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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

Endo-PAT 2000 for the early detection of atherosclerosis

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PRIORITISING SUMMARY

REGISTER ID: 000149

NAME OF TECHNOLOGY: ENDO-PAT 2000 FOR THE ASSESSMENT OF ENDOTHELIAL FUNCTION

PURPOSE AND TARGET GROUP: PATIENTS BEING ASSESSED FOR EARLY ATHEROSCHLEROSIS

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 |
| <input checked="" type="checkbox"/> No | |
| <input type="checkbox"/> Not applicable | |

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
US		✓	
Germany	✓		

IMPACT SUMMARY:

The Endo-PAT 2000 is a device designed to measure endothelial function (EF) in the finger tip of a patient. EF measurements may be useful for a variety of reasons but in particular the degradation of EF is an early marker of atherosclerosis. A non-invasive method for screening for early atherosclerosis may be an important tool for preventive medicine.

BACKGROUND

Atherosclerosis is a disease affecting the function of arteries. Atherosclerosis is the underlying cause of several major diseases including stroke, heart attacks and other cardiovascular diseases. These diseases are some of the highest causes of morbidity and mortality in Australia. Atherosclerosis is an inflammatory disease which involves the endothelium of the arteries. The arteries harden and stiffen and become blocked with plaques. This leads to decreased function of these arteries which, at first, is asymptomatic but at later stages can block blood supply to the heart or brain with subsequent morbidity and mortality. Early identification of those at risk of

atherosclerosis and therefore cardiovascular disease would be an important step in the prevention of several major diseases.

The Endo-PAT 2000 is based on the concept of peripheral arterial tonometry (PAT), which can be used to assess the function of the endothelium in the finger. EF has been shown to be a predictor of cardiovascular disease (Frick & Weidinger 2007). The Endo-PAT 2000 uses a pressure cuff that covers the distal two thirds of the finger. When blood flow is occluded by the application of a pressure cuff to the forearm, blood flow to the finger is prevented. This occlusion causes a lack of oxygen in the finger inducing reactive hyperaemia (the increased blood flow to a body site due to an occlusion and is mediated by nitric-oxide). The lack of oxygen induces various degrees of hyperaemia depending on the function of the endothelial cells in the finger. The Endo-PAT 2000 device has a finger cuff that is pneumatically inflated both for securing the device to the finger and for measuring pulse volume changes in the finger tip. The patient's non-occluded arm is used as a control (Figure 1).



Figure 1 The Endo-PAT device (Itamar Medical 2008)

Measurements from both fingers are collected by the device and displayed on a computer where a final value is determined (Figure 2). A normal response consists of a sudden increase in blood flow after occlusion is stopped when compared to baseline. An abnormal response shows little if any increased blood flow to the finger when compared to baseline after the removal of the occlusion.

Theoretically, CVD should be preventable by lifestyle modification therefore an early detection or monitoring device for CVD would be an invaluable tool.

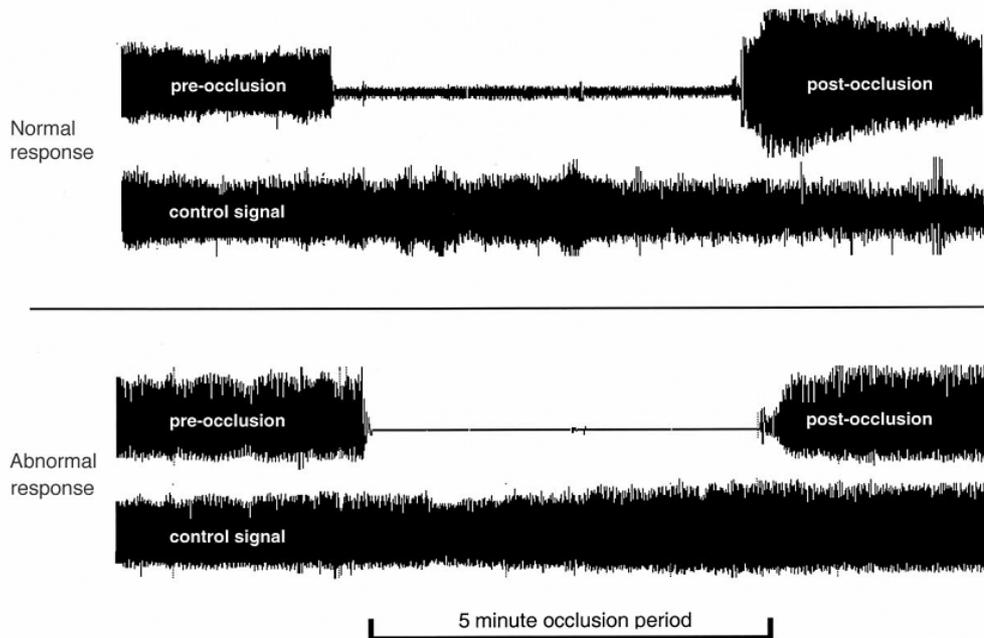


Figure 2 Normal and abnormal pulse amplitude response to occlusion as measured by the Endo-PAT 2000 device (Bonetti et al 2004)

CLINICAL NEED AND BURDEN OF DISEASE

Cardiovascular disease (CVD) is the major cause of mortality in Australia, accounting for 37 per cent of all deaths. Additionally, CVD causes a large proportion (18 %) of the total disability adjusted life years in Australia. Important health outcomes of CVD are ischemic heart disease and stroke. 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 3.67 million Australians, with 1.1 million suffering long-term disability due to these diseases. With the ageing population the prevalence is expected to increase in the future (Heart Foundation 2004).

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) and 27,757 separations for diseases of the arteries, arterioles and capillaries (ICD code I70-79) (AIHW 2008). In New Zealand during 2002-03 there were 4,690 separations from public hospitals for diseases of the arteries, arterioles and capillaries (ICD code I70-79) with a mean stay of 10 days. In addition there were 131 day cases for the same indication. During the same period there were 27,309 separations for ischaemic heart disease (ICD code I20-25) with a mean stay of seven days. There were 3,317 day cases for this indication (data supplied by the NZ Health Information Service).

DIFFUSION

No evidence was found supporting the diffusion of the Endo-PAT 2000 into Australia.

COMPARATORS

The gold standard for determining EF is the coronary endothelial function test. This is an invasive test where the responsiveness of the endothelium of the epicardial vessels is assessed using catheters, pharmacological agents and angiography. The agents are introduced into the vessels through catheters and the response is quantified using angiography to image the vasoconstriction or vasodilation of the targeted vessel (determined by diameter measurement before and after agent introduction). The blood vessel diameter changes indicate the function of the endothelium. For one pharmacological agent, acetylcholine, normal patients undergo a vasodilation whereas patients with atherosclerotic vessels display a vasoconstriction. Other tests may also be performed at the same time to test for disease symptoms diagnostic for a specific disease type (Barac et al 2007).

SAFETY AND EFFECTIVENESS ISSUES

Several studies have compared the Endo-PAT 2000 to other methods of EF testing and also used the Endo-PAT 2000 as a non-invasive diagnostic tool for EF assessment.

Kuvin et al compared the Endo-PAT 2000 to brachial artery ultrasound scanning (BAUS¹), another method for the determination of EF, in a population of 89 patients (mean age 54 ± 2 years) presenting for examination for chest pain. BAUS was performed in a similar way to Endo-PAT 2000 except ultrasound was used to determine EF. The dilatory response due to occlusion was imaged using ultrasound and compared to baseline data. The Endo-PAT 2000 measurements were performed as recommended and simultaneously with the BAUS test. This comparison showed a linear relationship between BAUS and Endo-PAT 2000 values, which were significantly correlated ($r=0.55$, $p<0.001$). Additionally, 68 subjects underwent direct measurement of coronary artery disease as determined by exercise myocardial perfusion imaging (ExMPI). Subjects with a positive test for ExMPI (signs of ischaemia or infarction) had significantly *lower* Endo-PAT 2000 scores (ExMPI *positive*, Endo-PAT 2000 score = 1.31 ± 0.02 ; ExMPI *negative*, Endo-PAT 2000 score = 1.62 ± 0.08 , $p = 0.004$) (Kuvin et al 2003) (Diagnostic evidence level III-2).

A second study investigated the ability of the Endo-PAT 2000 device to identify subjects with coronary endothelial dysfunction in a population of 94 consecutively recruited subjects who were referred to the clinic for a coronary angiogram. Coronary artery blood flow was determined using the gold standard, a coronary endothelial function test. Of the 94 patients, 55 were found to have dysfunctional EF and 39 had normal EF, as determined by the coronary endothelial function test. The Endo-PAT 2000 scores were significantly *higher* in *normal* patients (1.78 ± 0.08) and *lower* in *dysfunctional* patients (1.27 ± 0.05 , $p<0.001$). Using ROC curve analysis, an Endo-

¹ Baus is an established non-invasive method for diagnosis of EF {Faulx, 2003 #8}

PAT 2000 score cut-off of 1.35 was found to be the best predictor of normal or abnormal coronary endothelial function. An Endo-PAT 2000 value of <1.35 gave a sensitivity of 80 per cent and a specificity of 85 per cent (Bonetti et al 2004) (diagnostic evidence level III-2).

As part of the Framingham Heart Study², the correlation between Endo-PAT 2000 results and cardiovascular risk factors was investigated. Of the 4,095 participants in the study, 1,957 were eligible³ for Endo-PAT 2000 assessment. Several known factors which are linked to higher rates of CVD were found to be *inversely* correlated to Endo-PAT 2000 scores. These factors included male sex, body mass index, ratio of total to high-density lipoprotein cholesterol, diabetes mellitus, smoking (all $p<0.01$), indicating that the Endo-PAT 2000 may be useful as a non-invasive predictor of CVD risk (Hamburg et al 2008) (prognostic evidence level IV).

The studies reviewed here show that the Endo-PAT 2000 results correlate well with other established methods of diagnosing EF dysfunction. The data are of moderate quality and prospective long term studies with controls could provide better data on the outcomes of patients who have low scores on the Endo-PAT 2000 and whether this is a truly predictive factor for CVD.

COST IMPACT

The suppliers of this device were contacted but no reply was forthcoming at the time of publication of this summary.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

From the early stage evidence examined in this summary, Endo-PAT 2000 scores appear to be predictive of coronary endothelial function. Low scores are also associated with known CVD risk factors. Given that the alternative diagnostic tests are invasive and are associated with significant safety risks, the Endo-PAT 2000 may be a useful device for the initial investigation of, and potentially screening for CVD through the early detection of atherosclerosis.

² Framingham Heart Study is directed by the National Heart, Lung and Blood Institute (NHLBI), and is aimed at identifying the common factors or characteristics that contribute to cardiovascular disease (CVD).

³ Endo-PAT 2000 diagnosis was started mid-recruitment, leaving 2217 eligible patients. 260 more patients were excluded due to inadequate study data (n=207) and a variety of other reasons and errors.

HEALTHPACT ACTION:

Although an early stage, non-invasive diagnostic test for atherosclerosis and CVD may be useful in the management and prevention of these diseases, there is little evidence of clinical effectiveness in the studies summarised in this assessment. Therefore HealthPACT has recommended that further assessment of this technology is no longer warranted.

NUMBER OF INCLUDED STUDIES

Total number of studies	
Level III-2 diagnostic evidence	2
Level IV prognostic evidence	1

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SEARCH CRITERIA TO BE USED:

Cardiovascular Diseases/ diagnosis
Hyperemia/ physiopathology
Endothelium, Vascular/ physiopathology
Peripheral Vascular Diseases/ physiopathology
Plethysmography/instrumentation/ methods

