

# Radioembolization in Hepatocellular Carcinoma. A New Ablative Tool

Javier Orcajo Rincón<sup>1\*</sup>, Alonso Farto Juan Carlos<sup>1</sup>

<sup>1</sup>Nuclear Medicine Department, H.G. University "Gregorio Marañón" Dr Esquerdo, Madrid, Spain.

\*Corresponding author: Javier Orcajo Rincón, Nuclear Medicine Department, Gregorio Marañón Hospital Dr Esquerdo, Madrid, Spain.

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## Opinion

Among the intra-arterial techniques used in primary and metastatic liver pathology, radioembolization with yttrium-90 microspheres has been the one that has evolved most dramatically in recent years and the one that has positioned itself in the earliest stages of management of hepatocellular carcinoma (HCC) in current clinical guidelines [1,2]. Currently, the technology available in most Centers performing transarterial radioembolization (TARE), comprising the incorporation of Cone Beam CT (CBCT), SPECT/CT gamma cameras and the design of dedicated software for voxel-based multi-compartment dosimetric analysis, allows for a much safer planning of the procedure and the implementation of highly personalized therapies [3, 4]. These new technological tools have allowed the transformation of this procedure, initially used with palliative intent, through the administration of low doses of radiation to large areas of liver tissue, to a new tool with radical intent.

This new approach, called radiation segmentectomy or radiation tumorectomy, differs from the conventional approach by its higher degree of selectivity. It consists of the administration of high doses of intra-arterial radiation, between 300 and 400 Gy to a very limited tissue extension. Especially suitable for lesions smaller than 5 cm, has shed light into the suitability of this treatment for patients with small lesions confined to  $\leq 2$  segments [5,6]. Results obtained in recent studies, such as the Dosisphere-01, multicenter phase II trial, or the SARAH, TARGET and LEGACY studies, reveal the benefit of high doses of radiation to the tumor, and multicompartamental dosimetry, as determining prognostic factors, significantly increasing the overall survival of these patients, reaching 93% OS in patients with transplant or resection following TARE at 3 years [7-11].

In addition to a reduction in the risk of radiation damage in the non-tumorous liver parenchyma and in extrahepatic tissues,

supraselective radio embolization has achieved oncological results comparable to those of ablative techniques such as radiofrequency ablation. In a recently published study by the renowned team at Northwestern University, Chicago, a pathological tumor necrosis rate of 100% was demonstrated in 67% of patients treated with radiation segmentectomy who underwent liver explants, with a median radiation dose of 240 (IQR: 136–387) Gy, while all patients receiving  $> 400$  Gy exhibited complete pathological necrosis [12].

Based on the new results of this supraselective procedure, very recently, the new BCLC guidelines for the management of hepatocarcinoma have been published, in which hepatic radio embolization, especially that directed at small lesions and with a radical objective, is considered in the earliest stages of the disease. In BCLC stage 0, defined as a solitary HCC  $< 2$ cm without vascular invasion or extrahepatic spread in a patient with preserved liver function and no cancer-related symptoms, or in early stage (BCLC A), its implementation is now contemplated in patients who are not candidates for percutaneous ablative therapies (radiofrequency or microwave) or surgery, even in lesions up to 8cm.

In our Center we have performed more than 50 procedures of radiation segmentectomies, with resin and glass microspheres, directed at lesions not amenable to ablative treatments, confined to one or two segments and calculating treatment doses with radical intention ( $>300$ Gy), obtaining response rates greater than 90%, with no data on serious adverse effects. Therefore, supraselective radio embolization has proven to be a safe technique, with a high impact on the evolution of the oncological disease, on the quality of life and, finally and very importantly, on the overall survival of patients diagnosed with HCC.

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