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Re: Determination of Absolute Left-Ventricular Volume from First-Pass Kinetics

In a recent article (*1*) the authors describe the use of first-pass kinetics to determine left-ventricular volume in absolute terms. We believe the method described is essentially equivalent to the standard cardiac output approach, in which the patient's blood volume is determined as described in the early seventies (*2,3*) and more recently by Hannan (*4*). We take this opportunity to substantiate this claim further and to describe our own work, which has demonstrated that absolute volume may also be calculated using red cells in vivo (*5,6*).

The method as described contains one assumption that we believe to be theoretically invalid. In their derivation the authors define B(t) as the sum of D(t) and S(t) divided by two, where D(t) and S(t) are the envelopes of the end-diastolic and end-systolic points, respectively. In practice, however, they measure the integral under the background-corrected first-pass curve obtained at one frame per second. In general this integral is not equal to B(t) as defined but will depend on the shape of the volume-time curve for that particular study. From Fig. 1 it can be seen quite clearly that during a typical cardiac cycle, at equilibrium, the mean count rate (which is proportional to the area under the volume-time curve) is dependent on the curve shape. The shape of the volume-time curve will similarly influence the first-pass integral, which will equal the defined B(t) only when the volume-time curve is perfectly symmetrical. This can be further demonstrated if one considers the measurements made in practice by the authors. If the area under the first-pass curve is used, then the final equation for volume should be exactly equivalent to the equations derived from the normal cardiac output approach. As defined by the authors, this only holds if the mean equilibrium count rate is equal to (D + S)/2, which is not necessarily true. It is therefore possible that the results were subject to a systematic error in the majority of cases. Had the true mean equilibrium count rate been measured instead, their method in practice would then be essentially equivalent to the standard cardiac output approach.

We have also described a method of estimating absolute volume based on first-pass kinetics. In our case, a pulsatile theoretical model for the cardiac circulation was used to describe the bolus passage, and the mean residual time for blood passing through the ventricle was shown to be equivalent to the area under the equilibrium volume-time curve divided by stroke volume. We demonstrated that the method was similar to the standard cardiac output approach, except that red cells labeled in vivo could be used and calculation of blood volume was not specifically required. Our use of an imperfect blood tracer (i.e. in vivo-labeled RBCs) for cardiac-output measurement is in agreement with the basic theory of indicator dilution as described by McIntyre and Bassingthwaighte (*7,8*). In their article, Harpen et al. make correct use of blood volume. In the case of a perfect blood tracer, a separately calculated blood volume may be used since, in this special case, the integral of the bolus curve and attenuated left-ventricular counts are logically distinct from the injected activity and concentration of activity in the blood at equilibrium. This logical distinction does not hold, however, if in vivo-labeled cells are used. In this case the same four measurements are necessary, but it is the bolus integral and injected activity that are logically distinct from the attenuated left-ventricular counts and the blood's activity concentration at equilibrium. The ratio of injected activity over blood concentration is not necessarily equal to blood volume in the case of an imperfect blood tracer. This point is overlooked in recent publications (*9,10*), which describe the use of in vivo-labeled cells, standard cardiac output equations being essentially misused in these papers. Our method is flexible and can be useful in practice since a small initial dose can be given as a bolus and a further dose given before the subsequent equilibrium study when the blood sample is taken. This avoids the need for deadtime correction during the first-pass collection, which with our instrumentation has been necessary for higher doses.

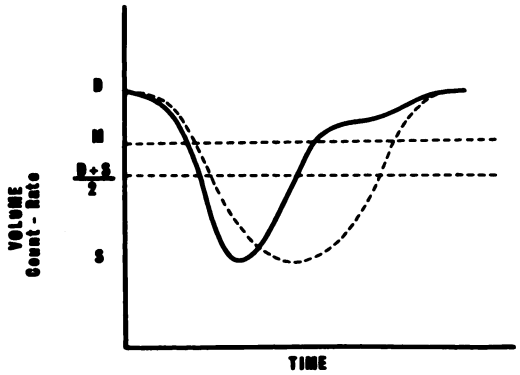

FIG. 1. Half sum of end-diastolic volume (D) and end-systolic volume (S) is equal to mean volume in case of symmetrical volume-time curve (- - -). In case of more usual curve (——) this is not true. (mean volume = M).

It is our belief that the method described by Hannan, and with modification Harpen's method, both allow an accurate absolute volume to be estimated. The advantage of a method using first-pass kinetics is that, unlike other methods, it does inherently correct for both attenuation and other effects such as detection geometry. Our own work demonstrates that similar methods can also be used with in vivo-labeled red cells.

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Reply

We have reanalyzed the patient data from our left-ventricular volume study (*1*) using the method of Hutton et al. (*2,3*) and have made the following observations:

1. In eight of the 12 patients, a well-defined end point to the volume-time curve obtained from the gated phase of the study could not be found. This is presumably due to fluctuations in heart rate occurring during the gated phase of the study. We were thus unable to determine the mean transit time needed to apply their method.

2. In the four patients in which a well-defined end point was found, the two methods yielded values for left-ventricular volume that differed by no more than 5%. The mean deviation was 2.8%.

In 16 additional patients, we have obtained similar results, which were not included in our original study.

Our model assumes that the time-averaged left-ventricular activity is the average of systolic and diastolic activities. While this may not be theorically justified, experience has shown that in practice the two averages are very nearly equal.

The use of RBCs labeled in vitro has a distinct advantage over in-vivo-labeled cells in that left-ventricular volumes and cardiac outputs may be found as percentages of total blood volume when this has not been determined. We have found a strong correlation between the cardiac output expressed as a percent of total blood volume and the conventional cardiac index. It may thus be possible to obtain an index of cardiac output without any wet-lab procedures.

While our model may not be theoretically perfect, it presents a conceptually and computationally simpler method for obtaining useful clinical information.

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Re: Normal Appearance and Reproducibility of Liver-Spleen Studies with Tc-99m Sulfur Colloid and Tc-99m Microalbumin Colloid

An ample and occasionally excellent literature documents the significance of specific imaging patterns in diagnosing hepatocellular disease (*1,2*). Inhomogeneity, bone-marrow uptake, enhanced splenic uptake, and lung uptake all have certain discriminant value in detecting disease. As expected, normal individuals imaged by Klingensmith et al. with sulfur colloid and with albumin colloid showed no such findings, except "normal" variability (*3*). Nevertheless, the authors reached a general conclusion about the relative clinical utility of these two RES-imaging agents. The process of inference demands more, and such a conclusion appears premature.

The work of Kloiber et al.—cited to support conclusions on differences in background—was performed with an agent quite different in character from that used by the authors (*4*). Further, the reference to higher background in albumin colloid images is not borne out by the authors' own data. They show comparable blood levels for the two agents at 30 min after injection, slightly faster hepatic extraction of albumin colloid, and essentially similar regional ratios otherwise (*3,5*). Finally, as indicated by labeling efficiency of 99%, any thyroid uptake seen over unmarked overexposed albumin colloid images is negligible. Such activity reflects the biodegradable nature of the new imaging agent and does not significantly enter dosimetry considerations.

Nonetheless, this technically well-performed trial is important to clinicians in re-emphasizing the wide variability in normal spleen-to-liver (S:L) uptake ratios of colloidal imaging agents. The S:L ratios of 0.97 ± 0.29 and 0.98 ± 0.33 obtained from sulfur colloid and albumin colloid, respectively, confirm earlier data of Wasnick et al. showing normal sulfur colloid S:L ratio and variability of 0.77 ± 0.2 (*6*).

As to the clinical utility of the albumin colloid kit, the article omits mention of the two technical reasons it was developed. First, the kit is "instant," requiring only the addition of technetium generator eluate. This eliminates the need for boiling or multiple chemical additions and reduces radiation exposure incurred in preparation. Second, unlike sulfur colloid, albumin colloid is biodegradable.

The agent was designed to simplify current clinical practice, not to change it. Indeed, the clinical studies of Klingensmith et al. confirm the essential equivalence of biodistribution of the two colloids. Data collected during clinical trials of albumin colloid in patients, in which the authors participated, document the utility of the new agent in detecting hepatocellular disease as well as space-occupying lesions.*

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FOOTNOTE

* Data on file, New England Nuclear Corp.

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