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Australia and New Zealand Horizon Scanning Network

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Horizon Scanning Technology Prioritising Summary

Laparoscopic hepatic artery infusion pump

October 2004
(Updated November 2005)



**Australian
Safety
and Efficacy
Register
of New
Interventional
Procedures -
Surgical**



**Royal Australasian
College of Surgeons**



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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 Interventional 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:

COUNTRY	LEVEL OF USE		
	Trials underway	Limited use	Widely Diffused
United States	✓		

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 portcath (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 ($p \geq .20$) 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.



2005 UPDATE

A search of relevant databases, online journals and the Internet was conducted in November 2005, following the recommendation in November 2004 that laparoscopic hepatic artery infusion pump be monitored for assessment in 12 months time. One new source of evidence on the safety and efficacy of this intervention has been located in the literature. A case series study conducted by Shimonov et al. (2005) examined 23 patients suffering from colorectal cancer and isolated liver metastases. These patients were treated with combined arterial infusion (HAI) of irinotecan (CPT-11) in conjunction with systemic chronotherapy infusion of 5-fluorouracil (FU), folinic acid and carboplatin.

A total of 15 patients completed the study. Of these, 10 patients have been previously treated with 5FU and leucovorin while the other 5 were chemo-naïve. Partial response was experienced by 6 patients (40%) and this was followed by laparoscopic radiofrequency ablation in 5 patients (33%). The disease was stabilized in 2 patients (13%) while 7 patients (46%) experienced disease progression.

Five patients suffered from grade 2 gastrointestinal tract pain while 9 patients experienced right upper quadrant pain during HAI treatment. In addition to this, there were grade 2 hematological complaints in two patients. Overall, the side effects were considered mild and this appears to be particularly true for patients who had previous treatments.

Reference:

- 1) Shimonov M, Hayat H, Chaitchik S, Brener J, Schachter P, Czerniak A. Combined systemic chronotherapy and hepatic artery infusion for the treatment of metastatic colorectal cancer confined to the liver. *Chemotherapy* 2005; **51** (2-3): 111-115.

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.

2005 Update: Based on the limited evidence, this procedure will be archived.

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| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input type="checkbox"/> Monitor | <input checked="" type="checkbox"/> Archive |

References:

Cheng J, Glasgow RE, O'Rourke RW, Swanstrom LL, Hansen PD. Laparoscopic radiofrequency ablation and hepatic artery infusion pump placement in the evolving treatment of colorectal hepatic metastases. *Surgical Endoscopy* 2003; 17:61-7.

Cheng J, Hong D, Zhu G, Swanstrom LL, Hansen PD. Laparoscopic placement of hepatic artery infusion pumps: technical considerations and early results. *Annals of Surgical Oncology* 2004; 11(6):589-97.

Fong Y, Cohen AM, Fortner JG, Enker WE, Turnbull AD, Coit DG, Marrero AM, Prasad M, Blumgart LH, Brennan MF.. Liver resection for colorectal metastases. *Journal of Clinical Oncology* 1997; 15:938-946.

Urbach DR & Hansen PD. Laparoscopic placement of a continuous hepatic artery infusion pump. *Seminars in Laparoscopic Surgery* 2000; 7(2):140-7.

Urbach DR, Herron DM, Yashodan SK, Swanstrom LL, Hansen PD. Laparoscopic hepatic artery infusion pump placement. *Archives of Surgery* 2001; 136:700-4.

Sources of Further Information:

Franklin ME & Gonzalez JJ. Laparoscopic placement of hepatic artery catheter for regional chemotherapy infusion: Technique, benefits, and complications. *Surgical Laparoscopy Endoscopy & Percutaneous Techniques* 2002; 12(6): 398-407.

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'.



This Horizon Scanning Prioritising Summary was prepared by Ms Lynette Cufone 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).