

## Development of $^{90}\text{Sr}$ - $^{90}\text{Y}$ generators using the cation exchange technique at IPEN/CNEN-SP

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**Introduction.** There is a widespread interest in the use of  $^{90}\text{Y}$  for various therapeutic applications, including radiolabeled tumor-specific antibodies for tumor therapy, radiolabeled particles for irradiation of malignant tumors in the liver, irradiation of solid tumors and treatment of rheumatoid arthritis of the knee joint.<sup>1-5</sup> Yttrium-90 is generated through the decay of reactor-produced  $^{90}\text{Sr}$  ( $t_{1/2}=28$  years) and isolated by methods like precipitation, extraction, electrochemical separation and ion exchange chromatography<sup>1</sup>. Because of its simplicity, the ion exchange methods are most commonly used in the generator systems for the separation of  $^{90}\text{Y}$  from  $^{90}\text{Sr}$  in very pure form. Most of these generators have been prepared using the Dowex-50 cation exchange resins, that can retain  $^{90}\text{Sr}$  while the  $^{90}\text{Y}$  daughter is eluted in various solvents such as citrate, oxalate, acetate, and ethylenediaminetetraacetic acid (EDTA). One must note that  $^{90}\text{Sr}$  is a bone-seeker and produces bone marrow depression, so the permissible  $^{90}\text{Sr}$  has a lifetime tolerance of 74kBq (2 $\mu\text{Ci}$ ) when fixed in bone<sup>6</sup>. The objective of this work is to develop a methodology for the preparation of  $^{90}\text{Sr}$ - $^{90}\text{Y}$  generators using a cation exchange resin method.  $^{90}\text{Sr}$  is strongly adsorbed in the resin and  $^{90}\text{Y}$  is eluted in 0.03mol.L<sup>-1</sup> EDTA. **Materials and methods.** All experiments were performed at the Radiopharmacy Center at

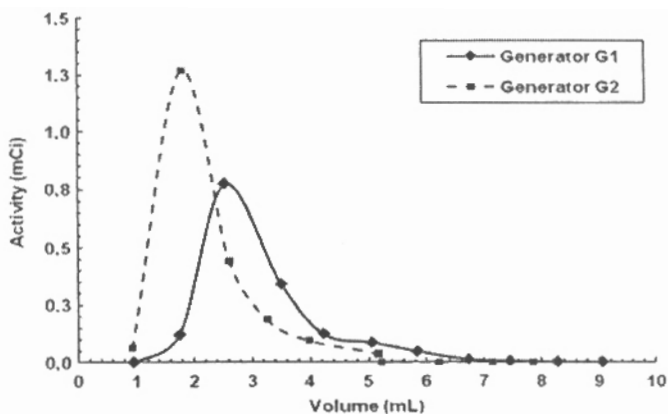


Figure 1.—Elution profile for ( $G_1$ ) and ( $G_2$ )  $^{90}\text{Sr}$ - $^{90}\text{Y}$  generators with  $0.03 \text{ mol}\cdot\text{L}^{-1}$  EDTA.

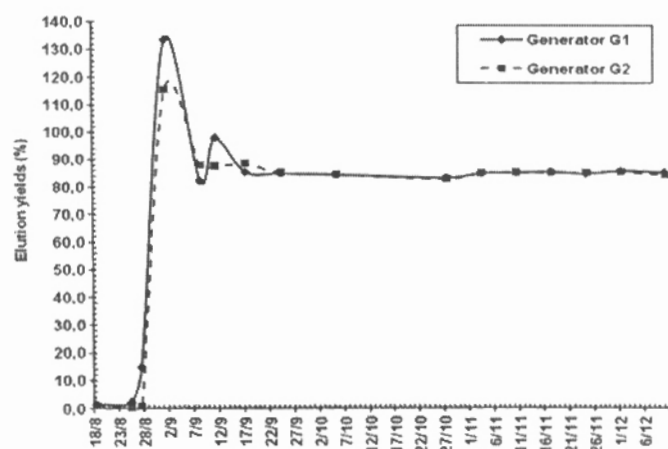


Figure 2.—Elution yields for ( $G_1$ ) and ( $G_2$ )  $^{90}\text{Sr}$ - $^{90}\text{Y}$  generators.

IPEN/CNEN-SP. Two generators ( $G_1$  and  $G_2$ ) were developed, both loaded with 3 mCi (111 MBq) of  $^{90}\text{Sr}$ . The solution containing the pair  $^{90}\text{Sr}/^{90}\text{Y}$  was prepared in  $1 \text{ mol}\cdot\text{L}^{-1}$  HCl. The cation exchange resin used in both generators was Dowex 50W-X8 (100-200 mesh, 11<sup>+</sup> form) that was converted to  $\text{Na}^+$  form with  $1 \text{ mol}\cdot\text{L}^{-1}$  NaOH and distilled water. After the activation, the resin was conditioned with 100 mL of  $0.003 \text{ mol}\cdot\text{L}^{-1}$  EDTA at  $\text{pH} = 4.55$ . The generator ( $G_1$ ) consisted of a glass chromatographic column with a 1 cm diameter and 10 cm high fitted with a glass frit at the bottom. The column was assembled vertically. The flow rate was 11 drops/min. The generator ( $G_2$ ) differed only in the diameter, 0.8 cm with a flow rate of 6 drops/min. The elutions for both generators for separation process were performed with  $0.003 \text{ mol}\cdot\text{L}^{-1}$  and  $0.03 \text{ mol}\cdot\text{L}^{-1}$  EDTA. The radioactivity measurements were performed using a Capintec CRC®-15 beta dose calibrator. A liquid scintillation counting analyzer (LSC) was also available for determination of the beta emitters ( $^{90}\text{Sr}$  and  $^{90}\text{Y}$ ) and an HPGe detector for the determination of the gamma emitter ( $^{85}\text{Sr}$  tracer). Pure samples of  $^{90}\text{Y}$  and  $^{90}\text{Sr}$ - $^{90}\text{Y}$  were used as standards in the LSC. The quality control performed for the two

generators system consisted of following the decay of  $^{90}\text{Y}$  in each elution and also by measuring the activities of  $^{85}\text{Sr}$  (HPGe) and  $^{90}\text{Sr}$  (beta counting). **Results.** Figure 1 shows the elution profile for the ( $G_1$ ) and ( $G_2$ ) generators eluted with  $0.03 \text{ mol.L}^{-1}$  EDTA. Generator  $G_2$  could be eluted with lower volumes (5 mL) than the generator  $G_1$  (8 mL). Figure 2 shows the elution yields for both generators. Initially (up to 28/8), the generators were eluted with  $0.003 \text{ mol.L}^{-1}$  EDTA with larger elution volumes and low yields. The concentration of EDTA was changed to  $0.03 \text{ mol.L}^{-1}$ , decreasing the elution volumes and increasing the elution yields. Both generators had the same behavior along the 4 months of use with average elution yields of 85%. The activity of each eluted sample was measured during 1 month for the  $^{90}\text{Y}$   $t_{1/2}$  determination. The results showed low deviation errors of the  $t_{1/2}$  obtained in relation to the theoretical one (2.6 to 6.5%) indicating a small presence of  $^{90}\text{Sr}$  during the elutions. It was noticed that for generator  $G_1$  the half-life started to lower in the last elutions, indicating a possible contamination with  $^{90}\text{Sr}$ . The same samples were analyzed for  $^{85}\text{Sr}$  (HPGe) and  $^{90}\text{Sr}$  (LSC) and it was not detected the presence of both radioisotopes, indicating a high radionuclidic purity of  $^{90}\text{Y}$ . **Conclusion.** A very promising methodology for the preparation of  $^{90}\text{Sr}$ - $^{90}\text{Y}$  generators was developed using the cation exchange technique. In this technique,  $^{90}\text{Sr}$  is strongly adsorbed in both generators, and  $^{90}\text{Y}$  eluted using  $0.03 \text{ mol.L}^{-1}$  EDTA. The results showed that chromatographic columns with smaller diameters presented a better performance during the elutions, with smaller elution volumes and larger radioactive concentrations. Next steps include the development of a methodology to destroy EDTA, the determination of  $^{90}\text{Sr}$  breakthrough using an ICP-OES technique and the gradual increase of the  $^{90}\text{Sr}$ - $^{90}\text{Y}$  activity.

### References

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