

# First evidence for a dose-response relationship in hepatic holmium-166 radioembolization

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## Background

Radioembolization is an intra-arterial therapeutic procedure with the aim to deliver a tumoricidal dose to tumors while sparing the healthy liver tissue. Since treatment with holmium-166 (<sup>166</sup>Ho)-microspheres can be preceded by a scout dose of identical microspheres that are imageable using SPECT, the treatment can be personalized based on pre-treatment quantification. To this end, a dose-effect relationship needs to be established, which is the aim of this study.

## Methods

Patients who were treated in the clinical phase 2 HEPAR II study and who underwent an FDG PET scan at baseline, at three months follow-up, and a post-therapy <sup>166</sup>Ho-SPECT/CT scan, were included for analysis.

The dose-response relationship was assessed by relating the change in total lesion glycolysis (TLG) between baseline and follow-up to measured absorbed tumor dose.

The <sup>166</sup>Ho-microspheres activity distributions following treatment were estimated with quantitative SPECT/CT reconstructions using a pre-calibrated fast Monte Carlo-based reconstructor (UMCS), which has been previously validated for <sup>166</sup>Ho.

Lesion masks were defined on baseline FDG-PET (PERCIST; threshold  $2 \times \text{SUL}_{\text{mean}}$  in aortic blood pool). The masks were transferred to the corresponding <sup>166</sup>Ho-SPECT reconstructions following affine co-registration of the CT scans of the PET and SPECT acquisitions. The tumor doses were estimated using these transferred masks. The entire microsphere dose was assumed to be absorbed in the 5x5x5 mm SPECT voxel.

Response was categorized according to the PERCIST criteria: complete response (CR) if 100% decrease in TLG; partial response (PR) if TLG decrease  $\geq 45\%$ ; progressive disease (PD) if TLG increase  $\geq 75\%$ ; otherwise stable disease (SD).

## Results

In total 30 patients with a total of 88 lesions were included. The lesions were categorized as CR (n=31), PR (n=17), SD (n=30) or PD (n=10). The corresponding median absorbed doses were 192 Gy (range 35-905) for CR, 138 Gy (6-608) for PR, 126 Gy (62-375) for SD and 78 Gy (38-204) for PD.

An objective response (CR and PR) was observed in 48 lesions (55%). Doses in these lesions were significantly higher than doses in lesions without objective response (Mann-Whitney U=604.0,  $z=-2.983$ ,  $p=0.003$ ).

## Conclusion

In this study, we have established that there is a significant effect of absorbed dose on lesion response in <sup>166</sup>Ho radioembolization, according to the PERCIST criteria. Further analysis will stratify these results according to tumor type and provide a dose threshold needed for a reliable tumor response.

Dear Sir, Madam,

We hereby submit our abstract on a dose-response relationship in hepatic holmium-166 radioembolization.

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Kind regards,

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