practice, but we acknowledge that it has to be confirmed with other studies and hope there will be a lot of further work on this topic.

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Lung Shunting: An Indicator of Survival, But Not Necessarily a Tool for Selecting Patients for Radioembolization

From

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Editor:

We read with great interest the article by Dr Narsinh and colleagues on lung shunt fraction (LSF) as a predictor of survival, which was recently published online in *Radiology* (1). The estimation of hepatopulmonary shunting is an essential part of radioembolization work-up, but can technetium 99m (^{99m}Tc) macroaggregated albumin (MAA) accurately predict LSF? A recent study in patients with liver metastasis showed that ^{99m}Tc-MAA structurally overestimates LSF when compared to the actual LSF after treatment (2). This can lead to inadequate exclusion of patients or a reduction of prescribed activity. The overestimation is even worse when non-attenuation-corrected single photon emission computed tomography (SPECT) or planar imaging is used.

Given these circumstances, it seems remarkable that Dr Narsinh and colleagues found LSF to be a predictor of survival. In their study, patients with an LSF greater than 10% had a 6.9-month survival, compared with a survival of 10.0 months for patients with a lower LSF. First of all, it is not specified in this article if outcome was corrected for administered activity and tumor dosimetry. Patients with a high LSF likely received a reduced amount of activity based on their LSF, which could have influenced tumor absorbed doses and outcome by itself. In addition, we think it is essential to include dosimetric parameters in the analysis because tumor absorbed doses are known to correlate with outcome (3,4).

Second, imaging of ^{99m}Tc-MAA more than 1 hour after injection can lead to an increased LSF (the study by Narsinh and colleagues used a 2-hour limit) (5). Most importantly, however, LSF was calculated with planar imaging only, which is known to overestimate LSF. Factors causing overestimation may include spillover of liver counts in the lungs due to organ overlap, scatter, and respiratory motion (2). It would be interesting to study whether LSF is still an independent prognostic factor, or perhaps an even stronger prognostic factor, in case LSF is more accurately calculated by using attenuation- and scatter-corrected SPECT/computed tomography (CT).

LSF as a prognostic factor could reflect a more aggressive tumor with immature vessels that allow arteriovenous shunting. Although these patients have a worse prognosis, it does not imply that they benefit less from radioembolization than do patients with an LSF of 10% or less. Therefore, there is at this moment no reason to withhold therapy from patients with an LSF greater than 10%.

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Response

From
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We greatly appreciate the interest and previous work of Dr Smits and colleagues with regard to the measurement and significance of LSF among patients undergoing radioembolization. Because patient survival has been found to correlate to tumor absorbed dose (1,2), we did investigate whether administered activity bore any relationship to LSF. However, we found that administered activity did not correlate with LSF in the cohort (Spearman correlation coefficient $\rho = -0.019$, $P = .65$, $n = 592$). Although the median and mean administered activity was slightly reduced in the group of patients with LSF of at least 20%, there was a considerable range of administered activity overlapping in all LSF categories, as dosing is also determined by body surface area and percentage tumor involvement (mean administered activity = 1.15 GBq ± 0.39 in patients with LSF ≤10% vs 1.11 GBq ± 0.36 in patients with LSF >10%).

^{99m}Tc-MAA scintigraphy may not model yttrium 90 (^{90}Y) microsphere distribution well. For example, Elschot et al (3) demonstrated that, when using holmium 166 (^{166}Ho) microspheres for treatment, LSF is often overestimated with ^{99m}Tc-MAA scintigraphy. This finding perhaps explains the low observed toxicity rate among patients receiving an absorbed lung dose calculated as more than 30 Gy (4). Our study was limited in its retrospective nature and inability to include novel techniques for improved radiation dosimetry (5). We look forward to future studies improving radiation dosimetry and treatment planning through a variety of strategies, including *(a)* development of better prescribed activity calculation methods for ^{90}Y resin microspheres that account for liver mass, lung mass, and microsphere distribution; *(b)* administering a scout dose of ^{90}Y microspheres followed by ^{90}Y positron emission tomography/CT (6); *(c)* administering a scout dose of ^{166}Ho microspheres followed by ^{166}Ho SPECT/CT that is attenuation- and scatter-corrected (3); and/or *(d)* incorporating expected reductions in LSF from adjunctive measures (eg, temporary balloon occlusion [7] or transarterial embolization [8]) into treatment planning. We agree that improved alternatives to ^{99m}Tc-MAA scintigraphy are needed to develop accurate and patient-specific radiation dosimetry plans, particularly if overestimation of calculated LSF is resulting in subtherapeutic treatment dosing in many patients.

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