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Scientific Article

Autoradiography and biopsy measurements of a resected hepatocellular carcinoma treated with 90 yttrium radioembolization demonstrate large absorbed dose heterogeneities

Jens Hemmingsson MS [a,*], Jonas Högberg PhD [b], Johan Mölne MD, PhD [c], Johanna Svensson MD, PhD [d], Peter Gjertsson MD, PhD [e], Magnus Rizell MD, PhD [f], Olof Henrikson MD, PhD [g], Peter Bernhardt PhD [a]

[a] *Department of Radiation Physics, The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden*
[b] *Department of Medical Physics, Linköping University Hospital, Linköping, Sweden*
[c] *Department of Pathology, The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden*
[d] *Department of Oncology, The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden*
[e] *Department of Clinical Physiology, The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden*
[f] *Department of Surgery, The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden*
[g] *Department of Radiology, The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden*

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Abstract

Purpose: Radioembolization is an alternative palliative treatment for hepatocellular carcinoma. Here, we examine the uptake differences between tumor tissue phenotypes and present a cross-section of the absorbed dose throughout a liver tissue specimen.

Methods and materials: A patient with hepatocellular carcinoma was treated with ^{90}Y radioembolization followed by liver tissue resection. Gamma camera images and autoradiographs were collected and biopsy tissue samples were analyzed using a gamma well counter and light microscopy.

Results: An analysis of 25 punched biopsy tissue samples identified 4 tissue regions: Normal tissue, viable tumor tissue with and without infarcted areas, and tumor areas with postnecrotic scar tissue. Autoradiography and biopsy tissue sample measurements showed large dose differences between viable and postnecrotic tumor tissue (159 Gy vs 23 Gy).

Conflicts of interest: The authors have no potential conflicts of interest relevant to this article.

* Corresponding author. Department of Radiation Physics, Sahlgrenska University Hospital, Gula Stråket 2B, Gothenburg 41345, Sweden.
E-mail address: jens.hemmingsson@phonsa.gu.se (J. Hemmingsson).

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Conclusions: Radioembolization of 90 yttrium with resin microspheres produces heterogeneous-absorbed dose distributions in the treatment of unifocal hepatic malignancies that could not be accurately determined with current gamma camera imaging techniques.

Introduction

Hepatocellular carcinoma (HCC) accounts for approximately 80% of primary liver cancers and is the third most common cause of cancer-related deaths worldwide.[1,2] Major risk factors for the development of HCC include hepatitis B or C infections and alcoholic liver disease. These risk factors also lead to the development of cirrhosis, which is present in 80% to 90% of patients with HCC.[3] Treatment options vary depending on the cancer stage and range from potentially curative treatments such as surgical resection, liver transplantation, or radiofrequency ablation to palliative treatments including sorafenib (tyrosine kinase inhibitor), transarterial chemoembolization, or radioembolization. During radioembolization, resin or glass microspheres that contain 90 yttrium (^{90}Y) are injected into the hepatic artery and spread throughout the injected liver, lobe, or segment, mainly reaching tumor tissue due to the predominantly arterial vascularization of liver tumors.[4] Radioembolization of ^{90}Y utilizes high-energy beta particles (E_{mean}: 0.934 MeV) and approximately 90% of the absorbed dose is delivered in the first 9 days after injection.

In 2014, Högberg et al. described the distribution of resin microspheres in the hepatic arterial tree of normal liver tissue as large clusters in arterioles or a string of spheres or single spheres in terminal arterioles.[5] This irregular arrangement leads to a heterogeneous-absorbed dose distribution that could be a contributing factor to the higher radiation tolerance that is observed in radioembolization relative to external beam radiotherapy along with the low-dose rate effects of ^{90}Y irradiation.[6] Similar estimates of tumor dose heterogeneity would be valuable to improve the evaluation of the therapeutic potential of radioembolization. Posttreatment imaging such as single photon emission computed tomography (SPECT) or positron emission tomography (PET) are important tools to evaluate activity distributions both intra- and extra-hepatic. From these images, the tumor-to-normal-tissue concentration (TNC) ratio can be calculated, which is a useful quantity in treatment planning (on pretherapeutic SPECT images) and efficacy evaluation, as follows:

$$TNC = \frac{A_T / V_T}{A_N / V_N} \quad (1)$$

where A is the activity in tumor (T) and normal tissue (N), respectively, and V is the corresponding volume of each of these regions.

Unfortunately, the poor resolution and noise properties of gamma cameras and PET make characterization of the dose distribution in tumors challenging. SPECT imaging of ^{90}Y requires additional processing to enhance image quality since images suffer from the low photon yield and positional uncertainties of bremsstrahlung interactions as well as scattered photons and septal penetration that result from the continuous high-energy spectrum (E_{max}: 2.28 MeV) that make window-based scatter rejection difficult.[7] Compared with bremsstrahlung, SPECT and PET images show superior contrast and resolution.[8] However, the low positron-branching ratio make for long scan times and noisy images.[9]

Here, we describe and compare the estimated absorbed dose distribution in resected HCC tissue at different levels of resolution, utilizing collected gamma camera images, ex vivo autoradiography measurements, activity quantification, and pathologic analysis.

Methods and materials

Radioembolization was performed at Sahlgrenska University Hospital as a neo-adjuvant treatment to lower the risk of recurrence at the resection boundaries for a 63-year-old man with a unifocal HCC in the noncirrhotic right lobe. All procedures were approved by the regional ethics review board in Gothenburg, Sweden and were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. A total of 2.0 GBq ^{90}Y resin microspheres were injected into the right lobe, which consisted of 450 ml and 1050 ml of tumor and normal tissue, respectively. SPECT images (Infinia Hawkeye, GE Healthcare, Milwaukee, WI) were collected for the pretherapeutic simulation with 150 MBq ^{99m}Technetium-MacroAggregate Albumin (^{99m}Tc-MAA; energy window: 126-154 keV) and similarly for ^{90}Y bremsstrahlung after the radioembolization (energy window: 55-285 keV). SPECT images were reconstructed using iterative, ordered-subset, expectation maximization with computed tomography (CT)-based attenuation correction. The normal and tumor areas were outlined in volumes of interest (VOI) for SPECT quantification using hepatic, arterial, phase CT images in the imaging platform PhONSAi developed in-house (T.Rydén et al.: Fast GPU-based Monte Carlo code for SPECT/CT reconstructions generates improved 177Lu images). The TNC was calculated from the counts in the normal liver VOI and the tumor VOI. The absorbed tumor doses were calculated applying the TNC values and assuming that the