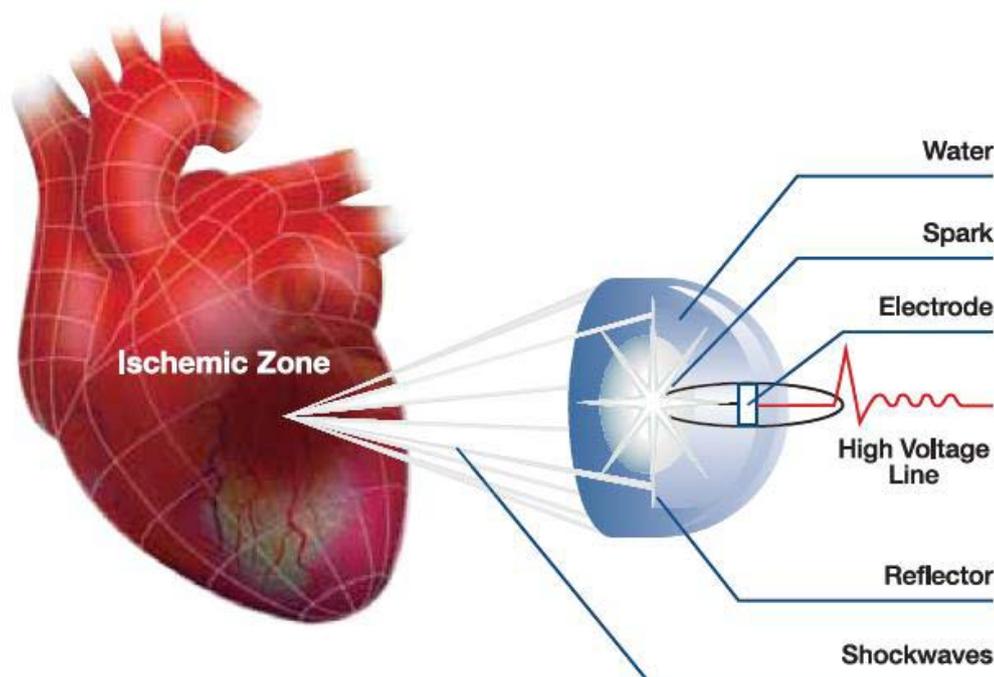


Figure 1 Main functional components used in ESMR™ technology (Medispec 2010).

<sup>1</sup> Factors include hypercholesterolaemia, hypertension, smoking, and diabetes.

The anticipated clinical impact of SWT is based on improved myocardial blood flow and enhanced angiogenesis. Increased blood flow after SWT is explained by nitric oxide, which is a potent vasodilator over short periods, while enhanced angiogenesis is thought to arise from up-regulation of vascular endothelial growth factors and their corresponding receptors, which has been observed after application of SWT (Jargin 2009).

### **CLINICAL NEED AND BURDEN OF DISEASE**

Ischaemic heart disease is a significant health outcome of cardiovascular disease (CVD), the major cause of mortality in Australia. CVD accounts for 34 per cent of all deaths nationally and causes a large proportion (18%) of the total disability adjusted life years in Australia. Potential years of life lost due to CVD in 2006 was estimated to be 191,600 person-years. The risk factors for CVD are smoking, high blood pressure, overweight, high cholesterol and low physical activity (BODCE 2007). It is estimated that CVD affects 3.7 million Australians, with 1.4 million suffering long-term disability due to these diseases (AIHW 2009).

In Australia, during the period 2006-07, there were 469,817 public hospital separations for diseases of the circulatory system. Of these, there were 162,328 separations for ischaemic heart disease (ICD code I20-25) (AIHW 2008). In New Zealand during 2002-03 there were 27,309 separations from public hospitals for ischaemic heart disease (ICD code I20-25) with a mean stay of seven days. In addition, there were 3,317 day cases for this indication (data supplied by the NZ Health Information Service).

### **DIFFUSION**

The technology has not yet diffused within Australia and New Zealand.

### **COMPARATORS**

Currently, management of ischaemic heart disease involves three main options. The first option is nitrate-based medication for which side-effects are common, including disabling headaches and dizziness. Continuous, long-term use of nitrates may lead to recurrent myocardial infarction (Thadani & Rodgers 2006). The remaining options are invasive procedures: percutaneous coronary intervention (PCI) which uses balloon dilation of narrowed arteries, and coronary artery bypass grafting (CABG) (Ito et al 2009).

### **SAFETY AND EFFECTIVENESS ISSUES**

Japanese researchers conducted clinical studies using SWT on a small group of patients with end-stage ischaemic heart disease (n=9), following promising results in experiments with pigs and rabbits (level IV intervention evidence). Patients (five men) were aged 55 to 82 years and not considered suitable for PCI or CABG, with a

number having already exhausted these treatment options. SWT was administered three times per week at intervals of one, three and 6 months. The treatments significantly reduced weekly use of nitroglycerin ( $p < 0.01$ ) and significantly improved Canadian Cardiovascular Society class scores compared to values obtained pre-treatment (mean scores  $> 2.5$  and  $< 2.0$ , respectively;  $p < 0.05$ ). Of the six patients with a score of three, five had a score of two and one patient had class one angina after 12 months. Additionally, imaging with scintigraphy indicated that myocardial blood perfusion was enhanced in ischaemic areas treated with SWT. No adverse events or complications were noted (Ito et al 2009).

An abstract presented at the 20<sup>th</sup> World Congress of the International Society for Heart Research described a study which was conducted to assess the efficacy of SWT for post-bypass ischaemic patients (level IV intervention evidence). Seventeen patients underwent angiography which confirmed that PCI and CABG were no longer viable treatments. Ten of these patients had previous myocardial infarction and six had angina pectoris. The Cardiospec<sup>TM</sup> unit (Medispec Ltd) was used to deliver three treatments per week, every four weeks for a total of nine treatments. Scintigraphy was performed at one and three-month follow-up. Overall, ten patients had an improvement in their symptoms, while three patients had significantly improved myocardial perfusion at rest, as measured at three-month follow up (no p-values were provided in the abstract). No improvement in ischaemia was observed during exercise in these three patients. The significant improvements were observed only among the patients without history of myocardial infarctions, suggesting SWT is more appropriately indicated for angina without a history of myocardial infarction. No adverse events or worsening of symptoms were observed (Takayama et al 2010).

A German study presented at the World Congress of Cardiology, 2006, recruited 25 patients who had refractory angina ( $n=15$ ) or chronic occlusion of one coronary vessel ( $n=10$ ) (level IV intervention evidence). All patients, with a mean age of 64 years, were treated using with SWT using Cardiospec<sup>TM</sup> at the appropriate ischaemic zone and followed up after three months. Canadian Cardiovascular Society class scores improved from  $3.22 \pm 0.43$  to  $2.2 \pm 0.68$  ( $p < 0.05$ ) at the end of the three months. Exercise tolerance and myocardial perfusion were also significantly increased (Gutersohn et al 2006).

### **COST IMPACT**

Medispec Ltd were contacted to provide information on cost of the Cardiospec<sup>TM</sup> unit, however no response was received.

### **ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS**

No issues were identified/raised in the sources examined.

## OTHER ISSUES

The sources examined in this summary provided evidence of statistical differences from baseline in outcomes for patients treated with SWT, but did not clearly define the clinical impact associated with these differences. On the basis of the Canadian Cardiovascular Society classification of angina definitions (Campeau 1976; SSCTS 2010) and the mean degree of change in this score from pre- to post-treatment, it would appear that improvement of angina symptoms, on an overall basis, is moderate in size. On a per patient basis, some patients would be expected to have had a large improvement in their symptoms, with corresponding ease in daily living activities.

Further information regarding the use of SWT for ischaemic heart disease is awaited in the results of a US trial presently being conducted in three US centres, however this trial also has a small patient sample (n=15, five per centre). Since SWT is usually intended for patients that are not amenable to alternative treatments for coronary artery disease, the best available evidence may be limited to studies that examine safety and efficacy.

A small randomised controlled trial (RCT) is currently being conducted by the Hadassah-Hebrew University Medical Center in Israel in conjunction with Medispec (ClinicalTrials.gov Identifier: [NCT00662727](#)). The trial commenced enrolment in 2008 and expects to be finalised by December 2010. Patients with refractory angina not amenable to revascularisation with angioplasty or bypass surgery (n=30) will be randomised to receive SWT or placebo, that is the same treatment but with no shockwaves delivered. The primary outcome is the total exercise time measured at six months follow-up and secondary outcomes are changes in stress-SPECT testing (to identify the ischemic areas) and angina pectoris Canadian Cardiac Society class also measured at six months.

A larger RCT (n=60) conducted by the Karachi Institute of Heart Diseases in conjunction with UNIQIP INTERNATIONAL, Pakistan is ongoing but is no longer recruiting patients (ClinicalTrials.gov Identifier: [NCT00776568](#)). Patients with refractory angina pectoris were randomised to receive either anti-hypertensive drugs (ACE inhibitors, Ca channel blockers, beta blockers, diuretics, cholesterol lowering agents) or extra-corporeal shockwave treatment (low intensity shock waves applied as 300 shocks per visit for 9 visits at weeks 1, 5 and 9). The shock wave treatment aims to induce the growth and development of new vasculature in regions of severe ischaemia, perfusing areas unreachable by PCI and/or CABG). The primary and secondary outcomes measured at six month follow-up were the alleviation of angina symptoms and changes in stress-SPECT testing compared to baseline. In addition, the University of Duisburg-Essen is currently recruiting patients for an RCT (n=60) (ClinicalTrials.gov Identifier: [NCT01241968](#)) for patients with refractory angina pectoris.

Concerns have been raised regarding the safety of SWT. Shock waves of sufficient power can injure cell membranes, small blood vessels and further contribute to ischaemia through the irreversible loss of cardiac muscle cells, which are incapable of mitosis (Jargin 2009). In the studies examined, no adverse reactions to SWT were apparent, but longer term follow-up with larger patient samples may be necessary to substantiate the early safety outcomes of this technology.

#### **SUMMARY OF FINDINGS**

Clinical studies of small sample size have been conducted on the basis of earlier promising results with animal studies for the application of SWT. It would appear that end-stage ischaemic heart disease patients who have exhausted other treatment options stand to experience at least moderate relief from symptoms of angina after a course of SWT with consequent improvement in daily living and less restrictions on physical activity. To date, the procedure has been shown to be safe within a 12 month follow-up period.

#### **HEALTHPACT ASSESSMENT:**

Although this assessment was based on low-level evidence with a lack of long-term follow-up data, several randomised controlled trials are expected to be completed and their results published in the near future. It would be prudent to await the results of these trials as shock wave treatment is considered an option of last resort for patients who have exhausted all other treatment avenues. HealthPACT have therefore recommended that this technology be monitored for further information in 24-months time.

#### **NUMBER OF INCLUDED STUDIES**

Total number of studies	3
Level IV evidence	3

#### **REFERENCES:**

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#### **SEARCH CRITERIA TO BE USED:**

Shockwave/shock wave therapy, angina

Extracorporeal

Ischaemic/ischemic heart disease, coronary artery disease

Ischaemia, myocardium\*