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Australia and New Zealand Horizon Scanning Network

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Horizon scanning prioritising summary

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Heartsbreath: Diagnostic test of grade III heart transplant rejection in heart transplant recipients.

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PRIORITISING SUMMARY

REGISTER ID: **000094**

NAME OF TECHNOLOGY: **HEARTSBREATH**

PURPOSE AND TARGET GROUP: **DIAGNOSTIC TEST OF GRADE 3 HEART TRANSPLANT REJECTION IN HEART TRANSPLANT RECIPIENTS**

STAGE OF DEVELOPMENT (IN AUSTRALIA AND/OR NEW ZEALAND):

- ☒ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☐ Nearly established
- ☐ Established
- ☐ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- ☐ Yes — ARTG number
- ☒ No
- ☐ Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States	✓		

IMPACT SUMMARY:

Menssana Research Inc. provides the Heartsbreath test with the aim of diagnosing grade 3 heart transplant rejection in heart transplant recipients. The technology is not yet available in Australia The test was approved in the United States in February 2004.

BACKGROUND

After a heart transplant, the recipient's immune system normally attacks the new organ as it identifies it as a foreign body (rejection). The standard treatment for prevention of organ rejection in transplant patients is to administer immune-suppressing drugs and to carefully monitor for signs of organ rejection throughout the life span.

The Heartsbreath test is a non-invasive breath test for markers of oxidative stress which may predict grade 3 rejection of heart transplants in recipients who were successfully transplanted in the previous twelve months. Grading of rejection is categorised according to The International Society of Heart and Lung Transplantation (ISHLT) grading system agreed in 1991 (Balk et al 1997)

Features of Grade 3A and 3B rejection are described as "mutifocal inflammatory infiltrates consisting of large aggressive lymphocytes with or without eosinophils and "diffuse

inflammatory process within several pieces of biopsy tissue. Myocyte damage is present as well as an aggressive inflammatory infiltrate of large lymphocytes and eosinophils with an occasional neutrophil" (Beckman et al 2001).

The Heartsbreath test consists of:

- An apparatus for collecting methylated alkanes from alveolar breath onto an absorbent trap. The apparatus also collects a separate sample of room air.
- Analysis of the methylated alkanes in alveolar breath and room air through gas chromatography and mass spectroscopy.
- Interpretation of the methylated alkanes with a proprietary algorithm in order to predict the probability of grade 3 heart transplant rejection.

The American Food and Drug Administration has approved the Heartsbreath test as an adjunct to, but not as a substitute for, endomyocardial biopsy. Results from the Heartsbreath test are compared to results of endomyocardial biopsy pathology results within the previous month to measure the probability of transplant rejection.

CLINICAL NEED AND BURDEN OF DISEASE

The clinical need for this technology is not high: the number of heart or heart-lung transplants in the year 2000 in Australia was 63 which represents a rate of 3.3 per million per year (AIHW, 2004).

DIFFUSION

Currently, the test is not being marketed in Australia.

COMPARATORS

The conventional procedure used in the diagnosis of all grades of heart transplant rejection is endomyocardial biopsy, a catheter procedure in which a small piece of tissue is cut from inside the heart and retrieved for laboratory analysis.

There are some reported difficulties in relying on endomyocardial biopsy alone: the biopsy sample may show a lower intensity of rejection than the rest of the heart (Nakhleh et al 1992, Sharples et. al 1992). Previous studies of heart transplant biopsy have also demonstrated high inter-observe variability in scoring the severity of heart transplant rejection (Nielsen et al. 1992, Shanes et al. 1987, Winters et al. 1996).

COST IMPACT

There may be potential to reduce resources allocated to biopsy procedures if the test were to replace endomyocardial biopsy in the short term. However, if the test is used as an adjunct to biopsy, it is unclear what the potential cost savings would be. The current price of the Heartsbreath test is $US500.00 (personal communication, Menssana Research Inc.).

EFFECTIVENESS AND SAFETY ISSUES

In a case-control study (intervention level III-2 evidence), results from 1061 breath samples taken from 539 heart transplant patients analysed with the Heartsbreath test were compared to breath samples from normal healthy age-matched controls. This was a predictive model to ascertain potential markers of transplant rejection. The heart transplant recipients with and without these identified rejection markers were then cross-classified according to the rejection grades derived from subsequent biopsy sampling (diagnostic level 3b evidence) (Phillips et al. 2002).

Breath test results revealed nine breath samples whose levels represented markers of grade 3 rejection. The cross-validated model, indicated that the Heartsbreath test had a sensitivity of 59.5% and specificity of 58.8% for detecting grade 3 heart transplant rejection, compared to biopsy. The negative predictive value of the breath test for grade 3 rejection was 97.3%, such that in a patient with a negative breath test, endomyocardial biopsy would contribute little additional clinical information.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

CONCLUSION:

There is limited published evidence currently available for the Heartsbreath test and there is limited clinical need for this adjunctive test in Australia. It is unlikely to have any significant policy or clinical impact on the public health system.

HEALTHPACT ACTION:

Therefore it is recommended that this technology be archived.

SOURCES OF FURTHER INFORMATION:

AIHW 2004 '*Interactive national hospital morbidity database'* [Internet] Available from: http://www.aihw.gov.au/pls/cvd/cvd_proc.show_report [Accessed May 20, 2004].

Balk, A. H., Zondervan, P. E. et al (1997). 'Effect of adopting a new histological grading system of acute rejection after heart transplantation', *Heart,* 78 (6), 603-607.

Beckman, E. N., Mehra M. R, Par M. H, Scott, R. L. (2001) 'Utility of Heart Biopsy in Transplant Patients' *Ochsner,* 3 (2), 219-22 [Internet] Available from http://www.ochsnerjournal.org/pdfserv/i1524-5012-003-04-0219.pdf [Accessed May 20, 2004].

Nakhleh, R. E., Jones, J. et al (1992). 'Correlation of endomyocardial biopsy findings with autopsy findings in human cardiac allografts', *J Heart Lung Transplant,* 11 (3 Pt 1), 479-485.

Nielsen, H., Sorensen, F. B. et al (1993). 'Reproducibility of the acute rejection diagnosis in human cardiac allografts. The Stanford Classification and the International Grading System', *J Heart Lung Transplant,* 12 (2), 239-243.

Phillips M, Boehmer J. et al (2002) 'Heart Allograft Rejection: Detection with Breath Alkanes in Low Levels (the HARDBALL study)', *J Am Coll Cardiol,* 1:12-13.

Shanes, J. G., Ghali, J. et al (1987). 'Interobserver variability in the pathologic interpretation of endomyocardial biopsy results', *Circulation,* 75 (2), 401-405.

Sharples, L. D., Cary, N. R. et al (1992). 'Error rates with which endomyocardial biopsy specimens are graded for rejection after cardiac transplantation', *Am J Cardiol,* 70 (4), 527-530.

Winters, G. L. & McManus, B. M. (1996). 'Consistencies and controversies in the application of the International Society for Heart and Lung Transplantation working formulation for heart transplant biopsy specimens. Rapamycin Cardiac Rejection Treatment Trial Pathologists', *J Heart Lung Transplant,* 15 (7), 728-735.

SEARCH CRITERIA TO BE USED:

Graft Rejection/classification/ diagnosis
Heart Transplantation
Allograft
Breath Alkanes