avoidance of radiomicrosphere hepatotoxicity (*3*). The converse is true: only a minority, that is, 16%, of patients may be at risk of significant tumor under-dosing or inadvertent radiomicrosphere hepatotoxicity. Considering the general complexity of $^{90}$Y radioembolization, most physicians will find these treatment odds favorable and consistent with best practice in the modern era of personalized medicine.

A conservative mean T/N ratio of 2 was used in this example of colorectal liver metastasis. Most patients have higher, more favorable mean T/N ratios (*4*), which enable deliberate escalation of the intended tumor mean absorbed dose beyond 120 Gy when within safety limitations to the nontumorous liver and lung. Hence, many patients can achieve better dosimetric results than presented in this example. Equation 1 has an infinite number of possible dosimetric scenarios, which the reader is encouraged to explore. A thorough understanding of the interplay between mean T/N ratios, intended mean absorbed doses, tissue masses, and hepatopulmonary shunting is paramount for safe and effective predictive dosimetry by partition modeling (*2,4*).

It has been common knowledge for years that $^{99m}$Tc-MAA is an imperfect surrogate for $^{90}$Y-resin microspheres (*5*), and no study has claimed otherwise. $^{99m}$Tc-MAA should be regarded as a tool, and the usefulness of any tool is only as good as its user and the complexity of the task at hand. For basic predictive dosimetry, partition modeling can be performed using a pocket calculator (*2*), and SPECT/CT (*4*) is now widely available to replace planar $^{99m}$Tc-MAA scintigraphy. For advanced predictive dosimetry, affordable and increasingly powerful computers and software can rapidly generate dose–volume histograms from $^{99m}$Tc-MAA SPECT/CT data (*6*). Correlation of $^{90}$Y SPECT or $^{90}$Y PET dose distributions with $^{99m}$Tc-MAA and newer microspheres as they appear will add further confidence in the utility of the treatment planning procedure, but for the moment, it is reasonable to proceed with $^{99m}$Tc-MAA. Today, the major barrier to the routine application of predictive dosimetry for $^{90}$Y radioembolization is no longer the state of the art but rather the state of our hearts.

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**Yung Hsiang Kao**
*Austin Hospital*
*Level 1, Harold Stokes Building*
*145 Studley Rd.*
*Melbourne, Victoria 3084, Australia*
*E-mail: yung.h.kao@gmail.com*



Published online Nov. 6, 2013.
DOI: 10.2967/jnumed.113.128553


**REPLY:** With great interest we read Dr. Kao's comments on our work. Advanced dosimetry and individualized treatment planning play a crucial role in further development and optimization of hepatic $^{90}$Y radioembolization. Pretreatment scout dose imaging is an important tool for this purpose. In our publication, we showed the limitations of $^{99m}$Tc-macroaggregated albumin ($^{99m}$Tc-MAA) as a scout dose to predict subsequent intrahepatic $^{90}$Y distribution (*1*). In 68% of all 225 evaluated liver segments (according to Couinaud's liver segmentation), a difference of more than 10% between $^{99m}$Tc-MAA and $^{90}$Y activity distribution was found. A difference of more than 20% and more than 30% of the mean activity per milliliter was found in, respectively, 97 (43%) and 72 (32%) of 225 segments. The overall mean difference between pretreatment and posttreatment distribution of activity concentration for all segments was −0.022 MBq/mL, with 95% limits of agreement of −0.581 to 0.537 MBq/mL (−28.9 to 26.7 Gy absorbed dose). Dr. Kao translated these findings to clinical practice and ultimately emphasized the utility of $^{99m}$Tc-MAA scout dose imaging for individualized treatment planning, using the so-called partition model (*2*), regardless of the reported limitations. We fully agree with Dr. Kao's suggestion that the drawbacks of scout dose imaging should not withhold us from using advanced treatment planning techniques, especially because the alternative methods, the often-used body surface area–based method for resin microspheres and the whole liver volume–based method for glass microspheres, leave much room for improvement and are highly inaccurate from a dosimetry perspective.

It is generally true that the partition method leads to higher administered activities, because it takes the differential dose between tumorous and nontumorous tissue (T/N ratio) into account, which is usually greater than 1 (*3*). In the example given by Dr. Kao, the aimed tumor-absorbed dose is 120 Gy. Because of expected differences between $^{99m}$Tc-MAA and $^{90}$Y distribution, the final expected tumor dose will not be 120 Gy in every patient, but a tumor dose greater than 90 Gy may still be reached in as many as 84% of the patients. This seems acceptable indeed. Moreover, this percentage will further increase with improvements in radioembolization techniques focused on diminishing the discrepancies between $^{99m}$Tc-MAA and $^{90}$Y distribution, such as selective administrations distal to major bifurcations and major side branches. In our study, these factors significantly influenced the distribution differences between $^{99m}$Tc-MAA and $^{90}$Y (*1*).

On the other hand, one has to keep in mind that it is not the absorbed dose to the tumors but rather the absorbed dose to the nontumorous liver tissue that is the dose-limiting factor, especially for whole-liver treatments. In Dr. Kao's example, the target nontumorous liver dose of 60 Gy will not be met in a significant number of patients. According to Dr. Kao's analysis, the upper acceptable limit of 70 Gy is expected to be crossed in as many as 16% of the patients. In the light of radioembolization-induced liver disease as a potential complication after high-dose radioembolization, this number seems to be unacceptably high. One should therefore choose a conservative approach when using the partition method for whole-liver treatments. In addition, Dr. Kao's scenario was sketched for a T/N ratio of 2; higher T/N ratios will lead to lower nontumorous liver doses. The uncertainty in estimating the nontumorous liver dose will then be less relevant. For lobar treatments, in which the partition method is mostly used today, the nontumorous dose is of course not that important because the contralateral lobe will be spared.

Although the partition method is definitely the preferred method in every radioembolization patient, its use in clinical practice is still limited. Besides the limited predictive value of $^{99m}$Tc-MAA scout dose imaging, the method is mostly hampered by segmentation difficulties. Delineation of the tumorous and nontumorous tissue is time-consuming and sometimes downright impossible because of the number and diffuse growth pattern of the tumors (*3*). Current research efforts therefore focus on new-generation scout dose microspheres (*4*), advanced administration techniques using specialized catheters (*5*), and improved image-fusion and segmentation techniques (*6*) to overcome these hurdles and move toward individualized treatment planning in radioembolization. The found limitations of $^{99m}$Tc-MAA scout dose imaging should be kept in mind when one is using it for treatment planning but should not stop us from aiming for optimized radioembolization dose planning.

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**Marnix G.E.H. Lam***
**Maurits Wondergem**
**Mattijs Elschot**
**Maarten L.J. Smits**
**University Medical Center Utrecht*
*Heidelberglaan 100*
*3584 CX Utrecht, The Netherlands.*
*E-mail: m.lam@umcutrecht.nl*



Published online Nov. 6, 2013.
DOI: 10.2967/jnumed.113.132852