Title:	**Selective Internal Radiation Therapy for Hepatic Metastases using SIR-Spheres – March 2002**
Agency:	Medical Services Advisory Committee (MSAC) Commonwealth Department of Health and Aged Care GPO Box 9848 Canberra ACT 2601 Australia **http://www.msac.gov.au**
Reference:	**MSAC application 1034. Assessment report**

Aim

To assess the safety and effectiveness of Selective Internal Radiation Therapy **(**SIRT) and the circumstances under which public funding should be supported for the treatment of non-resectable hepatic metastases secondary to colorectal cancer in the absence of extrahepatic metastases and in combination with hepatic arterial or systemic chemotherapy.

Conclusions and results

Safety

Patient safety The randomised trials provided limited information regarding patient safety. It appears that SIRT plus hepatic arterial chemotherapy may result in additional elevation of hepatic enzymes (alkaline phosphatase), and more nausea and vomiting than hepatic arterial chemotherapy alone. SIRT plus systemic chemotherapy appeared to result in more grade 3-4 toxicities (including granulocytopenia and mucositis) than systemic chemotherapy alone. There was one treatment related death in the combined treatment arm of this trial. Uncontrolled evidence suggests SIRT commonly result in liver enzyme elevations, fatigue and lethargy, anorexia, nausea and/or vomiting and gastrointestinal symptoms. There have been a small number of cases of fatal radiation hepatitis, gastrointestinal ulceration or haemorrhage, and radiation pneumonitis.

Personnel safety The doses of radiation delivered to personnel appear to be reasonably low and within the ranges recommended by the National Occupational Health and Safety Commission, Australia.

Effectiveness

There is some evidence that SIRT plus hepatic chemotherapy may be more effective than hepatic chemotherapy alone in terms of tumour response in the liver, depending upon how this was measured. When measured by changes in tumour volume, there was a trend favouring SIRT plus hepatic chemotherapy in tumour response and when measured by tumour area, there were significantly more tumour responses in those treated with hepatic chemotherapy plus SIRT than with chemotherapy alone. There is also some evidence to suggest that SIRT plus systemic chemotherapy improves both 'first integrated" and 'best confirmed" tumour response.

SIRT plus hepatic chemotherapy may prolong time to disease progression in the liver, depending upon how this was measured. If disease progression was measured by tumour volume, there was a trend favouring SIRT plus hepatic chemotherapy. If measured by tumour area, there was a significant difference favouring SIRT plus hepatic chemotherapy ($p=0.033$, Gray's test).

There is insufficient evidence from the trial of hepatic chemotherapy plus SIRT to determine the effect of SIRT on progression-free or overall survival. Evidence was also not available on quality of life measures.

Cost-effectiveness

It is not possible to give a reliable estimate of cost per life year saved or cost per quality adjusted life year due to the lack of reliable evidence regarding benefit on these outcomes. The incremental cost-effectiveness ratio for SIRT also varied considerably depending upon the assumptions used in the analysis. A comprehensive Australian-based assessment of costs and effects associated with systemic chemotherapy, hepatic arterial chemotherapy and SIRT is needed to provide a basis for a comparison between systemic therapy and hepatic chemotherapy with or without SIRT.

Recommendation

MSAC recommended against public funding since there is currently insufficient evidence of effectiveness and cost-effectiveness. The data suggests SIRT is reasonably safe and has anti-tumour activity, but it is not clear whether this translates into a survival or quality of life benefit.

Method

The National Health and Medical Research Council (NHMRC) Clinical Trials Centre at the University of Sydney conducted a systematic review of the literature on SIRT (with eligibility criteria defined *a priori*). The search was undertaken from commencement until 13 February 2001, of biomedical electronic databases, the Internet and international health technology assessment organisation websites. Additional published and unpublished data was also obtained from the applicant.