Studies of Labeling Procedures for the preparation of ^{188}Re-DMSA(V)

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Introduction. Radionuclide therapy (RNT) is emerging as an important tool of nuclear medicine. Apart from the well established ^{131}I, several other promising radionuclides have been identified, among them ^{188}Re, ^{90}Y and ^{177}Lu are considered to be the most promising radionuclides for *in vivo* therapy.[1] ^{188}Re has received a lot of attention in the past decade, due to its favourable nuclear characteristics: $t_{1/2}$ 16.9 h, $E_{\beta\,max}$ 2.12 MeV and E_{γ} 155 keV (15%) suitable for imaging, including the fact that it is carrier-free and can be obtained cost-effectively through the generator ^{188}W-^{188}Re. Besides the therapeutic usefulness of ^{188}Re, the emission of the 155 keV gamma photon is an added advantage since the biodistribution of ^{188}Re-labeled agents can be evaluated *in vivo* with a gamma camera. Biodistribution studies of ^{188}Re-DMSA(V) have shown that its general pharmacokinetic properties are similar to that of ^{99m}Tc-DMSA(V), so this agent could be used for targeted radiotherapy of the same tumors, i.e., medullary thyroid carcinoma, bone metastases, soft tissue, head and neck tumors.[2,3] In therapy of medullary thyroid carcinoma, the ^{188}Re-DMSA(V) would be an excellent alternative, once this specific type of tumor doesn't uptake ^{131}I.[4] The aim of this work is to evaluate two labeling procedures for the preparation of ^{188}Re-DMSA(V) by two different methods. **Materials and methods.** Initially ^{188}Re-DMSA(V) was prepared using a commercial kit of

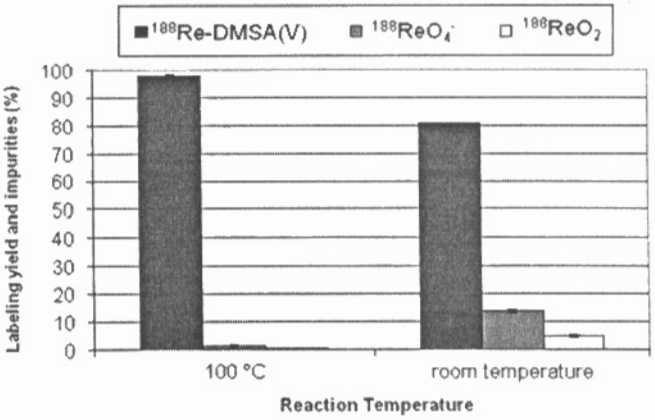

Figure 1.—Labeling yield with the variation of reaction temperature.

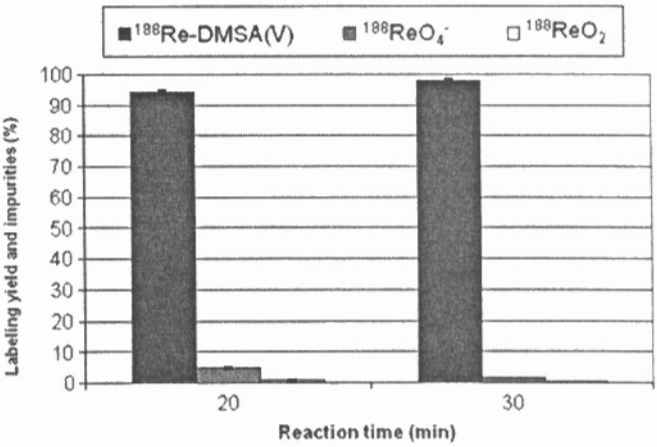

Figure 2.—Labeling yield with the variation of reaction time

DMSA (III) for labeling with ^{99m}Tc (IPEN-CNEN/SP). The labeling was done with 1 mL of $^{188}ReO_4^-$ (~185MBq) and the reaction time was 30 minutes at high temperature (100 °C). The variables studied were: reaction temperature (100 °C and room temperature), reaction time (20 and 30 minutes) and volume of $^{188}ReO_4^-$ (1.0 and 2.0 mL). The second method was prepared in a vial containing 2.5 mg of DMSA (dimercaptosuccinic acid), 1.00 mg of $SnCl_2.2H_2O$ and 30 mg of sodium oxalate, in a total volume of approximately 1 mL. The pH was adjusted to about 5 with 37% HCl. The labeling was done with 1 mL of $^{188}ReO_4^-$ (~185MBq) and the reaction time was 15 minutes at room temperature. The variables studied were: reducing agent mass (0.2; 0.6; 1.0; 1.5 e 2.0 mg) and mass of DMSA (1.25; 2.5 e 5.0 mg). The radiochemical purity was determined using TLC-SG developed with two different solvent systems. Acetone was used in order to separate ReO_4^- (R_f 1) from ^{188}Re-DMSA(V) and ReO_2 (R_f 0) and 5% glycine was used in order to separate ReO_2 (R_f 0) from ^{188}Re-DMSA(V) and ReO_4^- (R_f 1). The distribution of radioactivity on the TLC-SG strips was determined using a calibrated Germanium hyperpure detector model GX1518 (HPGe) coupled to a multichannel analyzer system (Canberra Inc., USA). **Results.** Figures 1,

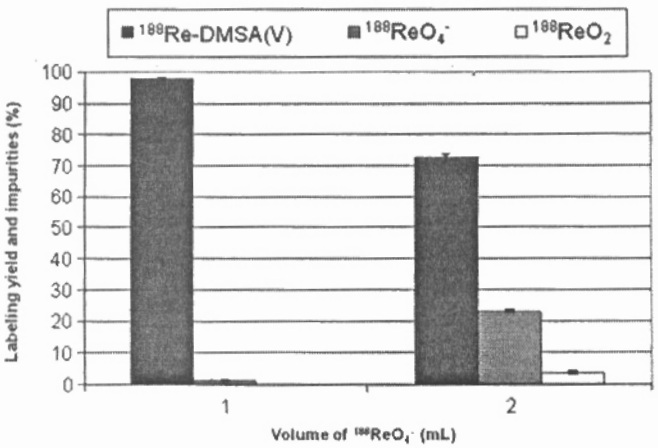

Figure 3.—Labeling yield with the variation of volume of $^{188}ReO_4^-$.

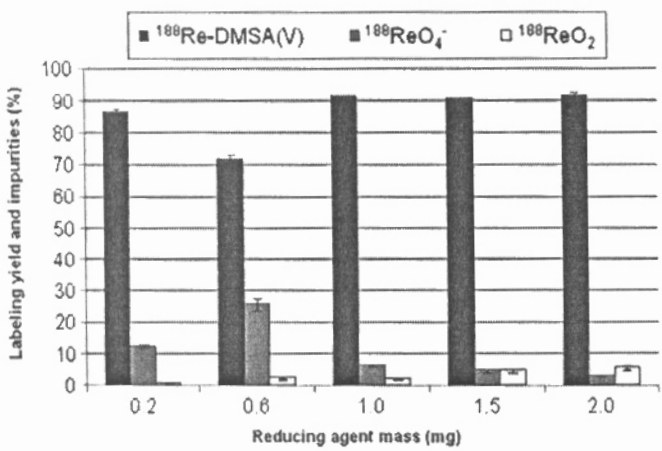

Figure 4.—Labeling yield with the variation of reducing agent mass.

2 and 3 show the results of the effect of the variation of reaction temperature and time and volume on the labeling efficiency of ^{188}Re-DMSA (V) prepared with a commercial kit of ^{99m}Tc-DMSA (III). The best results of labeling yield (> 98%) were achieved when it was used 30 minutes of reaction time with heating at 100 °C and 1 mL of $^{188}ReO_4^-$. Figures 4 and 5 show the results of the effect of the variation of the reducing agent and DMSA masses, respectively on the labeling efficiency of ^{188}Re-DMSA (V) prepared with method II. The best labeling yield was achieved using 1.0 mg of $SnCl_2.2H_2O$ and 2.5 mg of DMSA but other parameters have to be studied for the optimization of the radiolabeling. The advantage of this method is that it does not require high temperatures to achieve good labeling yields due to the use of oxalate. This compound complexes with Re in a more appropriate geometry and kinetics promoting a more efficient reduction of $^{188}ReO_4^-$ when compared with the method I. Conclusion. Preliminary results for both methods of labeling ^{188}Re-DMSA(V) showed that the labeling yield was >90% but method II requires milder conditions. Further experiments are also necessary to optimize the labeling methodology of ^{188}Re-DMSA(V).

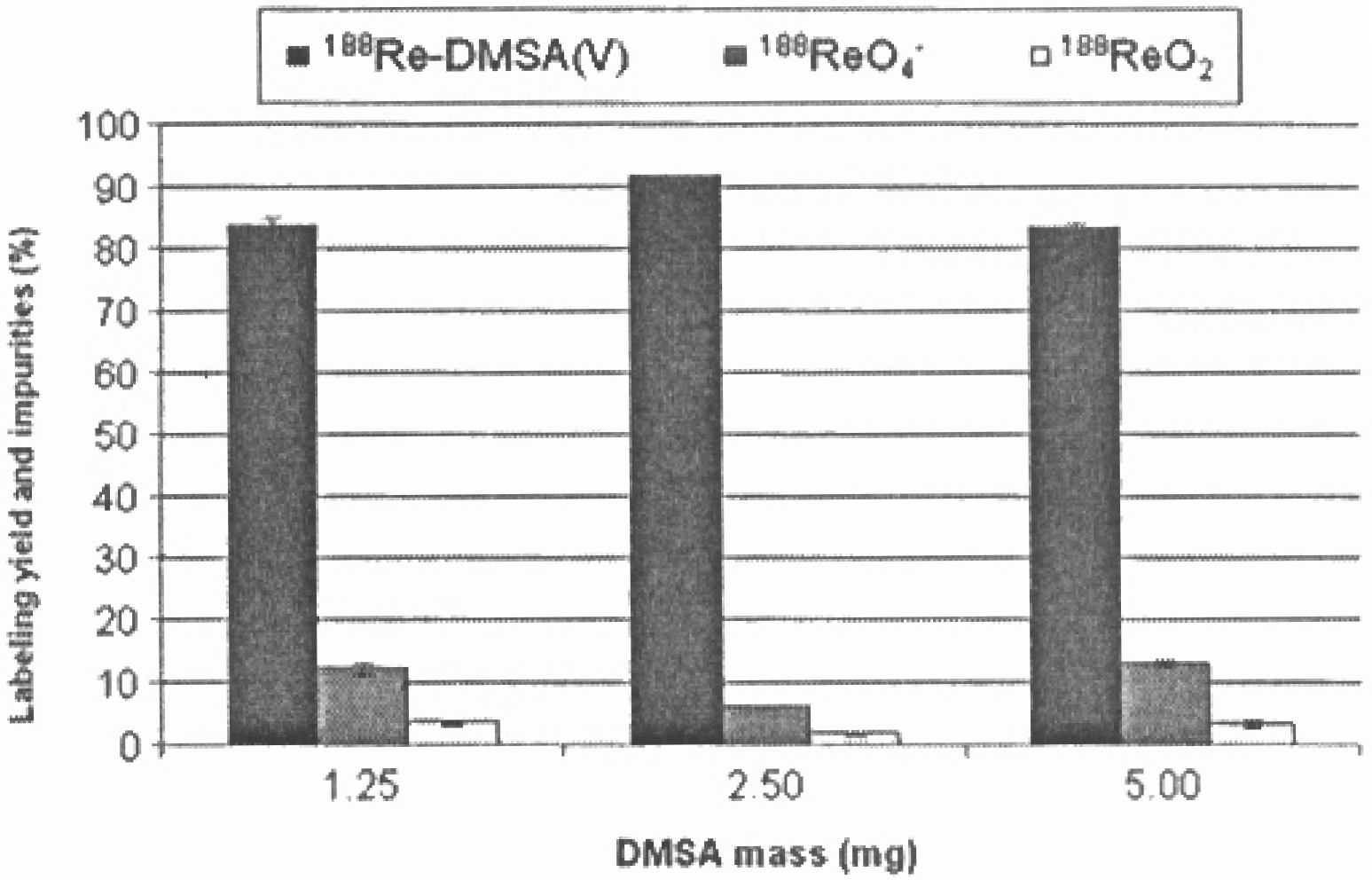

Figure 5.—Labeling yield with the variation of DMSA mass.

References

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