A primary activity standard for the alpha-emitting radionuclide Ra-224

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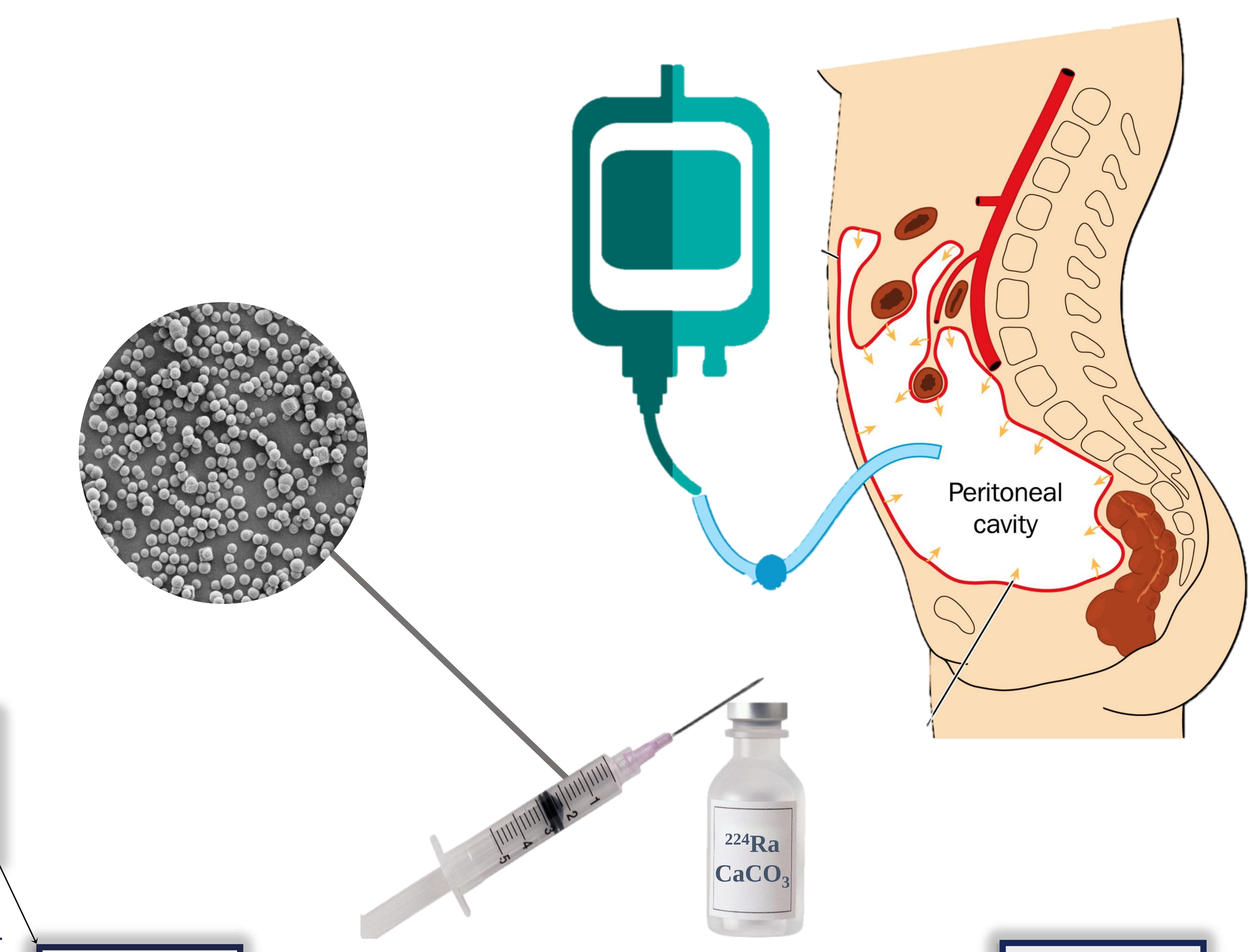
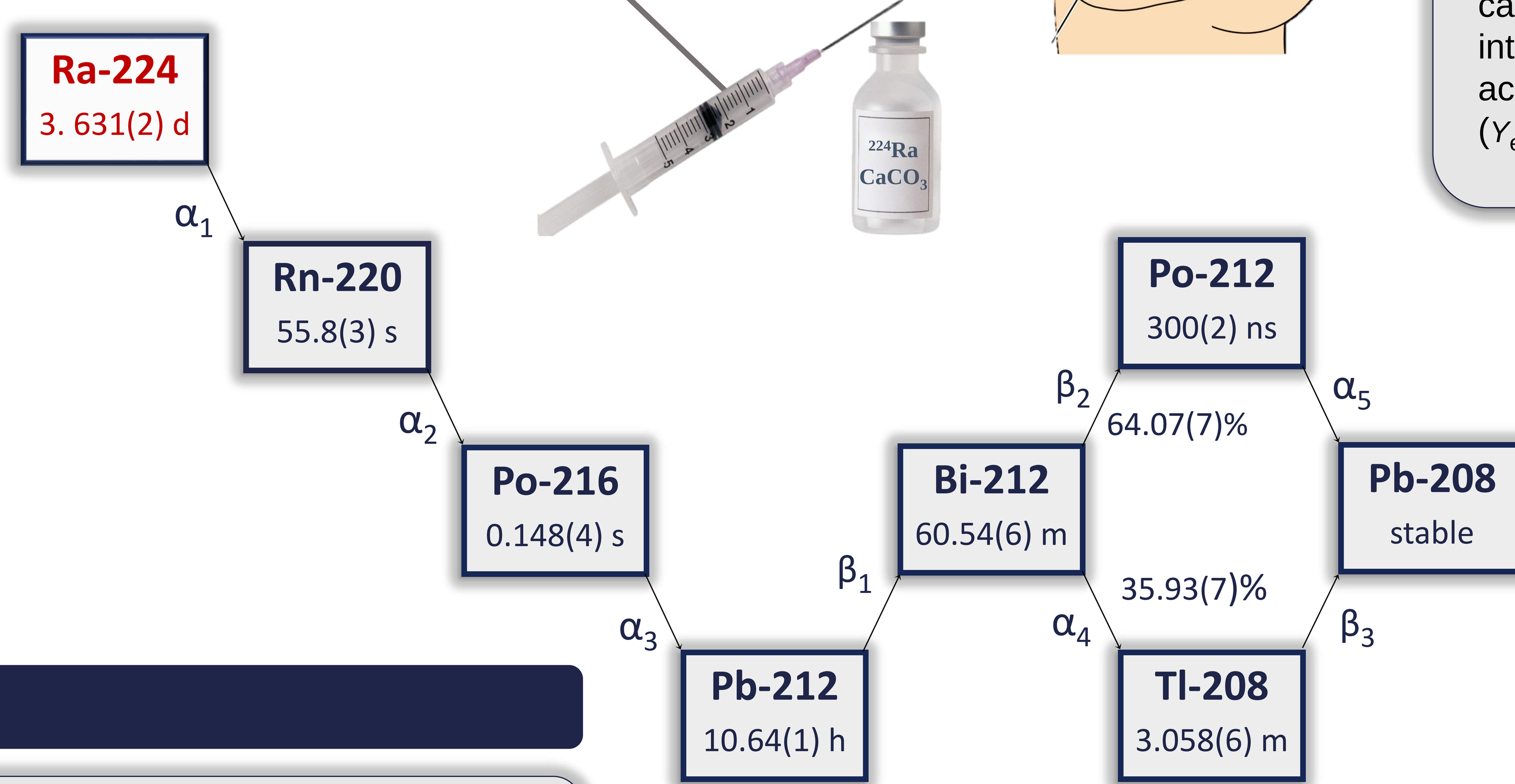
ABSTRACT

Alpha-emitting radiotherapies can offer cancer patients highly effective treatments with minimal side effects. For cavitary micro-metastatic diseases, a new therapy consisting of a suspension of injectable microparticles labeled with ^{224}Ra is showing promise in pre-clinical studies. With a 3.631(2) d half-life and a decay scheme that includes the emission of four energetic alpha particles, ^{224}Ra can deliver a high dose of therapeutic radiation to the metastasis, resulting in double-strand DNA breaks with minimal toxicity to surrounding healthy tissues. Prior to commencing clinical trials, it is essential to develop a radioactivity standard for ^{224}Ra to assure consistent dosage administration.





Daughter nuclide	Beta-Gamma transitions					
	A	P_{br}	B	P_{br}	C	weight
^{212}Pb	$\beta_{0,3}\gamma_{3,1}\gamma_{1,0}$	0.0499	$\beta_{0,2}\gamma_{2,0}$	0.817	$\beta_{0,0}$	0.1331
^{208}Tl	$\beta_{0,2}\gamma_{2,1}\gamma_{1,0}$	0.492	$\beta_{0,3}\gamma_{3,1}\gamma_{1,0}$	0.221	$\beta_{0,4}\gamma_{4,2}\gamma_{2,1}$	0.287

Tab.1 Simplified decay scheme for the beta-emitting daughters of ^{224}Ra used in MICELLE2 efficiency calculations. Branch probabilities (P_{br}) are renormalized such that "missing" decays are assigned to energetically similar cascades.

METHODS

The primary activity standardization was performed at NIST, with two liquid scintillation-counting based methods: live-timed $4\pi\alpha\beta$(LS)-γ(NaI) anticoincidence counting (LTAC) and triple-to-double coincidence ratio (TDCR) counting. Monte Carlo simulations were used to model instrument responses, assuring appropriate corrections and establishing theoretical links between methods.

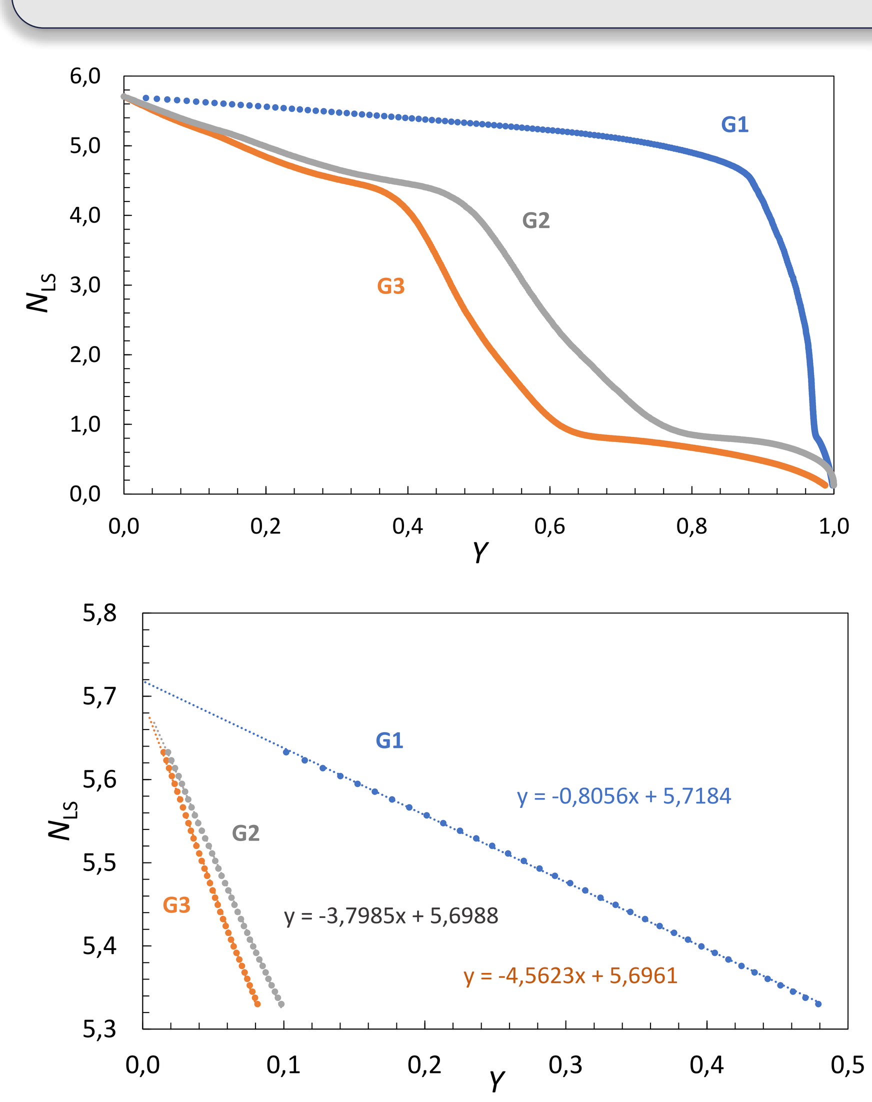


Fig. 1 LS channel count rates as a function of inefficiency, *Y*. The blue, orange, and gray data correspond to data acquired with G1, G2, and G3, respectively. Efficiency variation is achieved by increasing the lower-level discriminator threshold for the LS channel. (Top) LS channel count rate as a function of inefficiency, *Y*. (Bottom) Extrapolations over linear regions give convergent intercepts at *Y* =0.

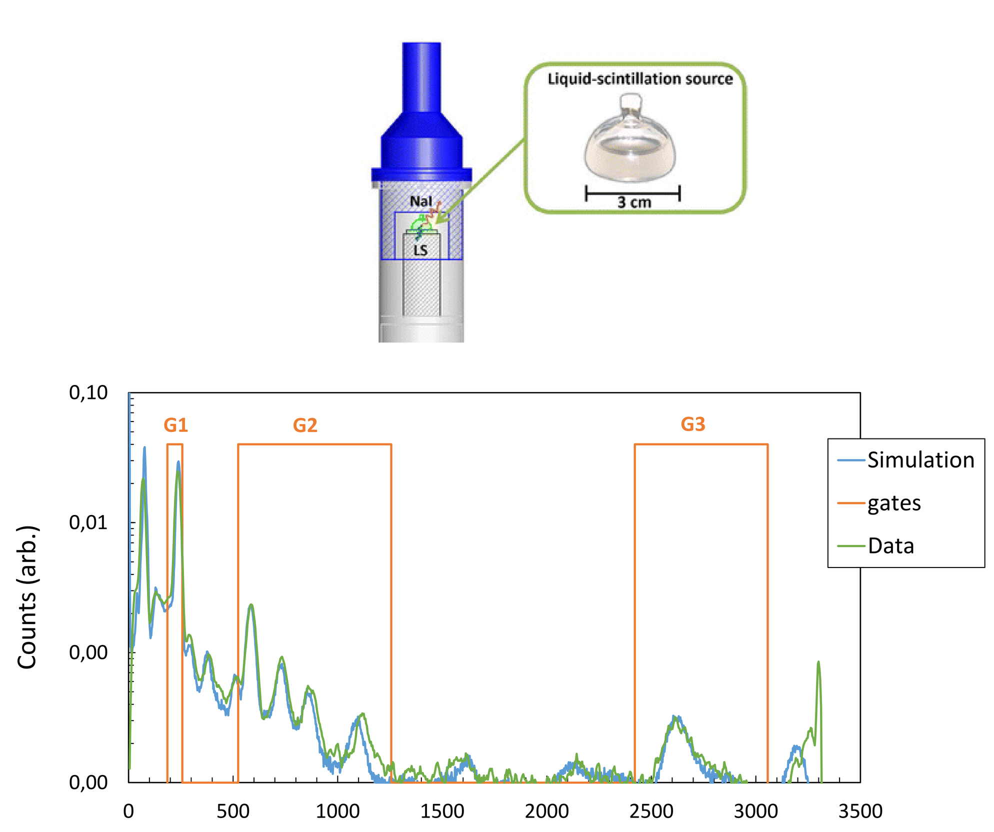


Fig.2 NaI(Tl) spectrum obtained with a ^{224}Ra source at secular equilibrium. The green trace is experimental data acquired in the γ-ray channel of the LTAC. The blue trace is from a Monte Carlo simulation. The anticoincidence gate settings are shown in orange.

RESULTS

Activity determinations using the TDCR method, were achieved by varying the efficiency with gray filters, achieving a triple-to-double coincidence ratio (K) range of (0.986 to 0.992) and corresponding to doubles counting efficiency (ε_D) range of (5.05 to 5.66) counts per ^{224}Ra decay, according to the MICELLE2 model. As expected for such a high-efficiency radionuclide, no trending with efficiency is seen in the calculated activities.
In LTAC experiments, all coincidence gates were set to monitor the LS counting efficiency for the different types of decay in the scheme All gates sampled yield also the LTAC data, with inefficiency extrapolations giving nearly convergent intercepts (Fig.1). Applying correction factors calculated from the Monte Carlo simulations, the accordance between intercepts obtained with different gates improved. For the final LTAC activity, an effective inefficiency:
($Y_{eff} = 0.29 * Y_1 + 0.67 * Y_2 + 0.04 * Y_3$) was used.

	EXP2		EXP3		EXP4	
	A / A_{TDCR}	u	A / A_{TDCR}	u	A / A_{TDCR}	u
TDCR	1	0.0019	1	0.0044	1	0.0024
LTAC	1.0023	0.0030	0.9998	0.0033	-	-
AutoIC	0.9983	0.0001	0.9981	0.0003	1.0002	0.0002
HPGe	0.9614	0.0222	0.9460	0.0141	-	-

Tab.2 Comparison of methods and experiments. Within each experiment (E2, E3, and E4), results are normalized to TDCR. For AutoIC, the given uncertainty (u) is the counting uncertainly only; all others are relative combined standard uncertainties (k = 1). The VIC results (orange band) are normalized by the K_{VIC} determined in E2 to provide and experiment-to-experiment comparison.

CAPINTEC IONIZATION CHAMBER		CRC-15R	CRC-55tR	CRC-35R	CRC-25PET	CRC-55tPET
5 mL ampoule		739(4)	736(4)	747(9)	739(5)	731(4)
20 mL ^{224}RaCl$_2$ in 20 mL vial		737(4)	735(4)	-	741(5)	-
2 mL ^{224}RaCl$_2$ in 20 mL vial		744(4)	740(4)	-	747(5)	-
12 mL ^{224}RaCl$_2$ in 20 mL syringe		753(5)	752(4)	762(9)	755(5)	747(4)
12 mL suspension of ^{224}Ra labeled CaCO$_3$ mp in 20 mL syringe		745(4)	745(4)	754(9)	747(6)	741(5)

Tab.3 Preliminary data dial settings determined by the calibration curve method to give the correct activity for 5 mL of a 1 mol/L HCl solution of ^{224}Ra in equilibrium with its daughters in a NIST standard 5 mL flame sealed ampoule and several other geometries. Uncertainties on the dial settings are given in parentheses and are expanded (k = 2) uncertainties.

CONCLUSIONS

The activities determined by multiple methods and across multiple experiments were consistent within uncertainties. The primary activity standard carries a combined standard uncertainty of 0.30 %.

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