

Selective internal radiation therapy for non-resectable colorectal metastases in the liver

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NICE interventional procedure guidance 401
guidance.nice.org.uk/ipg401

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1 Guidance

This document replaces previous guidance on selective internal radiation therapy for colorectal metastases in the liver (interventional procedure guidance 93).

- 1.1 Current evidence on the safety of selective internal radiation therapy (SIRT) for non-resectable colorectal metastases in the liver is adequate.
- 1.2 The evidence on its efficacy in chemotherapy-naive patients is inadequate in quantity. Clinicians should offer eligible patients who have not been previously treated by chemotherapy entry into well-designed research studies such as the FOXFIRE trial (www.octo-oxford.org.uk/alltrials/trials/FOXFIRE). For patients who are not eligible or who prefer not to enter a research trial, the procedure should be used with special arrangements for clinical governance, consent and audit.
- 1.3 For patients who have previously been treated with chemotherapy, there is evidence that SIRT can prolong time to progression of hepatic metastases, but more evidence is required on survival and quality of life (see section 1.7). Therefore for patients who have been previously treated with chemotherapy this procedure should be used with special arrangements for clinical governance, consent and audit.
- 1.4 Clinicians undertaking the procedure for patients outside research studies should take the following actions.
 - Inform the clinical governance leads in their Trusts.
 - Ensure that patients and their carers understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/guidance/IPG401/publicinfo).
 - Clinicians should enter details for all patients undergoing selective internal radiation therapy for non-resectable colorectal metastases in the liver onto the [national SIRT register](#) and review clinical outcomes locally.

- 1.5 Patients should be selected for SIRT or entry into trials by a hepatobiliary cancer multidisciplinary team including an interventional radiologist, in liaison with a colorectal cancer multidisciplinary team.
- 1.6 SIRT should only be carried out by clinicians with specific training in its use and in techniques to minimise the risk of side effects of the procedure.
- 1.7 The Committee considered that SIRT is a potentially beneficial treatment for patients with non-resectable colorectal metastases in the liver, but that more research and data collection are required to demonstrate its efficacy. A recommendation about research trials for chemotherapy-naive patients is given in 1.2 above. For patients who have previously been treated with chemotherapy, comparative trials are needed to determine whether SIRT prolongs survival compared with best standard treatment, and to determine its effect on quality of life. There is also a need to identify which subgroups of patients are likely to derive clinical benefit from SIRT. Research studies should clearly describe the characteristics of treated patients, and the extent and histological details of their tumours. Outcomes should include survival and quality of life. Downstaging of metastases allowing resection or ablation should be clearly documented.
- 1.8 NICE may review the procedure on publication of further evidence.

2 The procedure

2.1 Indications and current treatments

- 2.1.1 Colorectal cancer is common and metastatic spread to the liver occurs frequently.
- 2.1.2 Treatment of hepatic metastases depends on their extent and location. Treatment options include surgical resection, thermal ablation, chemotherapy, different types of arterial embolisation and external beam radiotherapy.

2.2 Outline of the procedure

- 2.2.1 SIRT is used for patients with limited or no extrahepatic disease for the treatment of colorectal cancer liver metastases that are unsuitable for resection or ablation. It may be used alone or in combination with chemotherapy. It aims to deliver radiation directly into the metastases, minimising the risk of radiation damage to healthy surrounding tissues.
- 2.2.2 With the patient under local anaesthesia, radioactive microspheres that are designed to embolise into small vessels around the metastases are injected into branches of the hepatic artery, usually via a percutaneous femoral approach.
- 2.2.3 A nuclear medicine liver-to-lung shunt study is usually carried out before the procedure to assess the risk of radioactive microspheres causing lung damage. Radiographic imaging and selective coil embolisation of arteries to the stomach and duodenum are also commonly carried out.
- 2.2.4 SIRT may be repeated, depending on the response achieved.

Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview, available at www.nice.org.uk/guidance/IP/228/overview

2.3 Efficacy

- 2.3.1 In a randomised controlled trial (RCT) of 70 patients with non-resectable colorectal liver metastases, mean survival after treatment by SIRT plus hepatic artery chemotherapy or hepatic artery chemotherapy alone was 23.5 and 18.4 months respectively ($p = 0.18$). An RCT of 44 patients treated by SIRT plus systemic chemotherapy or systemic chemotherapy alone reported median overall survival of 10.0 and 7.3 months respectively ($p = 0.80$). Ten out of 23 patients in the control arm crossed over to SIRT at progression and this is likely to have confounded survival data. An RCT of 21 patients treated by SIRT plus systemic chemotherapy or systemic chemotherapy alone reported median

survival of 29.4 months and 12.8 months respectively (hazard ratio 0.33, 95% confidence interval [CI] 0.12 to 0.91; $p = 0.025$).

- 2.3.2 The RCT of 70 patients reported better tumour response following SIRT plus hepatic artery chemotherapy than hepatic artery chemotherapy alone at minimum 3.5-year follow-up ($p = 0.01$). The RCT of 44 patients treated by SIRT plus systemic chemotherapy or systemic chemotherapy alone reported median 'time to liver progression' of 5.5 months and 2.1 months respectively (hazard ratio 0.38, 95% CI 0.20 to 0.72; $p = 0.003$).
- 2.3.3 Downstaging, which enabled potentially curative surgical resection, was reported in 2 of 50 (4%) patients treated by SIRT in a case series.
- 2.3.4 In the case series of 50 patients treated by SIRT mean anxiety levels were significantly reduced (compared with pre-treatment levels) in 14 patients who were questioned 6 weeks after treatment ($p < 0.01$).
- 2.3.5 The Specialist Advisers listed key efficacy outcomes as tumour response rates, survival and downstaging to allow surgery, or chemoresponsiveness.

2.4 Safety

- 2.4.1 In a case series of 100 patients, 1 patient died from radiation hepatitis 9 weeks after SIRT, and another patient died from acute pancreatitis with peptic ulceration.
- 2.4.2 The RCT of 44 patients treated by SIRT plus systemic chemotherapy or systemic chemotherapy alone reported grade 3 toxicity in 5% (1/21) and 27% (6/22) of patients respectively ($p = 0.10$). The RCT of 70 patients reported that there was no significant difference between the groups (SIRT plus hepatic artery chemotherapy or hepatic artery chemotherapy alone) in the total number of grade 3 or 4 toxicity adverse events.
- 2.4.3 Liver abscess requiring drainage was reported in 9% (1/11) of patients (timing not stated) in the systemic chemotherapy plus SIRT arm of the RCT of 21 patients.

- 2.4.4 A case series of 140 patients treated by SIRT reported that radiation-induced liver dysfunction occurred in 2% (3/140) of patients (median follow-up 9 months).
- 2.4.5 The Specialist Advisers listed adverse events as pain, vomiting, anorexia, fatigue, portal hypertension, and impaired delivery of radioembolic material after antiangiogenic agent use. They considered theoretical adverse events to include pneumonitis, gastrointestinal haemorrhage or ulceration, cholecystitis, biliary strictures, pancreatitis, radiation dermatitis and radiation hepatitis.

2.5 Other comments

- 2.5.1 The Committee noted that observational studies report large numbers of patients previously treated by chemotherapy who have received SIRT, but that the number of these patients reported in comparative trials was very small. The Committee considered quality of life after any kind of treatment to be of great importance for these patients. These considerations formed the basis of the recommendations for further research.
- 2.5.2 The Committee considered that SIRT may be a potential option for patients with limited extra-hepatic disease for whom chemotherapy has failed.
- 2.5.3 The Committee noted that there have been a small number of reports of SIRT downstaging colorectal metastases to the extent that treatment by resection or ablation became possible. However, it considered that there was insufficient evidence to comment on the potential use of the procedure with this intent.
- 2.5.4 The Committee also considered a number of patient commentary questionnaires from patients who described benefits from SIRT.

3 Further information

- 3.1 For related NICE guidance see www.nice.org.uk

Information for patients

NICE has produced information on this procedure for patients and carers ('Understanding NICE guidance'). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind. See www.nice.org.uk/guidance/IPG401/publicinfo

Changes since publication

May 2013: recommendation 1.4 was updated to include details of the national SIRT register.

About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE [interventional procedures guidance process](#).

It updates and replaces NICE interventional procedure guidance 93.

We have produced a [summary of this guidance for patients and carers](#).

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this

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