with ^{99m}Tc-labeled antimelanoma antibody F(ab')2 fragments, 225.28S, illustrate this point.

Patient 1 (Fig. 1) had combined immunolymphoscintigraphy and immunoscintigraphy 2 yr after the excision of a primary melanoma from her right ankle. There were no palpable lesions in the areas of increased uptake and the patient has yet to develop disease in these areas 14 mo after the study. The uptake is thought to be due to entrapped antibody-antigen complexes resulting from the binding of the antibody to sequestered antigen within the lymphatics. Patient 2 (Fig. 2) showed a pattern of uptake normally observed in patients receiving second or subsequent injection of murine monoclonal antibody and had increased uptake in the liver, spleen, and bone marrow. Since this patient had no known previous exposure to mouse IgG, it was thought that the pattern of uptake could be due to clearance of circulating immune complexes, caused by pre-existing HAMA, by the reticuloendothelial system.

While the formation of immune complexes, be they antibody-circulating-antigen or antibody-antibody, can alter the clearance rate and biodistribution of injected monoclonal antibodies they can contribute to the nonspecific uptake observed during early imaging times especially when radionuclides such as ^{99m}Tc are used. The immune complexes could be entrapped within the vasculature and disrupted architecture of tumours where the large intracapillary pores of newly grown capillary beds permit the extravasation of the complexes into the interstitial space. Increased macrophage activity, especially when there is associated tumour necrosis, may result in ingestion of the complexes. The immediate effect of these is an observed increased (nonspecific) uptake on early imaging (probably up to 24 hr). However, ingestion of the complexes by macrophages within the tumour results in rapid removal of the radiolabel, which results in the lower count rates, lower target-to-background ratios, and high false-negative results observed by many authors on late imaging. This is in addition to interference with tumour targeting by anti-idiotypic HAMA and the effects of faster clearance of the antibody.

The occurrence of pre-existing HAMA in some patients makes it desirable that this should be evaluated before murine monoclonal antibodies are administered for diagnostic purposes. The effect of circulating immune complexes should also be borne in mind when the choice of antibody radiolabel makes imaging beyond 24 hr impracticable.

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Right Ventricular Ejection Fraction by First-Pass Curve Oscillations

TO THE EDITOR: The high frequency sampled first-pass radioventriculogram consists of the low-frequency curve undulated by the successive spikes, each reflecting intra-beat ventricular time-volume relationships. Besides poor signal-to-noise ratio, calculating ventricular ejection fraction (EF) from the magnitude of the few well defined spikes is a simple, well known method.

Recently Iwata proposed a correction for the method and applied it to the right ventricle (*1*). Iwata's correction contains a principal error, but it is potentially useful if used as modified below.

Denote by V(ed) the ventricular volume at end-diastolic time (ed) and by V(es) its volume at the time of the succeeding end systole (es). By definition it stands:

$$EF = 1 - V(es)/V(ed). \quad (1)$$

If A(t) is the ventricular count rate and if V(t)~A(t), Equation 1 then reads:

$$EF = 1 - A(es)/A(ed.) \quad (2)$$

Equation 2 is used in standard method. Iwata, however, introduced ventricular indicator concentration, c(t), and proposed the following correction of Equation 2:

$$EF = 1 - (c(ed)/c(es)) \cdot A(es)/A(ed). \quad (3)$$

The apparent idea was that proportionally V(t) ~A(t) holds if indicator concentration does not change in the time from ED to ES. On the contrary, the ratio c(ed)/c(es), depicted from the low-frequency first-pass curve, can be used to correct for it. However, here and in Iwata's article the time from arbitrary diastole, ED, to the succeeding systole, ES, is the ejection phase, when all inputs to the ventricle are suspended and, assuming perfect mixing, the indicator concentration does not change. Consequently, as long as one analyzes only the ejection phases (descending limbs of the spikes), the equality, c(es) = c(ed), renders Equations 2 and 3 equivalent, which obviates the need for the correction of the standard method. In order to make more efficient use of these data, one can also analyze the filling phases (ascending limbs of the spikes), when es is arbitrary end-systole and ed is the succeeding diastole. Then

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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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.

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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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