Overview of selective internal radiation therapy: from work-up to follow-up

Thomas Helmberger *
Institut für Diagnostische und Interventionelle Radiologie, Neuroradiologie und Nuklearmedizin Klinikum Bogenhausen, München, Germany

1. Rationale
Hepatic malignancies are one of the most challenging presentations in oncology, not only because of their high incidence but because of their recurrent nature and the limited efficacy of current treatments. With multiple sequential lines of therapy, the risk of additive toxicities increases overall, often with concurrent functional changes to the liver.

External beam radiation therapy (EBRT) is the cornerstone of curative and palliative therapy in many malignancies, and is often used synergistically with chemotherapy to improve outcome. However, until recently, radiotherapy has not been applied with much success to the liver due to the low tolerance of liver parenchyma to doses above 35Gy. This is below the required dose of 45Gy or above (usually with concurrent radio-sensitising chemotherapy) for the radical treatment of microscopic disease from adenocarcinomas, particularly of rectal origin, and for macroscopic disease such as liver metastases.

Seminal works by Withers (1988) and Lawrence have shown that complications do not occur unless the threshold of liver damage exceeds the functional reserve. Small portions of the liver can tolerate irradiation well above 35Gy without significant complications, as long as sufficient normal liver is spared from radical dose radiation exposure. These principles have been applied successfully for stereotactic body radiation therapy of small liver metastases and also for selective internal radiation therapy (SIRT) in the treatment of primary and secondary liver tumours.

SIRT is a form of brachytherapy, which utilises the high-density microvascularisation, present in almost all malignant tumours (greater than 5–10 mm diameter), to deliver high local doses of irradiation to liver tumours via the hepatic arterial branches. The concept of SIRT was born in the 1950s, but its wider adoption followed the development of the current generation of products such as SIR-Spheres microspheres (yttrium-90 labelled resin microspheres) and TheraSphere (yttrium glass microspheres) that were approved in the early 2000s.

*Correspondence: Thomas Helmberger, M.D., EBIR, Professor of Radiology, Institut für Diagnostische und Interventionelle Radiologie, Neuroradiologie und Nuklearmedizin, Klinikum Bogenhausen, Englschalkinger Str. 77, 81925 München, Germany. Tel.: +49 89 9270 2201. E-mail address: thomas.helmberger@klinikum-muenchen.de (T. Helmberger).
2. Patient selection

SIRT with 90Y-resin microspheres is indicated for the management of liver-dominant or liver-only primary or secondary liver tumour(s) in patients who have a life expectancy of at least 3 months (without infections and no evidence of pulmonary insufficiency) and no significant hepatic functional deficit.

For each patient, the appropriateness of SIRT is also governed by a number of well-established and accepted parameters for liver reserve and vascular access. Liver function must be adequate, without ascites, with normal synthetic liver function (e.g., albumin >3 g/dL), and normal total bilirubin of less than 2.0 mg/dL (≤34 µmol/L). A small number of patients are found to be unsuitable for treatment due to the presence of either aberrant vessels that prevent the isolation of the liver arterial tree from gastric and small-bowel branches or arteriovenous fistulae in tumours that allow for more than 20% of the microspheres to pass through the liver capillary bed to the lungs. Understanding these exclusion criteria (as outlined by Goin) is key to preventing avoidable complications with SIRT.

3. Multidisciplinary teams and the continuum of care

Ideally SIRT should be undertaken at centres that employ a multidisciplinary approach to planning, delivering and reviewing cancer treatment, or upon referral from a multidisciplinary team familiar with the procedure. In particular, multidisciplinary team members should be consulted with regard to the likely interactions between SIRT and any prior, concurrent or planned biological, chemotherapeutic, locoregional ablative, surgical or external beam radiation therapies. A detailed clinical history, blood tests (full blood count, serum renal and liver function tests) as well as evidence of liver-dominant disease based on contrast-enhanced positron emission tomography (PET), computed tomography (CT) or magnetic resonance imaging (MRI) are key to informing the decision to treat.

SIRT is one element in the continuum of care. It is often given during a treatment hiatus or following disease progression with chemotherapy.

4. Treatment work-up

Treatment work-up includes a thorough angiographic evaluation in order to detect extrahepatic vessels that irrigate liver tumors and to detect, and eventually occlude, aberrant vessels arising from hepatic arteries that may feed the gastrointestinal tract (mainly gastroduodenal artery and right gastric artery). During this arteriography, with the tip of the catheter in the same position where 90Y-resin microspheres will be delivered, technetium-99m labeled macroaggregated albumin (99mTc-MAA) is injected as a tracer, to measure the hepatopulmonary shunt. Planar or SPECT/CT gamma-camera images are then used to detect any misplacement of 99mTc-MAA in the gastrointestinal tract and to estimate the dose of radiation to tumour and non-tumoral tissue.

5. Treatment

Eligible patients are then invited back for the treatment procedure. Immediately prior to the administration of 90Y-resin microspheres, an angiogram is conducted to confirm that all aberrant vessels are occluded. The calculated implanted activity may be adjusted if there are concerns over the extent of pre-treatment and/or potential subsequent toxicity. The microspheres are then administered as a single or sequential lobar application immediately followed by a Bremsstrahlung scan to confirm the correct targeted deposition of the microspheres. Patients are then closely monitored for 2 to 4 days after the procedure and post-embolisation syndrome is managed, as necessary.

6. Summary

In summary, the key to successful treatment with SIRT is appropriate selection of patients with a controllable and identifiable tumour load and sufficient hepatic functional reserve. SIRT is one element in the continuum of care for patients managed by a multidisciplinary team. Diligent pretreatment work-up is essential with close post-treatment follow-up to manage complications and to prepare for subsequent treatment.

Conflict of interest statement

The author has no conflict of interest.

REFERENCES


