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REFERENCES AND APPLICABLE DOCUMENTS

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LIST OF ACRONYMS AND ABBREVIATIONS

PET	Positron Emission Tomography
TTY	Thick Target Yield [MBq/μAh], radionuclide production efficiency with the target thick enough to degrade the energy of the projectile to the reaction threshold
TY	Target Yield [MBq/μAh], radionuclide production efficiency in the energy window above the nuclear reaction threshold
EOB	End of Bombardment

EXECUTIVE SUMMARY

The production yields and radioisotopic purity of the medically interesting scandium radioisotopes were measured. The feasibility of the cyclotron produced ^{43}Sc and ^{44m,g}Sc is confirmed. However, the direct cyclotron production of ^{47}Sc is associated with too high impurity level for practical use.

INTRODUCTION

Radioisotopes of scandium offer a variety of applications in the field of nuclear medicine. Both positron emitters ^{43}Sc and ^{44g}Sc are promising PET isotopes (respectively: $T_{1/2}$ = 3.89 h and 4.04 h, β+ branching = 88% and 95%, max. β+ energy = 1.20 MeV and 1.47 MeV). Additionally, ^{44m}Sc ($T_{1/2}$ = 58.6 h) can be used as ^{44m}Sc/^{44g}Sc long-lived in-vivo generator as it decays mainly by a low energy gamma transition to the ^{44g}Sc ground state. Meanwhile, ^{47}Sc is a β- emitter with favourable characteristics for therapeutic purposes (average β- energy = 162 keV, $T_{1/2}$ = 3.35 d).

MATERIALS AND METHODS

Production of the medical radioisotopes ^{43}Sc, ^{44g}Sc and ^{47}Sc was investigated by Warsaw University using proton, deuteron and alpha particle beams. Four cyclotrons were employed: the U200P variable energy heavy ion cyclotron and the PETtrace commercial cyclotron (p and d beams) at the University of Warsaw, the locally built C30 proton cyclotron in the National Centre of Nuclear Research in Świerk near Warsaw and the C70 Arronax cyclotron at Saint Herblain, France. The external station for solid sample high current irradiations was built for the PETtrace cyclotron.

These accelerators were used to irradiate targets of $^{nat}CaCO_3$, enriched $CaCO_3$, ^{nat}Ca, ^{nat}KCl, $^{nat}TiO_2$ and enriched TiO_2. After the irradiation, targets were measured using gamma-ray spectroscopy techniques to determine the (Thick) Target Yields (TTY or TY) and isotopic purities of produced radioisotopes.

RESULTS AND DISCUSSION

The determined yield of production of the scandium isotopes with the use of proton, deuteron and alpha particle beams are presented in Table 1, Table 2 and Table 3 correspondingly [1,2]. Their application possibilities are also affected by the available target enrichment and the level of produced impurities. The obtained values were compared with the available cross-section data and the evaporation model predictions (Figures 1–5). Examples of the produced EOB activities and relative impurities are shown in Tables 4–5 (proton and deuteron beams), Table 6 (alpha particle beam, ^{44g,m}Sc production) and Figure 6 (alpha particle beam, ^{43}Sc production).

Our measurements indicate that the **4 h irradiation of $^{nat}CaCO_3$ with 20 MeV alpha beam of the 25 μA intensity and in the energy range 20→0 MeV would produce around 6 GBq ^{43}Sc with negligible contamination of ^{44g}Sc and ^{47}Sc at the level of 0.03%** (Fig. 6). These data are of particular interest when a high intensity alpha beam will become available at GANIL from the SPIRAL2 linac. The productions using the ^{nat}KCl targets provided significantly higher radioactive contaminants (around 10%).

Similar to the alpha particle beam and ^{nat}Ca targets, the production **of ^{43}Sc with the use of the deuteron beam provides comparably high yield with less than 1% radioactive contaminants but the enriched ^{42}Ca target** is required.

The 15 MeV proton beam can be used for the production of ^{44g}Sc even with natural calcium target, yielding 50 MBq/µA in 4 h irradiation accompanied by 3% of radioactive impurity (Table 4). The use of commercially available **enriched ^{42}CaCO3 target almost completely eliminates the contaminants and increases the produced activity to 2200 MBq/µA**. The use of 29 MeV alpha beam is also possible, but produces around 15 times less ^{44g}Sc activity.

As shown in Tables 1 and 3–5, the **production of the ^{47}Sc radioisotope with the proton beam is doable but contaminated with high amount of long-lived radioactive Sc impurity** (26% of ^{48}Sc in case of ^{48}Ca target or 66% ^{44m}Sc for ^{48}Ti target), while the production with the alpha beam has unacceptably low yield (even on the enriched target). However, we intend to still investigate the production and the feasibility of a ^{47}Ca/^{47}Sc generator.

Additionally, all three projectiles can be used for the production of the ^{44m}Sc/^{44g}Sc generator. As shown on Fig. 7 they are comparable, yet with heavier projectiles, the population of the high-spin isomer ^{44m}Sc is favored and less decay is needed to get rid of excess ^{44g}Sc. Around 1 GBq of ^{44m}Sc/^{44g}Sc generator can be obtained in one irradiation of an enriched target, with less than 1% of long-lived radioactive impurity for each beam type.

We are also currently working on the labelling of the produced Sc isotopes for the formation of radiopharmaceuticals. Several methods are currently investigated at ARRONAX and in collaborations with the Institute of Nuclear Chemistry and, using a small animal PET by a team from the University of Warsaw Biological and Chemical Research Centre.

CONCLUSIONS

^{43}Sc can be produced with high yield and good purity with α particle beam and natural calcium target or with deuteron beam and enriched ^{42}Ca.

The optimal production of ^{44g}Sc was achieved with the use of proton beam and the enriched ^{44}Ca target (although natural target can be considered).

With the same beam current, a comparable activity of ^{44m}Sc can be obtained with proton, deuteron or α particle beams.

The production of ^{47}Sc with protons has too much radioisotopic impurities while the production with alpha particles has too low yield.

The research on optimal Sc radiochemistry and the ^{47}Ca/^{47}Sc generator is underway.

TABLES

Table 1. Comparison of the measured Thick Target Yield [MBq/μAh] of the medical Sc radioisotopes for the different $CaCO_3$ targets irradiated with proton beams with various energies [1].

Isotope:	**^{43}Sc**	**^{44g}Sc**		**^{44m}Sc**	**^{47}Sc**
Target and enrichment:	$^{43}CaCO_3$ (90%)	$^{nat}CaCO_3$	$^{44}CaCO_3$ (94.8%)	$^{44}CaCO_3$ (94.8%)	$^{48}CaCO_3$ (97.1%)
p energy [MeV]			**TTY [MBq/μAh]**		
7.6	61(6)	2.6(4)	120(20)	0.13(5)	
9.7	109(11)	6.1(4)	280(20)	0.40(4)	0.47(5)
10.7	180(20)	8.2(9)	370(40)	0.84(5)	2.1(2)
11.3		8.7(9)	400(40)	1.5(1)	
11.9	200(20)	11(1)	500(50)	1.3(2)	6.8(8)
12.8	240(20)	11.9(1.0)	540(50)	2.0(2)	10(1)
14.3	260(30)	16(1)	730(50)	2.7(3)	21(2)
15.2	317(14)	17.2(6)	780(30)	3.6(1)	31(2)
17.5	410(40)				
21.8		23(1)	1030(50)	5.9(3)	94(6)
22.0		22(2)	980(100)	7.5(8)	
22.4					98(5)
22.8		21(1)	940(40)	7.0(2)	105(6)
28.2					136(8)
28.5		23(1)	1020(50)	8.0(4)	139(16)

Table 2. Comparison of the measured Thick Target Yield [MBq/µAh] of the medical ^{43}Sc radioisotope irradiated with deuteron beams in two energy ranges [1].

Isotope:	**^{43}Sc**
Target and enrichment:	^{42}CaCO$_3$ (95.9%)
d energy [MeV]	**TTY [MBq/µAh]**
4.7-0	5.6(8)
6.8-0	45(4)

Table 3. Yields of Sc and ^{44}Ti radioisotopes produced by alpha particle beams [2].

Radioisotope	**Target chemical form**	**α-particle energy range (MeV)**	**TTY or *TY* [MBq/µAh]**
^{43}Sc	^{nat}CaCO$_3$	29-0	110(20)
		20-0	84(4)
	^{nat}Ca	29-0	240(20)
		20-0	190(30)
	^{40}CaCO$_3$	20-0	88(13)
	^{nat}KCl	29-19	*4.2(6)*
	^{41}KCl (95.4 %)	29-19	*60(9)*
^{44g}Sc	^{42}CaCO$_3$ (68 %)	29-12	31(5)
	^{42}CaCO$_3$ (95.9 %)	29-12	44(7)
	^{42}CaCO$_3$ (68 %)	29-20	*25(4)*
	^{42}CaCO$_3$ (95.9 %)	50-12	54(8)
	^{nat}KCl	20-2	4.3(8)
	^{41}KCl (95.4 %)	20-2	60(10)

^{44m}Sc	^{42}CaCO3 (68 %)	29-12	3.3(6)
	^{42}CaCO3 (95.9 %)	29-12	4.7(8)
	^{42}CaCO3 (68 %)	29-20	*2.7(4)*
	^{42}CaCO3 (95.9 %)	50-12	9.7(6)
	^{nat}KCl	20-2	0.21(3)
	^{41}KCl (95.4 %)	20-2	3.0(6)
^{47}Sc	^{nat}CaCO$_3$	20-0	0.020(2)
	^{44}CaCO$_3$ (98 %)	20-0	0.93(9)
^{44}Ti	^{42}CaCO$_3$ (68 %)	29-12	$3.9\cdot10^{-5}$(1.0)
	^{42}CaCO$_3$ (95.9 %)	29-12	$5.5\cdot10^{-5}$(1.0)
	^{42}CaCO$_3$ (95.9 %)	56-12	$2.6\cdot10^{-4}$(5)

Table 4. Examples of the deduced EOB activities and relative impurities in medical Sc samples, produced with the commercially available, most enriched $CaCO_3$ targets using proton and deuteron beams.

		^{43}Sc	**^{44g}Sc**		**^{47}Sc**
irradiation time		4 h	4 h		8 h
		proton beam (1 µA)			
energy [MeV]		15.2 – 2.2	15.2 – 2.2	15.2 – 2.2	22.8 – 17.1
target		$^{43}CaCO_3$ (90%)	$^{nat}CaCO_3$	$^{44}CaCO_3$ (94.8%)	$^{48}CaCO_3$ (97.1%)
EOB [MBq]		910(40)	50(2)	2240(80)	420(40)
relative activity at EOB	^{43}Sc	100	3.0(2)	0.0049(6)	0.25(4)
	^{44g}Sc	12.0(1.5)	100	100	0.106(13)
	^{44m}Sc	0.95(12)	0.62(3)	0.62(3)	0.0077(9)
	^{46}Sc				≤0.07*
	^{47}Sc	0.0131(17)	0.56(7)	0.0033(4)	100
	^{48}Sc	0.025(3)	1.1(1)	0.0063(8)	26(3)
	^{47}Ca	0.00033(5)	0.014(2)	8.4(1)E-5	13.0(1.6)
	^{43}K				0.00096(13)
		deuteron beam (1 µA)			
energy [MeV]		6.8-0			
target		$^{42}CaCO_3$ (95.9%)			
EOB [MBq]		129(11)			
relative activity at EOB	^{43}Sc	100			
	^{44g}Sc	0.25(16)			
	^{44m}Sc	0.0054(19)			
	^{47}Sc	0.0019(2)			
	^{48}Sc	0.06(2)			

*calculated from detection limit

Table 5. ^{47}Sc production results extrapolated for 8 h irradiation time with 1 µA of proton beam and a $^{48}TiO_2$ (99.63%) target for proton energy 28.0 – 18.3 MeV.

projectile energy		**28.0-18.3 MeV**	
^{47}Sc TY [MBq/µAh]		2.6(5)	
measuring time		at EOB	40 h post-EOB
activity ^{47}Sc [MBq]		20(4)	14(3)
relative activities	**^{47}Sc**	100	100
	^{43}Sc	4.3(1.2)	0.0048(14)
	^{44g}Sc	170(40)	71(19)
	^{44m}Sc	80(20)	66(18)
	^{46}Sc	0.033(9)	0.046(12)
	^{48}Sc	0.08(2)	0.058(15)
	^{48}V	190(50)	250(60)

Table 6. Relative composition of the activities EOB induced by a 12 h alpha particle bombardment of enriched ^{42}Ca targets for two energy ranges.

Isotope	**29-12 MeV 68 %**	**29-20 MeV 68 %**	**29-20 MeV 95.9 %**
^{44m}Sc	100	100	100
^{44g}Sc	481(92)	466(93)	466(93)
^{43}Sc	318(46)	157(37)	12(3)
^{46}Sc	0.044(15)	0.053(13)	0.018(4)
^{47}Sc	0.44(20)	0.28(8)	0.09(3)

FIGURES

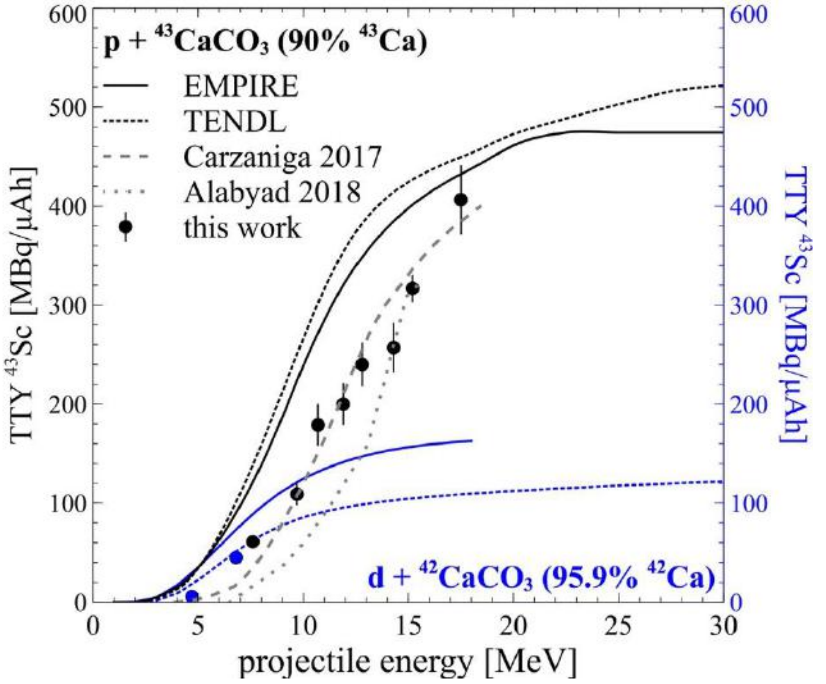

Fig. 1. Comparison of the experimentally determined ^{43}Sc Thick Target Yield with the theoretical estimates for a deuteron beam impinging on an isotopically enriched ^{42}CaCO$_3$ target and protons impinging on enriched ^{43}CaCO$_3$.

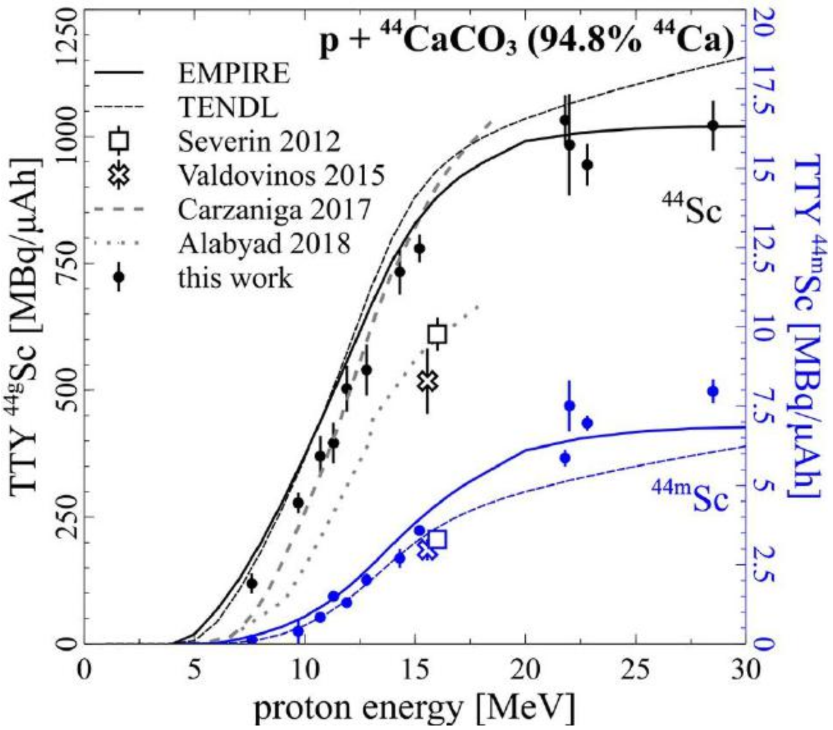

Fig. 2. Measured Thick Target Yields of ^{44g}Sc and ^{44m}Sc radioisotopes produced in the ^{44}Ca(p,n) reaction compared with the theoretical predictions based on TENDL cross-section and EMPIRE reaction code calculations.

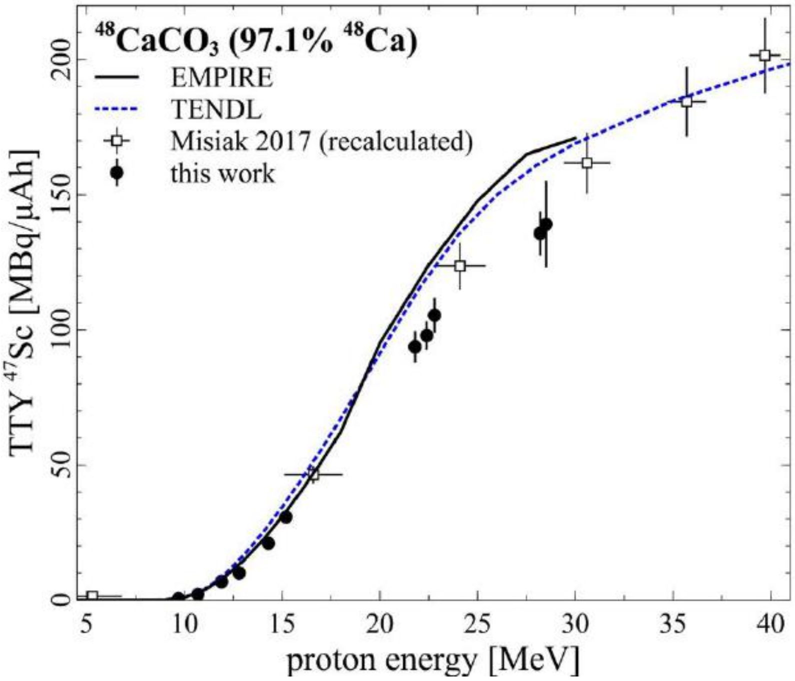

Fig. 3. Measured Thick Target Yield of ^{47}Sc obtained using the ^{48}Ca(p,2n) reaction with theoretical predictions based on EMPIRE reaction code calculations and TENDL predictions.

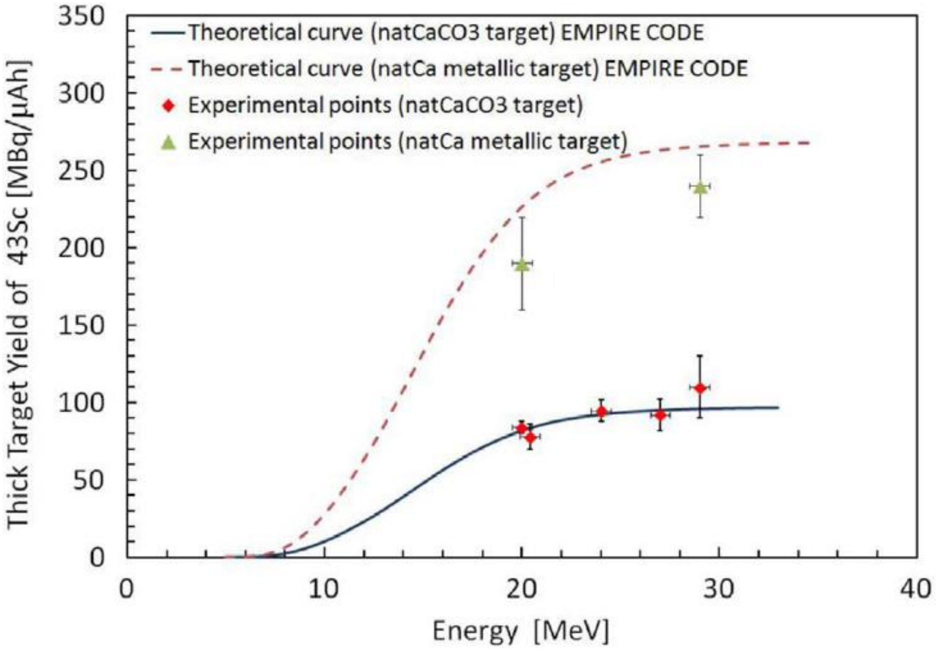

Fig. 4. Comparison of the experimental and theoretical Thick Target Yield (TTY) for the production of the ^{43}Sc radioisotope by an alpha-particle beam incident on ^{nat}CaCO$_3$ and metallic ^{nat}Ca targets.

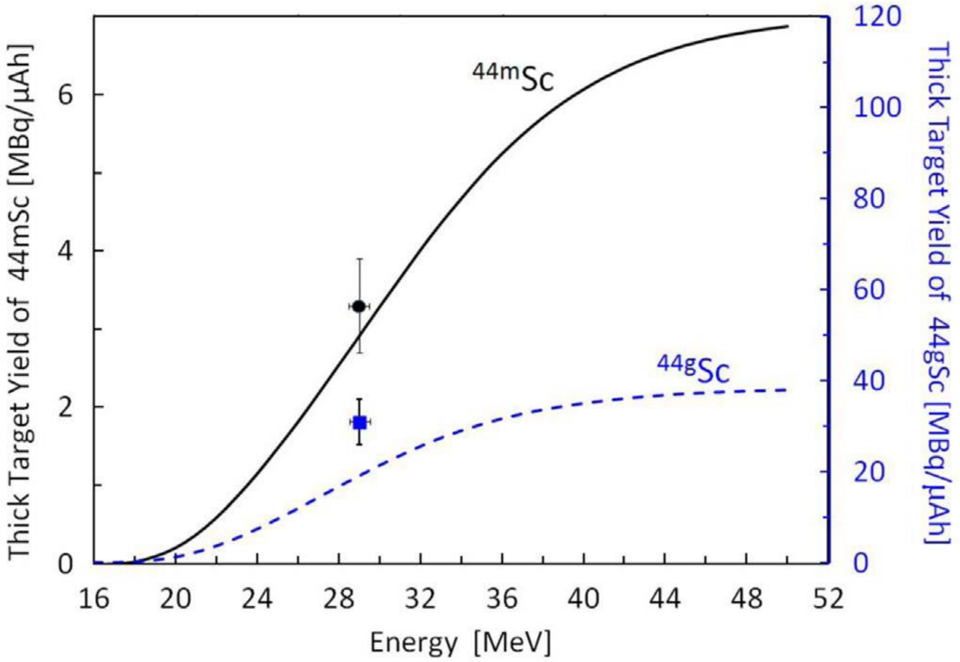

Fig. 5. Comparison of the theoretical (lines) and experimental (points) Thick Target Yields for the production of ^{44g}Sc isomers with a ^{42}CaCO$_3$ (enriched 68%) target.

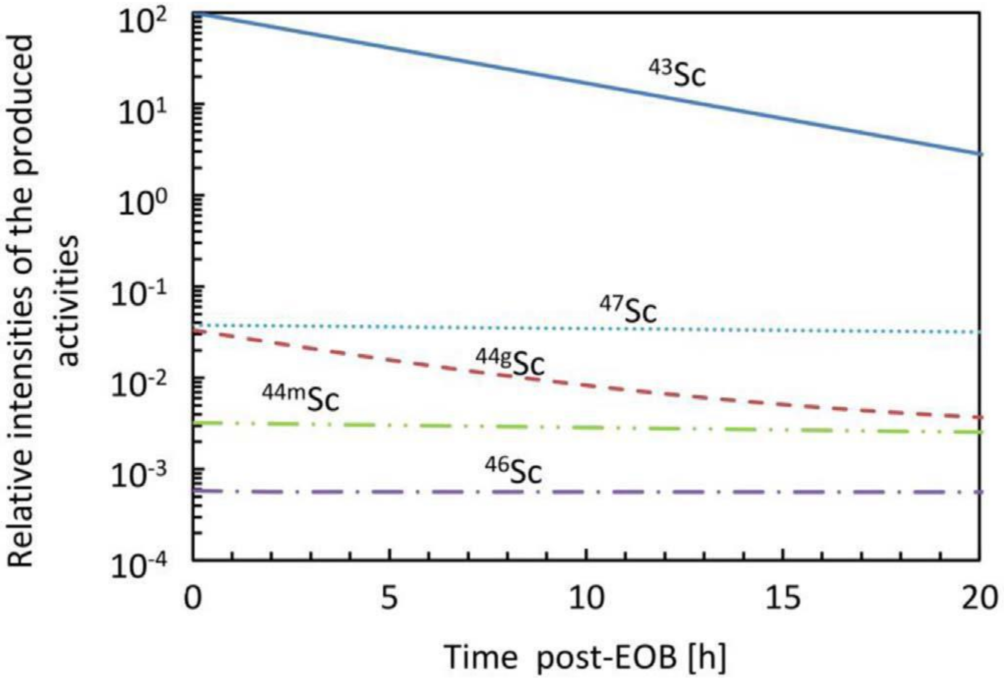

Fig. 6. Evolution with time of the relative intensities of Sc radioisotopes produced during a 4 h irradiation of a ^{nat}CaCO$_3$ target with a 20 MeV α-particle beam.

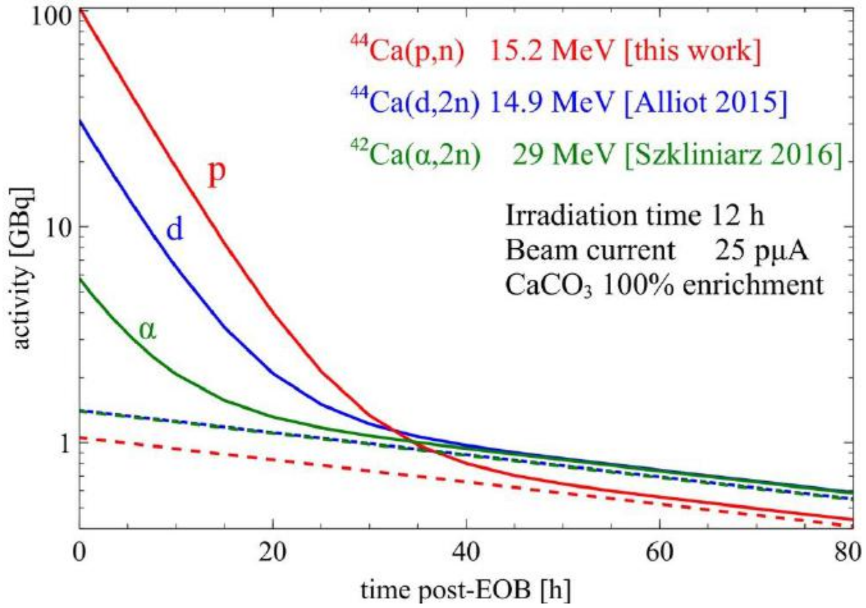

Fig. 7. Activity of produced samples of ^{44m,g}Sc after 12 h irradiation time of a thick target with proton, deuteron and alpha particle beams of 25 pμA intensity.