



**FIGURE 3.** Angiography confirmed the scintigraphic findings by showing high grade renal artery stenosis in right kidney.

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## Fractionated Cold-Kits: Address the Critical Issues to Obviate Problems

**TO THE EDITOR:** The recent letter on fractionated cold-kits by Decristoforo and Riccabona (1) was interesting. It was surprising to note the unexpected high rate of failure with fractionated MAG3 kit after storage for 6 days, especially when eluate from different generators were used.

We have been using fractionated MAG3 for the last 3 yr without a single incidence of failure. A whole MAG3 kit was reconstituted in 2.6 ml of saline for injection and fractionated into five aliquots (0.5 ml) in  $\text{N}_2$ -filled Amersham vials using 27 G insulin syringe. These vials were stored in  $-20^\circ\text{C}$  freezer. The fractionated kits were reconstituted with 600-1300 MBq of  $^{99m}\text{Tc}$ -pertechnetate in 1.5 ml saline (final volume 2.0 ml), boiled for 10 min and cooled for 15 min before use. The radiochemical purity was  $>96\%$  on the day of fractionating or after storage at  $-20^\circ\text{C}$  for 2 yr.

The rapid fall in the radiochemical purity from 97% to  $63.6\% \pm 48\%$  within 6 days of storage at  $-10^\circ\text{C}$  was surprising as described by Decristoforo and Riccabona (1). The problem might be attributed to high volume of saline (2.5 ml) in the fractionated kit; 0.5 ml aliquots seem to offer better stability over a 2-yr period of storage. The arguments used by

the authors regarding the higher amounts of dissolved oxygen oxidizing tin (II) is the major issue. The fractionation method using smaller reconstitution volume (0.5 ml of saline, preferably  $\text{N}_2$ -purged) and smaller gauge needles (27 G) would minimize the possibility of oxygen assimilation during storage and seem to offer better radiochemical purity ( $>90\%$ ).

Various methods were described to fractionate cold-kits such as HMPAO (2,3), MIBI (4,5), ECD (6), MAG3 (7) and Ultratag (8). The following factors are of considerable importance when kits are fractionated: (a) use a small volume to reconstitute the kit, the ideal volume for fractionation is 0.1-1.0 ml; (b) store in  $\text{N}_2$ -filled vials at temperatures at or below  $-20^\circ\text{C}$ ; and (c) use right amount of tin (II) augmentation where required. The resultant fractionated product seem to give radiochemical purity of  $>90\%$  irrespective of the length of storage time. The underlying factor seem to be the preservation of an optimum concentration of tin (II) which plays a central role in the stability of technetium-labeled radiopharmaceuticals. The ligand concentrations seem to be present in adequate quantity in the whole kit or after fractionation.

In the case of HMPAO, concentration of tin (II) is a critical issue. It has only  $7.6 \mu\text{g}$  tin (II) compared to  $25 \mu\text{g}$  tin (II) present in MIBI kit. We fractionated HMPAO into five aliquots (0.1 ml) after stannous PYP augmentation. The fractionated kits after storage for 18 mo at  $-70^\circ\text{C}$  seem to give radiochemical purity  $>90\%$ ; higher amounts of tin (II) interacts with HMPAO and produces secondary HMPAO after reconstituted with  $^{99m}\text{Tc}$ -pertechnetate, whereas lower amounts of tin leads to free pertechnetate (3). A MIBI kit fractionated into five 0.5 or 1-ml aliquots in saline and stored frozen could be used after stannous augmentation ( $10-20 \mu\text{g}$ ) after months of storage (5); up to 10 GBq of  $^{99m}\text{Tc}$ -pertechnetate could be added per fractionated kit with radiochemical purity  $>96\%$ . In our study, a whole MIBI kit could be reconstituted with 20 GBq of  $^{99m}\text{Tc}$ -pertechnetate in 5 ml saline which was stable for  $>8$  hr postreconstitution (radiochemical purity  $>96\%$ ) indicating that sufficient amount of tin (II) is present as the reducing agent, suggesting a stabilizing role for tin (II).

While I appreciate that fractionated procedures are a variation to the recommended original protocols, the unexpected results could be overcome by adapting the right strategy to preserve optimum tin (II) levels during fractionation. Besides legal consideration, a good radiopharmacy practice is to standardize the fractionation methodology which is proven in your own laboratory, especially to establish stability over a period of storage and to use the fractionated products that satisfy quality control requirements before using them for patients.

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