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LETTER TO THE EDITOR

Reply

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Dear Sir,

We appreciate the interest of Dr. Durand and colleagues in our study "In vivo radionuclide uptake quantification using a multi-pinhole SPECT system to predict renal function in small animals" [1], in which we showed a high agreement between the radioactivities determined in vivo by SPECT and ex vivo in a gamma counter. We would like to take this opportunity to respond to their specific comments:

1. Concerning statistics, Durand et al. suggest that the standard error of estimate would have been more appropriate for analysis of our data. We agree that the regression analysis that we used was somewhat rudimentary. However, the article referred to [2] describes the comparison of two indirect, unrelated measurement methods with an unknown true value. In contrast, in our study we compared radioactivity levels determined in vivo by SPECT with values determined ex vivo in the gamma counter. In this experimental setting, the gamma counter is our gold standard. In our opinion the regression analysis appears to be the right method; however, indication of the confidence and prediction intervals of the regression curve would have improved the significance. We indicate these values in Fig. 1 of this reply.
2. In the second paragraph of their letter [3], Durand et al. dispute whether it is possible to assess renal function with the technique described, as they do not consider absolute DMSA uptake a valid marker for renal function. We are convinced that the new technique, multi-pinhole SPECT, can indeed be used to assess renal function in vivo. The reference given [4] describes considerable overestimations of renal function in a model assuming unilateral kidney function impairment. However, the use of high-dose peptide receptor radionuclide therapy (PRRT) with [^{177}Lu-DOTA^{0},Tyr^{3}]octreotate results in a symmetrical reduction of renal function. Therefore, the model cited [4] does not apply to our experimental setting. Furthermore, we found a convincing relation between the ^{99m}Tc-DMSA uptake and 1/creatinine (r^2=0.772, p<0.001) (Fig. 2) as well as a relation between the reduction of ^{99m}Tc-DMSA uptake and total protein excretion into the urine in rats [5, 6], showing the value of ^{99m}Tc-DMSA in assessing renal function after PRRT.

Neither in the title nor in the introduction had we focussed exclusively on ^{99m}Tc-DMSA. The aim of this work was to validate NanoSPECT for the assessment of renal function in vivo after PRRT. ^{99m}Tc-DMSA appeared to be a suitable tracer for this purpose. However, the high sensitivity of the camera allows the acquisition times to be kept very short, which in turn allows dynamic SPECT imaging. Therefore it is, for example, also possible to acquire and quantify dynamic ^{99m}Tc-MAG3 SPECT images [7]. Considering the whole collection of tracers available, it would be possible to investigate and quantify different aspects of renal function in vivo with the technique described, as indicated in the title of our manuscript [1].

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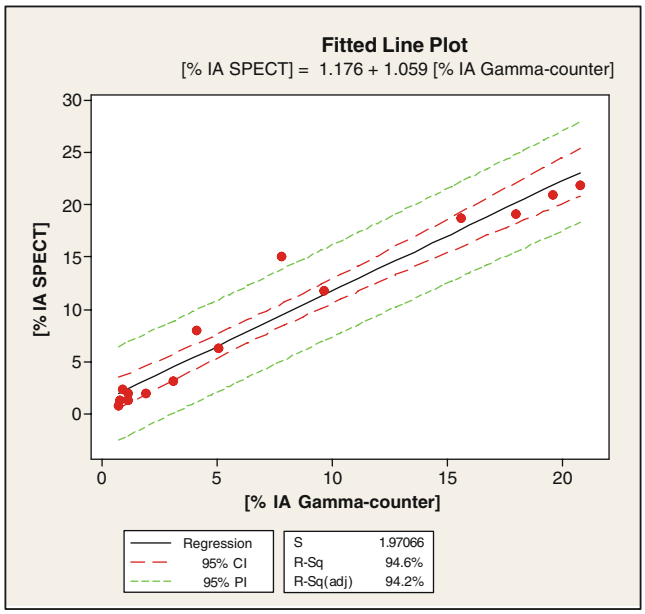

Fig. 1 Linear regression analysis of the data from [1], with indication of the 95% confidence interval (*CI*) and the prediction interval (*PI*)

3. We fully agree that the description of the pharmacokinetics of ^{99m}Tc-DMSA was somewhat basic. This was done because our manuscript is a short communication to prove a principle and to demonstrate the potential of a new technique. ^{99m}Tc-DMSA was not the main focus of this article.

The renal handling of ^{99m}Tc-DMSA is the source of controversy, and besides peritubular uptake several authors have reported tubular reabsorption as well [8, 9].

4. As stated in the fourth paragraph of the letter from Durand et al., it has indeed been questioned whether ^{99m}Tc-DMSA is a marker of tubular function. It is, however, indisputable that ^{99m}Tc-DMSA is a marker for functioning tubules. Again, we would like to point out that we found a very good relation between ^{99m}Tc-DMSA uptake and generally accepted clinical markers. We therefore believe that ^{99m}Tc-DMSA is an excellent marker to quantify renal function in rats after high-dose PRRT with [^{177}Lu-DOTA^0,Tyr^3]octreotate and we shall continue to use this technique in this setting.

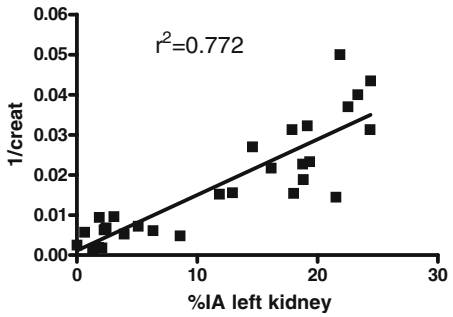

Fig. 2 Linear correlation of percentage injected activity (%IA) in the left kidney 4 h after injection of 50 MBq ^{99m}Tc-DMSA measured with NanoSPECT (x-axis) and 1/creatinine values (y-axis) in rats treated with 278 or 555 MBq [^{177}Lu-DOTA^0,Tyr^3]octreotate with or without amifostine or D-lysine as renoprotective drugs [6]

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