(perhaps by the liver). It is well recognized that the retention of ^{111}In-B72.3 by normal liver tissue is greater than that for ^{131}I-B72.3 (*3*).

The more rapid distribution of ^{131}I-B72.3 from the central to the peripheral compartments is indicated by the much shorter mean transit time in the central compartment (MTTc) for ^{131}I-B72.3 than for ^{111}In-B72.3 (9 hr versus 41 hr, respectively). Analogous to the situation in the peripheral compartment, the mean residence time in the central compartment (MRTc) was similar for ^{131}I-B72.3 and ^{111}In-B72.3 despite the much shorter MTTc for ^{131}I-B72.3. This once again suggests much greater recycling of ^{131}I-B72.3 from the peripheral back to the central compartment. A much longer time is spent by an individual indium-labeled B72.3 molecule in passing through the central compartment than is spent by an iodine-labeled B72.3 molecule. Iodine-labeled B72.3 is recirculated between the central and peripheral compartments a greater number of times (n = 14.6) than indium-labeled B72.3 (n = 4.5).

The most important difference between our results and those of Dr. Webster is that we did not detect an effect of elevated levels (>4 U/ml) of circulating TAG-72 antigen on the values for various pharmacokinetic parameters associated with ^{131}I-B72.3. We could find no difference in distribution half-life ($T1/2\alpha$), elimination half-life ($T1/2\beta$), mean residence times in the body (MRT_B) or central compartment (MRTc), mean transit times in the central compartment (MTTc) or probability of distribution (PRD).

In the study by Dr. Webster, the mean $t1/2\alpha$ for ^{111}In-B72.3 was much shorter in patients with elevated serum TAG-72 than in those patients with normal serum TAG-72 levels (0.2 versus 12.3 hr respectively). In our study with ^{131}I-B72.3, the mean $T1/2\alpha$ was very similar for patients with elevated or normal serum TAG-72 (1.8 versus 2.2 hr respectively). The mean $t1/2\beta$ for ^{111}In-B72.3 was 74 hr in patients with normal serum TAG-72 but only 34.8 hr in patients with elevated serum TAG-72. In comparison, the $T1/2\beta$ for ^{131}I-B72.3 was similar for patients with normal or elevated serum TAG-72 (56 versus 62 hr, respectively). The MRT_B was also much shorter for ^{111}In-B72.3 in patients with elevated serum TAG-72 (50.1 hr) compared to those with normal serum TAG-72 (100 hr). In our study of ^{131}I-B72.3, the MRT_B was similar for patients with elevated or normal serum TAG-72 (88.5 versus 79.8 hr, respectively). The MRTc was shorter and the MTTc was much shorter for ^{111}In-B72.3 in patients with elevated serum TAG-72 compared to those with normal TAG-72 (43.5 versus 79.0 hr and 2.1 versus 40.5 hr, respectively). Once again, in our study of ^{131}I-B72.3, the MRTc and MTTc were very similar for patients with elevated and normal serum TAG-72 (59.6 versus 59.8 hr and 7.1 versus 10.1 hr, respectively). Finally, the PRD was much higher for ^{111}In-B72.3 if the patients exhibited elevated serum TAG-72 (95.2%) than if the serum TAG-72 was normal (50.2%). In our study, the PRD for ^{131}I-B72.3 was almost identical for patients with elevated or normal serum TAG-72 (89.3 versus 87.8%, respectively).

Although evidence of immune complex formation in the serum is not shown in the paper by Dr. Webster, it is proposed that rapid formation of antibody-antigen complexes in the serum may be responsible for the decreased $T1/2\alpha$ and MRTc for ^{111}In-B72.3 in patients with elevated TAG-72 in the serum. In our study, less than 10% immune complexes were detected by FPLC when serum from patients with elevated TAG-72 was incubated in vitro with ^{131}I-B72.3. This may partially explain the fact that we did not find a significant difference in pharmacokinetics in patients with elevated serum TAG-72. We were unable to detect significant levels of immune complexes in the serum of such patients despite in-vitro testing of the ^{131}I-B72.3 which demonstrated an immunoreactivity ranging from 40%–70% as well as positive radioimmunoscintigraphy results in these patients.

No hypothesis for the decrease in MRT_B for ^{111}In-B72.3 in patients with elevated serum TAG-72 is proposed by Dr. Webster, however one possible explanation may be that the formation of immune complexes in the serum may result in increased RES uptake and subsequent degradation of the radiolabeled antibody. A similar phenomenon has been previously reported for ^{131}I-HMFG1 antibody which was administered to patients with high levels of HAMA (*6*).

It is important to realize that although statistical moment theory and mean time parameters may allow a comparison of the disposition characteristics of various radiopharmaceuticals, experimental evidence is not as yet available to definitively assign biological interpretations to these parameters. Nevertheless, it allows one to speculate as to the biological behavior of various radiopharmaceuticals based on a pharmacokinetic non-compartmental model approach. The study by Dr. Webster and colleagues has provided the stimulus for such an approach to the analysis of pharmacokinetic data obtained in clinical trials of radiolabeled monoclonal antibodies. This type of analysis may provide new insights into the different disposition characteristics of these antibodies labeled with different radionuclides. An awareness of these characteristics will be very useful in deciding on the appropriate immunopharmaceutical for use in imaging or therapy studies in cancer patients.

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REPLY: Reilly and Thiessen have raised a question about the influence of specific antigen TAG-72 on the pharmacokinetics of ^{111}In-B72.3. They did not observe an effect for ^{131}I-B72.3 with TAG-72 serum concentrations >4 U/ml. We feel this is most likely due to clearance of the ^{131}I-B72.3 radioactivity by dehalogenation and urinary excretion when compared to the clearance of ^{111}In-B72.3 radioactivity by tissue deposition and less by urinary excretion (*1*). However, we feel our most important finding

was the suggestion of a different pharmacokinetic profile for patients without tumor secreting the specific antigen TAG-72.

The differences in MRT_B, a widely reported (but poorly understood) parameter should be emphasized. Yokoyama et al. (*2*) showed that whole-body clearance of ^{131}I-B72.3 correlated with the urinary excretion of activity, while the clearance of ^{111}In-B72.3 was not correlated with excretion. It is important to note the definition of AUMC/AUC (MRT_B). This parameter represents the aggregate residence time of molecules *eliminated* from the body and not the residence time of the remaining activity.

Several other points are raised by Reilly and Thiessen. We have not investigated in vitro immune complex formation with patients' serum, but we have previously reported that the circulating activity at 8 days after administration appears to be the intact antibody (*2*). In our report in the *Journal* (*3*), we noted that similar volumes of distribution for ^{111}In-B72.3 have been reported by others. We look forward to the complete report for ^{131}I-B72.3, soon to be published by Reilly et al. (*4*).

Lastly, we call attention to the assumptions associated with traditional pharmacokinetics that limit the validity for volumes of distribution and half-life. Accurate pharmacokinetic representation requires that the terminal phase be followed to >90% elimination and that elimination be from a single compartment. We cannot make these assumptions with Mabs radiolabeled with ^{111}In, which have a physical half-life of 2.83 days and are eliminated from both the vascular and tissue compartment. For mean time pharmacokinetics, it is only necessary to assume linear elimination (not distribution) of activity. The objective of our article (*3*) was to apply mean time pharmacokinetic methods and models to radiolabeled Mabs. The addition by Reilly et al. (*4*) of mean time pharmacokinetic studies with Mabs radiolabeled with ^{131}I increases our knowledge of the temporal distribution of Mab activity.

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CORRECTION

Due to a production error, Figures 1 and 3 in the article "Correction for Attenuation in Technetium-99m-HMPAO SPECT Brain Imaging" by Kemp et al. were printed incorrectly. The corrected figures are printed below.

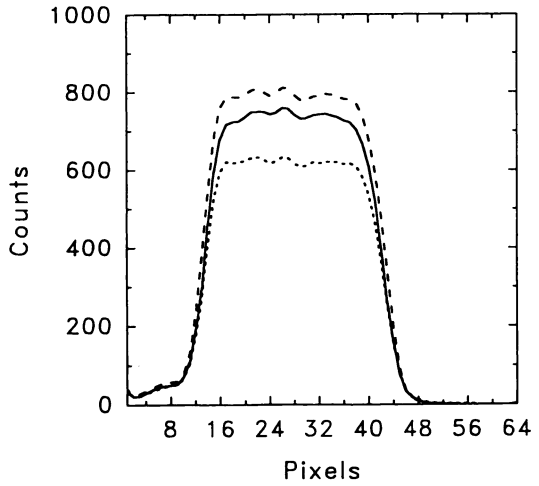

FIGURE 1. Profiles through images of the human skull filled with a uniform mixture of ^{99m}Tc and gelatin. Solid line: image corrected for attenuation with $\mu_w = 0.12$ cm^{-1}; dotted line: image corrected for attenuation with $\mu_w = 0.09$ cm^{-1}; dashed line: image corrected for attenuation with $\mu_w = 0.12$ cm^{-1} and $\mu_b = 0.15$ cm^{-1}. Note the increase in the count density at the center compared to the edges when the image is corrected for water attenuation with $\mu_w = 0.12$ cm^{-1}.

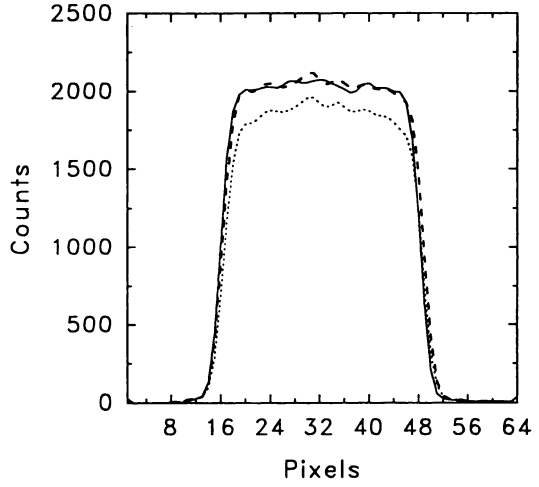

FIGURE 3. Profiles through images of the Jaszczak phantom filled with a uniform mixture of ^{99m}Tc and water. Solid line: phantom without aluminum, $\mu_w = 0.12$ cm^{-1}; dotted line: phantom with aluminum, $\mu_w = 0.12$ cm^{-1}; dashed line: phantom with aluminum, $\mu_w = 0.12$ cm^{-1}; $\mu_a = 0.27$ cm^{-1}.