Health Policy Advisory Committee on Technology

Technology Brief

Surefire Infusion System

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ASERNIP-S
Australian Safety and Efficacy Register of New Interventional Procedures – Surgical

Royal Australasian College of Surgeons

HealthPACT
emerging health technology

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This brief was prepared by Robyn Lambert from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

Summary of findings

The Surefire Infusion System (SIS) is a novel anti-reflux catheter developed for use in radioembolisation or chemoembolisation of liver cancer. There are several SIS models available. The devices have widespread regulatory approval and are available within Australia.

The SIS is intended to replace standard end-hole catheters and coils used in radioembolisation or chemoembolisation. The novel design of the SIS is intended to prevent non-target embolisation of healthy tissue during therapeutic procedures, and negates the need for coil embolisation of hepatic blood vessels. At this stage the clinical literature reflects its use in the liver for selective internal radiation therapy (SIRT), trans-arterial chemoembolisation (TACE), and drug-eluting bead trans-arterial chemoembolisation (DEB-TACE)[1] of primary and secondary liver cancer.

Two comparative studies found that use of the SIS reduces the total procedure time, fluoroscopy time, contrast agent dose and radiation dose associated with pre-treatment angiography for SIRT. This is because coil embolisation does not need to be performed. With respect to the actual SIRT procedures, no statistically significant changes in these outcomes were observed. Overall the published literature reports successful use of the SIS for SIRT and chemoembolisation procedures. In terms of safety, a single case of catheter occlusion was reported, but there were no observed instances of non-target embolisation.

One study compared the costs of consumables when performing SIRT using coil embolisation and a standard end-hole catheter or the SIS. The authors reported a cost-saving from SIS as it precluded the use of coils. Potential cost-savings in the Australian context are dependent upon the local negotiated price of the SIS, the type and cost of standard catheters, the type, cost and number of coils used, and whether repeat embolisation is required.

The included studies reported conflicts of interest and the identified ongoing clinical trials were sponsored by the manufacturer. No high-level evidence is currently available to support a claim of superior tumour response when the SIS is used as compared to a standard end-hole catheter and coil embolisation.

HealthPACT Advice

The Surefire® infusion system for the treatment of primary or secondary hepatic tumours offers advantages over conventional chemoembolisation catheters in that it prevents backflow into the collateral circulation and does not require the use of beads or coils. There is currently little evidence describing patient outcomes with the use of the Surefire® system. RCTs are required in order to ascertain the clinical utility of this technology and technologies like it.

HealthPACT does not support public investment in the Surefire® system in clinical practice at this time; however, HealthPACT recommends that the evidence for the Surefire® system be reviewed once the results of three ongoing RCTs have been published.

Technology, Company and Licensing

Register ID	**WP235**
Technology name	**Surefire® Infusion Systems**
Patient indication	**For the treatment of primary and secondary liver cancer**

Description of the technology

The Surefire Infusion System (SIS) (Figure 1) is intended for delivering radiopaque media and therapeutic agents to selected sites in the peripheral vascular system.[2] The device appears to be most commonly used in selective internal radiation therapy (SIRT), which delivers millions of tiny radioactive microspheres or beads directly to malignant liver tumours (radioembolisation). Surefire Medical, Inc. (Colorado, USA) make several catheters, of which the Surefire Precision is the latest. The Surefire Precision Infusion System is depicted in Figure 1 below with the tip deployed and not deployed.

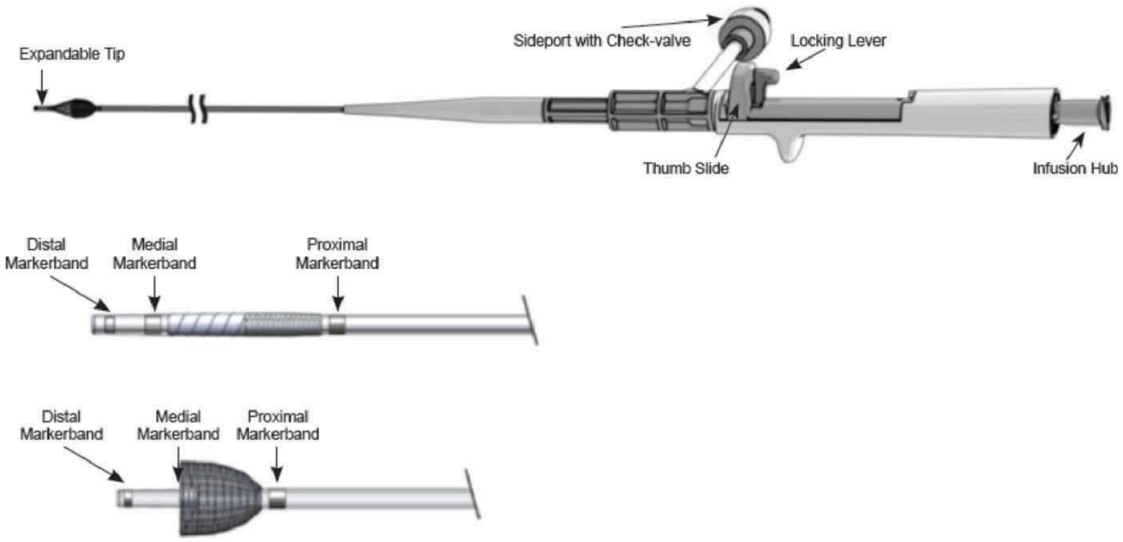

Figure 1 The Surefire Precision Infusion System with tip non-deployed and deployed[3]

The novel feature common to all of Surefire Systems is the patented, expandable tip. The SIS is known as an anti-reflux catheter because it prevents the backward flow of injected agents to other parts of the liver or other organs. Liver tumours contain regions of high pressure that limit blood flow and make it difficult to deliver therapeutic agents. The tip of the SIS expands to the vessel wall, effectively stopping any backward (retrograde) flow of an injected agent around the catheter. The therapeutic agent can then be delivered to the tumour against a pressure gradient using infusion pressure.[4] By this mechanism embolic agents (materials used to block blood flow through a vessel) can be delivered to a liver tumour without the need for coil embolisation of surrounding blood vessels.

The Precision catheter has a smaller outer and inner diameter than its predecessors, the mT and LT, and is equipped with a lever mechanism for tip expansion rather than requiring retraction of an outer sheath.[2] The Surefire microcatheters have a larger outer diameter

than a standard end-hole catheter and require a guiding catheter.[4] Surefire Medical, Inc. sell three different guiding catheters that can accommodate all of the infusion systems, but any guide catheter of sufficient inner diameter can accommodate the infusion systems.[4] The device is a single use item.

Company or developer

Surefire Medical, Inc., Colorado, United States of America.

Reason for assessment

The SIS is a new type of microcatheter designed to maximise embolisation efficiency whilst reducing reflux of embolising agents in the treatment of liver cancer. Use of the SIS removes the need for coil embolisation of arteries in selective internal radiation therapy (SIRT), trans-arterial chemoembolisation (TACE), and drug-eluting bead trans-arterial chemoembolisation (DEB-TACE) and may have time and cost saving implications.

Stage of development in Australia

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

Licensing, reimbursement and other approval

Surefire Medical, Inc. reported receiving TGA, CE Mark[5], United States Food and Drug Administration and Health Canada approval for its devices. An ARTG public summary document for an embolisation prevention implant manufactured by Surefire Medical was identified (216086 listed 15/10/2013)[6], but it is not clear whether the ARTG listing covers any of the catheters. Surefire Medical, Inc. has FDA 510(k) approval for the following products:[7]

- Surefire Infusion System, K160662 (approval, 11/03/2016)
- Surefire Infusion System 021, K143588 (approval 12/01/2015)
- Surefire high flow angiographic catheter, K122506 (approval 12/09/2012)
- Surefire High-Flow Microcatheter, K121677 (approval 14/06/2012)
- Surefire Infusion Catheter System, K110459 (approval 24/06/2011).

A search of the 510(k) database also identified approval for a Surefire guiding catheter (K140034) and a Surefire guide sheath (K113737). Health Canada approval for the Surefire Infusion Systems was also identified.[8]

Australian Therapeutic Goods Administration approval

☒ Yes ARTG number: 216086

☐ No

☐ Not applicable

Technology type **Device**

Technology use **Therapeutic**

Patient Indication and Setting

Disease description and associated mortality and morbidity

The SIS has been used in the treatment of patients with primary and secondary liver cancer. Primary liver cancer is a malignant tumour that begins in the liver, of which there are three forms. The most prevalent is hepatocellular carcinoma (HCC). Other forms are cholangiocarcinoma and angiosarcoma.[9] Secondary liver cancer refers to cancer of any origin which has spread to the liver. Secondary liver cancer is more common than primary liver cancer and has an extremely poor prognosis. While most cancers can spread to the liver, the most common are breast, stomach and bowel cancer. Primary and secondary liver cancers have a poor prognosis. The five-year survival rate at diagnosis is 16 per cent[10]; the biggest known risk factors for primary liver cancer in Australia are Hepatitis C and B infections[9]; and, males are three times more likely than females to be diagnosed with primary liver cancer in Australia. [10]

Number of patients

Primary liver cancer

Worldwide, primary liver cancer is the second leading cause of cancer death. HCC arises predominantly in the setting of chronic liver disease, with most patients having underlying cirrhosis of the liver.[11] For all Australians, liver cancer is among the 20 most commonly diagnosed cancers.The age-standardised incidence of liver cancer has increased from 1.8 to 6.4 per 100,000 persons between 1982 and 2014,[10] with the incidence increasing with age. Reliable national data on the diagnosis of cancer for Indigenous Australians are not readily available[10], but the age-standardised incidence rate reported by the AIHW was 2.8 times higher for Indigenous Australians than for non-Indigenous Australians.[10]

In New Zealand the number of liver cancer cases over the 1994 to 2011 period was 3,195 (2,192 of which were in men). Although the one-year survival from 1998-99 to 2010-11 improved, the five-year survival remained low at 15 per cent. In an analysis of cancer registrations and mortality rates in persons over the age of 50 years, it was shown that Māori men older than 65 years were most likely to be registered with and die from prostate, lung, colorectal, stomach and liver cancers. The incidence of liver cancer in Māori men aged

50 to 64 years in 2005-2007 was 46.6 per 100,000 persons and in the older than 65 years group it was 106.7 per 100,000. For non-Māori men, the incidence was 11.2 per 100,000 persons in the 50- to 64-year age group and 29.2 per 100,000 in the older than 65 years age group.

Secondary liver cancer

The Australian Cancer Council reported that approximately 28,000 people are diagnosed with secondary liver cancer each year.[9] Secondary site cancer (including the liver) is the most common diagnosis for palliative cancer care in Australia, accounting for 23 per cent of all cancer-related palliative care provided. [10] Information regarding secondary liver cancer incidence in New Zealand could not be identified.

Speciality	**Oncology**
Technology setting	**Hospital or specialist hospital**

Impact

Substitution technology

The SIS is a substitute for standard end-hole catheters used in the delivery of embolic agents during liver cancer treatments such as SIRT, TACE or DEB-TACE. When coil embolisation of the hepatic vasculature is indicated, the use of a SIS may negate the need for coils.

Current technology

Treatments for liver cancer include potentially curative interventions such as surgical resection, liver transplantation and tumour ablation.[12-14] However, intermediate or advanced stage liver cancer patients or those ineligible for surgical or ablative therapies often receive treatment intended to achieve localised control, palliate symptoms, extend life and, in some cases, downstage the tumour as a "bridge" to surgery or transplant. These treatments may include TACE, [12] DEB-TACE[15] and SIRT[16]. TACE is the delivery of chemotherapeutic agents to the liver through a trans-arterial route and DEB-TACE combines the chemotherapeutic agents used in TACE with tiny beads that enable embolisation of the vessels as well as administration of local chemotherapy (chemoembolisation). SIRT uses radioactive microspheres or beads to kill the cancer cells.[17]

The rationale for using intra-arterial, liver-directed therapies follows from the liver's dual blood supply. The liver receives blood flow from the portal vein (providing the majority of blood) and the hepatic artery; however, liver cancers are primarily perfused by the hepatic artery.[4] By infusing chemotherapy or radiotherapy agents into the hepatic artery these agents are preferentially delivered to tumour tissue. Delivery of these agents is usually accompanied by blocking the feeding vessel associated with the tumour to induce ischaemic tissue death. Currently these agents are delivered using a standard end-hole microcatheter in conjunction with metal coils or other agents to block the blood vessel. [4, 18]

Patients undergo a diagnostic hepatic angiogram and imaging to ensure that their anatomy is suited to the procedure and to define the need for embolisation of gastric or gastro-duodenal vessels, thereby avoiding release of the chemotherapy or radiotherapy agents into the gut.[4, 12] The SIS is a novel catheter for the delivery of embolic agents to the liver which can avoid the use of vessel embolisation with metal coils. Coil embolisation takes time to perform and coils can migrate, or if left in permanently, can result in tumours recruiting new hepatic arteries; therefore, requiring occlusion at subsequent procedures.[19]

TACE reportedly confers a survival benefit when compared with best supportive care[20] and a randomised controlled trial of DEB-TACE and SIRT suggests they are equivalent in terms of overall survival and progression-free survival rates. [16]

Diffusion of technology in Australia

The extent of diffusion of the SIS in Australia is linked to the level of diffusion of the SIRT, DEB-TACE and TACE procedures in Australia. TACE appears to be an established treatment option for primary liver cancer in Australia[9, 12], but the diffusion of DEB-TACE and SIRT within Australia is unknown. Some items on the MBS were identified that are relevant to these procedures (see cost infrastructure and economic consequences). It is also unclear whether current practice more commonly employs standard catheters or the SIS. However, given that the exclusive distributor of Surefire Medical, Inc. products in Australia[21] is Sirtex Medical Limited, it is likely that the SIS has been used in SIRT procedures within Australia. Sirtex Medical Limited is an Australian company that commercialised a targeted radioactive treatment for use in SIRT procedures called SIR-Spheres® Y-90 resin microspheres that is used globally. [9, 22]

International utilisation

The clinical literature is derived mostly from the United States of America; however, clinical trials in Europe were also identified. What is not clear is to what extent the device has penetrated into routine use; some of the included literature report that the system has been available at their institution for a number of years.

Country	Level of Use		
	Trials underway or completed	Limited use	Widely diffused
Australia		✓	
Canada		✓	
Europe		✓	
United States of America		✓	

Cost infrastructure and economic consequences

The DRGs that the SIS could be being used under are H61A, H61B, and H61C and the cost to the healthcare system associated with the SIS is the cost of the system.

The SIS catheter is a substitute for standard end-hole catheters in liver-directed therapies, including SIRT, TACE and DEB-TACE that can remove the need for coil embolisation of liver blood vessels. Since other aspects of the treatment do not change, the cost implications associated with the procedure relate to differences in consumable costs of catheters, guidewires and coils (which are not required when using the SIS). The SIS systems would be used by interventional radiologists in hospitals with an angiography suite. No specific training requirements for the SIS systems have been identified.

Morshedi et al[19] reported the cost of the SIS (including the guiding catheter) to be $4,002[a]. This figure is based on a report from the United States of America and uses historical price data. No current Australian cost data could be identified.

The SIS is a single use device so the cost will differ depending on the number of treatments required. For example, a TACE procedure may be repeated several times until a response is observed; however, in the case of SIRT the safety of repeated radioembolisation is less established.[12, 23]

Reimbursement for TACE, DEB-TACE and SIRT

A search of the MBS did not reveal a specific item number associated with TACE; however, item 35321 for peripheral arterial or venous catheterisation could potentially represent part of the TACE procedure.[24]

Searches of the MBS identified several items for the delivery of SIRT which do not appear to preclude the use of the SIS systems. These items are for the treatment of hepatic metastases secondary to colorectal cancer. Primary liver cancer is not a listed indication. The item numbers, description and fees are listed below.

- 35404: Dosimetry, handling and injection of SIR-spheres for selective internal radiation therapy of hepatic metastases which are secondary to colorectal cancer and are not suitable for resection or ablation, used in combination with systemic chemotherapy using 5-fluorouracil (5FU) and leucovorin (Fee: $346.60)[24]
- 35406: Trans-femoral catheterisation of the hepatic artery to administer SIR-Spheres to embolise the microvasculature of hepatic metastases which are secondary to colorectal cancer and are not suitable for resection or ablation, for selective internal radiation therapy used in combination with systemic chemotherapy using 5-fluorouracil (5FU) and leucovorin (Fee: $813.30)[24]

a AUD = 0.731 USD, currency conversion performed on 12 May 2016, source XE Currency Converter

SIR-Spheres are also listed on the prostheses list with a minimum benefit of $8,230 (billing code SE001).[25] The delivery apparatus is also listed in the prosthesis list description. It is not clear whether the delivery apparatus would be different when using the SIS systems.

The Medical Services Advisory Committee has received an application "1242 - yttrium-90 microsphere radioembolisation to embolise the microvasculature of hepatic primary and secondary cancers". The status of the application is unclear; however, the final PICO confirmation was completed in September 2012.[26]

Ethical, cultural, access or religious considerations

No ethical, cultural, access or religious considerations were identified that may limit the use of this technology.

Evidence and Policy

Safety and effectiveness

One randomised controlled trial (level II interventional evidence) and one retrospective, non-randomised comparative trial (level III-3 interventional evidence) were identified for inclusion in this Technology Brief. Two case series (level IV interventional evidence, one with a randomised serial infusion protocol) were also identified. Both studies were subsequently omitted following clinician feedback on the limited relevancy of the reported endpoints (blood pressure changes[27], distribution of 99m-MAA[28]) and the lack of long-term data (personal communication, Discipline of Surgery, University of Adelaide).

Table 1 Included study characteristics

Study/design	Inclusion criteria	Exclusion criteria	Follow-up & number of patients	Conflicts of interest
Fischman et al 2014[29] Level II evidence (prospective) Single centre United States of America	Patients with primary or secondary liver cancer selected for SIRT at a multidisciplinary tumour board	Target tissue not distal to the gastro-duodenal artery as determined by CT or MR imaging	Patients were treated between March and September 2013, length of follow-up NR N = 30 Losses to follow-up NR	The study was funded by a restricted research grant from Surefire Medical. The lead author is a paid consultant for Surefire Medical and other device manufacturers. Four of the six other authors also declared conflicts of interest.
Morshedi et al 2015[19] Level III-3 evidence (retrospective) Single centre United States of America	Patients with primary or secondary liver cancer who underwent first-time radioembolisation using SIR-spheres of a single lobar or sub-lobar liver volume through a single hepatic artery	Use of glass microspheres, prior coil embolisation or occlusion of the hepatic arterial system or its communicating arteries, prior Y-90 procedures to the lobe being evaluated, protection that included coil and SIS or no coil or SIS and unavailability of data on endpoints	Mean follow up: Coil group = 132.4 days; SIS group = 86 days N = 14 Losses to follow-up NR	Three of the four study authors reported conflicts of interest that include being a consultant or receiving an honorarium from Surefire Medical. One author also reported association with SIRTEX medical (manufacturer of SIR-spheres).

SIRT: selective internal radiation therapy; NR: not reported; CT: computed tomography; MR: magnetic resonance; SIS: Surefire infusion system.

The included studies reported using SIS; however, the exact model used in each study was unclear. Participants included patients with primary and secondary liver cancer, and the vast majority underwent SIRT with Y-90 microspheres. Several conference abstracts were available that reported on the use of the SIS, but many had potential patient overlap with the included studies, and therefore were not included.

Fischman et al 2014[29]

Fischman et al (2014) reported the results of a prospective, randomised controlled trial comparing coil embolisation with the SIS in a SIRT procedure. Thirty patients with primary liver cancer or metastatic liver disease who were selected for SIRT were randomly assigned to coil embolisation of non-target vessels, macroaggregated albumin (MAA) infusion and SIRT with a standard microcatheter system or MAA infusion and SIRT with the SIS and no coil embolisation. The mean age of patients in the embolisation group was 64.7 years (standard deviation [SD] 10) and 62.8 years (SD 10.7) in the SIS group. In the coil embolisation group, the target area was the right lobe in 11 patients, the left lobe in three and the whole liver in one patient. In the SIS group the right hepatic lobe was treated in 12 patients and the left lobe was treated in three. Neither patients nor outcome assessors were blinded to treatment assignment and no statistically significant differences in baseline characteristics were observed between groups. Positioning of the catheter was into the hepatic arterial branch supplying the tumour(s).

The primary endpoint was fluoroscopy time during the planning angiography, as measured from insertion of the microcatheter or SIS (after completing diagnostic angiography) until confirmation of safe position for infusion. Secondary endpoints during planning angiography included: deployment time; total procedure radiation dose; total contrast agent dose; contrast agent dose administered from the time of insertion to confirmation of safe position for infusion; procedure time and complications related to embolisation. Secondary endpoints during the SIRT procedure included: intended infusion dose; delivered infusion dose; procedure time; contrast agent dose; infusion fluoroscopy time; total infusion time and recanalization rate of coil-embolised arteries. The authors reported that at a power of 80 per cent, the sample size of 30 was sufficient to detect a significant difference in fluoroscopy time for planning angiography.

Safety

One patient in the coil embolisation group died from rapid disease progression before undergoing SIRT. The authors reported no major or minor complications in either group and stated that there were no instances of arterial constriction, tearing, blood clotting or coil migration in any patient.

Effectiveness

The planning angiography was completed in all patients; however, two patients (one in each group) did not undergo the subsequent SIRT procedure due to a hepatopulmonary shunt ratio in excess of 20 per cent. The SIRT procedure was performed a median of 21 days (between 9 and 57 days) after planning angiography for all patients. During the planning angiography the SIS group had, on average, shorter procedure times, shorter fluoroscopy times and shorter deployment times than the coil embolisation group. Additionally, the total contrast agent dose and radiation dose was smaller in the SIS group. A total of 51 coils were placed in the coil embolisation group. The gastro-duodenal artery was embolised in all patients and was the only embolisation site in nine patients. Table 2 reports the results for coil embolisation versus SIS in the planning angiogram. A statistically significant difference was observed for all endpoints.

Of the SIRT procedure secondary endpoints, only the total contrast agent dose differed between the groups: 49.2 mL (SD 8.5) in the SIS group and 61.6 mL (SD 18.3) in the coil embolisation group ($p<0.05$). No statistically significant differences were observed among the other outcomes.

Table 2 Endpoints from the planning angiogram[29]

Endpoint	Coil embolisation (N = 15) mean (SD)	SIS (N = 15) mean (SD)	*p* value
Fluoroscopy time (minutes)	6.0 (4.3)	1.8 (1.2)	0.002
Procedure time (minutes)	30.5 (13.6)	16.2 (5.0)	<0.001
Deployment time (minutes)	16.2 (9.3)	3.8 (2.1)	<0.001
Total contrast agent dose (mL)	92.5 (22.5)	56.3 (13.8)	<0.001
Contrast agent dose(mL)*	23.0 (7.4)	9.6 (4.7)	<0.001
Dose–area product (Gy cm2)	336 (241)	189 (98)	0.04

*Dose of contrast agent used only during deployment time; SD: standard deviation; SIS: Surefire infusion system; Gy: gray; cm: centre metres.

Morshedi et al 2015[19]

Morshedi et al (2015) report the results of a retrospective, non-randomised comparative study in which 14 patients were treated with SIRT using Y-90 resin microspheres using coil embolisation (7 patients) or the SIS (7 patients). The authors reported using the latest generation SIS anti-reflux catheter, but the exact model was not stated. Of 58 patients who had undergone SIRT at their institution in the five years prior to publication, those who had undergone a planning angiogram followed by single lobar or sublobar SIRT with only the SIS or coil embolisation were included. Included patients had a mean age of 64 years (SD 6) in the SIS group and 57 years (SD 3) in the coil group. Patients included those with primary or secondary liver cancer. SIRT in the SIS group was delivered to the right lobe in six patients and the left lobe in one; SIRT in the coil group was delivered to the right lobe in five patients

and to the left lobe in two. Treatment was delivered through a single hepatic artery. No statistically significant differences in baseline characteristics were detected between the groups.

Parameters investigated included, procedure time (defined as time from initial arterial puncture to closure), fluoroscopy time, contrast dose, and radiation dose (from pre-treatment angiography and SIRT delivery). This study also reported cost data on the consumable materials used for preventing radioembolisation of non-targeted healthy tissue, (these data are reported below under 'Economic evaluation').

Safety

None of the patients in either group displayed symptoms of gastrointestinal ulceration or other non-target delivery of Y-90 microspheres. Mean follow-up in the coil and SIS groups were 132.4 and 86 days, respectively. No other safety outcomes were reported, and it is not clear whether other events did not occur or were not reported.

Effectiveness

This study reported that for the pre-treatment angiogram the SIS catheter reduced procedure time, fluoroscopy time and contrast material dose when compared with coil embolisation (see Table 3). However, for the SIRT procedure parameters, no significant differences in procedure time, fluoroscopy time, radiation dose or contrast material dose were identified.

Table 3 Endpoints from the planning angiogram[19]

Endpoint	Coil embolisation (N = 15) mean (SEM)	SIS (N = 15) mean (SEM)	*p* value
Fluoroscopy time (minutes)	49.7 (6.6)	14.3 (4.6)	0.0016
Procedure time (minutes)	192.1 (11.4)	102.6 (13.2)	0.0004
Total contrast agent dose (mL)	265.0 (16.8)	174.3 (22.6)	0.0098
Radiation dose (mGy)	4442.4 (897.1)	1931.3 (544.2)	0.05

SIS: Surefire infusion system; SEM: standard error of the mean; mGY: milligray.

Economic evaluation

No formal economic evaluation of the SIS was identified. However, Morshedi et al (2015) retrospectively reviewed 14 patients who underwent SIRT for the treatment of primary or secondary liver cancer and reported on differences in consumable costs, including the pre-treatment angiogram and delivery procedure, between SIRT with the SIS system (7 patients) and with the standard catheter and detachable coils for embolisation (7 patients).

The authors calculated costs according to the overall unique consumable materials used for preventing non-target radioembolisation in both procedures. In the SIS catheter group these

materials were: non-SIS microcatheters, micro-guidewires, the SIS device and SIS guide catheter. In the standard catheter and coil group the materials included microcatheters, micro-guide wires and coils. The cost calculations do not include base material costs, procedure room costs or hospital costs that were common to both procedures. Local hospital resource costs were used that may not be applicable outside this institution.

Overall, the average cost per patient of consumables using the SIS catheter was 62per cent lower than for the coils ($ 5,897±116 versus 15,428±3,023).[b]

The difference was attributed to the cost of the coils (55 coils were used in six patients), and it was noted that the type of coils used was a significant contributor to costs.

Treatment was provided using the more expensive detachable coils, which may have been a driver of consumable costs in the standard treatment group. The authors also noted that cost savings associated with the SIS catheter will be attenuated if patients require repeat treatment because the subsequent SIRT procedure would require a new SIS device. In contrast, when repeating a standard catheter SIRT the coil embolisation component of the procedure does not need to be repeated.

Hence, the potential for cost saving with the SIS catheter is dependent on the number of radioembolisation procedures required in each patient and to the institutional preference for other consumables.

Ongoing research

Three clinical trials investigating the use of SIS in radioembolisation and chemoembolization of primary or secondary liver cancer were identified from a search of ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Registry. All three are randomised controlled trials in which the comparator is a standard end-hole catheter. Information regarding these studies is presented in Table 4.

b AUD = 0.787 USD, currency conversion performed on 12 May 2016, source XE Currency Converter. The price of the system was reported in a publication from 2014 and using rates from 3 July 2014 the price was $4,544 ± 123 versus $11,888 ± 2,330

Table 4 Details of clinical trials identified on the Surefire Infusions System

Trial ID; location	Study design	Estimated enrolment	Intervention(s)	Outcome measure(s)	Status	Estimated completion
NCT02446925 United States	Randomised controlled trial, open label (single centre)	20 patients	Yttrium-90 (Y-90) radioembolisation using: 1. Surefire Infusion System 2. Standard end-hole catheter	Primary: Y-90 distribution and concentration within and around the targeted tumour as determined by post-embolisation PET-CT scan Secondary: length of duration of arteriogram; fluoroscopy duration; number of vessels requiring coiling; tumour response; toxicities; time to progression of tumour; vessel injury; Child-Pugh score; non-target embolisation; time to death.	Enrolling by invitation only	May 2016
NCT02208804 Netherlands	Randomised controlled trial, single blind (outcome assessors) (single centre)	25 patients	Holmium-166 radio embolization using: 1. Surefire Infusion System 2. Standard end-hole catheter	Primary: post-treatment tumour to non-tumour activity concentration ratio on SPECT/CT scan Secondary: mean absorbed radiation dose; post treatment tumour response on CT scan (3 months); predictive value of holmium-166 scout dose; dose-response relationship between tumour and dose on SPECT/CT scan; infusion efficiency; overall survival; clinical and laboratory toxicity.	Currently recruiting	November 2016
NCT02748161 United states	Randomised controlled trial, open label (number of centres unknown)	140 patients	Transarterial chemoembolisation with doxorubicin-eluting beads using: 1. Surefire® Infusion System 2. Standard End-hole catheter	Primary: objective tumour response (at 3 months) Secondary: objective tumour response (1 month); dose of beads delivered; contrast dose; fluoroscopic time; repeat procedures per lesions; complications of embolisation; contrast retention; changes in alpha-fetoprotein blood levels	Enrolling by invitation only	August 2018

PET-CT: Positron emission tomography–computed tomography; SPECT/CT: Single-photon emission computed tomography/ computed tomography.

Other issues

Each of the studies reported herein identified conflicts of interest that included authors receiving honorariums from, or, were consultants to or shareholders in Surefire Medical, Inc, or that study funding was provided by Surefire Medical, Inc.

Some of the authors were also consultants for Sirtex Medical Limited, which manufactures Sirtex SIR-Spheres used in radioembolisation and sponsor SIS in Australia.

Chemoembolisation

The majority of clinical evidence has reported on the use of the Surefire catheter system in SIRT procedures; however, the system also has a role in other transarterial liver cancer therapies such as chemoembolisation (drug-eluting beads) and 99mTc MAA infusions. [1]

The manufacturer claims that the system may increase tumour uptake of therapeutic agents through pressure, but as yet the published clinical evidence has not investigated whether use of the SIS confers any advantage over standard end-hole catheters with respect to treatment response with DEB-TACE, TACE or SIRT. However, a conference abstract[30] from a single centre reported on the modified Response Evaluation Criteria in Solid Tumours results in a cohort of 11 patients treated with DEB-TACE using the SIS for delivery who had previously been treated using a standard end-hole catheter. The authors report that follow-up imaging after initial treatment was available for six patients with 15 lesions: 12 of the 15 (80%) lesions had complete response, two (13%) demonstrated partial response (PR) and one lesion had stable disease. Some patients were down-staged to being eligible for a liver transplant; however, due to limited available information it wasn't clear how many patients were available for follow-up, were down-staged or had repeat treatments. [30]

Pasciak et al 2015[28]

This study indicated that, relative to a standard end-hole catheter, the SIS results in increased uptake of an injected material to distal tumour and a decrease in deposition in non-target liver tissue. This study was deemed to have been of limited or no clinical relevance (personal communication, Dr Markus Trochsler) and hence is not included in safety and effectiveness. Pasciak et al (2015) reported the results of a prospective trial in which nine patients with primary or secondary liver cancer underwent a serial infusion protocol to determine whether there were differences in the hepatic distribution of embolic particles depending on the use of a standard end-hole catheter as compared to the SIS. Patients were aged 48 to 86 years and sex was not reported. Each patient was treated with Y-90 microspheres using the SIS; however, as shown in Figure 2 below, each patient also underwent two same-day sequential infusions of technetium 99m-MAA via a standard end-hole catheter and an SIS (anti-reflux catheter). Single-photon emission computed tomography (SPECT) imaging was used to evaluate the differences in technetium 99m-MAA distribution in the target and non-target sites.

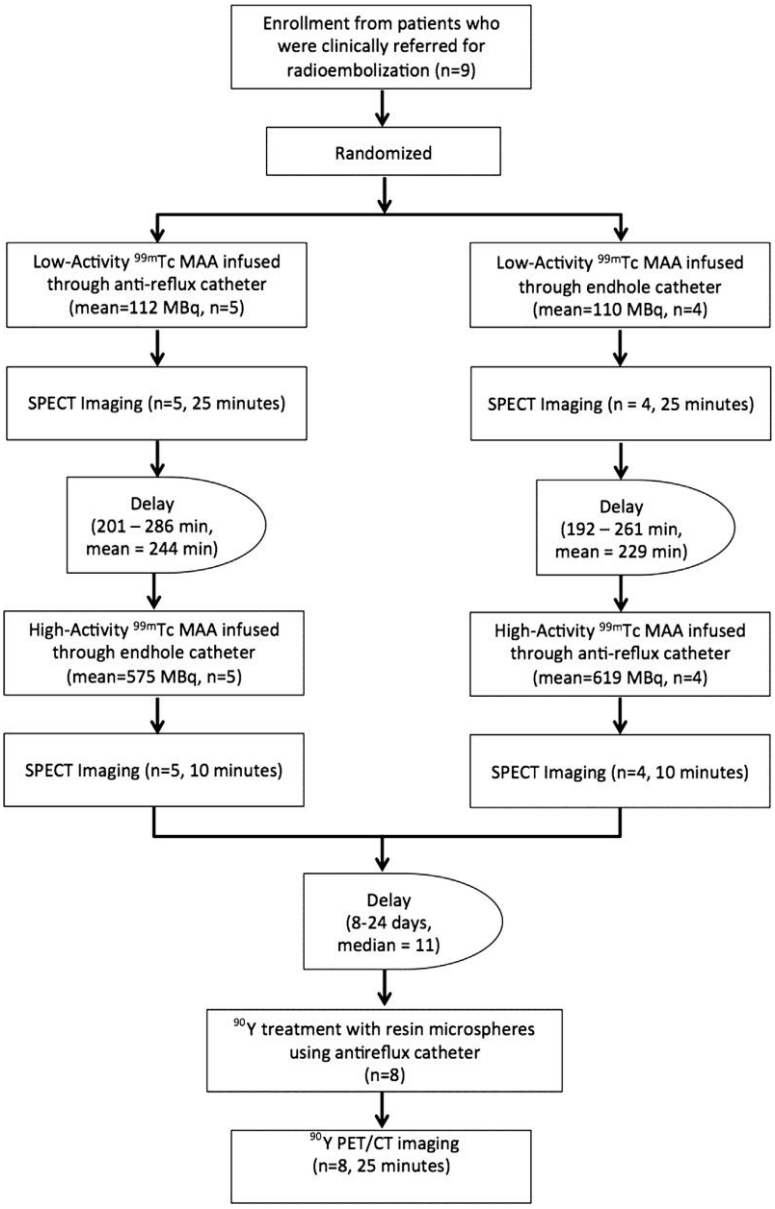

Figure 2 Dual infusion protocol

The qualitative analysis of the SPECT scans showed more uniform and extensive tumour coverage with increased relative activity deposition when SIS was used. They also reported that semi-quantitative analysis indicated the increases in uptake in distal tumour in all patients. With respect to standard end-hole catheters the SIS was associated with a 33 to 90 per cent increase in 'region of interest' MAA deposition ($p<0.05$). The authors also report decreased MAA deposition in non-target liver tissue; they report this decrease to be statistically significant ($p<0.05$).

There were a total of 17 embolisation procedures performed in nine patients (with MAA or Y-90 microspheres) and one instance of catheter occlusion was recorded during Y-90 microsphere infusion. The authors report that a second treatment was given on the same day to match the undelivered portion of the original planned dose. One of the nine patients

never received the SIRT treatment because of escalating liver-function tests post MAA and pre-treatment.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies:	2
Total number of Level II studies:	1
Total number of Level III-3 studies:	1

Search criteria to be used (MeSH terms)

Surefire

Date searched

22/3/2016

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