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LETTER TO THE EDITOR

^{90}Y-radioembolization of hepatocellular carcinoma from a theranostic perspective: towards a personalized approach

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Dear Sir,

We have read with great interest the paper by Ho and colleagues describing the usefulness of dual tracer ^{11}C-acetate and ^{18}F-FDG PET-CT for the individualized dose calculation in patients affected by hepatocellular carcinoma submitted to treatment with ^{90}Y-labeled glass microspheres [1]. We would like to congratulate the authors for this publication and thank them for focusing on a relevant question. The two tracers (i.e., ^{11}C-acetate and ^{18}F-FDG) were proposed as complementary biochemical probes to characterize hepatocellular carcinoma before undergoing the administration of ^{90}Y-labeled glass microspheres, as the more aggressive hepatocellular lesions are generally ^{18}F-FDG-avid, while the more differentiated ones can be visualized using ^{11}C-acetate.

A growing amount of scientific data concerning ^{90}Y-radioembolization in hepatocellular carcinoma has demonstrated its significant impact on outcomes [2]. To date, ^{90}Y-radioembolization represents a well-standardized procedure in which two commercially available devices (glass or resin microspheres) can be used. In this scenario, the study performed by Ho and coworkers provides an opportunity to elaborate this innovative therapeutic approach from a theranostic perspective. The theranostic approach is a typical feature of nuclear medicine in which diagnostic imaging and therapy are often performed using the same molecules labeled with different radionuclides [3]. By extension, theranostics represent a combination of diagnostic and target therapy in order to achieve a personalized approach for every patient's needs and characteristics.

In this regard, the authors correlated the biological aggressiveness of hepatocellular carcinoma, determined by its affinity for ^{18}F-FDG or ^{11}C-acetate, with the dose delivered to the lesions, calculated on ^{90}Y-PET-CT, and the response to ^{90}Y-radioembolization assessed with PET-CT. As a higher cut-off in tumor dose/response was found in ^{18}F-FDG avid lesions in comparison with those detected by ^{11}C-acetate, an individualized algorithm has been proposed for the prescription of ^{90}Y-glass microspheres. In this context, PET imaging with a specific molecular probe was used to define the most appropriate therapeutic approach. However, it has to be pointed out that acetate is labeled with ^{11}C with a short 20-min half-life, limiting the use of this radiopharmaceutical only to PET-centers with on-site cyclotron. To overcome these drawbacks, ^{18}F-choline, a surrogate biomarker of membrane lipid synthesis, has been introduced for the PET imaging of well-differentiated hepatocellular carcinoma, with a sensitivity ranging from 63 to 100% [4]. In our experience, the complementary use of ^{18}F-FDG and ^{18}F-choline may be particularly useful for the PET evaluation of plurifocal hepatocellular carcinoma before ^{90}Y-radioembolization, as hepatic nodules within the same patient may present different grade of biological aggressiveness (Fig. 1).

It should be noted that Ho et al. [1] defined the response to ^{90}Y-treatment as a decrease in metabolic tumor volume calculated on the PET-CT performed 2 months after the procedure. Which the best time point and imaging method are to assess tumors following therapy with ^{90}Y-microspheres is still under debate. Nevertheless, several published papers suggested that an early metabolic evaluation of hepatic tumors after loco-regional treatments can be feasible as soon as 1 month after the procedure [5]. In a recent report from our group, the decrease in total lesion glycolysis (metabolic tumor volume × SUVmean) calculated on ^{18}F-FDG PET at baseline and 1 month after ^{90}Y-radioembolization resulted in a significant prognostic factor in patients affected by poorly differentiated

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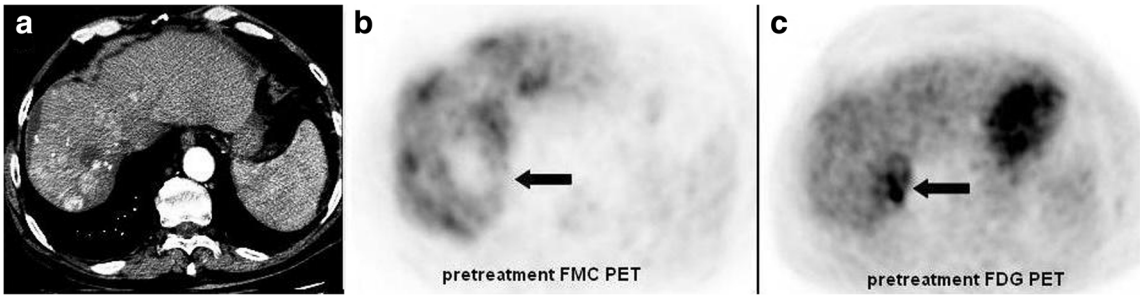

Fig. 1 Dual tracer ^{18}F-metilcholine (FMC) and ^{18}F-FDG PET-CT acquired in a 69-year-old male patient affected by plurifocal hepatocellular carcinoma submitted to ^{90}Y-radioembolization. **a** Contrast-enhanced multislice CT axial slice (arterial phase) showed multiple hypervascularized nodules in hepatic parenchyma. **b** FMC PET axial slice demonstrated multiple focuses of tracer uptake in liver and a relatively hypoactive area in the medial portion of the VII hepatic segment (*black arrow*). **c** ^{18}F-FDG PET axial slice detected focal tracer uptake in the medial portion of the VII hepatic segment (*black arrow*), thus demonstrating the presence of nodules at different grades of biological aggressiveness within the same patient

hepatocellular carcinoma and portal vein tumor thrombosis [6]. We believe that a metabolic evaluation of hepatic tumors after therapy with ^{90}Y-microspheres can be performed as early as at 1 month after therapy, in order to readily identify non-responders patients who would benefit from other therapeutic options.

It would be worthwhile to further investigate how much the complementary use of different PET molecular probes (i.e., ^{11}C-acetate, ^{18}F-choline, ^{18}F-FDG) might be useful for the biological characterization of hepatocellular carcinoma in order to achieve a personalized approach to ^{90}Y-radioembolization.

Compliance with ethical standards

Conflict of interest Luca Filippi, Orazio Schillaci, and Oreste Bagni declare that they have no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Not applicable, this is a Letter to the Editor.

References

1. Ho CL, Chen S, Cheung SK, et al. Radioembolization with ^{90}Y glass microspheres for hepatocellular carcinoma: significance of pretreatment ^{11}C-acetate and ^{18}F-FDG PET/CT and posttreatment ^{90}Y PET/CT in individualized dose prescription. Eur J Nucl Med Mol Imaging. 2018. https://doi.org/10.1007/s00259-018-4064-6.
2. Salem R, Lewandowski RJ, Kulik L, Wang E, Riaz A, Ryu RK, et al. Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma. Gastroenterology. 2011;140(2):497–507.
3. Ahmadzadehfar H, Essler M. It is time to move forward into the era of Theranostics. EJNMMI Res. 2018;8(1):9 https://doi.org/10.1186/s13550-018-0364-x.
4. Haug AR. Imaging of primary liver tumors with positron-emission tomography. Q J Nucl Med Mol Imaging. 2017;61(3):292–300 https://doi.org/10.23736/S1824-4785.17.02994-6.
5. Ma W, Jia J, Wang S, Bai W, Yi J, Bai M, et al. The prognostic value of 18F-FDG PET/CT for hepatocellular carcinoma treated with transarterial chemoembolization (TACE). Theranostics. 2014;4(7):736–44.
6. Filippi L, Di Costanzo GG, D'Agostini A, Tortora R, Pelle G, Cianni R, et al. Decrease in total lesion glycolysis and survival after yttrium-90-radioembolization in poorly differentiated hepatocellular carcinoma with portal vein tumour thrombosis. Nucl Med Commun. 2018. https://doi.org/10.1097/MNM.0000000000000879.