introduces additional errors due to statistical noise. This probably worsens accuracy rather than improving it. Dr. Decostre et al. underestimate the importance of a reproducible test. It is true the purpose of the test is to recognize changes in renal function, but one cannot recognize a change in renal function unless one has a reproducible test so that a change in function would represent a true change rather than simply a statistical variance. Dr. Decostre et al. have published the statement "One can only hope by choosing a ROI which is a compromise between the different structures, to approximate the true background" (*1*). Another important difference which may affect our differing conclusions is that we use the camera technique only to estimate relative renal function and depend on blood sampling for an absolute value. Dr. Decostre et al. use a technique which also employs the externally derived blood disappearance curve. I stand by my statement that we have not yet learned what the true background is nor the best way to deal with it. I believe that the approach suggested by Dr. Piepsz et al. is promising, but it still requires broader application and confirmation as stated in my review.

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Breakage of Technetium-99m-Sestamibi Vial with the Use of a Microwave Oven

TO THE EDITOR: A microwave oven heating method was first proposed by Gagnon et al. (*1*) as an alternative heating technique to prepare ^{99m}Tc-sestamibi. We have confirmed that it takes 10 sec heating time in a microwave oven to label ^{99m}Tc-sestamibi maintaining an average radiochemical purity (RCP) of 97% over the 24-hr storage period (*2*). Based upon the report of Gagnon et al. (*1*) and our previous observations (*2*), we believe that the microwave oven heating method is a rapid and reliable way to make ^{99m}Tc-sestamibi available for either routine or emergency use. However, two recent incidents of breakage of ^{99m}Tc-sestamibi vials during the microwave heating process prompt us to caution the nuclear medicine community on adopting this new method. The consequences of such an "accident" are not only very costly (averaging $300 per vial) but could also delay and jeopardize patient care, especially in emergency cases, due to contamination of the microwave oven, which is rendered unsuitable for use. Two out of 84 ^{99m}Tc-sestamibi vials have been broken since we began utilizing a microwave oven to prepare ^{99m}Tc-sestamibi for clinical studies. Although the incidence rate (2/84 = 2.38%) is not very high for any individual institution, it does pose a much more serious problem when a similar "accident" rate is applied to the nuclear medicine community nationwide or even worldwide.

Two vials of ^{99m}Tc-sestamibi burst while being heated in a commercial microwave oven (Fig. 1). In both instances, the labeling procedures for ^{99m}Tc-sestamibi using a microwave oven heating method that we described previously (*2*) were carefully followed. As shown in Figure 1, both vials were broken from the side wall and the base, while the vial top including the metal cap and rubber stopper remained intact. Previous experiments indicate that excessive pressure may build up inside the vial and can cause ejection of the rubber stopper if the vial is not vacuumed (*2*). After carefully examining the broken vials, we noticed that both bases of the vials of the Cardiolite® (E. I. du Pont de Nemours & Co., N. Billerica, MA) kits were much thinner than the ones that we had previously used (*2*) (Fig. 2).

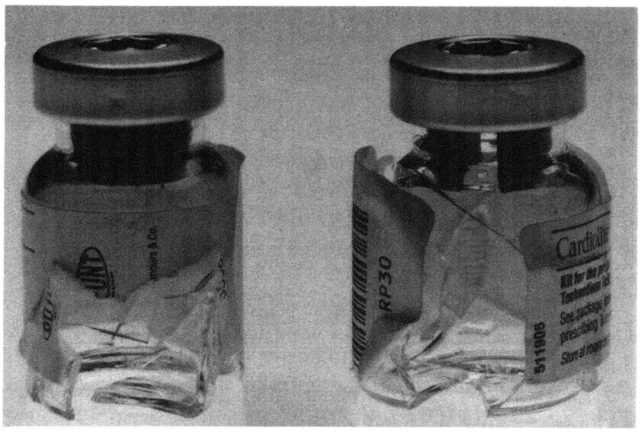

FIGURE 1. Two shattered vials of ^{99m}Tc-sestamibi prepared with the microwave oven heating method.

Table 1 presents the average measurement of the empty vial weight (without the metal cap and rubber stopper) and the thickness of the vial's thinnest portion for two different types of Cardiolite® kits (i.e., black and red labels where the lot numbers were imprinted). The black-label kits were the same type of vials that we had used for evaluating the microwave oven heating process (*2*), and the red-label Cardiolite® kits were utilized to prepare ^{99m}Tc-sestamibi for patient studies. Table 1 indicates that there were not only major differences between the weights of each type of vial (difference = 0.43 ± 0.05 g, $p < 0.001$), but there was also a noticeable 1.5-fold difference ($p < 0.001$) in thickness of

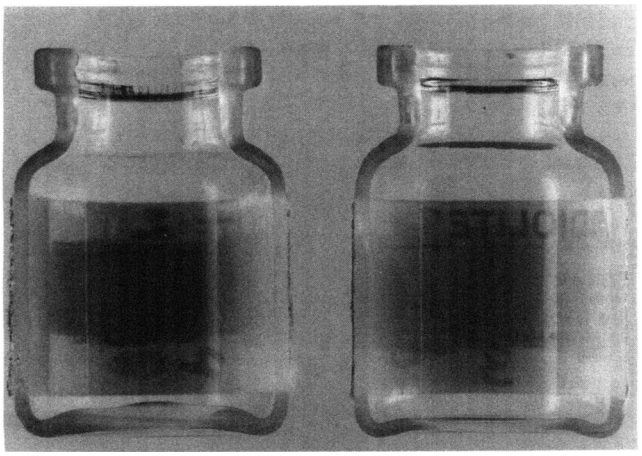

FIGURE 2. Cross-section view of two Cardiolite® kits: a black-label vial (left) and a red-label vial (right). There is a significant difference in the base thickness between the two types of vials.

TABLE 1
Comparison of Two Different Types of Cardiolite® Vials

Label	Lot no.	n	Weight (g)	Thinnest thickness (mm)
Black	3521	7	9.12 ± 0.04	1.31 ± 0.01*
Red	3530, 3536	12	8.70 ± 0.13	0.89 ± 0.13†

All measurements are expressed in mean ± s.d.
* Side wall of the vial.
† Central base of the vial.

the thinnest section. The thinnest part of the vial was selected for comparison because it would be the weakest point for the glass vial to rupture. Based on our findings (Table 1) and the fact that uneven heat distribution and rapidly rising pressure may be generated within the vial when heated in the microwave oven, we think that the thinner vial of the Cardiolite® kit is responsible for the tendency of the vial to break during microwave preparation. With the increasing demand for Cardiolite® kits and the unique application of ^{99m}Tc-sestamibi in acute myocardial conditions, the microwave oven heating method will undoubtedly gain popularity rapidly. This problem could be solved by future replacement of the thinner glass vials with a thicker base vial.

In the interim, we have designed an acrylic-plastic container with a screw cap (Fig. 3) to prevent contamination of the microwave oven. Any spill of radioactivity caused by either ejection of the rubber stopper or shattering of the vial will be retained inside the container. Because of the addition of the 5-mm thick acrylic plastic which surrounds the ^{99m}Tc-sestamibi vial, we have re-evaluated the microwave heating parameters (e.g., heating time and output power of the microwave oven). By maintaining the same heating conditions (e.g., 10 sec and 452.5 watt) as described in (*2*), an acceptable labeling efficiency (92.0% ± 0.7%, n = 3) (*3*), although lower than previous results (96.9% ± 1.4%, n = 30) (*2*), was obtained after reconstitution. An additional 2 sec were then added to overcome the extra acrylic-plastic shielding, which may interfere with the microwave heating process. Figure 4 demonstrates that an overall average RCP value of 96.9% ± 1.1% (n = 30) was achieved over a 24-hr evaluation period. There is, however, an additional 8.3 ± 1.1 sec (n = 20) of radiation exposure to nuclear medicine personnel while handling the ^{99m}Tc-sestamibi vial in and out of the plastic container. Assuming that the radiation exposure rate for 1 mCi (37 MBq) of ^{99m}Tc at 0.5 m is 0.31 mR/hr (3.1 mSv/hr) (*2*), the radiation exposure from this process of holding a vial of 150 mCi (5,550 MBq) ^{99m}Tc-sestamibi for 8.3 ± 1.1 sec is only 0.11 ± 0.02 mR (1.1 ± 0.2 mSv).

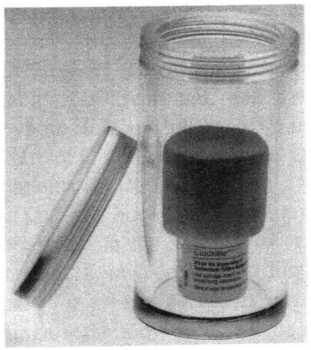

FIGURE 3. A screw-cap container (height: 10 cm, inside diameter: 4 cm, thickness: 0.5 cm) made of acrylic plastic. The ^{99m}Tc-sestamibi vial top is covered with styrofoam to prevent sparking.

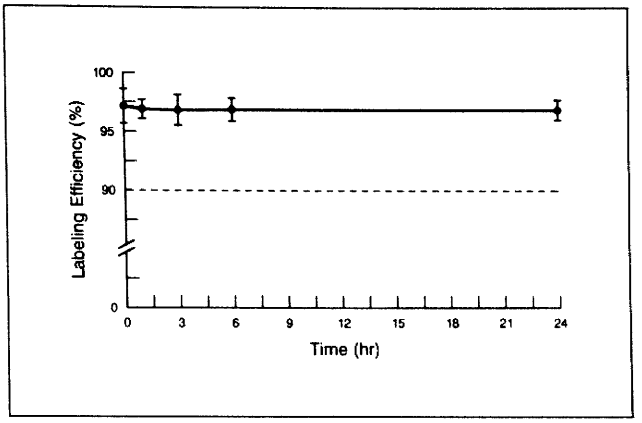

FIGURE 4. RCP graph of six vials of ^{99m}Tc-sestamibi prepared with the use of a plastic container and the microwave heating technique. An average of 156 mCi (5,772 MBq) of ^{99m}Tc activity in 3 ml were added to each Cardiolite® kit. The dotted line represents the minimum acceptance level of RCP for ^{99m}Tc-sestamibi (i.e., 90%) (*3*).

The Nuclear Regulatory Commission (NRC) has recently amended, on a three-year interim basis, its regulation in the Code of Federal Regulations, Title 10, Parts 30 and 35 relating to the preparation and uses of radiopharmaceuticals (*4*). The interim final rule (*5*) allows NRC licensees to depart from the manufacturer's instruction (i.e., package insert) for the preparation of reagent kits provided the licensees meet certain conditions and limitations. The rule restricts that such deviation be applied only to "obtain medical results not otherwise attainable or to reduce medical risks to particular patients because of their medical condition" (*5*). In our institution, we restrict the use of the microwave oven heating method for the preparation of ^{99m}Tc-sestamibi only in cases of emergency (e.g., spontaneous chest pain or acute myocardial infarction). Unlike ^{201}Tl, ^{99m}Tc-sestamibi undergoes no significant redistribution over an extended period once it is in the myocardial tissue. This unique physiological property of ^{99m}Tc-sestamibi offers a much more flexible imaging schedule than ^{201}Tl. As a result, adequate patient care, e.g., thrombolytic therapy, can be promptly initiated without concern for losing imaging information. However, due to the lengthy time required to prepare ^{99m}Tc-sestamibi as per the manufacturer's instructions (i.e., "recommended" boiling water bath method) (*2,3*), acutely ill patients may not receive the radiopharmaceutical in a timely manner. This delay would not only have a negative impact on the diagnostic outcome, but also may pose "medical risks" to the patients because of their acute myocardial condition.

In our opinion, we think that each NRC licensee should be able to use the microwave oven heating method to prepare ^{99m}Tc-sestamibi on an emergency basis. Based on the fact that important medical results that are otherwise impossible to obtain with other agents and that the medical risks can be clearly diminished, this deviation from the manufacturer's instructions of Cardiolite® (*3*) should be permissible under the current NRC interim rule (*5*). According to the interim rule (*5*), the specific departure requested by the authorized user/physician must state the nature of the departure, a specific description of the departure, and the reasons for such a departure. This written directive must be kept along

with a record of the number of patient administrations of ^{99m}Tc-sestamibi prepared with the microwave oven heating method for a period of 5 yr (*5*).

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