ameter is not linear, and therefore it is difficult to make a generally applicable statement about sensitivity. We recommended a standardized phantom 15 cm in diameter to represent the head, and one 25 cm in diameter to represent the body, because these are close to the average dimensions of the ellipses describing the MIRD standard man's head and torso (excluding the arms) (*4*). We disagree with the use of a steel-walled phantom, because of its inhuman attenuation characteristics.

We all believe that standardized measurements have become a necessity, but we must beware of blind acceptance of excessively simplified statements of performance (*1*,*5*. As Einstein said: "We should make things as simple as possible, but no simpler."

JONATHAN M. LINKS
HENRY N. WAGNER, JR.
The Johns Hopkins Medical Institutions
Baltimore, Maryland

FOOTNOTE

* Popper & Sons, Inc., 300 Denton Ave., New Hyde Park, NY 11040.

REFERENCES

1 LINKS JM, WAGNER HN: Specification of performance of positron emission tomography scanners. *J Nucl Med* 23:82, 1982
2. PHELPS ME, HOFFMAN EJ, HUANG SC, et al: Effect of positron range on spatial resolution. *J Nucl Med* 16:649-652, 1975
3. DERENZO SE: Precision measurement of annihilation point spread distributions for medically important positron emitters. Lawrence Berkeley Laboratory Report LBL-9169, 1979
4. SNYDER WS, FISHER HL, FORD MR, et al: Estimates of absorbed fractions for monoenergetic photon sources uniformly distributed in various organs of a heterogeneous phantom. *J Nucl Med* MIRD Supplement 3, 1969
5. HOFFMAN EJ: Comments on specifying the performance of a positron tomograph. *J Nucl Med* 23:82-83, 1982

Quantification of In Vivo Distribution of Platelets Labeled with Indium-111 Oxine

The recent paper by Scheffel et al. (*1*) in the *Journal of Nuclear Medicine* raises some important questions in regard to the sites of platelet sequestration and the accuracy of the different methods used to quantitate the in vivo distribution of platelets labeled with In-111 oxine. The observation that there is no appreciable increase in splenic and hepatic radioactivity at the end of platelet life span raises the question of where the nearly 50% of the injected dose that remained unaccounted for was deposited, and whether this occurs in the bone marrow as has been suggested by Klonizakis et al (*2*).

We have improved the accuracy of our original method (*3*) of in vivo quantification of In-111-labeled platelets in organs (*4*) and present some of the relevant results with this method. This may throw some light on the sites of final disposal of platelets.

Briefly, autologous platelets were labeled with In-111 oxine as previously described (*5*). Anterior and posterior images of the whole body were acquired every second day with a scintillation camera and a computer-assisted imaging system. The geometrical mean method of correcting for attenuation was used for in vivo measurement of whole-body and organ radioactivity. Distribution of In-111 activity at equilibrium and at the end of platelet life span was determined by fitting the data with the method of linear least squares regression analysis. The geometrical mean counts were expressed as a percentage of the total body's geometrical counts to eliminate the effect of scintillation camera efficiency calibration and the influence of organ radiation attenuation. The corrected counts calculated by this method represent the radioactivity of the organ as if it were situated in the mid anteroposterior plane of the body (*4*).

The results of In-111 distribution, at equilibrium and at the end of platelet survival, as measured in normal volunteers are given in Table 1. There was a slight but significant increase in splenic radioactivity with time. Hepatic activity increased threefold. Total-body In-111 activity decreased minimally.

The accuracy of the method of quantification was verified, and the sites of deposition of In-111 determined in 10 baboons (*Papio ursinus*). The equilibrium and final in vivo In-111 distributions, determined with the scintillation camera, are given in Table 2. Radioactivity in both the liver and spleen increased. In the baboon the spleen is a more active site of platelet sequestration than in man, but hepatic activity increased twofold with time. The baboons were killed at the end of the study and the excised organs measured. As is evident from Table 2, there is a close agreement between in vivo and ex vivo measurements. Dissection of the skeleton revealed that (14.4 ± 1.7)% of radioactivity was located in the bone marrow at the end of platelet life span. Most of the In-111 activity lumped under "other organs" was accounted for by muscle and skin (6.7 ± 1.4)%, gastrointestinal system (4.9 ± 1.6)%, and kidneys (2.5 ± 0.6)%.

These results, and studies performed in a phantom (*4*), clearly validate the accuracy of the geometrical mean method for the in vivo quantification of In-111 activity.

The discrepancies between our results and those of Scheffel et al. (*1*) are difficult to explain if they are not due to differences in the techniques of In-111 quantification. We find it difficult to accept the suggestion that the bone marrow is responsible for 35-40% of platelet sequestration (*2*). The bone-marrow activity of 14.4% that we found in the baboon corresponds closely to the 14% measured in rabbits (*1*). Our results favor the liver as a major site of platelet sequestration. Analysis of the data given by Scheffel et al. (*1*) in their Table 4 with Student's t-test for paired data also shows that hepatic activity in subjects 1, 4, 6, 7, 8, and 9 increased significantly ($P < 0.01$) during the time from 90 min after injection of labeled platelets to the final measurement of In-111 activity. Although the spleen, liver, and bone marrow are the major components of the reticuloendothelial system, the wide distribution of this tissue throughout the body may account for the final distribution of the remainder of In-111 activity. Some platelets may also be utilized in the vascular system, but we have not been able to measure this in vivo in normal subjects (*3*).

TABLE 1. IN VIVO QUANTIFICATION OF IN-111 ORGAN RADIOACTIVITY IN NORMAL HUMAN SUBJECTS (n = 6)

Organ	Equilibrium % activity	Final % activity
Whole body	100 ± 0	96.6 ± 5.2*
Spleen	31.1 ± 6.1	35.6 ± 9.7*
Liver	9.6 ± 1.2	28.7 ± 8.3*

* Whole-body In-111 activity did not decrease significantly ($p > 0.1$), but that of the spleen ($p < 0.01$) and liver ($p < 0.005$) did increase significantly with time (student's t-test for paired data).

TABLE 2. IN VIVO AND EX VIVO QUANTIFICATION OF IN-111 RADIOACTIVITY IN BABOONS (n = 10)

Organ	In Vivo Quantification: Equilibrium % activity	In Vivo Quantification: Final % activity	Ex Vivo Quantification
Whole body	100 ± 0	95.2 ± 3.7*	100 ± 0
Spleen	17.3 ± 3.2	33.5 ± 3.1*	33.7 ± 5†
Liver	15.6 ± 2.0	35.2 ± 6.5*	36.7 ± 7.1†
Bone marrow	—	—	14.4 ± 1.7
Other organs	68.1 ± 4.5	31.4 ± 4	15.5 ± 4.0

* Whole-body In-111 activity did not decrease significantly ($p > 0.05$), but that in the spleen ($p < 0.001$) and liver ($p < 0.0005$) did increase highly significantly with time. (Student's t-test for paired data).
† In vivo and ex vivo quantification of splenic and hepatic In-111 activity did not differ statistically ($p > 0.1$).

Our results confirm the validity of the geometrical mean method for the in vivo quantification of labeled platelets. The results also confirm the findings of Aster (*6*), who in his classical studies showed that the liver and spleen are the major sites of platelet sequestration. The role of the bone marrow has certainly been underestimated in this regard, but it seems to play a relatively subsidiary role to that of the liver and spleen.

ANTHON DUP HEYNS
MATTHEUS G LÖTTER
HARRY F KOTZÉ
HENRY PIETERS
PAULA WESSELS
University of the Orange Free State
Orange Free State
Republic of South Africa

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REFERENCES

1. SCHEFFEL U, TSAN M-F, MITCHEL TG, et al: Human platelets labeled with In-111 8-Hydroxyquinoline: Kinetics, distribution, and estimates of radiation dose. *J Nucl Med* 23: 149-156, 1982
2. KLONIZAKIS I, PETERS AM, FITZPATRICK ML, et al: Radionuclide distribution following injection of ^{111}Indium-labelled platelets. *Br J Haematol* 46:595-602, 1980
3. HEYNS A DUP, LÖTTER MG, BADENHORST PN, et al: Kinetics, distribution, and sites of destruction of ^{111}Indium labelled human platelets. *Br J Haematol* 44:269-280, 1980
4. VAN REENEN O, LÖTTER MG, HEYNS A DUP, et al: Quantification of the distribution of ^{111}In-labelled platelets in organs. *Eur J Nucl Med* 7:80-84, 1982
5. HEYNS A DUP, BADENHORST PN, PIETERS H, et al: Preparation of a viable population of Indium-111-labelled human blood platelets. *Throm Haemostas 42:* 1473-1482, 1980
6. ASTER RH: Studies of the fate of platelets in rats and man. *Blood* 34:117-128, 1969

Reply

We thank Dr. Heyns and his colleagues for their interest in our work with In-111 platelets and their comments on our recent paper in this Journal (*1*).

Since the publication of our paper (*1*), we have (a) validated our in-vivo quantification method based on the modified geometric mean for correction of attenuation, and (b) studied the role of bone marrow in the sequestration of platelets in rabbits (*2*). Our results, details to be published elsewhere, showed that there was good correlation between the values obtained by in vivo quantification and those obtained by postmortem measurements of the radioactivity in the liver and the spleen. In 32 rabbits, $r = 0.854$ for liver and 0.899 for spleen, and the ratios of in-vivo to sacrifice values were 1.05 and 1.10 respectively. Using this method, we also showed that after infusion, the In-111 platelets rapidly accumulated in these two organs, reaching 35% and 12% of the injected dose in the liver and spleen respectively by one day. Thereafter there was little change. On the sixth day, when In-111 platelets had cleared from the circulation, there was 40% in the liver, 14% in the spleen, and 28% in the bone marrow (Table 1). The radioactivity in the bone marrow was derived by assuming that the total bone-marrow mass in rabbits was 2.2% of the body weight (*3,4*). Our earlier estimate of 14% (*1*) was based on measurements we made on three complete rabbit skeletons, freed from adhering muscle and fat after autoclaving the carcass. The radioactivity in bone (approximately 3%) had been subtracted from the total skeleton activity. We suspect that some of the In-111 in the bone marrow may have been lost during autoclaving. Therefore, in our current study, we have used the previously published values (*3,4*) in estimating rabbit bone-marrow mass.

Our results suggest that in addition to liver and spleen, bone marrow plays an important role in sequestering platelets in rabbits. Our results in humans and rabbits (*1,2*) differ from those of Heyns et al. (*5*) in that there was little change of the radioactivity in the liver and spleen after one day. We postulate that the initial localization of In-111 platelets in the liver and spleen was in part due to pooling, while at later days, it was due to sequestration of platelets by the macrophage system in these organs. The role of bone marrow in the sequestration of platelets in man is not clear, since no direct measurement in humans have been carried out. However, in view of the visualization of In-111 radioactivity in areas corresponding to the distribution of bone marrow in *man* (*1,6*), bone marrow may also play an important role in the sequestration of platelets in man. Heyns's recent results in *baboons* (*5*) point to the same conclusion.

URSULA SCHEFFEL
ROBIN HILL-ZOBEL
MIN-FU TSAN
The Johns Hopkins Medical Institutions
Baltimore, Maryland 21205