Optimising Dose to Tumour with Selective Internal Radiation Therapy (SIRT)

Recently published 2016 **European Society for Medical Oncology (ESMO) Clinical Guidelines** recommend **TARE/SIRTwith ^{90}Y microspheres** for the treatment of **colorectal cancer liver metastasis** and inoperable **intrahepatic cholangiocarcinoma, complementing existing guidelines for SIRT/TARE use in HCC.**[1,2,3]

Selective Internal Radiation Therapy (SIRT) or transarterial radioembolisation (TARE) involves injection of ^{90}Y-containing microspheres through the hepatic artery into liver tumours. This therapy combines two approaches: irradiation of tumour tissue and embolisation of blood vessels.

Two different types of ^{90}Y microspheres currently exist in the market: glass microspheres (TheraSphere™, BTG) and resin microspheres (SIR-Spheres®, Sirtex).[4-6] Aside from resin microspheres having a slightly larger diameter compared to glass microspheres (20–60 µm vs. 20–30 µm) the main difference is the activity per microsphere at calibration: 50 Bq for resin and 2500 Bq for glass.[7]

Higher specific activity of glass microspheres means that fewer microspheres are administered to achieve the desired dose. As a result, glass microspheres have minimal embolic effect.[8] This allows glass microspheres to lodge deeper inside the tumour, where their primary mechanism of action is radiation.[8] Because of their differing characteristics, the two ^{90}Y microsphere products lie at opposite ends of a radioembolisation spectrum. Resin microspheres rely on a combination of embolisation with lower levels of radiation, whereas glass microspheres are minimally embolic with high levels of radiation.[9] As such, the term "selective internal radiation therapy" more accurately describes therapy with glass microspheres.

A key benefit of high activity glass microspheres is the ability to achieve high absorbed dose in the tumour. Modelling shows that total administered activity with glass microspheres is higher, leading to greater absorbed dose coverage with fewer numbers of microspheres.[10] Retrospective dosimetric correlations have demonstrated that higher tumour absorbed doses drive tumour response and lead to improved patient outcomes.[11–15]

The properties of glass microspheres allow for unique treatment options in the clinic. Not being limited by the number of microspheres provides flexibility to adjust radiation dose according to individual patient needs, enabling clinical utility for downstaging, bridge to transplant, and radiation segmentectomy. Glass microspheres have demonstrated success in a range of scenarios: curative or palliative, livers with single or multifocal tumours, portal vein thrombosis (PVT) in primary or chemorefractory secondary liver cancer, and using segmental or lobar approaches.[9,11–13,15–23]

The ability to deliver high dose to tumour does not come at the cost of compromised patient safety. A consistently favourable toxicity profile for glass microspheres has been reported in numerous studies.[9,11–13,15–19,24] Minimally embolic radiotherapy reduces the risk of stasis, resulting in fewer incidents of reflux and gastric ulceration. Modelling studies have illustrated that lower numbers of glass microspheres lead to their limited distribution in normal tissue compared to more embolic microspheres, which may also contribute to the higher observed dose tolerance.[25] Therapy with embolic effects increases risk to patients with compromised portal venous flow. SIRT with glass microspheres has tolerable adverse effects combined with promising survival rates even in patients with PVT.[12,15,16,20]

Selectively delivering the maximal dose while maintaining patient safety is fundamental to achieving long term benefit.[26,27] The observation that improved responses are seen above certain absorbed dose thresholds opens the way to exploring personalised dosimetry with glass microspheres, with the goal of optimising dose according to patient and tumour characteristics.[12]

Common side effects of TheraSphere™ include mild to moderate fatigue, pain and nausea for about a week. For details on rare or more severe side effects, please refer to the TheraSphere™ package insert at www.therasphere.com.[4,9,12]

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In the EU, TheraSphere™ is used in the treatment of hepatic neoplasia.[4] In Canada, TheraSphere™ may be used in the treatment of hepatic neoplasia in patients who have appropriately positioned arterial catheters.[5]

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