Iwata's correction in Equation 3 may prove useful, especially for the right ventricle and the tight bolus, when rapid changes in indicator concentration occur.

Finally, Iwata simulated c(t) by the gamma-variate function fitted to end-systolic first-pass points. Alternatively, one may use the cycle-averaged sampled curve, which requires acquiring the data in the list mode, allowing for multiple reformatizations. Therefore, the curve sampled in accordance with the heart rate is directly proportional to indicator concentration, there is no referring to any particular model, even multimodal bolus is allowed, and recirculation need not be distinguished from the first-pass data.

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Davor Eterović
Department of Nuclear Medicine
Clinical Hospital Firule
Split, Yugoslavia

REPLY: I think that the perfect mixing in the indicator within the right ventricle will not occur for the short period between diastole, ed, to the succeeding systole, es, in the case of the tight bolus in the first-pass method and rapid change in the indicator concentration.

I showed how the imperfect mixing influenced the determination of right ventricular ejection fraction, and that the influence could be attenuated by using Equation 3 in the Eterovic letter, when the spatially averaged concentration c(t) in the right ventricle at time t was given. However, in the present stage, c(t) is unknown. I assumed that c(t) was represented by the gamme-variate function fitted to end-systolic first-pass points. Naturally, the possibility exists that other estimations of c(t), better than my own, are found. If any, the error in my correction will be caused from the estimation of c(t). Namely, if the indicator is well mixed with turbulent blood flow in right ventricle during the ejection phases, the modification of my estimation of c(t) or c(ed)/c(es) in Equation 3 will be needed. However, at least in my phantom experiments, ejection fraction after my correction agreed well with the known phantom ejection fraction.

Kazuro Iwata
Nara Medical University
Kashihara-city, Nara, Japan

Splenic Dynamics of Indium-111-Labeled Platelets in Idiopathic Thrombocytopenic Purpura (ITP)

TO THE EDITOR: In a recent paper by Syrjälä et al. (*1*) on platelet kinetics in idiopathic thrombocytopenic purpura (ITP), the authors concluded that the closed two-compartmental model frequently put forward to represent platelet exchange between blood and the splenic platelet pool was not valid for short-lived platelets.

Their data, however, do not in any way invalidate the two-compartmental model. It is widely accepted that this model is only considered to be effectively "closed" for platelet life spans measurable in days rather than hours, but that a "runoff" component (due to platelet destruction) becomes increasingly significant as the mean life span becomes shorter. Heat damaged red blood cells, for example, provide a special case for this model in which about half the cells entering the spleen on each pass fail to get out again while the other half transit the spleen with a mean time of ~15 min (*2,3*). Syrjälä et al. (*1*) make no reference in their paper to this "destruction" rate constant and imply that the two exponentials seen on the splenic uptake curve represent two separate pooling compartments with different equilibrium time courses, similarly to red cells in splenomegaly (*4*). It would be expected from this implication, i.e., that the true model has three compartments, that the blood-pool curve should also be bi-exponential. The fact that there was no correlation between the exponential components of the blood-pool curve and those of the splenic uptake curve is meaningless.

Fitting a bi-exponential function to splenic platelet uptake curves of a duration of only 40 min is of questionable reliability because of the uncertainty that a plateau value (i.e., equilibrium) has been reached. The illustrated examples in their paper could have been fitted with a single exponential approaching an asymptote, as would be the case for a two-compartmental model with insignificant "runoff." It would be interesting to know if a bi-exponential fit was significantly better than a monoexponential fit in all the cases that they describe as bi-exponential. We took their illustrated example and indeed showed no significant difference between the respective standard errors of monoexponential (plus asymptotic constant) and bi-exponential fits.

Finally, there is no reason why deconvolution analysis applied to the spleen should be invalidated when platelets are being taken up or exchanging at sites in addition to the spleen. It was for the very reason that such additional sites were likely with short lived platelets that we applied a deconvolution analysis in patients with reduced platelet survivals in order to measure mean platelet transit time through the spleen (*5,6*). Indeed, in patients with very short platelet survivals, we observed splenic retention functions that were monoexponential and approached an asymptote that we interpreted as representing the fraction of incoming platelets that were irreversibly removed in the spleen. The raw splenic uptake curves in such cases have precisely the bi-exponential appearance that Syrjälä et al. (*1*) described in their paper.

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A. M. Peters
M. J. Myers
Hammersmith Hospital
London, England

REPLY: We very much appreciate the willingness of Peters and Myers to discuss our analysis (*1*) of splenic dynamics of radiolabeled platelets in idiopathic thrombocytopenic purpura (ITP). Before responding to the specific issues raised in their letter, we would like to comment briefly on general aspects of using mathematical models for describing biologic systems. It must be remembered that models are only a means to provide a better understanding of biologic mechanisms and should, therefore, not be classified as being strictly "right" or "wrong." The usefulness of a selected model is determined by its universality, i.e., its applicability to various pathophysiologic conditions. This does not mean that it is unjustified to use a model applicable only to a particular condition, e.g., the use of a closed two-compartmental model for the study of the dynamics of normal platelets. It was with these considerations in mind that we suggested the use of biexponential curve fitting instead of a closed two-compartmental model for analyzing splenic dynamics in ITP.

Our data may not totally invalidate the two-compartmental model in ITP. In fact, we observed a monoexponential time-activity course in 4 out of 33 ITP patients. We have not made any reference to a possible 'runoff' component due to platelet destruction because we have not as yet addressed this possibility by appropriate experiments, and are not fully convinced that data obtained from studying the splenic uptake of heat-damaged red cells can be applied to the kinetics of ^{111}In-labeled platelets. Peters and Myers correctly point out that our blood-pool curve is also biexponential and that this indicates the use of a three-compartmental model. The observation that there was no correlation between the exponential components of the blood-pool curve and that of the splenic curve is by no means meaningless. On the contrary, the lack of correlation strongly implies that the system contains other important components. However, in a closed two-compartmental system the blood-pool and splenic curves can be assumed to be complementary. In a forthcoming paper, we have compared the two- and three-compartmental models with each other and have shown the superiority of the latter in providing meaningful information on the effects of platelet autoantibodies on splenic dynamics.

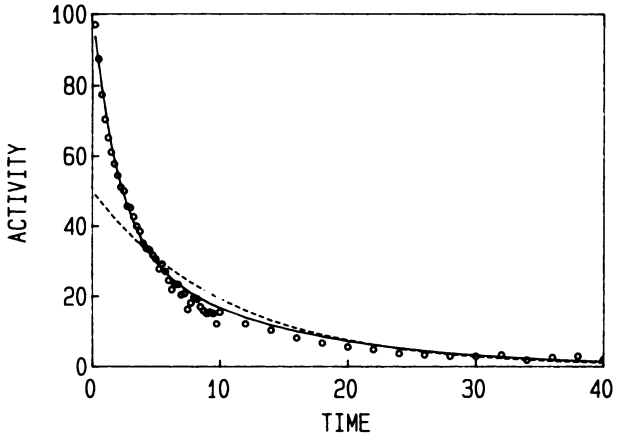

FIGURE 1
Inverted splenic time-activity curve observed after injection of ^{111}In-labeled platelets (circles) and fitting of biexponential (solid line) and monoexponential (dashed line) functions to the data.

It is true that the curve fitting procedure is very dependent on the residual function detection and that there are rare ITP patients in whom a splenic plateau value has not been reached after 40 min, but this does not preclude fitting a two-exponential function to the observed curve in these cases. It is our experience that a 40-min imaging time is sufficient for reliable data analysis and prolongation of the imaging time does not give additional information (most of our patients were imaged for 60 min).

We have now performed a statistical comparison of biexponential and monoexponential fits to the splenic time activity curves (Fig. 1) of each case studied. The goodness of each fit was calculated by reduced chi square test (*4*). The reduced chi square values of biexponential fits were significantly lower than the monoexponential ones ($p < 0.005$, two-tailed Student's t-test for paired samples), clearly demonstrating the biexponential nature of the function. In fact, in only three cases was the monoexponential fit superior to the biexponential one. In eight additional cases, the two fits were equally good but in the majority (22 cases) the biexponential was better.

According to Peters et al. (Ref. 3 page 143): "A potential error in deconvolution analysis is the assumption that the blood-pool signal recorded by the gamma camera is a true reflection of the arterial input into the spleen. This assumption would not be valid if some degree of platelet sequestration in the lungs or in the bone marrow of the chest wall, occurring during the course of dynamic imaging, was included in the blood-pool region of interest." Although these workers might now have changed their opinion concerning the usability of deconvolution analysis in platelet dynamics, we still share their earlier opinion with one essential amendment: deconvolution analysis under these methodologic circumstances is invalidated only if platelets taken up by extrasplenic sites are also partly released during the imaging period.

For the above reasons we are of the opinion that a closed two-compartmental model is not the best one for deriving information about splenic dynamics of short-lived platelets in ITP.

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