Calcium targets for production of the medical Sc radioisotopes in reactions with p, d or α projectiles

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Sources of the medical radioisotopes:

reactions induced by n – i.e. reactors

naturally decaying isotopes and so called generators

and nowadays …. alternative methods (accelerators)

mainly ‘sparked’ by unplanned close-down of reactors causing the shortage of the isotopes widely used.

The studies of the alternative methods were triggered not only by the reactors but development of diagnostic techniques enhanced this search as well

Research for replacements of so far routinely applied isotopes of short half-lives such as e.g. 18F (110 min), or 68Ga (68 min).

	Reactors neutrons	generators decays	Cyclotrons p, d, α or heavy ion beams
advantages	+ high production efficiency + one production centre able to supply large regions	+ isotopes available at spot, no need of transport + usually long life-time + easy to use	+ production of β+ emitters for PET diagnostic + decentralisation + high activity + much lower investment cost comparing to reactors
drawbacks	- high costs (operational and investment) - shortage if unexpected shutdown	- safety concerns - 'milking' requires educated personnel at hospital	- production limited by the available energy of the beams - in case of use of solid targets wet chemistry procedures are required

Scandium radioisotopes

- **Diagnostic:**
  - ✓ positron emitting ^{43}Sc (β+ 3.89 h) and ^{44g}Sc (β+ 3.97 h) which can compete with commonly in use ^{68}Ga with ~68 min).
  - ✓ ^{44g}Sc offers unique possibilities in the three-photon PET technique.
  - ✓ The ^{44m}Sc (58.6 h) which decays to the ground state ^{44g}Sc mainly by low energy transition can be used as in vivo $^{44m}Sc/^{44g}Sc$ generator.

- **Therapeutic**
  - ✓ ^{47}Sc (3.4 d; β-, 162 keV) - has favourable characteristic for therapeutic application. It is perfect match for theranostic pair with 43 and 44Sc for targeted therapy.

They can be produced in reactions induced by p or n on Ti,

(48Ti(p.2p)47Sc, 47Ti(n,p)47Sc)

using metal or oxide form of Ti.

But majority of studies is performed using reactions on Calcium, natural or enriched, with proton, deuteron and α irradiation

Isotope produced	U200P (α) / energy	PETtrace (p and d) and C30 (p)
^{43}Sc (^{nat} and ^{40}Ca)	^{40}Ca(α,p) / 20 MeV ^{40}Ca(α,n)^{43}Ti → ^{43}Sc	^{42}Ca(d,n) / 8 MeV ^{43}Ca(p,n) / 16 MeV
^{44}Sc (^{42}Ca)	^{42}Ca(α,2n) / 29 MeV	^{44}Ca(p,n) / 16 MeV
^{47}Sc (^{nat}Ca)	^{44}Ca(α,p)	
$^{44m/44g}$Sc *in-vivo* generator	^{42}Ca(α,2n)	^{44}Ca(p,n) / 16 MeV ^{44}Ca(d,2n) / 8 MeV

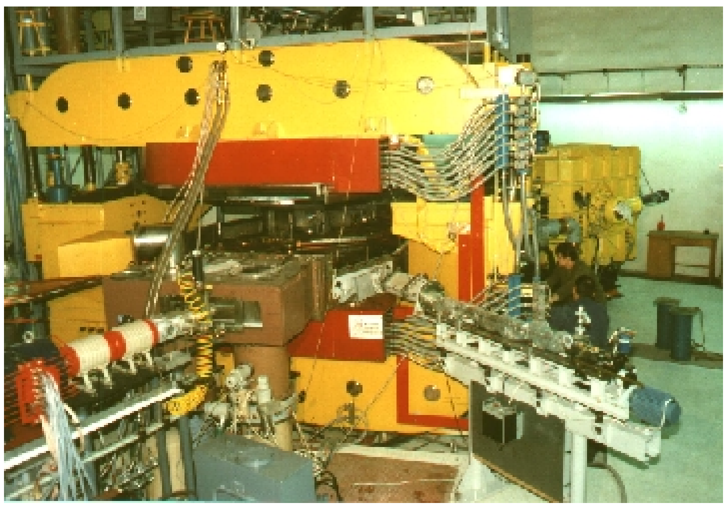
paper available on line at
App Rad Isotop, 118(2016)182

paper available on line at
App Rad Isotop, 142(2018)104

^{44}Ti/^{44g}Sc	*^{42}Ca (α,2n) / 29 MeV*	

Warsaw Heavy Ion Cyclotron

For radioisotopes production the He^{+} internal beam is used:
max energy 32 MeV
max intensity 1 μA



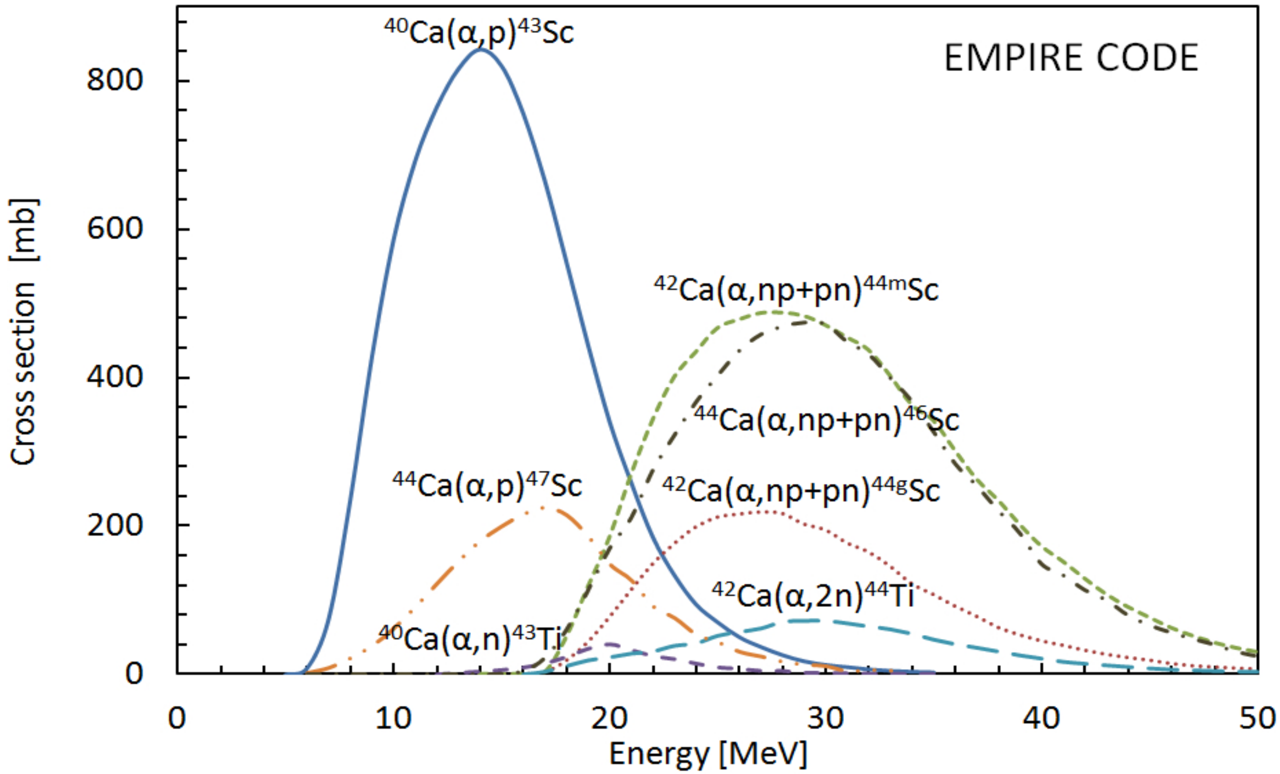
PETtrace

p/d high current cyclotron

p 16.5 MeV, intern. 80 μA
d 8.0 MeV, intern. 40 μA

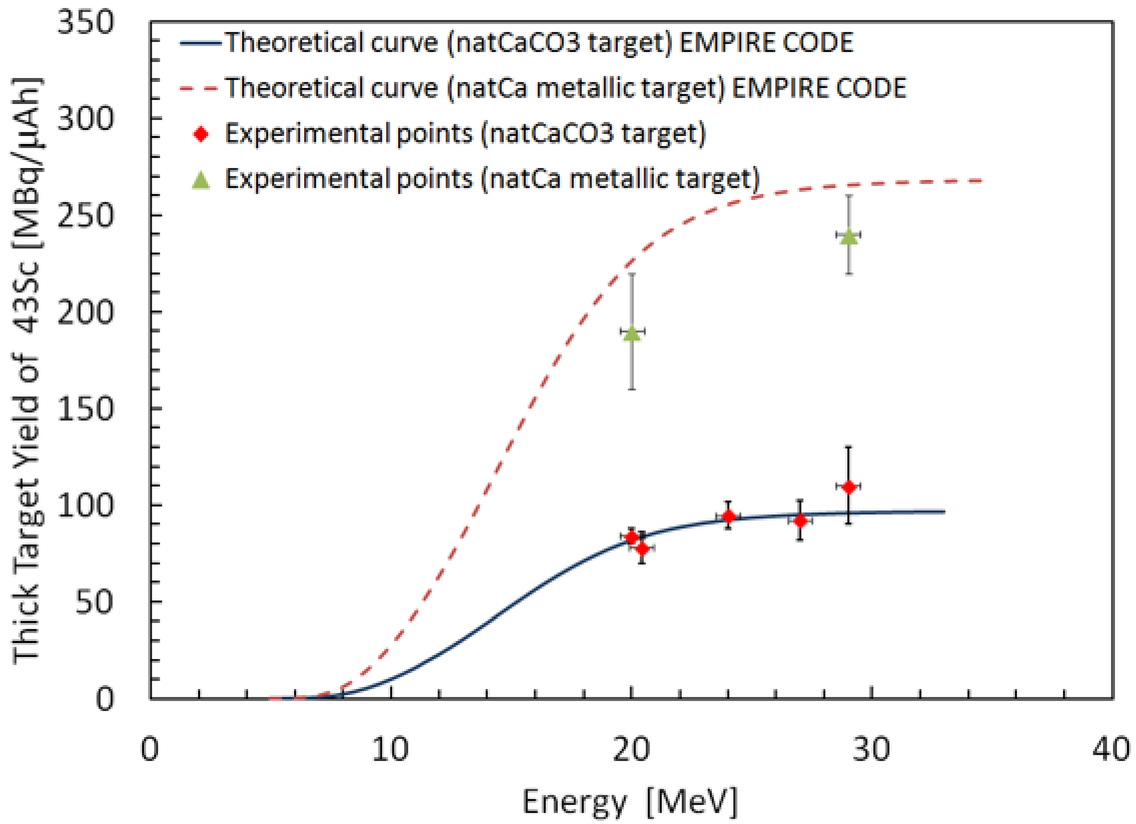
Cyclotron C30 *– located at NCBJ, Świerk, home made, delivering p with low intensities but with higher than PETtrace energies (up to 28 MeV)*

Sc with α particles



natCa:	40Ca	42Ca	43Ca	44Ca	46Ca	48Ca
%	96.64	0.647	0.135	2.086	0.004	0.187

$^{40}Ca(\alpha,p)^{43}Sc$



α 20 MeV

$^{nat}CaCO_3$, 25 µA, 4 h

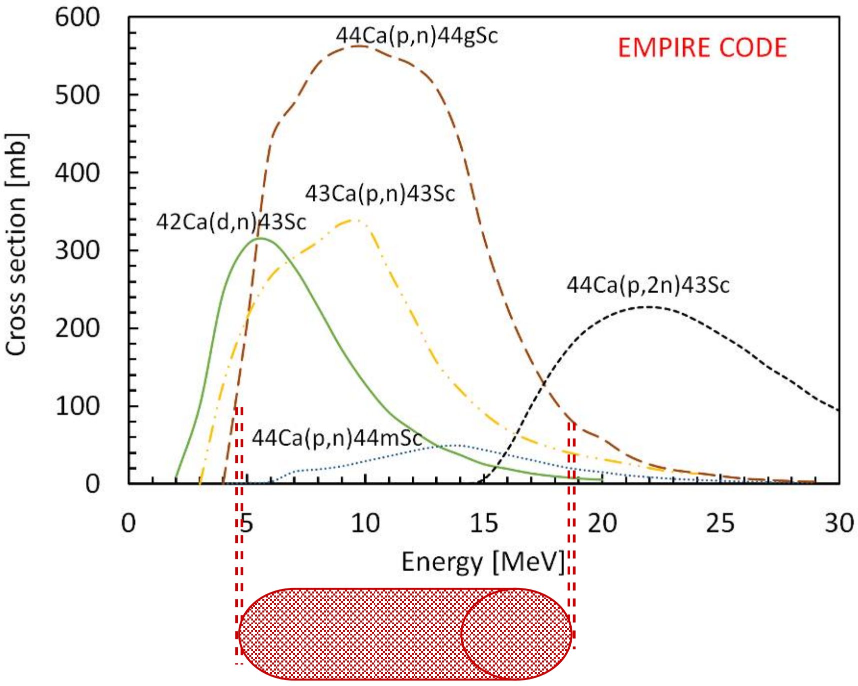
=

6 GBq ^{43}Sc

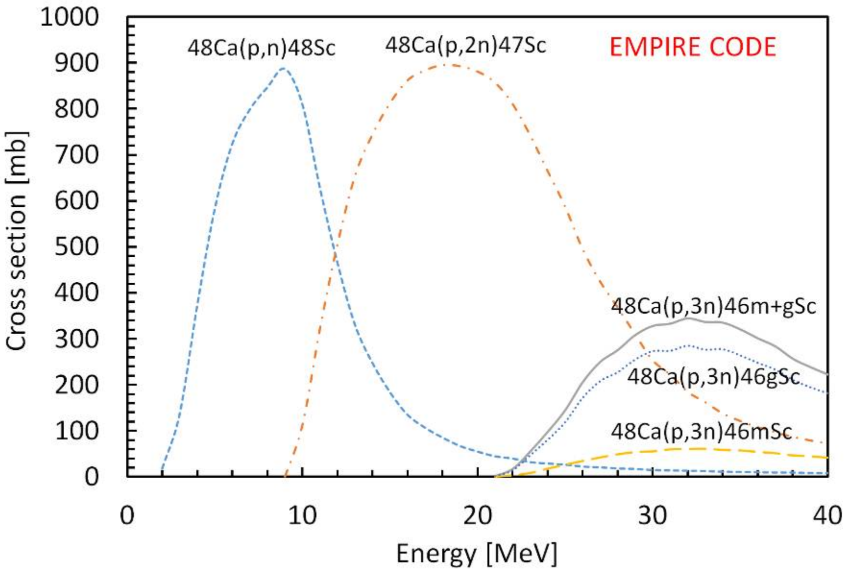
(18 MBq impurities)

Estimation for 25 µA beam current

Sc with p or d



Calculated cross sections for the production of ^{43}Sc and ^{44}Sc radioisotopes with p and d beams using 42, 43 or 44Ca targets.

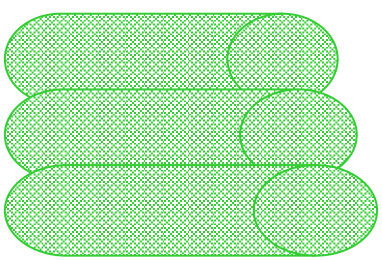


Calculated cross sections for production of 46, 47, 48Sc isotopes in proton induced reactions on the ^{48}Ca target.

Chemical form	$CaCO_3$ The only form of the enriched materials available commercially	CaO Obtained by (easy) conversion; thermal decomposition the CaCO3	Ca Needs conversion; it's two steps procedure
	Ready to be used for target preparation. Encapsulated pellets, pressed into holder	Unstable in the air so requires handling in the inert atmosphere	Very unstable in the air so requires handling in the inert atmosphere
beam 	Decomposes under the beam producing CaO+CO2 and, although short lived but, big amount of 13N (decaying in ~10 min via β+ to 13C) Under more intensive beam targets cracks due to this change	Low production of 13N 	If not sufficient cooling can melt under the beam
Treatment after irradiation	Dissolves very easily in a weak acids	Dissolving is a bit more difficult	Dissolves even in water
efficiency??			

$$CaCO_3 \Rightarrow CaO + CO_2$$
$$2CaO + Zr \Rightarrow Ca + ZrO_2$$

	Range of 16 MeV p/ *25 MeV α* [mg/cm²]	Stop. power MeV/(mg/cm²)	nucl/(mg/cm²) $N \times A_v \times 10^{-3}$	Thermal conductivity
$CaCO_3$ 2.71 g/cm³ 825 °C/decomp.	348.59 *67.208*	0.02576 *0.2157*	3.48 *0.67*	??
CaO 3.35 g/cm³ 2613 °C / 2850 °C	368.50 *72.025*	0.02450 *0.2028*	6.58 *1.28*	??
Ca 1.55 g/cm³ 842°C / 1484°C	389.05 *77.066*	0.02345 *0.1922*	9.72 *1.92*	201 W/(m·K)



1

1.05

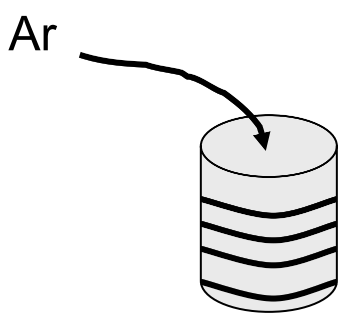
1.11

$$A = \Phi N \sigma (1-e^{-\lambda t})$$

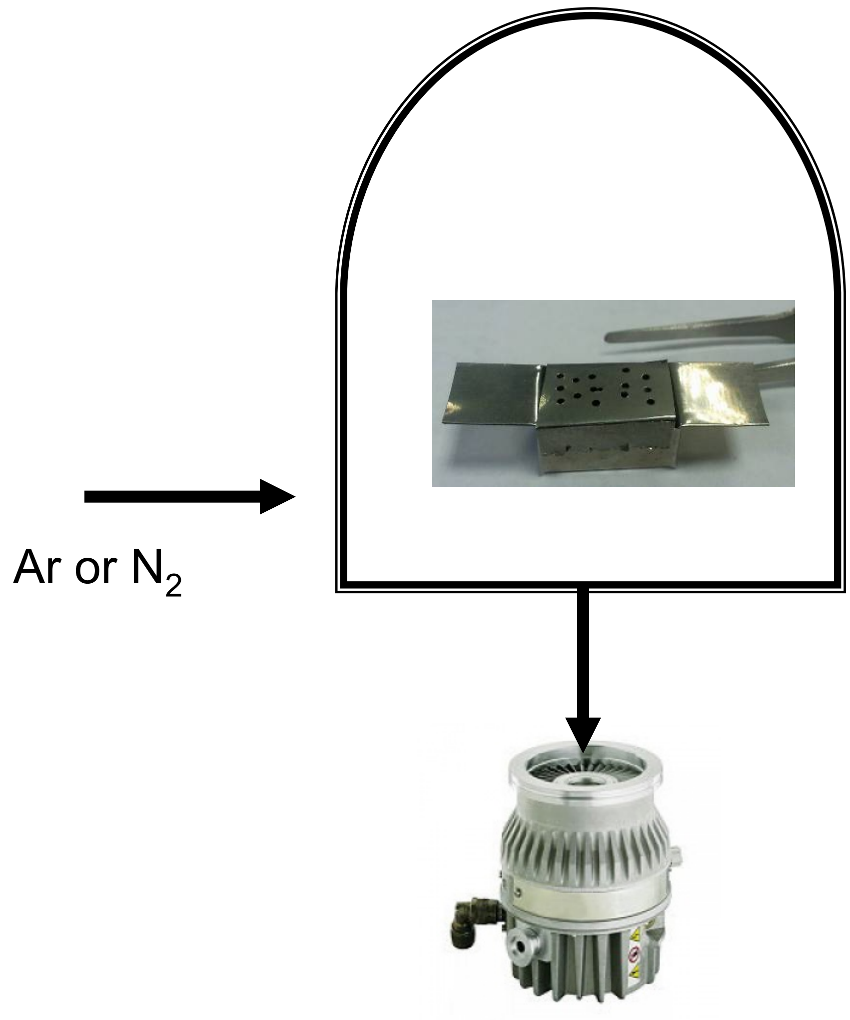
A activity
Φ beam intensity
N number of nuclei in the target
σ reaction cross section
λ decay constant ($=\ln 2/T_{1/2}$)
t irradiation time

$CaCO_3$: CaO : Ca 1: 2 : 3

By heating in presence of Ar flow



or in a vacuum



Isotope produced	Target price		$ /MBq	
	p	α	p	α
^{43}Sc	101460 $ (^{43}Ca)	1 $ (^{nat}Ca)	109 $	6.3 $
^{44m}Sc	6850 $ (^{44}Ca)	5025$ (^{42}Ca)	527 $	279 $
^{44g}Sc	11900 - 3827 $	15450 – 3075 $	4 – 5 $	30-300 $
^{47}Sc (^{44}Ca)	140107 - 46530 $	989 $	250 – 550 $	267 $

Conclusions

1. Since isotopes are sold in form of $CaCO_3$ but their price is related to the element, using CaO as target the double activity of the isotope in request can be produced at the same cost of the target material.
2. Much lower amount of side activity (due to 13N production) is released during irradiation with protons.
3. The heat dissipation from the target remains similar to the situation of use of carbonate and still needs to be solved.

International projects

- French-Polish, COPIN, GANIL/SPIRAL2
  ”***Radioactive Nuclei for Medical Applications”,*** 2013…
- ENSAR2, WP15,
  “***Matched pair of scandium isotopes for Theranostics”***

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Production of the Sc-based radiopharmaceuticals for PET diagnostic,
IChTJ/INCT, and POLATOM, HIL UW/ŚLCJ UW, NCBCH UW;
2016 - 2018


Thank you