

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of ex-vivo hepatic resection and reimplantation for liver cancer

Liver cancer may develop initially in the liver or may spread to the liver from other parts of the body. In some patients, the tumour may develop in parts of the liver that are dangerous or technically impossible to treat with surgery, for example, when the tumour is very close to the blood vessels that connect to the liver. This procedure involves removing the liver from the body, cutting away the tumour, and reimplanting the residual tumour-free liver into the patient.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in October 2008.

Procedure name

- Ex-vivo hepatic resection and reimplantation for liver cancer

Specialty societies

- Association of Upper Gastrointestinal Surgeons
- British Association for the Study of the Liver
- British Association of Surgical Oncology

Description

Indications and current treatment

This procedure can be carried out in patients with primary or secondary (metastatic) liver cancer. Primary liver cancer most commonly includes hepatocellular carcinoma and cholangiocarcinoma. Metastasis to the liver may occur from any primary cancer site but is particularly common in colorectal cancer.

Treatment strategies for liver cancer patients depend on tumour origin, location, number and size. Overall, primary liver cancer has a poor prognosis, and treatment intent is usually palliative. Some patients may benefit from liver transplantation, and some from liver resection surgery. If surgically operable, metastatic liver disease, particularly from primary colorectal cancer, has a better prognosis.

Some liver tumours can be removed by open or laparoscopic resection. Bleeding during surgery is a particular problem associated with this procedure and various methods can be used to control it, including the Pringle manoeuvre (continuous or intermittent), vascular clamping, inflow occlusion and total hepatic vascular exclusion. However, such occlusive vascular control measures can lead to iatrogenic damage to the liver. Resection may be particularly difficult when the tumour is located close to, or infiltrating into, the inferior vena cava.

A number of non-resective treatment modalities can also be used, sometimes in combination with surgery. These may include trans-arterial chemoembolisation and 'open' or percutaneous radiofrequency or microwave ablation.

What the procedure involves

The procedure is carried out with the patient under general anaesthesia. The liver is removed from the patient via upper abdominal incision, and perfused with a preservation solution. A bloodless transection of hepatic parenchyma can then be performed allowing complex reconstruction of hepatic veins or portal structures. The liver is then reimplanted into the patient. The procedure can be performed under total hepatic vascular exclusion, with or without venovenous bypass.

List of studies included in the overview

This overview is based on approximately 30 patients from one case series ¹, and three case reports ^{2, 3, 4}.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Efficacy

A case report of 24 patients (22 with cancer) treated by ex-vivo hepatic resection for liver cancer reported resection and auto-transplantation was possible in 92% (22/24) of patients (91% (20/22) of patients with cancer). Sixty-three per cent (15/24) of patients and (59% (10/13) of patients with cancer) survived the ex-vivo resection and were discharged at a mean follow-up of 36.5 days. Sixty-seven per cent (10/15) of these discharged patients died of tumour recurrence between the 12-month and 36-month follow-up; among those with cancer, 77% (10/13) died of tumour recurrence between the same follow-up period.¹

The mean survival time among the 10 patients with colorectal metastases was 21 months. Two patients with focal nodular hyperplasia were alive at 5 and 9 year follow up.

A second case report of 8 patients reported that 1 of 4 patients who underwent ex-vivo resection died 15 days after the operation because of respiratory and renal failure, and 1 patient died 30 months after the operation with right renal adenocarcinoma, infiltration of the inferior vena cava, and pulmonary and spinal metastases. The other 2 patients who underwent ex-vivo resection were alive at 5-month follow-up, 1 with recurrence of the tumour in the bone². In the same study a clear resection margin was recorded in 3 of 4 patients who underwent ex-vivo resection.

A case report of 16 patients included 2 who underwent ex-vivo resection. One of the 2 patients, who had hepatocellular carcinoma, was alive and disease free at 52-months follow-up. The other patient, who had a colorectal metastasis, died from sepsis associated with a perforated small bowel at 4-month follow-up, but was free of hepatic disease. All vascular reconstructions were found to be patent at last follow-up (4 to 52 months)³.

A case report of a patient with a large hepatocellular carcinoma with involvement of the circumference of the inferior vena cava, the hepatic vein, and the right portal pedicle reported that the patient was alive with no recurrence 1 year after ex-vivo hepatic resection⁴.

In the case report of 24 patients (22 with cancer) the mean operative time was 13.54 hours, and the mean anhepatic phase was 6.67 hours¹.

Safety

In a case report of 24 patients (22 with cancer) 29% of patients (7/24) and 32% (7/22) of patients with cancer required a liver transplantation either immediately (2 patients) or with a subsequent procedure (5 patients)¹.

In a case series of 8 patients, of 4 patients undergoing ex-vivo resection 1 had no complications; 1 had haemopneumothorax, respiratory and renal failure at 2-day follow-up; 1 developed pleural effusion, which needed drainage, and inferior vena cava obstruction, which needed percutaneous endoluminal

stenting; and 1 patient reported urinary retention (follow-up period not stated)

².

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to ex-vivo hepatic resection and reimplantation for liver cancer. Searches were conducted of the following databases, covering the period from their commencement to 7 October 2007: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy).

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with liver cancer.
Intervention/test	Ex-vivo hepatic resection.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Microwave ablation for the treatment of metastases in the liver. NICE interventional procedures guidance 220 (2007). Available from www.nice.org.uk/IPG220
- Microwave ablation of hepatocellular carcinoma. NICE interventional procedures guidance 214 (2007). Available from www.nice.org.uk/IPG214
- Radiofrequency-assisted liver resection. NICE interventional procedures guidance 211 (2007). Available from www.nice.org.uk/IPG211
- Living-donor liver transplantation. NICE interventional procedures guidance 194 (2006). Available from www.nice.org.uk/IPG194
- Laparoscopic liver resection. NICE interventional procedures guidance 135 (2005). Available from www.nice.org.uk/IPG135
- Selective internal radiation therapy for colorectal metastases in the liver. NICE interventional procedures guidance 93 (2004). Available from www.nice.org.uk/IPG93
- Radiofrequency ablation for the treatment of colorectal metastases in the liver. NICE interventional procedures guidance 92 (2004). Available from www.nice.org.uk/IPG92
- Radiofrequency ablation of hepatocellular carcinoma. NICE interventional procedures guidance 2 (2003). Available from www.nice.org.uk/IPG2

Technology appraisals

- None relevant

Clinical guidelines

- None relevant

Public health guidance

- None relevant

Table 2 Summary of key efficacy and safety findings on ex-vivo hepatic resection and reimplantation for liver cancer

Abbreviations used: HCC, hepatocellular carcinoma; IVC, inferior vena cava.			
Study details	Key efficacy findings	Key safety findings	Comments
Oldhafer K J (2000) ¹ Case series Germany n = 24 (22 with cancer) Study period: Feb 1998 to Feb 1998 Study population: hepatic metastases n = 13; or primary liver cancer n = 9; extended focal nodular hyperplasia n = 2. Age: 51.3 years (mean) Sex: 63% male Inclusion criteria: no history of chronic hepatitis or cirrhosis. Technique: venovenous bypass. Hypothermic liver perfusion commenced in situ. Ex-vivo hepatectomy with resection following the segmental structure of the liver (degree of resection varied between patients) and portion of the vena cava. Vascular reconstruction as necessary. Reimplantation of the remnant liver. Follow-up: mean 20.3 months (range 2 weeks to 9 years) Conflict of interest: not stated	Patient outcome Ex-vivo resection and auto-transplantation was possible in 92% (22/24) of patients. Among patients with cancer, ex-vivo resection and auto-transplantation was possible in 91% (20/22) of patients. 63% (15/24) of patients survived the ex-vivo resection and were discharged at a mean follow-up of 36.5 days. 67% (10/15) of these patients died of tumour recurrence between 12-month and 36-month follow-up. Among patients with cancer, 59% (10/13) of patients survived the procedure and were discharged alive. Among these 13 survivors, 77% (10/13) died of tumour recurrence. Follow-up periods were the same for all patients. The mean survival time among the 10 patients with colorectal metastases was 21 months, and the 2 patients with focal nodular hyperplasia were alive at 5 and 9 years follow up. Surgical parameters Mean operative time was 13.54 hours, and anhepatic phase 6.67 hours (including the time to transplantation in 2 patients) or 5.67 hours in the remaining 22 patients.	Complications 29% of the patients (7/24) needed a liver transplant. Among the patients with cancer, 32% (7/22) required a liver transplant either immediately (2 patients) or in conjunction with a subsequent procedure (5 patients) 41% (9/22) of patients with cancer died postoperatively during the same admission episode as the operation.	Patients were selected for ex-vivo resection because it was considered the only chance for surgical resection treatment (17 patients), or to improve the radicality of resection and to perform meticulous vascular repair (7 patients). No details are provided on the follow-up point at which the complications or their sequelae occurred. Baseline clinical characteristics are not well described. Some patients were treated with ex-vivo surgery while transplantation was planned, and seven received a transplant following ex-vivo resection. One patient was lost to follow-up because they lived abroad. It is not clear if the survival time for patients with colorectal cancer represents only those who survived to discharge or to the sub-group as a whole.

Abbreviations used: HCC, hepatocellular carcinoma; IVC, inferior vena cava.			
Study details	Key efficacy findings	Key safety findings	Comments
Lodge JPA (2000) ² Case report UK n = 8 (4 ex-vivo) Study period: Feb 1995 to Feb 1999 Study population: hepatic metastases from colorectal cancer with IVC involvement. Age: 57 years (mean) Sex: 50% male Period between colorectal surgery and hepatectomy: 2 to 14 years Inclusion criteria: not stated Technique: general anaesthesia. Transverse upper abdominal incision with upper midline extension. Venovenous bypass. Ex-vivo hepatectomy with reimplantation of either segments 2 and 3 (three patients) or 4b, 5, and 6 (1 patient), IVC reconstruction with Dacron tube, saphenous vein graft, or Gore-Tex tube graft. Follow-up: mean 11 months Conflict of interest: not stated	Survival Of the four patients undergoing ex-vivo resection: - one patient died at 15-day follow-up following left haemopneumothorax, respiratory and renal failure - one patient died at 30-month follow-up with right renal adenocarcinoma, infiltration of the IVC, and pulmonary and spinal metastases - two patients were still alive at 5-month follow-up, one with recurrence in the bone. Surgical parameters A clear resection margin was reported in three of four patients. Mean postoperative length of stay was 19 days, and blood transfusion requirement was 9.5 units.	Complications Of the four patients who underwent ex-vivo resection: - one had no complications - one had haemopneumothorax, respiratory and renal failure on the second postoperative day - one developed pleural effusion (needing drainage) and IVC obstruction (needing percutaneous endoluminal stenting) - and one had urinary retention (follow-up period not stated).	All procedures were undertaken by the same surgeon. One patient received chemotherapy following hepatectomy. The follow-up period was reported for the whole study cohort and not just the four patients who underwent ex-vivo resection. Adjuvant treatments are not well described.

Abbreviations used: HCC, hepatocellular carcinoma; IVC, inferior vena cava.			
Study details	Key efficacy findings	Key safety findings	Comments
Hemming A W (2002) ³ Case report USA n = 16 (2 ex-vivo) Study period: 1996 to 2001 Study population: patients needing hepatic resection with hepatic vein reconstruction. One patient with HCC, and one with colorectal metastases. Involvement of the IVC, the hepatic vein, and portal structures. Inclusion criteria: not stated Technique: transverse upper abdominal incision with upper midline extension. Venovenous bypass. Ex-vivo liver resection (segments 1, 4 to 8 and parts of 2 and 3) as well as reconstruction of the hepatic veins and IVC. Reimplantation of part of segment 2 and 3. Resection of the right diaphragm in one patient. Assessment of vascular patency by ultrasound prior to discharge. Follow-up: 4 to 52 months (range) Conflict of interest: not stated	Survival One patient (with HCC) was alive and disease free at 52-month follow-up. One patient with colorectal metastasis died disease free at 4-month follow-up from sepsis associated with a perforated small bowel and diaphragmatic hernia. Surgical parameters Mean cold ischaemic time was 115 minutes and mean warm ischaemic time was 25 minutes. All vascular reconstructions were patent at the last follow-up.	Safety outcomes were not reported on.	Clinical, demographic and follow-up details of the two patients treated by ex-vivo resection are not reported separately to the rest of the study cohort. Case selection for ex-vivo surgery was determined by the site of the tumour and the involvement of the IVC, the hepatic veins, and portal structures. The clinician's experience is not described. The authors state that this technique requires a specialist centre with surgeons familiar with complex hepatobiliary surgery and liver transplantation.

Abbreviations used: HCC, hepatocellular carcinoma; IVC, inferior vena cava.			
Study details	Key efficacy findings	Key safety findings	Comments
Lechaux D (2002) ⁴ Case report France n = 1 Study period: not stated Study population: one patient with a large HCC in a non-cirrhotic liver, with involvement of the circumference of the IVC, the hepatic vein confluence, and the right portal pedicle Age: 40 years Sex: female Inclusion criteria: not stated Technique: 6 months of chemotherapy. Transverse upper abdominal incision with upper midline extension. Venovenous bypass. Ex-vivo liver resection (segments 5 to 8 extended to the posterior segment of 4 and the upper part of 2) and well as reconstruction of the hepatic veins and IVC using gore-tex conduits. Reimplantation of the remnant liver with reorientation 180 degrees in the sagittal plane. Postoperative anticoagulation medication. Follow-up: 12 months Conflict of interest: none	Patient 1 The procedure's operative time was 12 hours and the anhepatic period was 5.5 hours. Nine units of blood were needed for transfusion during the procedure. Liver function returned to normal within 5 days. Histopathological analysis confirmed HCC and no hepatic parenchymal resection margin involvement. Follow-up was uneventful and the patient was discharged at 21-day follow-up. One year after surgery the patient was alive with no recurrence.		The ex-vivo resection procedure followed a 6-month course of chemotherapy. It is difficult to disaggregate the efficacy of the surgical procedure in itself. Few clinical outcomes are reported. The explanted liver was perfused, and cooled in 4°C solution during bench resection. The decision to undertake ex-vivo surgery was based on the estimated duration of vascular reconstruction because of the involvement of the hepatic vein triad.

Validity and generalisability of the studies

- There is a very limited evidence base in terms of quantity.
- The extent of resection, and involvement of the IVC, varied between studies; techniques for vascular reconstruction varied between and within studies.
- Survival may be influenced by extrahepatic disease (primary or metastatic tumours at other body sites).
- Some studies included patients with primary liver cancer, some with metastases (mostly colorectal), and some included a mixed cohort.
- Two of the series reported the outcomes of ex-vivo resection within larger series of liver resection.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr J Buckles (Association of Upper Gastrointestinal Surgeons), Mr P Lodge (Association of Upper Gastrointestinal Surgeons), Mr G Poston (British Association of Surgical Oncology).

- All three of the Specialist Advisers considered this procedure to be novel and of uncertain safety and efficacy.
- Adverse events relating to the procedure known anecdotally or from the literature include mortality, liver failure, bleeding/blood transfusion, and wasted donor livers.
- No additional theoretical adverse events were identified.
- The key efficacy outcome by which to evaluate this procedure should be mortality survival cost.
- The main comparators for this procedure are palliative chemotherapy or in-situ liver resection with vascular exclusion and perfusion.
- There is no survival benefit over palliative chemotherapy in patients whose disease is so bad that the only surgical option is this procedure.

- The procedure is only available at one UK centre and no training is available at present.
- The procedure would be best undertaken by surgeons with experience in liver transplantation.
- It should only be carried out in major liver units able to offer liver resection and transplantation.
- Concern exists about the efficacy of such a high-risk procedure, which is often performed in a non-curative setting.

Issues for consideration by IPAC

- Non-English language study reports were excluded from this overview.
- Both hepatocellular carcinoma and colorectal metastases indications are included in this overview.
- Many interventional procedures guidance documents have already been published for liver procedures in these indications. Please see appendix B.

References

- 1 Oldhafer KJ, Lang H, Schlitt HJ et al. (2000) Long-term experience after ex situ liver surgery. *Surgery* 127:520–27.
- 2 Lodge JPA, Ammori BJ, Prasad KR et al. (2000) Ex vivo and in situ resection of inferior vena cava with hepatectomy for colorectal metastases. *Annals of Surgery* 231:471–79.
- 3 Hemming AW, Reed AI, Langham MR et al. (2002) Hepatic vein reconstruction for resection of hepatic tumors. *Annals of Surgery* 235:850–58.
- 4 Lechaux D, Megevand JM, Raoul JL et al. (2002) Ex vivo right trisegmentectomy with reconstruction of inferior vena cava and "flop" reimplantation. *Journal of the American College of Surgeons* 194:842–45.

Appendix A: Additional papers on ex-vivo hepatic resection and reimplantation for liver cancer

There were no additional papers identified.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2

Appendix B: Related NICE guidance for ex-vivo hepatic resection and reimplantation for liver cancer

Guidance	Recommendations
Interventional procedures	Microwave ablation for the treatment of metastases in the liver. NICE interventional procedures guidance 220 (2007). 1.1 Current evidence on the safety and efficacy of microwave ablation for the treatment of metastases in the liver does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to use microwave ablation for the treatment of metastases in the liver should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information, including about other treatment options. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG220publicinfo). • Audit and review clinical outcomes of all patients having microwave ablation for the treatment of metastases in the liver. 1.3 Patient selection should be carried out by a multidisciplinary team that includes a hepatobiliary surgeon. 1.4 The procedure should be performed under appropriate imaging guidance. 1.5 As a number of devices are available, and there is some uncertainty about the energy levels that should be used, any adverse events relating to this procedure should be reported to the Medicines and Healthcare products Regulatory Agency. 1.6 Further research on the procedure would be useful. The Institute may review the procedure upon publication of further evidence.

	Microwave ablation of hepatocellular carcinoma. NICE interventional procedures guidance 214 (2007). 1.1 Current evidence on the safety and efficacy of microwave ablation of hepatocellular carcinoma appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection should be carried out by a multidisciplinary team that includes a hepatobiliary surgeon. 1.3 The procedure should be performed under appropriate imaging guidance. 1.4 A number of devices are available, and there is some uncertainty about the energy levels that should be used. Any adverse events relating to this procedure should be reported to the Medicines and Healthcare products Regulatory Agency. 1.5 Further research on long-term survival outcomes and comparisons of microwave ablation with other ablative techniques will be useful. Radiofrequency-assisted liver resection. NICE interventional procedures guidance 211 (2007). 1.1 Limited evidence on the safety and efficacy of radiofrequency (RF)-assisted liver resection appears adequate to support the use of this procedure as one of the options for liver resection, provided that the normal arrangements are in place for consent, audit and clinical governance.
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	Living-donor liver transplantation. NICE interventional procedures guidance 194 (2006). 1.1 Current evidence on the efficacy of living-donor liver transplantation and its safety profile appears adequate to support the use of this procedure for suitable recipients. 1.2 However, current evidence suggests that living-donor liver transplantation carries a significant risk of morbidity and a small risk of death for donors. Therefore clinicians wishing to undertake this procedure should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that donors and recipients undergo thorough physical and psychological screening, and receive counselling about the morbidity and risks associated with this procedure. They should also be provided with clear written information. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG194publicinfo). • Audit and review clinical outcomes of all people donating liver tissue for transplantation. 1.3 Living-donor liver transplantation should only be performed on patients selected using UK Transplant Liver Advisory Group standards in specialist centres and in the context of a multidisciplinary team. 1.4 Clinicians should enter all donors and recipients into the UK & Ireland Liver Transplant Audit (www.rcseng.ac.uk/surgical_research_units/ceu/projects/proj_liver.html). Laparoscopic liver resection. NICE interventional procedures guidance 135 (2005). 1.1 Current evidence on the safety and efficacy of laparoscopic liver resection appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection for laparoscopic liver resection should be carried out by a multidisciplinary team. Surgeons undertaking laparoscopic liver resection should have specialist training and expertise both in laparoscopic techniques and in the specific issues relating to liver surgery.
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	Selective internal radiation therapy for colorectal metastases in the liver. NICE interventional procedures guidance 93 (2004). 1.1 Current evidence on the safety of selective internal radiation therapy (SIRT) for colorectal metastases in the liver appears adequate. With regard to efficacy, the procedure may reduce tumour bulk, but there is a lack of evidence of symptom relief or increased survival, and combination with other treatments makes interpretation of the published literature difficult. 1.2 Clinicians wishing to undertake selective internal radiation therapy for colorectal metastases in the liver should take the following actions. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. Use of the Institute's Information for the Public is recommended. • Audit and review clinical outcomes of all patients having selective internal radiation therapy for colorectal metastases in the liver. 1.3 Publication of research studies with outcome measures which include survival will be useful in reducing the current uncertainty about the efficacy of the procedure. The Institute may review the procedure upon publication of further evidence. Radiofrequency ablation for the treatment of colorectal metastases in the liver. NICE interventional procedures guidance 92 (2004). 1.1 Current evidence on the safety of radiofrequency ablation of colorectal metastases in the liver appears adequate. However, the evidence of its effect on survival is not yet adequate to support the use of this procedure without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake radiofrequency ablation of colorectal metastases in the liver should take the following actions. • Ensure that patients offered it understand the uncertainty about the procedure's efficacy and provide them with clear written information. Use of the Institute's Information for the Public is recommended. • Audit and review clinical outcomes of all patients having radiofrequency ablation for the treatment of colorectal metastases in the liver.
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	1.3 Publication of research studies with outcome measures which include survival will be useful in reducing the current uncertainty about the efficacy of the procedure. The Institute may review the procedure upon publication of further evidence. Radiofrequency ablation of hepatocellular carcinoma. NICE interventional procedures guidance 2 (2003). 1.1 Current evidence of the safety and efficacy of radiofrequency ablation (RFA) for hepatocellular carcinoma appears adequate to support use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 It is recommended that: • patient selection should be carried out by a multidisciplinary team that includes a hepatobiliary surgeon • the procedure should be monitored by CT or ultrasound.
Technology appraisals	None relevant
Clinical guidelines	None relevant
Public health guidance	None relevant

Appendix C: Literature search for ex-vivo hepatic resection and reimplantation for liver cancer

Database	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	07/10/2008	Issue 3, 2008	0
Database of Abstracts of Reviews of Effects – DARE (CRD website)	08/10/2008	-	0
HTA database (CRD website)	08/10/2008	-	1
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	07/10/2008	Issue 3, 2008	9
MEDLINE (Ovid)	07/10/2008	1950 to September Week 4 2008	197
MEDLINE In-Process (Ovid)	07/10/2008	October 06, 2008	10
EMBASE (Ovid)	07/10/2008	1980 to 2008 Week 40	132
CINAHL (NLH Search 2.0/)	07/10/2008	1981 – Present	0
BLIC (Dialog DataStar)	08/10/2008	1995-present	3
National Research Register (NRR) Archive	08/10/2008	-	0
UK Clinical Research Network (UKCRN) Portfolio Database	08/10/2008	-	0
Current Controlled Trials <i>metaRegister</i> of Controlled Trials - <i>mRCT</i>	07/10/2008	-	1
Clinicaltrials.gov	07/10/2008		Prospective randomized trial of laparoscopic versus open liver resection for HCC Alternative to two-stage hepatectomy Study on clinical outcome of vascular inflow occlusion in open liver resection

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	exp Liver Neoplasms/
2	((liver\$ or hepat\$) adj3 (neoplasm\$ or cancer\$ or carcinoma\$ or adenocarcinom\$ or tumour\$ or tumor\$ or malignan\$ or trauma\$)).tw.
3	(hepatectom\$ or ((liver\$ or hepat\$) adj3 (segmentectom\$ or sectionectom\$))).tw.
4	((liver\$ or hepat\$) adj3 (excision\$ or resect\$ or transect\$ or ablat\$ or cut\$ or remove\$ or bench\$)).tw.
5	hemihepatectom\$.tw.
6	((Liver\$ or wedge\$) adj3 resection\$).tw.
7	Hepatectomy/
8	hepatect\$.tw.
9	or/1-8
10	(Ex-vivo or Exvivo or In-vitro or Invitro).tw.
11	(external\$ or outside\$ or exterior\$).tw.
12	Portal Vein/su [Surgery]
13	Portal System/
14	(Port\$ adj3 (vein or system\$)).tw.
15	Extracorporeal Circulation/
16	Liver Circulation/
17	((Extracorp\$ or liver\$ or hepat\$) adj3 circulat\$).tw.
18	(veno\$ adj3 bypass).tw.
19	or/10-18
20	19 and 9
21	Replantation/
22	(Surgical\$ adj3 (reimplant\$ or reattach\$ or replant\$ or reinsert\$ or return\$ or replace\$)).tw.
23	(Replantat\$ or reattach\$ or reimplant\$ or reinsert\$ or replace\$ or reinsert\$).tw.
24	or/21-23
25	24 and 20
26	animals/
27	humans/
28	26 not (26 and 27)
29	25 not 28
30	from 29 keep 1-197