Answering reviewers

Comments from Reviewer No. 1560036:

1) Very good paper with only one question: You stated elsewhere that central necrosis is in all liver Mts from HAS. On the other hand, figure 1d and figure legend show that Mts had dense packed Lipiodol retention without the central necrotic area. I would like to know is it some contradiction? Or tumor necrosis is able to be densely enhanced by Lipiodol?

Response:

Thank you for raising this appropriate issue. In our study, we observed most of the liver metastases from HAS exhibited tumor necrosis regardless of tumor size. Our results also suggested that TACE, similarly to its role in HCC treatment, may serve as a local therapy for liver metastases of HAS.

For the HAS patient mentioned in Figure 1, we agree that the range of packed Lipiodol in liver tumors covered most part of the previous necrotic area. We believe this phenomenon is mainly caused by the passed Lipiodol droplets through the hepatic sinusoids into the central tumor necrosis. Similar to the pharmacokinetics in HCC, the oily nature of Lipiodol may allow transient dual (arterial and portal) embolization for the liver metastases of HAS [1]. When superselective TACE was done via the inserted microcatheter, the increased intravascular pressure and the relative leaky tumor microvessels would facilitate the injected Lipiodol to pass through the hepatic

sinusoids into the central necrosis [2]. The other possible minor mechanism to explain the smaller central necrotic region in the liver metastasis of HAS after the TACE is the influence of the metallic artifact from injected Lipiodol.

Reference:

1. Kan Z. Acta Radiologica 1996;37:7–24.
2. Zhu AX, et al. Nature Reviews Clinical Oncology 2011;8:292–301.

On behalf of all authors,

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