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## Maximizing Thallium Stress/Redistribution Scans

TO THE EDITOR: In an effort to maximize the utility of the thallium scan, the subject of the reinjection of thallium has become an issue of recent concern (*1*). The rationale of the reinjection procedure is the observation that a stress/reinjection comparison does a better job of identifying viable myocardium than a stress/redistribution scan.

Some authors propose performing stress/redistribution scans with reinjection of thallium in those patients with a fixed defect on the redistribution scan (*2,3*). The problem with this technique is that it involves a third set of images and is disruptive of the imaging schedule. Some laboratories prefer a 24-hr delayed imaging session, but this is also disruptive to a busy schedule as well as inconvenient for outpatients.

Some authors (*4*) propose a reinjection of thallium 20 min before the performance of the redistribution scan. The problem with this approach is the fact that a very tight stenosis of a coronary vessel (the type that causes 'pseudo-fixed' stress-induced defects) can cause defects on rest studies that 'fill-in' over time (*5*). Thus, some viable regions will still be considered as areas of myocardial scarring.

To avoid these problems we propose the following sequence:

1. Perform a stress thallium scan in the standard manner. Leave the injection line in the patient's arm in place during the scanning procedure.
2. At the end of the stress images (about 35–40 min after the termination of exercise), inject the booster dose of thallium and remove the i.v. line.
3. Obtain a 4-hr redistribution scan later that day.

We find that this procedure gives us the maximum clinical information with a minimum disruption to the department's function. As far as the patient is concerned, it does not even involve having an extra needle stick.

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REPLY: We wish to thank Drs. Makler, Schwartz, Shapiro, and Scheff for their concerns in the limited value of current technique of stress-delayed thallium scan for assessing tissue viability (*1–3*). Many scientists are now pursuing alternative methods for enhanced detection of "redistribution" in the ischemic myocardium. The 24-hr delayed scan (*4*) or reinjection thallium scan (*5–9*) have been proven to be useful for identifying additional ischemia which often fails to show redistribution on the routine thallium-201 scan.

The reinjection of thallium immediately after the stress scan seems to work well based on the concept of increasing plasma concentration of thallium, which may redistribute during post-exercise hyperemia (*10*). However, since majority of ischemic segments already show redistribution on the 3–4-hr delayed scan, it may be difficult to delete the delayed scan. At present, we think that reinjection may not be necessary when the redistribution is already observed on 3–4-hr delayed scan. Such a new technique seems to be valuable only when the routine scan shows a persistent defect, although the third set of images might be disruptive to the imaging schedule. Perhaps, we need more clinical information on the reinjection scan before eliminating the 3–4-hr delayed scan. We do hope that the clinical investigations of Dr. Makler et al. will demonstrate that their procedure will really enhance detection of redistribution in the ischemic myocardium and that these areas will be reversible in cardiac function after restoration of blood flow.

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**FIGURE 1.** Tumor-activity curve indicates progressive decline in tumor activity.

# Importance of the Terminal Portion of Tumor Time-Activity Curve in Determining Tumor Dosimetry in Radioimmunotherapy

TO THE EDITOR The fine article by Eary et al. concerning the Seattle experience in treating lymphoma patients with the $^{131}$I-labeled pan B-cell antibody MB-1 (*1*) was of considerable interest to us in view of our own ongoing experience with this same antibody (*2*). One aspect of this article which particularly intrigued us was the description of the methodology used to choose an appropriate antibody protein dose to achieve optimal tumor radiation doses relative to background. The general claim was made that higher protein doses resulted in more favorable tumor/normal organ dosimetry in patients without high tumor burdens. We have had the opportunity to study $^{131}$I MB-1 biodistribution using 40-mg and 200-mg protein doses in three B-cell lymphoma patients with relatively low tumor burdens selected from a total of twelve patients in our series (*2*). Similar to the Seattle group's results, increasing the protein dose from 40 to 200 mg (given intravenously over 2 hr) resulted in slower blood clearance of radioantibody activity. We have also observed an increase in the predicted radiation doses delivered to tumors and normal organs with a higher protein dose per mCi administered. In our limited experience, however, we have not been able to demonstrate an increase in tumor radiation dose *relative* to normal tissues with the higher protein dose. Although our maximum protein dose was not as high as that used by Eary et al., our differing results from the Seattle experience prompted us to further examine the dosimetric methodology employed by the Seattle group.

Eary et al. state that their patients were imaged during the week following the injection of increasing antibody protein doses to calculate residence times in tumors and the normal organs, these residence times then being used for dosimetric determinations using the MIRD formalism. In examining their Figure 6 on page 1263 where these parameters are plotted for Patient 1 of the series, it is apparent that tumor/normal tissue radioantibody uptake ratios are substantially lower in the first 2 days following the higher antibody protein dose than at the lower protein dose. Only at later time points does the "dosimetric advantage" to tumor of the higher protein dose become apparent—due to what is plotted as an increased retention time in the tumors. In fact, the curve-fit provided suggests that the antibody-delivered radioactivity is completely retained in the tumors forever at the highest (1100 mg) protein dose, and this is so stated in the text.
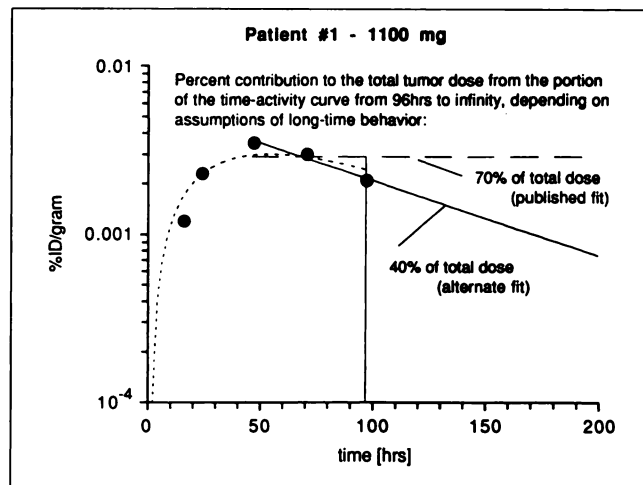
While complete tumor retention of iodinated antibody may be the case in their other patients, in the example shown (Patient 1, Figure 6) at the 1100-mg dose, image data points are only presented through 96 hr postinjection, making fitting the terminal portion of the curve difficult. An alternate, and we believe more appropriate, fitting of the tumor-activity curve (our Fig. 1) indicates a progressive decline in tumor activity from 48 through 96 hr following injection, despite the authors' chosen graphical indication that the tumor does not lose any radiolabeled antibody. If the curve is fitted as "flat" beyond 96 hr, (i.e., no radiolabeled antibody clearance from the tumor), 70% of the total radiation dose to the tumor is from the curve tail (i.e., from beyond the last data point), while if the tumor activity from 24–96 hr and beyond is plotted as a downsloping exponential function, only 40% of the total tumor radiation dose is from the curve tail. With a flat tumor clearance curve, there is a 100% increase in predicted radiation dose to the tumor over that present if the declining clearance curve is used (i.e., 850 cGy versus 425 cGy). Thus, the quality of the data and the method chosen for fitting the terminal portion of the antibody activity curve are critical to the dosimetric estimate and to the conclusion that increased protein dose improves relative tumor dosimetry.

In summary, while we agree that higher antibody protein doses will prolong the circulation of the MB-1 radioactivity in the blood and accept that increased protein doses of MB-1 *may* increase absolute and relative tumor dosimetry/mCi, we believe that longer data acquisitions (beyond 4–5 days) and a multi-exponential fitting of tumor clearance data are essential for an accurate dose estimate. This is particularly true if the tail of the tumor radioactivity clearance curve is relatively flat (and thus contributing substantially to the radiation dose). In our experience, it is most unusual for antibody-delivered radioactivity, particularly $^{131}$I activity, to be fully retained in any tumor site over time. If such radioactivity is retained in tumors with this degree of avidity, substantially delayed imaging points would be useful in confirming and better understanding the phenomenon.

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