Horizon Scanning Technology
Prioritising Summary

Laparoscopic hepatic artery infusion pump

October 2004
This work is copyright. You may download, display, print and reproduce this material in unaltered form only (retaining this notice) for your personal, non-commercial use or use within your organisation. Apart from any use as permitted under the Copyright Act 1968, all other rights are reserved. Requests and inquiries concerning reproduction and rights should be addressed to Commonwealth Copyright Administration, Attorney General’s Department, Robert Garran Offices, National Circuit, Canberra ACT 2600 or posted at http://www.ag.gov.au/cca

Electronic copies can be obtained from http://www.horizonscanning.gov.au

Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

DISCLAIMER: This report is based on information available at the time of research and cannot be expected to cover any developments arising from subsequent improvements to health technologies. This report is based on a limited literature search and is not a definitive statement on the safety, effectiveness or cost-effectiveness of the health technology covered.

The Commonwealth does not guarantee the accuracy, currency or completeness of the information in this report. This report is not intended to be used as medical advice and it is not intended to be used to diagnose, treat, cure or prevent any disease, nor should it be used for therapeutic purposes or as a substitute for a health professional's advice. The Commonwealth does not accept any liability for any injury, loss or damage incurred by use of or reliance on the information.

The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers’ Advisory Council (AHMAC) supports HealthPACT through funding.

This Horizon scanning prioritising summary was prepared by staff from the Australian safety and Efficacy Register of New Intervventional Procedures – Surgical (ASERNIP-S).
Name of Technology:
Laparoscopic hepatic artery infusion pump placement

Purpose and Target Group:
Laparoscopic hepatic artery infusion pump placement is a minimally invasive procedure, which enables long-term continuous hepatic chemotherapy infusion via an implantable pump, in patients with non-resectable colorectal liver metastases.

Stage of Development (in Australia): Yet to emerge in Australia
- Experimental
- Investigational
- Nearly established
- Established
- Established but changed indication or modification of technique
- Should be taken out of use

International Utilisation:

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>LEVEL OF USE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trials underway</td>
</tr>
<tr>
<td>United States</td>
<td>✓</td>
</tr>
</tbody>
</table>

Impact Summary:

Background
Colorectal cancer is the fourth most common malignancy, behind cancers of the lung, breast and prostate (http://www.livertumor.org). Up to 50% of patients with colorectal cancer eventually develop liver metastases (http://www.ellisfischel.org/liver/cryotherapy.shtml). In approximately 30% of those patients with metastases, the cancer is still confined to the liver at the time of metastatic diagnosis (http://www.livertumor.org). Of the patients with colorectal metastases confined to the liver, only 10-20% are surgical candidates due to tumour size, distribution, accessibility of the tumour(s), vascular involvement, poor hepatic reserve or poor general condition (Cheng et al. 2003).

Systemic chemotherapy has traditionally been the primary treatment modality for non-surgical candidates; however, patients rarely tend to live beyond five years. Due to the high mortality rate amongst these patients, alternative treatments such as radiofrequency ablation and cryotherapy have since been developed. Although these treatments have shown to be effective in the destruction of some tumours, they have been associated with complications due to the delivery of thermal energy to healthy tissue.

Laparoscopic hepatic artery infusion pump placement is a minimally invasive technique which enables continuous hepatic infusion therapy, for unresectable liver metastases. Liver...
metastases derive 95% of their blood supply from the hepatic artery, while normal liver parenchyma is supplied primarily by the portal vein (Franklin et al. 2002). Therefore a high concentration of drug can be delivered to the liver bed, maximising the therapeutic effect whilst high first pass hepatic extraction minimises systemic toxicity (Franklin et al. 2002).

Clinical Need and Burden of Disease
The five-year survival following resection of isolated colorectal cancer liver metastases can be as high as 38% (Fong et al. 1997). However, for the estimated 80% of patients with isolated colorectal cancer liver metastases who are not amenable to surgical resection, systemic chemotherapy is widely employed. Systemic chemotherapy is associated with only a 20-40% response rate with little impact on long-term survival (http://www.ellisfischel.org/liver). In Australia, 7094 new cases of colorectal cancer were registered in 1983. Each year this figure has increased, with 12405 cases registered in 2000.

Estimated Speed, Geographic and Practitioner Use Patterns of Diffusion in the Health System
Regional liver infusion chemotherapy has been in use for several decades in attempt to treat isolated hepatic metastases from colorectal cancer. The procedure was originally performed via laparotomy with an external pump; however, this has been associated with a high incidence of morbidity and mortality (Urbach et al. 2000). In 1996, the laparoscopic approach was used for implantation of the pump. It provided an alternative to laparotomy by enabling access whilst minimising morbidity and mortality (Cheng et al. 2003). A non-randomised comparative study conducted by Cheng et al. (2003), evaluated safety and efficacy between laparoscopic hepatic artery infusion pump placement and radiofrequency ablation, on 45 consecutive patients. In June 2004, Cheng et al. published early results and technical considerations for the procedure on 38 patients; however, there seems to be some overlap with their earlier publication.

Existing Comparators
- Hepatic artery infusion pump placement via laparotomy
- Alcohol-injected ablation
- Cryotherapy ablation
- Electrolysis ablation
- Radiofrequency ablation
- Systemic chemotherapy

Estimated Cost Impact
The costs associated with laparoscopic pump placement in Australia are not available. The cost of surgery involving pump placement via laparotomy in Australia is also not available. However, reimbursement fees as stated by the Medicare Benefits Schedule for laparotomy with insertion of portacath for administration of cytotoxic therapy including placement of
reservoir is approximately $525 (Item number 30400). Loading of an implanted pump or reservoir with a cytotoxic agent or agents is approximately $80 (item number 13939) and accessing of long term devices is approximately $43 (item number 13945, 14221).

According to the HIC, for the 2003/2004 financial year there were 16 claims to Medicare for laparotomy placement of a portacath (item number 30400) (http://www.hic.gov.au).

**Efficacy and Safety Issues**

The short and long-term safety and efficacy data exist from two comparative studies conducted by Cheng *et al.* (2003, 2004). There is an overlap of patients reported in these studies and a study conducted by Urbach *et al.* (2001).

The comparative studies evaluated patients who received laparoscopic radiofrequency ablation (LRFA) (n=20), laparoscopic hepatic artery infusion pump placement (LHAIP) (n=10) or both LRFA and LHAIP (n=15). Patients were excluded from the radiofrequency ablation group if their tumour involved the bifurcation in the hepatic hilum and a 1 cm margin could be obtained. This therefore resulted in patients in the LHAIP group having a more diffuse distribution of disease.

Patients who received both LRFA and LHAIP had the longest operative time (389.2 [77.7] min) (p<0.05) but there was no increase in blood loss or hospital stay compared to patients who received LHAIP alone (Cheng *et al.* 2003). Variant hepatic arterial anatomy was present in 18/38 (47%) patients who had LHAIP. The presence of a variant hepatic artery did not result in increased pump complications, operative time or blood loss (p≥.20) compared to patients with non-variant arterial anatomy (Cheng *et al.* 2004). There were no intraoperative or perioperative deaths. One patient in 45 (2.2%) who received LRFA and LHAIP developed pulmonary embolus (Cheng *et al.* 2003). A further 2/45 (4.4%) patients had an ileus that resulted in a prolonged hospital stay (Cheng *et al.* 2003). In 3/38 (7.9%) patients, who had LHAIP alone, misperfusion was identified by methylene blue injection, two were corrected intraoperatively and one postoperatively (Cheng *et al.* 2004). Cheng *et al.* (2004) reported a 13% pump-related complication rate.

At the mean 11.5 [7.8] month follow-up, survival was 70%, 67% and 50% for LRFA, LRFA + LHAIP and LHAIP respectively. The number of patients who were alive and tumour-free was 12/14 (86%), 7/10 (70%) and 0/10 (0%) in the LRFA, LRFA + LHAIP and LHAIP groups respectively. Kaplan-Meier survival curves estimate mean survival times of 25.4 [3.4] months in LRFA patients, 15.2 [1.7] months in LRFA + LHAIP patients and 12.6 [2.3] months in LHAIP patients (Cheng *et al.* 2003).

The limited evidence for the safety and efficacy of laparoscopic hepatic artery infusion pump placement is mainly based on Cheng *et al.* (2003), as other studies are still ongoing. With no comparison to placement via laparotomy, benefits and risks can not be determined.
Ethical Issues: No issues were identified from the retrieved material.

Cultural or Religious Considerations: No issues were identified from the retrieved material.

Other Issues: Before the laparoscopic hepatic artery infusion pump placement procedure, a cholecystectomy is performed to avoid postoperative chemotherapy-related cholecystitis. All studies published using a laparoscopic technique and implantable pump device were conducted by the same study group resulting in an overlap of patients.

Conclusion:
Limited evidence exists on the safety and efficacy of laparoscopic hepatic artery infusion pump placement. Long-term safety and efficacy data from randomised controlled trials are required before this procedure can be widely accepted.

References:


Sources of Further Information:
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 September 2004.

Search terms used were: ‘laparoscopic hepatic artery chemotherapy’, ‘laparoscopic hepatic arterial infusion’, laparoscopic implantable infusion and hepatic artery’ and ‘hepatic artery infusion pump and laparoscopy’.