



Australian Government
Department of Health and Ageing



Horizon Scanning Technology
Prioritising Summary
Radiofrequency assisted liver resection

May 2007
(Updated May 2008)



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



**Royal Australasian
College of Surgeons**

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PRIORITISING SUMMARY

REGISTER ID: S000032

NAME OF TECHNOLOGY: RADIOFREQUENCY-ASSISTED LIVER RESECTION

PURPOSE AND TARGET GROUP: PATIENTS WITH LIVER TUMOURS REQUIRING HEPATECTOMY

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | | |
|---|-------------|-----|
| <input type="checkbox"/> Yes | ARTG number | N/A |
| <input checked="" type="checkbox"/> No | | |
| <input type="checkbox"/> Not applicable | | |

INTERNATIONAL UTILISATION:

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

IMPACT SUMMARY:

Radiofrequency-assisted liver resection is designed for blood loss reduction, reduced operating time and decrease in the occurrence of biliary leaks. The Habib 4X liver resection sealer is currently the only device which has received approval from the FDA and is also licensed for use in Europe. The device is currently not available in Australia.

BACKGROUND

Hepatectomy is the term given to surgical resection of the liver. Hepatectomies are generally performed for the treatment of benign or malignant liver tumours. The most common benign tumours include hemangioma and focal nodular hyperplasia (Arnoletti and Brodsky 1999). The most common malignant tumours of the liver include metastases which may arise from any primary malignant neoplasm, however those arising from the colon, lung, stomach, pancreas and breast are the most common (Kahn and Macdonald 2007). In terms of primary tumours of the liver, hepatocellular carcinoma (HCC) is the most common, accounting for over 80% of all primary liver cancers (Kassahun et al. 2006).

Although other treatment options including chemotherapy, radiotherapy, percutaneous ethanol injection, cryoablation, microwave coagulation therapy, laser-induced thermotherapy and radiofrequency ablation exist, surgical resection remains the gold standard for the treatment of both primary and secondary liver tumours (Ayav et al. 2007, Kahn and Macdonald 2007). Unfortunately, very few patients are suitable for surgical resection due to a variety of reasons related to the stage of the disease and the patient's liver function (McGahan and Dodd 2001). In the instances where surgery is possible, intra-operative blood loss presents a major hazard (Dixon et al. 2005). Intra-operative blood loss is associated with higher rate of post-operative complications and shorter long-term survival (Weber et al. 2002, Kooby et al. 2003). Liver failure is also a concern for patients undergoing liver resection with approximately 1% to 2% of patients dying as a result of liver failure after surgery (Personal Communication 2007, Professor Guy Maddern, Director, Division of Surgery, The Queen Elizabeth Hospital).

Methods including vascular clamping and Pringle's manoeuvre during liver resection surgery permit the surgeon to clamp the inflow vessels during surgery and reduce bleeding during resection (Ayav et al. 2007). The use of these techniques has led to a significant reduction in intra-operative blood loss and the requirement for intra-operative blood transfusion (Jarnagin et al. 2002). Unfortunately, these methods are not completely effective and some even carry a further risk of causing liver dysfunction in patients suffering liver disease (Farges et al. 1999).

Radiofrequency-assisted liver resection involves the induction of necrosis in healthy liver tissue at the resection plane with the aim of creating a safe and bloodless way of dissecting the parenchyma during minor and major resections by sealing vascular and biliary structures (Ayav et al. 2007). The use of heat to create coagulative necrosis is not new. Radiofrequency ablation of liver tumours has been performed previously (Curley et al. 1999). Radiofrequency-assisted liver resection is novel because coagulation of normal liver tissue, which coagulates much quicker than cancerous tissue, is performed in order to obtain bloodless surgical resection, thus reducing the associated risks with intra-operative blood loss (Weber et al. 2002).

In the present summary, studies reporting the results of radiofrequency-assisted liver resection using different radiofrequency devices are presented. However, all devices appear to have great similarities to the Habib 4X sealer (RITA Medical Systems; California, United States). The Habib 4X sealer is currently the only device designed for open-surgery radiofrequency-assisted liver resections. The device consists of an array of four cooled-tip radiofrequency probes connected to a generator. These probes contain an exposed electrode and a thermocouple on the tip (to monitor temperature and impedance of the tissue) to produce controlled necrosis of healthy parenchyma. A laparoscopic version of the Habib 4X sealer is also available and use of this device has been noted.

CLINICAL NEED AND BURDEN OF DISEASE

In 2001, the Australian incidence of liver cancer was 617 cases per 100,000 males and 236 cases per 100,000 females (AIHW 2004). The mortality rates for sufferers of liver cancer during 2001 were 538 deaths per 100,000 males and 239 deaths per 100,000 females (AIHW 2004). Projections for the number of new cases of liver, gallbladder and pancreas cancer show that the new cases of this group of cancers is projected to increase by 27% from 1,469 in 2001 to 1,863 in 2011 (95% prediction interval from 1,426 to 2,489) for females. For males, an increase of 43% from 1,836 in 2001 to 2,624 in 2011 (95% prediction interval from 2,223 to 3,160) is projected (AIHW 2005).

Additionally, liver metastases have been identified in approximately 30% to 70% of cancer sufferers making the liver the second most common site of metastasis (Virtual Medical Centre 2006). In Western countries such as Australia liver metastases are more common than primary liver cancer (Virtual Medical Centre 2006).

DIFFUSION

The Habib 4X sealer and the Habib 4X Laparoscopic sealer have both received marketing approval from the FDA. They are the only systems specifically designed and marketed for the performance of liver resection. The Habib 4X sealer is also licensed for use in Europe. The Habib 4X sealer is currently not available in Australia.

COMPARATORS

Intra-operative manoeuvres to reduce risk of intra-operative bleeding during liver resection surgery (Jarnagin et al. 2002):

- Hypotensive anaesthetics
- The Pringle manoeuvre
- Total vascular exclusion

Comparators to radiofrequency-assisted liver resection (Kahn and Macdonald 2007):

- Radiofrequency ablation of liver tumours
- Standard surgical resection
- Hepatic arterial infusion chemotherapy
- Percutaneous ethanol injection
- Cryoablation
- Microwave coagulation therapy
- Laser-induced thermotherapy

SAFETY AND EFFECTIVENESS ISSUES

Ayav and colleagues reported their experience of radiofrequency-assisted liver resection in 156 consecutive patients over four years (Ayav et al. 2007). The patients involved had a mean of 1.77 (range: 1 to 10) tumours each with a mean size of 44 ± 30 mm. A total of thirty major hepatectomies¹ and 126 minor hepatectomies² were performed with 275 tumours resected. In this series, a cooled-tip radiofrequency probe and a 500 kHz radiofrequency generator (model RFG-3D, Radionics Europe, NV, Wettdren, Belgium) were used. The procedures were performed in a mean (\pm standard deviation) operative time of 241 ± 89 minutes including a mean resection time³ of 75 ± 51 minutes.

¹ Major hepatectomy: defined as resection of more than three segments.

² Minor hepatectomy: defined as tumorectomy, segmentectomy or bi-segmentectomy.

³ Resection time: time from start of radiofrequency ablation to completion of parenchymal transection.

The mean intra-operative blood loss for all patients was 139 ± 222 mL with major hepatectomy patients experiencing significantly greater blood loss than minor hepatectomy patients (271 ± 256 mL versus 109 ± 203 mL, $p = 0.005$). Intra-operative blood transfusion was required in nine patients (16% transfusion rate; six major hepatectomy and three minor hepatectomy patients) with the transfusion requirement being greater for patients who had undergone major hepatectomy ($p = 0.001$). This compares favourably to previously reported median volumes of 450 mL to 1450 mL and transfusion rates of 55% reported in the scientific literature (Cunningham et al. 1994, Melendez et al. 1998, Poon et al. 2004).

Changes in haemoglobin (Hb), bilirubin, albumin, aspartate transaminase (AST) and alanine transaminase (ALT) were measured pre-operatively and post-operatively on days one and seven to demonstrate the effect of radiofrequency-assisted liver resection on liver function. All variables except haemoglobin were significantly ($p < 0.001$) altered on post-operative day one but returned to near pre-operative levels by day seven (Table 1).

Table 1 Mean values of indicators of liver function

Indicator	Pre-operative	Day 1	Day 7
Hb (g/dL)	12.9 ± 1.7	11.9 ± 1.6	12.1 ± 1.4
Bilirubin (mmol/L)	11.1 ± 9.6	25.7 ± 15.6 *	19.7 ± 14.7
Albumin (g/L)	36.4 ± 4.4	28.8 ± 7.9 *	35.8 ± 8.9
AST (IU/L)	32 ± 17	569 ± 509 *	51 ± 29
ALT (IU/L)	30 ± 20	518 ± 436 *	102 ± 85

* $p < 0.001$

Ayav et al. (2007)

Post-operative complications were reported in 36 (23%) patients, with six developing more than one complication. Complications included pleural effusion ($n = 18$), intra-abdominal collection ($n = 17$), biliary leak ($n = 4$), post-operative liver failure ($n = 2$) and hepatic ischemia ($n = 1$). One re-operation was required to reconstruct a right hepatic artery injured during extended left hepatectomy and hepaticojejunostomy for cholangiocarcinoma in the case of hepatic ischemia. In two of the four cases of biliary leak, leakage was reported from the resection margin perhaps indicating incomplete coagulation in that specific region of the resection plane. Despite this the authors state that none of the complications reported were directly reported to the resection technique used.

There were no deaths intra-operatively, however, five patients died post-operatively (period at which the patients died was not reported). Two died from post-operative liver failure while the remaining patients died of multi-organ failure (none began with liver failure). A further five patients were admitted into the intensive care unit post-operatively (two for prolonged general anaesthesia and three for pre-operative respiratory and cardiac problems).

Fifty one patients (33%) experienced recurrence of the disease (26 hepatic, 15 extrahepatic and 10 both). In 34 of the 36 cases of hepatic recurrence, the recurrence was distant (more than 1 cm away) from the resection margin. In the remaining two patients initial histology demonstrated a negative resection margin suggesting that these two new tumours were new. When compared with nine other liver resection series presented by the authors, the present study had comparable rates of morbidity (23% versus range: 16 to 45%) and mortality (3.2% versus range: 0 to 5%) but much lower mean blood loss (139 mL versus range: 250 to 1700 mL) and transfusion rate (5% versus range: 6.9 to 62.3%) (Ayav et al. 2007).

Navarra et al. (2004) reported the results of radiofrequency-assisted liver resection in 42 patients, possibly reporting on a subset of patients also reported by Ayav et al. 2007. Thirteen major and 29 minor resections were performed. The number and size of tumours as well as the operating time of the patients was not reported. Despite this, a median resection time of 50 minutes (range: 30 to 110 minutes) was reported. The median intra-operative blood loss was

reported at 30 mL (range: 15 to 992 mL) with no requirement for intra-operative blood transfusion in any patient. As with the study by Ayav et al. (2007) the results compared favourably to the blood loss and transfusion rates reported in the literature.

Changes in haemoglobin, bilirubin, aspartate transaminase and alanine transaminase were measured pre-operatively and post-operatively on days one and seven to demonstrate the effect of radiofrequency-assisted liver resection on liver function. Bilirubin, aspartate transaminase and alanine transaminase levels were increased following the procedure but decreased to near-normal levels by the seventh post-operative day (Table 2). No statistical tests were performed.

Table 2 Mean (\pm SD) values of indicators of liver function

Indicator	Pre-operative	Day 1	Day 7
Hb (g/dL)	13.7 \pm 1.6	11.8 \pm 1.4	n/a
Bilirubin (mmol/L)	11.1 \pm 5.0	23.6 \pm 12.6	17.6 \pm 12.7
AST (IU/L)	30.4 \pm 13.7	730.7 \pm 653.5	57.5 \pm 23.5
ALT (IU/L)	40.1 \pm 61.6	702.3 \pm 516.1	128.8 \pm 67.4

Navarra et al. (2004)

No operative or post-operative deaths were reported. Most patients tolerated the surgery well with all but one being sent to the surgical ward soon after surgery. The remaining patient was sent to the ICU due to concomitant heart failure. Five days post-operatively another patient was transferred to the ICU due to a biliary leak from hepatico-jejunostomy. One week post-operatively blood transfusion was required in one patient due to another biliary leak from hepatico-jejunostomy. Two additional post-operative complications were also reported: subphrenic abscess (one patient) and chest infection (one patient). Only the occurrence of subphrenic abscess was related to the technique.

Hompes and colleagues reported the first series of patients who had undergone laparoscopic radiofrequency-assisted liver resection (Hompes et al. 2007). Forty-five patients were enrolled in the study with 25 undergoing laparoscopic liver resection without radiofrequency assistance and 20 undergoing laparoscopic liver resection with radiofrequency assistance. Allocation to radiofrequency was performed by the surgeon and was not random. Patients had a median number of one (range: 1 to 3) tumours with a median maximum diameter of 40 mm (range: 8 to 170 mm). Thirty-eight minor and nine major resections were performed. The study used a monopolar radiofrequency generator (frequency not reported) and a single cool-tip electrode manufactured by Tyco Healthcare and Radionics Europe respectively.

The median operative time for all patients was 115 minutes (range: 45 to 360 minutes) with the resection time not reported. A comparison between both groups demonstrated similar operation times for the non-radiofrequency assisted and the radiofrequency assisted groups (105 and 120 minutes, respectively). Median intra-operative blood loss was the same for both groups at 200 mL. Additionally, there were no significant differences between groups in terms of complications, mortality (none reported) and length of hospital stay. This small short term study suggests that when performing laparoscopic liver resection, radiofrequency assistance offers little (if any) advantage. This is in contrast to observations from open-surgery studies in which radiofrequency assistance is associated with a reduction in bleeding and better patient outcomes. The study also identifies that the surgical procedure is the main determinant in amount of intra-operative blood loss (Hompes et al. 2007).

COST IMPACT

A search of the published literature and website of the manufacturer of the Habib 4X Sealer (Rita Medical Systems; California, United States) did not reveal the cost of performing radiofrequency-assisted liver resection.

The Medicare Benefits Schedule reimbursement fees for procedures related the resection of liver tumours is listed in Table 3:

Table 3: Medical Benefits Schedule of fees for procedures related to resection of liver tumours (Department of Health and Ageing 2007)

Category	Item Number	Benefit (AUD)	Number of Claims (July 2005 to June 2006)
Subsegmental resection of liver	30414	\$609.55	204
Segmental resection of liver	30415	\$1219.05	192
Lobectomy of liver	30418	\$1058.70	221
Tri-segmental resection (extended lobectomy) of liver	30421	\$1764.30	59

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

No issues were identified from the retrieved material.

RECOMMENDATION:

The evidence currently available on radiofrequency-assisted liver resection is limited. There are currently no randomised comparative studies available, however the evidence presented in this summary suggests that under open surgery settings radiofrequency assisted liver resection may be associated with intra-operative blood loss and transfusion rate improvements. Given the potential high impact of this technology and lack of comparative studies it is recommended that this technology be monitored.

SOURCES OF FURTHER INFORMATION:

Ferko A, Lesko M, Subrt Z, Melichar B, Hoffman P, Dvorak P, Vacek Z, Liao L, Habib N, Koci J, Motycka P. A modified radiofrequency-assisted approach to right hemihepatectomy. *European Journal of Surgical Oncology* 2006; 32(10): 1209-1211.

Haghighi K, Wang F, King J, Daniel S, Morris D. In-line radiofrequency ablation to minimize blood loss in hepatic parenchymal transection. *The American Journal of Surgery* 2005; 190(1): 43-47.

Stavrou G, Tzias Z, von Falck C, Habib N, Oldhafer K. Hepatic resection using heat coagulative necrosis. First report of successful trisegmentectomy after hypertrophy induction. *Langenbeck's Archives of Surgery* 2007; 392(1): 95-97.

Zacharoulis D, Tzovaras D, Rountas C, Poultisidis A, Katsogridakis E, Sioka E, Hatzitheofilou C. Modified radiofrequency-assisted liver resection: A new device. *Journal of Surgical Oncology* 2007 [Epub ahead of print].

LIST OF STUDIES INCLUDED

Total number of studies 3
Level IV intervention evidence

SEARCH CRITERIA TO BE USED:

Radiofrequency
Radio-frequency
Liver resection
Resection
Radiofrequency assisted liver resection
RFALR
Hepatectomy
Liver
Liver cancer

REFERENCES:

AIHW, AACR & NCSG: Ian McDermid 2005. Cancer incidence projections, Australia 2002 to 2011. Canberra: Australian Institute of Health and Welfare (AIHW), Australasian Association of Cancer Registries (AACR) and the National Cancer Strategies Group (NCSG).

Australian Institute of Health and Welfare (AIHW) & Australasian Association of Cancer Registries (AACR) 2004. Cancer in Australia 2001. AIHW cat. No. CAN 23. Canberra: AIHW (Cancer Series no. 28).

Arnoletti J and Brodsky J. Surgical treatment of benign hepatic mass lesions. *American Surgeon* 1999; 65(5): 431-433.

Ayav A, Bachellier P, Habib N, Pellicci R, Tierris J, Milicevic M, Jiao L. Impact of radiofrequency assisted hepatectomy for reduction of transfusion requirement. *The American Journal of Surgery* 2007; 193(2): 143-148.

Cunningham J, Fong Y, Shriver C, Melendez J, Marx W, Blumgart L. One hundred consecutive hepatic resections. Blood loss, transfusion, and operative technique. *Archives of Surgery* 1994; 129(10): 1050-1056.

Curley S, Izzo F, Delrio P, Ellis L, Granchi J, Vallone P, Fiore F, Pignata S, Daniele B, Cremona F. Radiofrequency ablation of unresectable primary and metastatic hepatic malignancies: Results in 123 patients. *Annals of Surgery* 1999; 230(1):1-8.

Department of Health and Ageing. Medicare Benefits Schedule. Last updated 2007. <http://www9.health.gov.au/mbs/> [Accessed March 2007].

Dixon E, Vollmer C, Bathe O, Sutherland F. Vascular occlusion to decrease blood loss during hepatic resection. *American Journal of Surgery* 2005; 190(1): 75-86.

Farges O, Malassagne B, Flejou J. Risk of major liver resection in patients with underlying chronic liver disease: a reappraisal. *Annals of Surgery* 1999; 229(2):210-215.

Fong T. Liver resection. Last updated 2002. http://www.medicinenet.com/liver_resection/article.htm [Accessed March 2007].

Hompes D, Aerts R, Penninckx F, Topal B. Laparoscopic liver resection using radiofrequency coagulation. *Surgical Endoscopy* 2007; 21(2):175-180.

Jarnagin W, Gonen M, Fong Y, DeMatteo R, Ben-Porat L, Little S, Corvera C, Weber S, Blumgart L. Improvement in perioperative outcome after hepatic resection. Analysis of 1,803 consecutive cases over the past decade. *Annals of Surgery* 2002; 236(4):397-407.

Kahn A and Macdonald S. Liver, Metastases. Last updated 2007.
<http://www.emedicine.com/radio/topic394.htm> [Accessed March 2007].

Kassahun W, Fangmann J, Harms J, Hauss J, Bartels M. Liver resection and transplantation in the management of hepatocellular carcinoma: A review. *Experimental and Clinical Transplantation* 2006; 4(2): 549-558.

Kooby D, Stockman J, Ben-Porat L, Gonen M, Jarnagin W, DeMatteo R, Tuorto S, Wuest D, Blumgart L, Fong Y. Influence of transfusion on perioperative and long term outcome in patients following hepatic resection for colorectal metastases. *Annals of Surgery* 2003; 237(6):860-869.

McGahan J and Dodd G. Radiofrequency ablation of the liver: Current Status. *American Journal of Roentgenology* 2001; 176(1):3-16.

Melendez J, Arslan V, Fischer M, Wuest D, Jarnagin W, Fong Y, Blumgart L. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. *Journal of the American College of Surgeons* 1998; 187(6): 620-625.

Navarra G, Lorenzini C, Curro G, Basaglia E, Habib N. Early results after radiofrequency-assisted liver resection. *Tumori* 2004; 90(1): 32-35.

Poon R, Fan S, Lo C, Liu C, Lam C, Yuen W, Yeung C, Wong J. Improving perioperative outcome expands the role of hepatectomy in management of benign and malignant hepatobiliary diseases: analysis of 1222 consecutive patients from a prospective database. *Annals of Surgery* 2004; 240(4): 698-708.

Virtual Medical Centre. Metastases to the liver. Last updated 2006.
<http://www.virtualcancercentre.com/diseases.asp?did=705> [Accessed April 2007].

Weber J, Navarra G, Jiao L, Nicholls J, Jensen S, Habib N. New technique for liver resection using heat coagulative necrosis. *Annals of Surgery* 2002; 236(5): 560-563.

PRIORITISING SUMMARY UPDATE (2008)

REGISTER ID:	S000032
NAME OF TECHNOLOGY:	RADIOFREQUENCY-ASSISTED LIVER RESECTION
PURPOSE AND TARGET GROUP:	PATIENTS WITH LIVER TUMOURS REQUIRING HEPATECTOMY

A search of all relevant databases was conducted in April 2008 following the recommendation in May 2007 that radiofrequency assisted liver resection be monitored for twelve months. A total of five articles were retrieved for inclusion in this update (Ayav et al. 2007a; Bachellier et al. 2007; Lupo et al. 2007; Mitsuo et al. 2007; Zacharoulis et al. 2007). Another six articles were excluded as they were of low level evidence or written in another language (Ayav et al. 2007b; Vaos 2007; Vávra 2007; Varshney et al. 2007; Milićević et al. 2007; Ferko et al. 2007).

2008 SAFETY AND EFFECTIVENESS ISSUES

In a randomised control trial by Lupo et al. (2007) 50 patients (36 men, 14 women, median age 62) who were to undergo curative liver resection for primary or secondary liver cancer were randomly assigned to receive either radiofrequency-assisted liver resection (n=24) or clamp-crushing method (n=26). There was no statistically significant difference between the radiofrequency-assisted and clamp-crushing groups for operation time (292 versus 278 minutes, $p = 0.340$), blood transfusion requirements (8/24 versus 13/26 patients required transfusions, $p = 0.232$), or length of hospital stay (median of 12 days in both groups). Postoperative temporary liver failure occurred in four patients (two in each group), but all made a full recovery. Eight patients in the radiofrequency-assisted group developed a total of ten other complications, compared to no other complications in the clamp-crushing group ($p < 0.001$). Complications included abscess (n=6), biliary fistula (n=3) and biliary stenosis (n=1). During a follow-up of between 14-25 months, four patients in each group with metastasis from colorectal cancer experienced a cancer recurrence, while two other patients with cholangiocarcinoma had recurrences within one year. The study results indicated that radiofrequency-assisted liver resection leads to higher rates of complications than the clamp-crushing method (Lupo et al. 2007).

Mitsuo et al. (2007) performed a nonrandomized comparative study which investigated hepatectomy with and without radiofrequency ablation and its effect on blood loss. Twenty patients had radiofrequency-assisted hepatectomy and 28 patients had hepatectomy without ablation. There was no significant difference between the groups for baseline characteristics (age, gender, coexisting liver disease, or preoperative liver function), and no significant differences for mean size of the resected tumour, operation time, clamping time, or length of hospital stay. There was significantly less blood loss in the radiofrequency group compared to the comparative 'no radiofrequency' group (209±180 versus 429±389 ml, $p < 0.05$). Three patients in the comparative group required a blood transfusion, compared to no patients in the radiofrequency group; however this difference was not statistically significant. ALT levels at days one, three and seven post-operation, and bilirubin levels at day three post-operation (measures of hepatocellular damage), were significantly higher in the radiofrequency group compared to the comparator ($p < 0.05$). Postoperative complications included pleural effusion (n=7), infection of a drain (n=3), bile leakage (n=3) and subcutaneous abscess (n=6). There was no difference in the incidence of postoperative complications except for bile leakage, which was significantly more frequent in the radiofrequency group ($p < 0.05$). No patients

required a re-operation, suffered liver failure, or died during their hospital stay. The results of this study indicate that radiofrequency assisted hepatectomy may decrease intraoperative blood loss compared to conventional hepatectomy, but can result in more compromised liver function as indicated by the markers of hepatocellular damage (Mitsuo et al. 2007).

In a different non-randomized comparative study by Ayav et al. (2007a) the outcomes of radiofrequency-assisted liver resections were compared to those of a standard technique (total vascular exclusion (TVE)). Seventy-eight patients underwent major hepatectomy with the radiofrequency-assisted (n=27) or TVE technique (n=51). There was no significant difference between the baseline characteristics of the groups, in terms of age, gender, diagnosis, or number and size of tumours. Blood transfusion rates were lower in the radiofrequency-assisted group compared to the TVE group (26% versus 53%, p=0.04). In terms of liver function, AST and ALT levels (postoperatively and at days one and seven post-operation) were not significantly different between the two groups. However, the radiofrequency-assisted group had lower levels of bilirubin at day one (p=0.006) and seven (p=0.005), and higher levels of albumin at day seven (p=0.02). Only two radiofrequency-assisted patients required admission to intensive care, compared to 47 patients in the TVE group (p<0.0001). Postoperative hospital stay was also shorter in the radiofrequency group (10 versus 17 days, p=0.04). Six TVE patients (11%) and one radiofrequency-assisted patient (3%) died (p=0.44). Complication rates were similar between the two groups, with 14 complications in 11 radiofrequency-assisted patients (40%) and 32 complications in 24 TVE patients (47%) (p=0.76). These complications included pleural effusion, intra-abdominal collection, biliary fistula, and liver failure. There was a reduction in the incidence of liver failure in the radiofrequency-assisted group compared to the TVE group which bordered on significance (0 versus 9 patients, p=0.05), while for the other complications there was no significant difference between groups. The study results indicate that using radiofrequency can decrease the rates of blood transfusion, postoperative liver failure, intensive care unit admission and hospital stay compared to TVE (Ayav et al. 2007a).

In a case series by Bachellier et al. (2007), radiofrequency-assist laparoscopic liver resection was assessed in eighteen patients. All operations were performed without vascular clamping and consisted of tumorectomy (n = 9), multiple tumorectomies (n = 2), segmentectomy (n = 2), and bisegmentectomies (n = 2). Mean blood loss was 121±68 mL, mean operative time was 213±59 minutes, mean resection time was 167±45 minutes, and mean length of hospital stay was 6±1.5 days. Levels of ALT, AST, and bilirubin were elevated at days one and three post surgery (p<0.05), but returned to baseline levels by day seven. Albumin levels dropped compared to baseline at days one and three post-operation (p<0.05), before also returning to baseline. No perioperative or postoperative blood transfusions were required. There were no deaths reported after surgery, although two patients had complications (pneumothorax during surgery (n=1) and transient liver failure (n=1)). At follow-up (mean 9.8±6.2 months) none of the patients with malignancy had recurrence at the resection margins, although one patient was found to have a new deposit elsewhere at five months after surgery (Bachellier et al. 2007).

Another case series, by Zacharoulis et al. (2007), undertook a modified radiofrequency assisted liver resection in ten patients using a new bipolar radiofrequency device. This bipolar device was designed specifically for liver resection to achieve a near bloodless resection. The operative technique is described in some detail, and includes the use of opposing pairs of electrodes and the release of a minimum amount of energy, in order to create a small area of desiccation around the tumor. Procedures performed on the ten patients using this device included segmentectomy (n=6), closed pericystectomy for hydatid disease (n=1) and a formal right hepatectomy (n=2). None of the patients required blood transfusions or intensive care admissions, and none had a bile leak. Hospital stay was between three and seven days. This device presents a potential advantage over other radiofrequency devices which were designed

for destruction of a solid tumour, and which release an uncontrolled amount of energy that can lead to excess dead tissue. The new device, with its controlled energy flow, allows resection with minimal blood loss and reduces tissue damage (Zacharoulis et al. 2007).

2008 HEALTHPACT ACTION

A randomised controlled trial is now available on the use of radiofrequency for resection of liver tumours, as well as several additional non randomised comparative studies. The randomised controlled trial found that radiofrequency does not provide any benefit over a standard clamp-crushing technique in terms of operation time, blood transfusion requirements or length of hospital stay, but that it may produce higher complication rates. The two included non-randomised comparative studies produced conflicting results. One study indicated that radiofrequency may decrease intraoperative blood loss compared to a conventional technique but produce more hepatocellular damage, and the other found that radiofrequency can decrease the rates of blood transfusion, postoperative liver failure, intensive care unit admission and hospital stay compared to a standard technique. The evidence available on radiofrequency-assisted liver resection remains limited, and the safety and effectiveness of this technology is still questionable. Based on these findings, radiofrequency assisted liver resection will be archived.

NUMBER OF INCLUDED STUDIES

Total number of studies	5
Level II Randomised control trial	1
Level III-2&3 Comparative studies	2
Level IV Case series	2

REFERENCES

- Ayav A, Navarra G, Basaglia E, Tierris J, Healey A, Spalding D, Canelo R, Habib N, Jiao L. Results of major hepatectomy without vascular clamping using radiofrequency-assisted technique compared with total vascular exclusion. *Hepatogastroenterology* 2007a; 54(75): 806-809.
- Bachelier P, Ayav A, Pai M, Weber J, Rosso E, Jaeck D, Habib N, Jiao L. Laparoscopic liver resection assisted with radiofrequency. *American Journal of Surgery* 2007; 193(4): 427-430.
- Lupo L, Gallerani A, Panzera P, Tandoi F, Di Palma G, Memeo V. Randomized clinical trial of radiofrequency-assisted versus clamp-crushing liver resection. *British Journal of Surgery* 2007; 94(3): 287-291.
- Mitsuo M, Takahiro T, Yasuko T, Masayasu A, Katsuya O, Nozomi S, Yoshihide O, Isamu K. Radiofrequency (RF)-assisted hepatectomy may induce severe postoperative liver damage. *World Journal of Surgery* 2007; 31(11): 2208-2212.
- Zacharoulis D, Tzovaras G, Rountas C, Poultisidis A, Katsogridakis E, Sioka E, Hatzitheofilou C. Modified radiofrequency-assisted liver resection: a new device. *Journal of Surgical Oncology* 2007; 96(3): 254-257.