Whole body counting of radium-223 for monitoring of staff in radionuclide therapy

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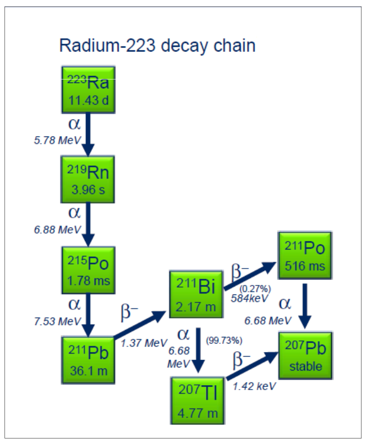
Introduction

Radionuclide alpha-therapy with Ra-223 dichloride (Xofigo™, Bayer Healthcare) is used in the treatment of prostate cancer patients with bone metastases. Prescribed activity is 50 kBq/kg body weight given 6 times at 4 weeks interval (Dauer et al. 2014). The half-life of Ra-223 is 11.43 d. A number of X-ray and gamma lines (1% of total energy) in the interval 80-400 keV allows for external detection with photon counting devices. For details see poster S10-P2



Technologists are wearing protective clothes, including mask and additional face shield, during activity drawing in the clean room and the subsequent injection in the dedicated therapy room.

Transport between the two is made in a special designed safe box with room for 8 syringes

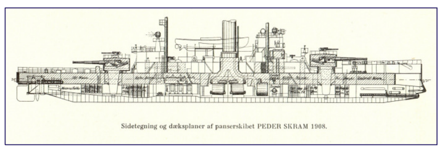
Dose coefficients for Ra-223 (ICRP 119) are high: 6.9 mSv/kBq for inhalation (assuming M = medium lung clearance) and 0.1 mSv/kBq for ingestion. Based on these numbers, the yearly dose limit for workers (20 mSv) may be received by a single inhalation of **3 kBq** (3 µL of injectate!), or by a constant body (lung) burden of **~140 Bq**. By ingestion, the limit for a weekly intake would be **4 kBq**.

Objective

To be licensed by the Danish authorities (NIRP/SIS) to use Ra-223 in the hospital, we had to demonstrate our ability to monitor staff and document that we comply with the dose limits for workers.

Methods

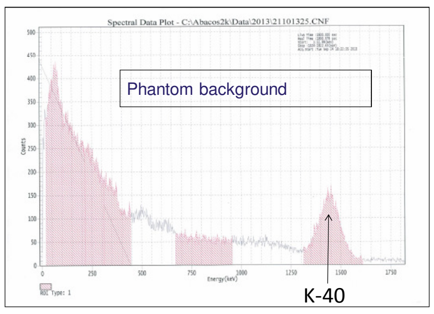
We used our low-background whole body counter (WBC) for this purpose, and tested/calibrated it by measuring a Ra-223 sample under realistic conditions. The WBC is underground in a construction built (1977) from selected low-activity materials. It is shielded with 15 cm of pre-WW2 steel and lined with Pb and Cd. The 4 uncollimated detectors are 6*4" NaI-cylinders placed 2 above and 2 below the bed.

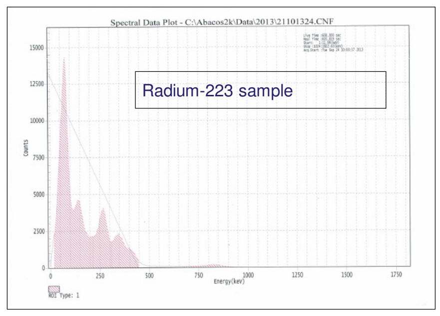


A whole body (WB) phantom of 1 L and 2 L bottles containing K-40 in a concentration relevant to human tissues can be configured to different person weights. Two fixed detector configurations have been used: STD (for WB) and LUNG (optimized for lung sensitivity).

One special bottle allows the centered insertion of, e.g., a 10 mL vial. Using this, a sample of 40 kBq Ra-223 was moved between bottle positions to simulate a uniform distribution or pure lung uptake. We compare the sensitivity (cps/Bq) to background to determine the critical level L_C, the detection limit L_D (or minimal detectable activity MDA), and the determination limit L_Q (or minimal quantifiable activity MQA) according to Currie (1968).

Results





Configuration		STD			LUNG	LUNG
Measuring time (s)			1800		1200	1200
Energy window (keV)			[20-445]		[20-445]	[210-445]
Phantom weight (kg)		55	77	88	77	77
Ra-223 calibration (Bq/cps)		34	38	39	7	21
Phantom background (cps)		27	30	32	37	12
Uncertainty (Bq)	σ_b	4.2	4.9	5.2	1.2	2.1
L_C Decision limit[1] (Bq)	$2.33{*}\sigma_b$	**10**	**11**	**12**	**3**	**5**
L_D Detection limit[2] (Bq)	$4.65{*}\sigma_b$	**20**	**23**	**24**	**6**	**10**
L_Q Quantification limit[3] (Bq)	$14.1{*}\sigma_b$	**59**	**69**	**73**	**17**	**29**

1: With (>)95% probability, a measured signal > L_C is a real "detection"
2: An activity larger than L_D can a priori be expected (>95%) to lead to a detection
3:Signals above L_Q are determined with <10% uncertainty

We received our license on March 4, 2014 and we have to date (August 18, 2015) performed 274 injections to 83 patients on 31 treatment days.
NO significant internal contamination with Ra-223 has been detected**.**

Discussion

Only counting statistics is considered and this underestimates the total uncertainty. The stated limits require that true individual background is predetermined for the involved staff, preferable on every treatment day to reflect actual level of K-40. Concurrent internal contaminations in Bq-amounts of other nuclides (e.g., Tc-99m, F-18) used in nuclear medicine is a challenge that must be considered by inspection of individual spectra.

In case of a contamination, the WBC gives very little spatial information and calculation of (effective) doses from measured activity would be highly uncertain. Assuming all measured activity present in the lungs is conservative.

The critical handling phases are dose drawing and injection, where aerosols with high activity concentrations might accidentally occur. Standard protection equipment minimizes the risk of inhalation and apparently most protection regulators have decided to neglect any remaining risk from these procedures.

Recently, SIS has accepted to base dose calculations on the use of F (fast) lung clearance for $RaCl_2$. The implied reduction in dose coefficient and demand on sensitivity will allow us to reduce the measuring scheme, using a standard background. It will further make it feasible to use a standard gamma camera at sites not having a WBC.

Conclusions

Our detection and quantification limits with the WBC are sufficient to document compliance with dose limits. Until now, no incidents have challenged the robustness of the procedures and equipment applied for protection.

References:

Currie LA: Limits for qualitative detection and quantitative determination: Application to radiochemistry. Anal. Chem. 1968;40;586-593

Dauer LT et al: Radiation safety considerations for the use of $^{223}RaCl_2$ in men with castration-resistent prostate cancer. Health Physics 2014;104:494-504

S. Holm and J. Mortensen are unpaid members of an advisory board for Bayer Healthcare on Xofigo.