

UNIVERSITY OF LATVIA
FACULTY OF CHEMISTRY

**CERN-MEDICIS ISOTOPE MASS SEPARATION
PROCESS OPTIMIZATION: THE CASE OF SCANDIUM
FOR RELEASE STUDY AND ON-LINE MONITORING OF
THE IMPLANTED ACTIVITY**

MASTER'S THESIS

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ABSTRACT

CERN-MEDICIS ISOTOPE MASS SEPARATION PROCESS OPTIMIZATION: THE CASE OF SCANDIUM FOR RELEASE STUDY AND ON-LINE MONITORING OF THE IMPLANTED ACTIVITY. Kalniņa P., supervisors: Dr. Phys. Duchemin C, Dr. Chem., asoc. prof. Pajuste E. Scientific co - supervisor: Mg. Chem. Mamis E. Master's thesis, 61 pages, 43 images, 10 tables, 59 references, 2 attachments, in English.

Scandium (Sc) isotopes are suitable for cancer diagnostics and therapy. Various production methods have been investigated, but challenges persist in achieving high molar activity and radiochemical purity for medical applications. The mass separation technique presents an alternative, but efficiency and yield remain sub-optimal for medical dose production. This study aims to systematically investigate the thermal release kinetics of Sc radionuclides from activated natural titanium foils in tantalum (Ta) environments of ISOL (Isotope Separation On-Line) target units. By elucidating the combination of target material structure and temperature conditions, enhanced release parameters were identified. Maximum Sc release from a non-embossed ^{nat}Ti foil samples was achieved at 1200 °C, for embossed ^{nat}Ti foil samples at 1450 °C and for ^{nat}V foil samples at 1600 °C, within an hour of reaching the set temperature. These findings offer insights into optimizing the mass separation process to improve the efficiency in Sc radionuclide production for medical applications. Upon the conclusion of the experiments, KROMEK detector GR-1+ was characterized. The data collected from the calibration will be used for the validation of various novel and innovative radioisotopes obtained within the MEDICIS facility.

Keywords: Thermal release, mass separation, target materials, scandium

ANOTĀCIJA

CERN-MEDICIS IZOTOPU MASAS ATDALĪŠANAS PROCESA OPTIMIZĀCIJA: SKANDIJA RADIONUKLĪDU TERMISKĀ IZDALĪŠANA UN “ON-LINE” AKTIVITĀTES MONITORINGS. Kalniņa P., zinātniskie vadītāji: Dr. Phys. Duchemin C, Dr. Chem., asoc. prof. Pajuste E. zinātniskais konsultants: Mg. Chem. Mamis E. Maģistra darbs, 61 lapas, 43 attēli, 10 tabulas, 59 atsauces, 2 pielikumi, Angļu valodā.

Ķīmiskā elementa skandija izotopi ir piemēroti vēža diagnostikai un terapijai. Lai arī ir pētīti dažādi skandija radionuklīdu ražošanas veidi, augstas molārās aktivitātes un radioķīmiskās tīrības sasniegšana medicīniskiem nolūkiem joprojām ir izaicinājums. Masu atdalīšanas tehnika sniedz alternatīvu pieeju, taču tās efektivitāte joprojām nav pietiekami augsta medicīniskās devas ražošanai. Šī pētījuma mērķis ir sistemātiski izpētīt skandija radionuklīdu termiskās izdalīšanas kinētiku tantala vidē no apstarotām dabiskā titāna folijām ISOL (*Isotope Separation On-Line*) mērķa iekārtās. Pētot mērķa materiāla struktūru un izdalīšanas temperatūras atkarību, tika noskaidroti skandija radionuklīdu termiskās izdalīšanas parametri. Maksimālā skandija radionuklīdu izdalīšana no neapstrādātām ^{nat}Ti folijām tika sasniegta 1200 °C, savukārt apstrādātām folijām maksimālā izdalīšana 1450 °C. ^{nat}V paraugiem maksimālās izdalīšanas temperatūra sasniedza 1600 °C, vienas stundas laikā pēc iestatītās temperatūras sasniegšanas. Iegūtie rezultāti sniedz ieskatu masas atdalīšanas procesa optimizēšanai, skandija radionuklīdu ražošanas efektivitātes uzlabošanai. Pētījuma noslēgumā tika raksturots KROMEK detektors GR-1+. No kalibrēšanas iegūtie rezultāti tiks izmantoti dažādu jaunu un inovatīvu radioizotopu validācijai MEDICIS iekārtā.

Atslēgas vārdi: Termiskā izdalīšana, masas atdalīšana, mērķa materiāli,

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ABBREVIATIONS

Avg	Average
CERN	European Organization for Nuclear Research
CHARM	CERN High Energy Accelerator Mixed-field
CZT	Cadmium Zinc Telluride detector
EOB	End Of the Beam
FRS	Fraction of radionuclides Reaching the sample's Surface
FWHM	Full Width at Half Maximum
GDP	Global Desorption Probability
HPGe	High-purity Germanium
ISOCS	In Situ Object Counting System
ISOL	Isotope Separation On-Line
ISOLDE	Isotope Separator On Line DEvice
LD	Detection Limit
MAb	Monoclonal Antibodies
MCA	Multi-Channel Analyzer
MDA	Minimum Detectable Activity
MEDICIS	Medical Isotopes Collected from ISOLDE
nat	Natural
ODF	Out-Diffusion Fraction
PET	Positron Emission Tomography
PSB	Proton Synchrotron Booster
RCS	Rail Conveyer System

SPECT	Single-Photon Emission Computed Tomography
TREC	Traceability of potential Radioactive Equipment at CERN
WHO	World Health Organization

INTRODUCTION

Scandium has gained substantial attention as a promising element in nuclear medicine due to its potential to provide a theranostic approach through its radioactive isotopes, including ^{43}Sc , $^{44\text{g}}\text{Sc}$, and ^{47}Sc , which are suitable for cancer diagnostics and therapy. However, the production of these isotopes has posed a significant challenge as high molar activity and radiochemical purity are difficult to achieve. Several methods have been explored to produce these isotopes, such as the irradiation of enriched or naturally abundant calcium (Ca), titanium (Ti), and vanadium (V) materials with different particle beams. At CERN (European Organization for Nuclear Research), the availability of various irradiation fields through the large accelerator complex has enabled the production of scandium radionuclides using various methods.

Recently, MEDICIS (**M**edical **I**sotopes **C**ollected from **I**SOLDE) has produced and mass-separated medical Sc radionuclides from irradiated cyclotron-compatible $^{\text{nat}}\text{Ti}$ and $^{\text{nat}}\text{V}$ target materials. Although high molar activity and radiochemical purity were achieved, the mass separation efficiency and yield remain unsatisfactory for medical dose activity production. Despite recent advancements in Sc mass separation at different facilities, efficiency and yield remain sub-optimal for medical dose production. Gamma-ray spectroscopy is an analytical technique that enables nondestructive detection and identification of various radioactive isotopes in a given sample. This technique is based on the measurement of the energy levels of incident gamma-rays that are detected using specific instruments. By comparing the energy levels of the detected gamma-rays with those produced by known radioisotopes, the identity of the emitter can be determined with high accuracy. CERN MEDICIS, in particular, employs two detector types for the purpose of radionuclide detection and analysis. The High-purity Germanium (HPGe) detector is primarily used to determine the final activity of implanted radionuclides, as well as their purity level after undergoing the mass separation process. On the other hand, the Cadmium Zinc Telluride detector (CZT), is used to monitor the activity accumulated during the collection process.

Purpose of work: address challenges in the production of scandium radionuclides for potential applications in nuclear medicine, focusing on achieving high molar activity and radiochemical purity while improving mass separation efficiency and yield by developing a method for radionuclide thermal release studies.

Tasks:

1. Review and analyse the most current scientific literature related to scandium radionuclide production (with a specific focus on the production challenges), radionuclide thermal release from target materials, and detection methods.
2. Develop a suitable set-up that can be used for radionuclide thermal release studies.
3. Conduct an experimental scandium thermal release series with two types of target materials to investigate the dependence of scandium thermal release on temperature.
4. Analyze the obtained data from the experimental series, and do the theoretical estimations using semi-empirical expressions which are based on detailed studies with specifically developed Monte Carlo models. Determine the best conditions for the release of scandium radionuclides from ^{nat}Ti and ^{nat}V target materials to obtain better mass separation conditions.
5. Calibrate the KROMEK detector efficiency for the on-line monitoring of the implanted activity.

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1.LITERATURE REVIEW

1.1 Scandium radionuclides for theranostic applications

According to the World Health Organization (WHO), an estimated 20 million new cases of cancer were reported in 2022. (Figure 1.1), with 9.7 million deaths resulting from the disease. About 1 in 5 people develop cancer in their lifetime, and approximately 1 in 9 men and 1 in 12 women die from it. Unfortunately, over 35 million new cancer cases are predicted in 2050., which marks a 77% increase from the estimated 20 million cases reported in 2022.¹

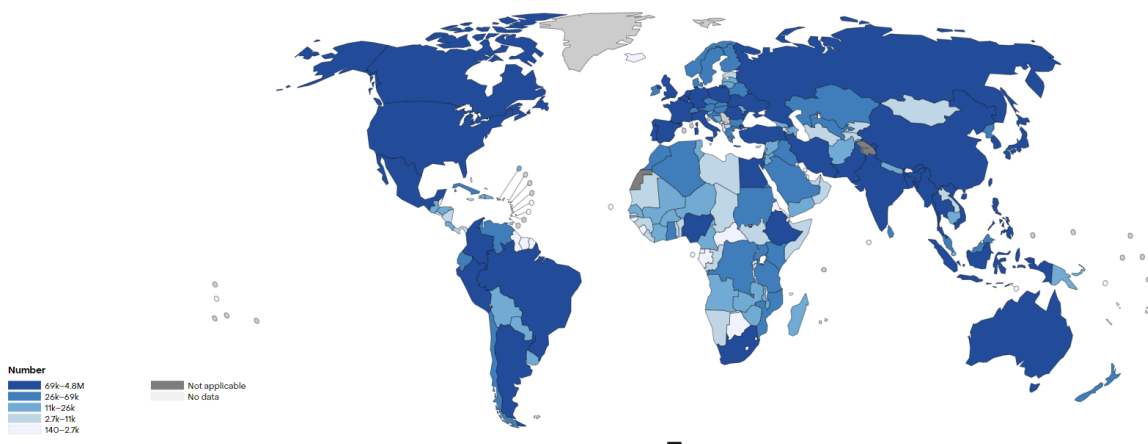


Figure 1.1: Absolute numbers, incidence, both sexes, in 2022., all cancers²

Radiology and nuclear medicine play a crucial role in the screening, treatment planning, response assessment, and long-term monitoring of cancer patients. A timely and accurate diagnosis is essential for successful management of oncological diseases. One of the primary approaches in controlling malignant tumors is timely treatment. Given the complexity of oncological diseases, it is crucial to use all available tools and techniques in the fight against cancer.

Nowadays, there is a growing interest in a new approach to medicine that combines diagnostic tools with therapeutic strategies.³ This approach is called theranostics and is especially well-suited to nuclear medicine. By using specific targeted diagnostic tests, it is possible to apply a personalized and accurate approach to treatment. The theranostics strategy uses specific biological pathways in the human body to acquire diagnostic images and deliver a therapeutic dose of radiation to the patient. The acquired image helps to identify the patient's response and estimate the appropriate dose of the therapeutic agent for the patient. With this approach, it is possible to provide the right treatment at the right time and with the right dose.⁴

Scandium is an element that has gained significant interest in the field of nuclear medicine due to its three radioactive isotopes - ^{43}Sc , $^{44\text{g/m}}\text{Sc}$, ^{47}Sc .⁵ These isotopes possess decay properties that make them suitable for theranostics. Scandium radionuclides have a significant advantage in "matched pair" radiopharmaceutical production as the chemical structure of the drug is identical for both the diagnostic and therapeutic agents.⁶

^{43}Sc (β^+ 88.1%, $T_{1/2} = 3.891(12)$ h) is a positron (β^+) emitter that holds a potential for immuno PET (Positron Emission Tomography) and macro-molecular imaging studies.⁷ $^{44\text{g}}\text{Sc}$ ($T_{1/2} = 4.042(25)$ h) is a radionuclide that is ideal for PET imaging due to its high branching ratio of positron emission ($E_{\beta^+} \text{ av} = 632$ keV, $I = 94.3\%$).⁸ Its half-life enables the acquisition of PET images several hours after the injection of the $^{44\text{g}}\text{Sc}$ -radiopharmaceutical.⁹ This makes it particularly useful for bio-molecules, providing slower kinetic profiles. ^{44}Sc -labeled PET radiopharmaceuticals could be also used for interoperate radio-guided surgery, including the detection of lymphatic metastases at later time points after injection.¹⁰ Currently, ^{44}Sc is most advanced in terms of production, as well as with pre-clinical investigations.¹¹ ^{44}Sc -DOTATOC and ^{44}Sc -PSMA¹² has already been employed in proof-of-concept studies in patients. ^{47}Sc ($T_{1/2} = 3.3492(6)$ d) is a β -emitter with a 159.4 keV (68.3 %) gamma-ray emission that would be suitable for therapeutic applications and single-photon emission computed tomography (SPECT) imaging.⁸ ^{47}Sc shows potential for use in radio-immunotherapy of tumors by being attachable to monoclonal antibodies (MAb) and conjugates.¹³ Nevertheless, the supply of these radionuclides is currently limited due to costly enriched target materials, their enrichment, availability and efficient production capabilities, accessible only at nuclear reactors or medium to high energy cyclotron centers.

1.2 Scandium radionuclide production

The production of ^{43}Sc , $^{44\text{g/m}}\text{Sc}$, and ^{47}Sc can be achieved through the irradiation of enriched calcium (Ca) and titanium (Ti) or naturally abundant metallic materials such as natural calcium ($^{\text{nat}}\text{Ca}$), titanium ($^{\text{nat}}\text{Ti}$), and vanadium ($^{\text{nat}}\text{V}$), using neutrons, protons, deuterons and alpha beams.¹⁴ It is important to optimize the enrichment levels of the materials used to minimize impurities that could compromise the radionuclide purity of the final sample. Despite being cost-efficient, the irradiation of natural target materials presents challenges due to the presence of other naturally occurring isotopes, and the involvement of various nuclear reaction pathways. The direct production of $^{44\text{g/m}}\text{Sc}$ in natural titanium occurs through various nuclear reactions including $^{47}\text{Ti}(p,\alpha)$, $^{48}\text{Ti}(p,n\alpha)$, $^{49}\text{Ti}(p,2n\alpha)$, and $^{50}\text{Ti}(p,3n\alpha)$.¹⁵ The long-lived ^{46}Sc ($T_{1/2} = 83.79$

d, $E_\gamma = 889 \text{ keV}$; 1120 keV) is produced via the $^{47}\text{Ti}(p,2p)$, $^{48}\text{Ti}(p,2pn)$, $^{49}\text{Ti}(p,2p2n)$, $^{49}\text{Ti}(p,\alpha)$, and $^{45}\text{Ti}(p,2p3n)$ nuclear reactions.¹⁶ The reactions with ^{48}Ti are the primary pathways due to its significant prevalence of 73.8% in natural titanium.¹⁷ Various methods to produce the therapeutic ^{47}Sc are documented, including utilizing reactors, cyclotrons, or electron linear accelerators. The main nuclear reactions of ^{47}Sc production are the $^{47}\text{Ti}(n,p)$, $^{48}\text{Ti}(p,2p)$, and $^{48}\text{Ca}(p,2n)$, which suggest the necessity to use enriched target materials to obtain sufficient radionuclide yield and purity. However, even with enriched material, the co-production of ^{46}Sc and ^{48}Sc cannot be fully avoided. Another way to produce ^{47}Sc is through $^{\text{nat}}\text{V}$ target irradiation with protons (^{50}V , 0.250% and ^{51}V , 99.750%). With this method, ^{47}Sc can be produced without contamination of ^{46}Sc , but the production yield is severely decreased.^{6,18} The attractiveness of utilizing natural Ti and V target materials is underlined by their cost-effectiveness, widespread availability, and achievable yield with a considerable number of medium-energy cyclotrons. However, this method also results in the generation of a diverse array of radionuclides, including Ti, Ca, V, and long-lived Sc isotopes, which are unsuitable for nuclear medicine and cannot be removed with chemical post-processing methods.¹⁹

At CERN it is possible to produce scandium radionuclides through various methods thanks to the different irradiation fields made available via the large accelerator complex, see Figure 1.2. Within the framework of this project, Sc production has been already achieved by target material direct irradiation with a 1.4 GeV proton beam provided by the CERN Proton Synchrotron Booster (PSB) at ISOLDE (**I**sotope **S**eparator **O**n **L**ine **D**Evice facility).²⁰ Another possibility is indirect irradiation by profiting from the fraction of the primary proton beam which did not interact with the ISOLDE target and from the secondary particles generated from the ISOLDE target's irradiation (also known as parasitic mode).^{21,22} By using these modes of irradiation and depending on the parameters, several GBqs of the medically important Sc radionuclides - ^{44}Sc and ^{47}Sc - activity can be reached.

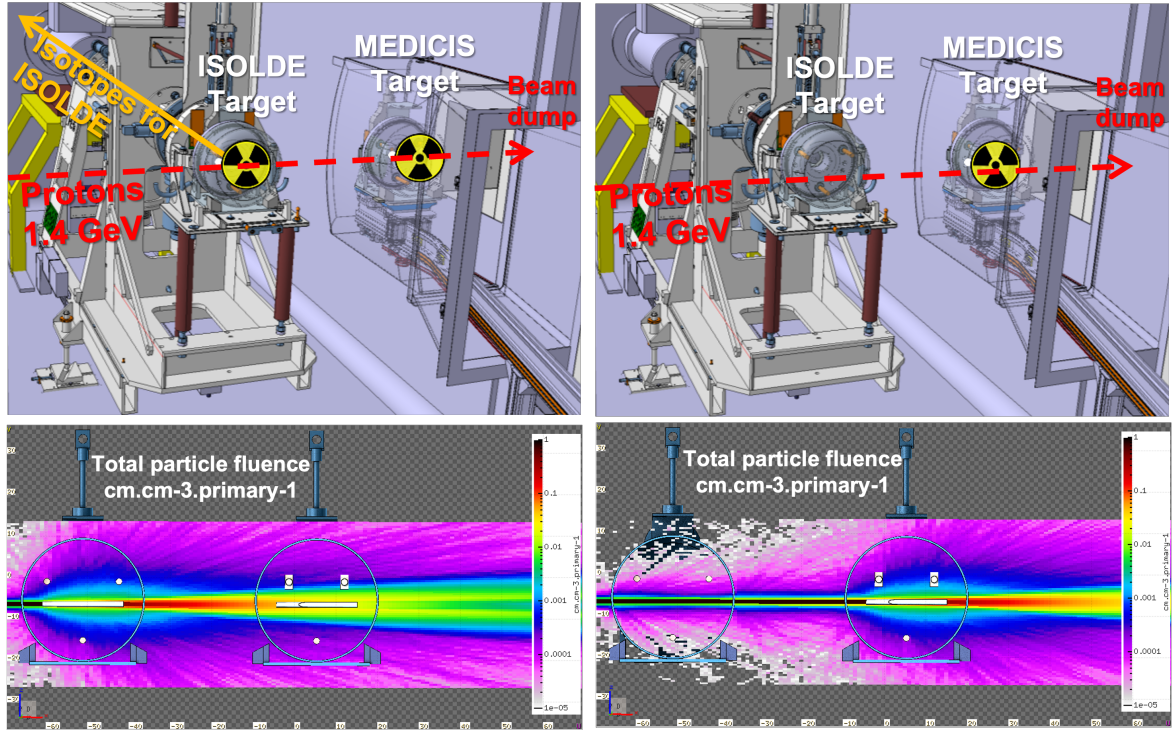


Figure 1.2: Indirect (left) and direct (right) irradiation at ISOLDE (1.4 GeV)²³

A third way that has been exploited within this project, to produce low activity samples, is via indirect target material activation using the secondary neutrons at the CERN High Energy Accelerator Mixed-field (CHARM) facility. The CERN CHARM facility (See Figure 1.3) specializes in the study of radiation effects on electronic components and the testing of various material shielding. This is done by using a 24 GeV/c proton beam extracted from the CERN proton-synchrotron, which is impinging onto a thick copper target. The radiation field generated by this process includes secondary neutrons²⁴ that has been used to activate indirectly ^{nat}Ti and ^{nat}V samples for ^{43}Sc , $^{44g/m}\text{Sc}$, ^{46}Sc , ^{47}Sc and ^{48}Sc radionuclide production.

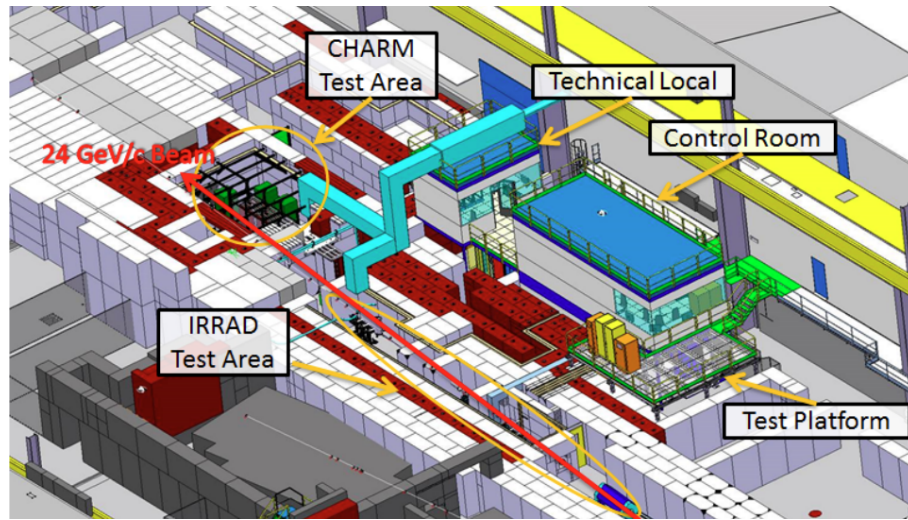


Figure 1.3: A screen-shot from the 3D Catia drawing of the IRRAD and CHARM facility, showing the different areas²⁵

1.3 The CERN-MEDICIS facility

CERN- MEDICIS is a facility located in the ISOLDE facility at CERN, designed to produce high-purity isotopes for developing the practice of patient diagnosis and treatment. CERN-MEDICIS is an isotope separator facility that operates in an "off-line" mode, which means that it is not directly connected to a driver beam for isotope production. Instead, the production process occurs elsewhere, and only isotope extraction and mass separation take place at MEDICIS.²⁶ In December 2017, the CERN-MEDICIS facility delivered its first radioactive ion beam at CERN in Switzerland to support research and development in nuclear medicine using non-conventional radionuclides. 14 institutes, including CERN, have joined the collaboration to improve research in imaging, diagnostics, radiation therapy, and personalized medicine at a unique installation. Since its commissioning, the CERN-MEDICIS facility has provided its partner institutes with non-conventional medical radionuclides such as ^{149}Tb , ^{152}Tb , ^{155}Tb , ^{153}Sm , ^{165}Tm , ^{167}Tm , ^{169}Er , ^{175}Yb , and ^{225}Ac with a high specific activity.²²

The CERN-MEDICIS facility processes for producing high purity isotopes are shown in figure 1.4. The chain starts with ISOLDE facility which directs a proton beam onto a thick target to produce desired isotopes. Only a fraction of the proton beam is absorbed, with the rest being lost into the beam dump. MEDICIS uses the transmitted protons to irradiate a second target to produce specific isotopes. Then targets are moved from the irradiation station to the radioisotope mass-separation beamline via an automated rail conveyer system (RCS) due to high levels of radiation. A KUKA robot is utilized to transport the target to the station where the desired isotope can be collected and radiochemically purified. This process requires heating the target

to extremely high temperatures, usually exceeding 2000°C , which results in the diffusion of the specified isotopes. The isotopes are then ionized and accelerated by an ion source to be transmitted through a mass separator, see section 1.3.1 for detailed described offline mass separation process. The mass separator extracts the desired isotope so that it can be implanted onto thin metallic (Al or Zn) or NaCl-coated foils for subsequent dispatch to biomedical laboratories for further scrutiny.²²

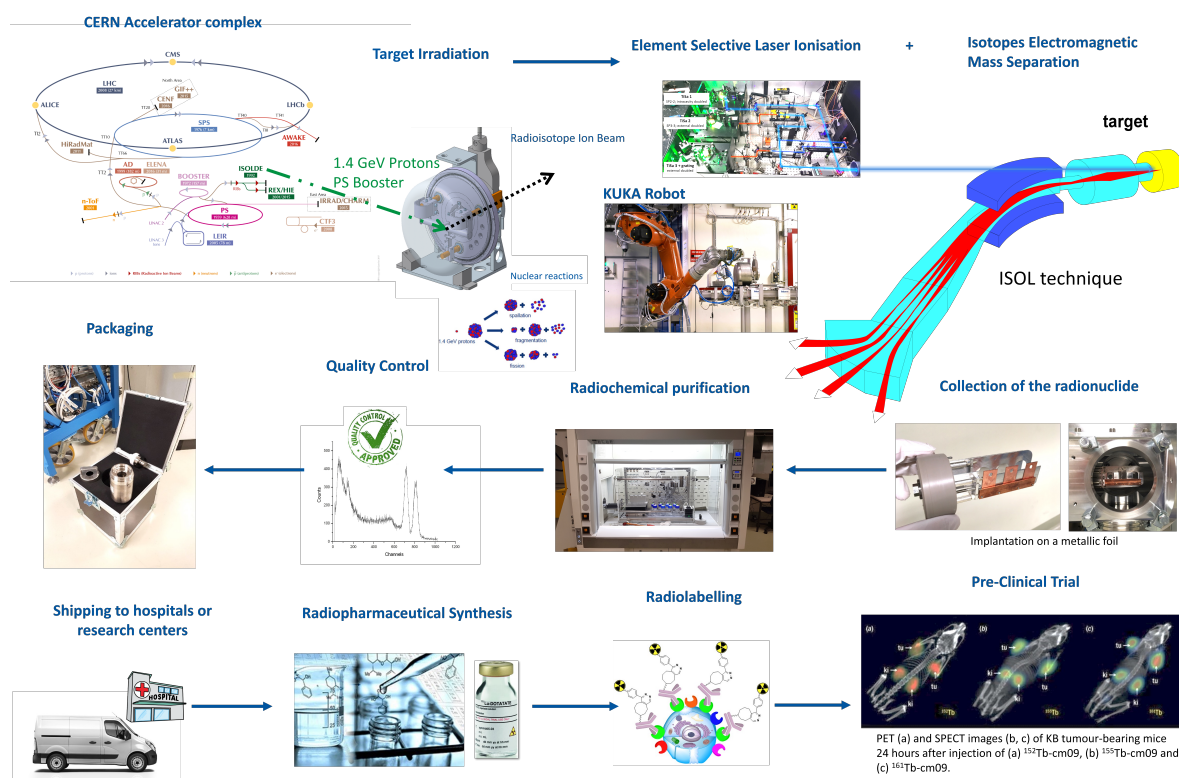


Figure 1.4: CERN-MEDICIS chain for high purity radionuclide production

1.3.1 Offline mass separation process

The previously discussed production methods in section 1.2 entails the co-production of Sc radioisotopes, which are not amenable to separation by radiochemical means. An alternative method for producing high molar activity, radiochemically pure, and medically suitable Sc radionuclides involves using a mass separation process. It is a technique that uses a dipole magnet to induce a magnetic field and separate accelerated, ionized isotopes according to their mass-to-charge ratio, through the Lorentzian principle. The magnetic rigidity of a particular ion beam relies on both the magnetic field from the dipole and the charged state of the isotope, mass, and energy. By blocking out unwanted trajectories, only pure beams of interest can be obtained. Unlike chemical separation, mass separation isolates isobars or atoms with the same

mass number (A) but different atomic number (Z) from the original sample. The ability of a mass separator to distinguish between closely spaced masses is measured by its mass resolving power, and some mass separators have enough resolution to separate isobars.^{27,28} This technique eliminates the need for enriched target material, as the various isotopes of Sc are naturally isolated during the separation process.²⁶ The MEDICIS facility at CERN is designed specifically for producing high-purity novel radionuclides for medical applications through mass separation.²² The mass separation method used at MEDICIS is adapted from the ISOLDE facility, but the isotopes are produced and mass-separated in a batch mode.²⁹ Clinically relevant activities of the targeted radionuclides are efficiently produced through the irradiation of thick targets with 1.4 GeV protons delivered by the CERN PSB.³⁰

Recently, MEDICIS has produced and mass-separated medical Sc radionuclides from irradiated cyclotron-compatible ^{nat}Ti and ^{nat}V target materials. Even though high molar activity and radiochemical purity were attained, the mass separation efficiency and yield are still unsatisfactory for medical dose activity production.²⁰ The conditions for Sc radionuclide release dynamics from metallic ^{nat}Ti and ^{nat}V foils within ISOL target units are not yet fully understood due to scandium's refractive properties, high adsorption enthalpy with tantalum (Ta) ISOL target unit structures, batch mode experiment limitations, and difficulties in extracting Sc radionuclides from the target units.

1.4 Radionuclide thermal release from target materials

The investigation of radionuclide thermal release from target materials is of paramount significance in facilitating effective mass separation process. Specifically, this entails understanding the thermally promoted out-diffusion of radionuclides, which refers to the process of radionuclides initially placed in the matrix of a solid escaping from it due to thermal diffusion. Upon reaching the surface of the object, radionuclides can either diffuse back into its bulk matrix or desorb from it.³¹ The release of radionuclides varies depending on the temperature of both the target material and the ionization line. Higher temperatures generally lead to increased release of radionuclides.

The phenomenon of diffusion in solids can be attributed to the Brownian motion of atoms or molecules.³² This motion is a result of their thermal energy, which causes them to oscillate around their equilibrium position in accordance with a Maxwell-Boltzmann velocity distribution. Generally, the majority of these oscillations will return the atoms to their initial equilibrium position, as they fall back into the potential well. However, on occasion, the energy of the oscil-

lations is sufficient to overcome this potential well, resulting in a shift in location. The diffusion coefficient, denoted by D , is a measure of the rate at which a given species diffuses within a host material at a specific temperature.^{31,33} It is expressed in units of $[\text{length}^2/\text{time}]$ and is typically quantified in $[\text{cm s}^{-1}]$. For metals, it is a function of temperature and can be expressed in accordance with the Arrhenius formula, as provided below:

$$D = A \cdot \exp\left(-\frac{Q}{RT}\right) \quad (1.1)$$

where $A [\text{cm}^2 \text{s}^{-1}]$ is the frequency factor, $Q [\text{J mol}^{-1}]$ is the activation energy, $T [\text{K}]$ is the absolute temperature and $R [\text{J K}^{-1} \text{mol}^{-1}]$ is the gas constant.

In order to gain a comprehensive understanding of the process by which scandium can be released from the target material during routine operation, it is necessary to estimate the rate at which it is emitted as a function of temperature and time. This can be accomplished through the monitoring of the gamma emission of the produced or collected radionuclide by means of a gamma ray spectrometer.

1.5 Gamma ray spectrometry and detectors used at CERN-MEDICIS

Gamma-ray (γ -ray) spectroscopy is a quick and nondestructive analytical technique that can be used to identify various radioactive isotopes in a sample. In gamma-ray spectroscopy, the energy of incident gamma-rays is measured by a detector. By comparing the measured energy to the known energy of gamma-rays produced by radioisotopes, the identity of the emitter can be determined. This technique has many applications, particularly in situations where rapid nondestructive analysis is required.³⁴ The system consists of a detector, electronics to collect and process the signals produced by the detector, and a computer with processing software to generate the spectrum and display and store it for analysis (see Figure 1.5).

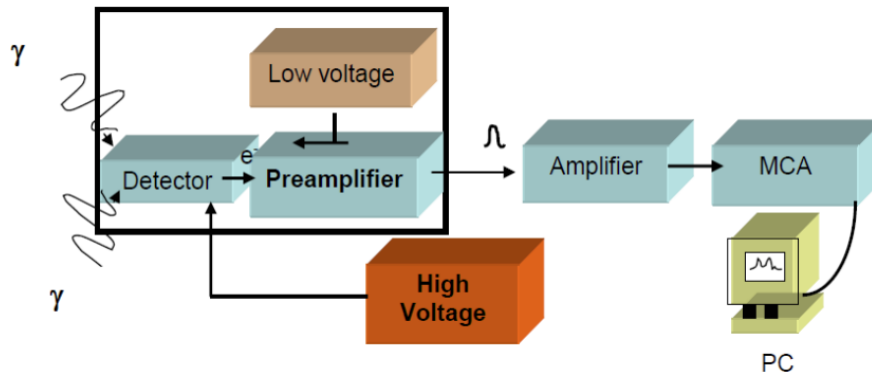


Figure 1.5: Block diagram of gamma ray spectrometer³⁵

Gamma-spectrometry allows for assessing quantitatively the radioactivity of a sample and is based on three fundamental interactions of radiation with matter- photo electric effect, Compton scattering and pair production, see Figure 1.6.³⁵

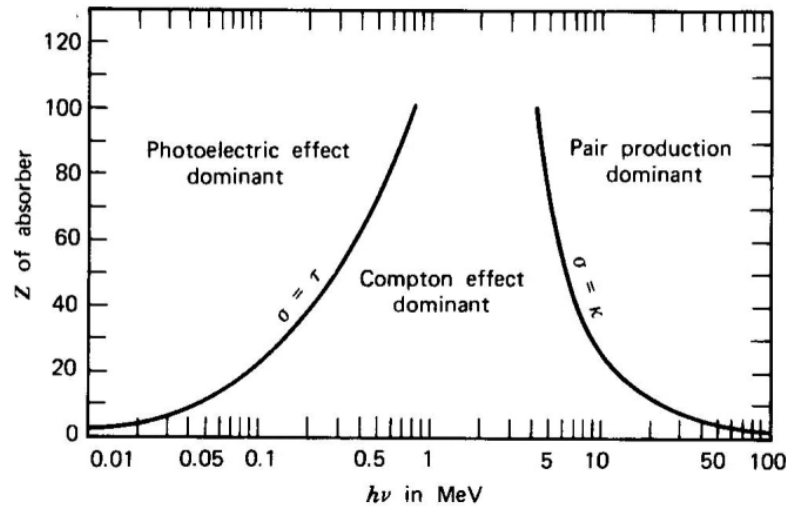


Figure 1.6: A graph depicting the various regions where the different gamma-ray interactions are dominant³⁶

The **photoelectric effect** is a prevalent interaction between a material and a low-energy photon. This phenomenon involves the transfer of all energy from the photon to an electron in the material, resulting in the ejection of the electron with an energy equivalent to the initial photon energy minus the electron's binding energy. Spectroscopy relies on this process, as it produces an output pulse in a detector proportional to the gamma-ray energy, enabling identification of the radioactive material by generating a characteristic full-energy peak in the spectrum. The photoelectric effect probability is strongly dependent on the atomic number and photon energy. It is the dominant process at low photon energy, see Figure 1.7.³⁷ The probability has discontinuities at the binding energies of the electrons in the constituent atoms. The probability of the photoelectric effect decreases when transitioning from a photon energy just above the binding energy of the electrons to an energy just below it.³⁸ In the **Compton effect** a gamma ray scatters from an electron transferring energy that depends on the angle of scatter. When a photon is moving towards a detector, it may scatter at a small angle and still hit the detector. However, this scattering process, known as Compton scattering, transfers some energy to the electron. As a result, the scattered photon will not deposit its full initial energy in the detector and will not contribute to the full-energy peak. In most cases, spectroscopic measurements count the number of photons in the full-energy peak. Therefore, a Compton-scattered photon is considered undesirable, even if it ends up depositing energy in the detector.³⁹ **Pair production**

is a process that can occur when a gamma-ray has an energy greater than 1.022 MeV. This process becomes significant at energies above 2.5 MeV. Pair production results in the creation of a positron and an electron pair, which slows down through scattering interactions within matter. When the positron comes to rest, it annihilates with an electron, creating a pair of 511 keV gamma rays that are emitted in opposite directions. The probability of pair production is zero up to the energy threshold of twice the electron mass ($1.022 \text{ MeV}/c^2$). However, the probability increases with energy and becomes constant at around 100 MeV.⁴⁰

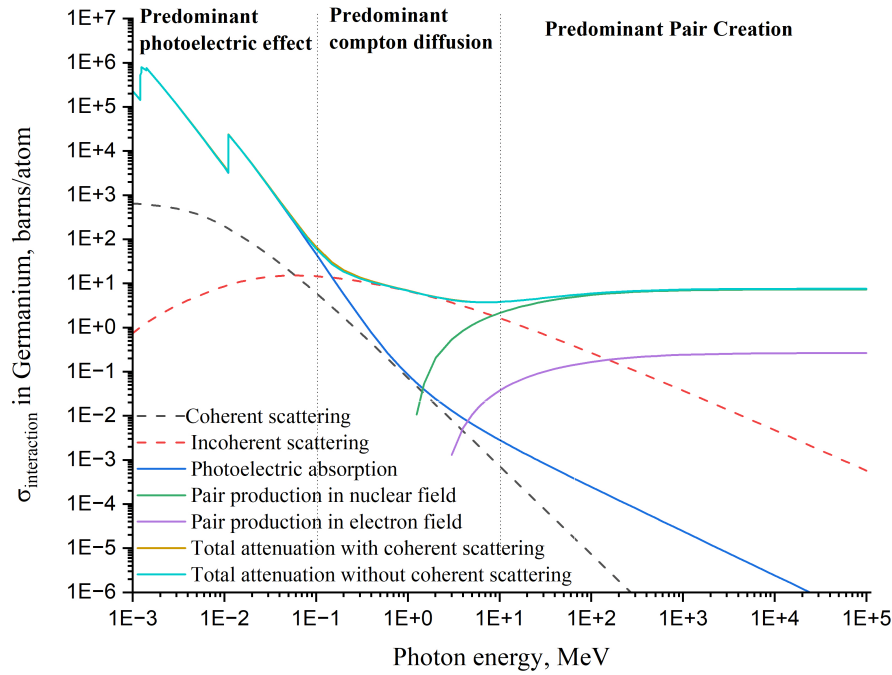


Figure 1.7: Cross-section of γ interaction processes in germanium

Depending on the detector used, gamma spectrometry can offer several advantages. Sample preparation for radionuclide analysis is straightforward and usually does not require a radiochemical separation process. The detection system provides data that are well-suited for computer processing, making it suitable for designing automatic analysis systems.⁴¹ With gamma spectrometry, different radionuclides can be simultaneously identified and their activity determined in a single counting source. The gamma-emitting radionuclides can be detected in the energy range of approximately 30 keV to 2000 keV. This method can detect low activities of radioactive substances as low as 0.1 Bq with sufficient certainty.⁴²

CERN-MEDICIS employs two types of detectors for the purpose of radionuclide detection and analysis. The first detector is a High-purity Germanium detector. HPGe radiation detectors are well established as a valuable tool in nuclear science and medical applications. HPGe detectors excel in gamma-ray spectroscopy, offering excellent energy resolution with large de-

detector sizes for high radiation detection efficiency.⁴³ The MEDICIS facility employs an HPGe detector (for the specification see subsection 2.1.4) as an offline spectrometer. This detector is mainly utilized to determine the final activity of implanted radionuclides and their purification level after the mass separation process and before shipping to partner institutes.

The second detector is made of Cadmium Zinc Telluride. It is a semiconductor that can convert X-rays or γ -ray photons into electrons and holes while operating at room temperature. CZT detectors are promising for medical applications due to their high resolution, room temperature operability and large count rate capability. CZT detectors don't require constant cooling like HPGe detectors, reducing the overall cost and complexity of the system.⁴⁴ At MEDICIS it is used as on line detector (see figure 2.15a) during radionuclide mass separation process to monitor the activity being collected as a function of the time and the target temperature, as well as to get the total collected activity on the collection foil at the end of the process.

⁴⁷Sc is known to emit a gamma radiation with a low energy range at 159.381 keV (I=68.3 (4) %). At CERN - MEDICIS the current configuration of the detection system allows for the easy detection of the first few hundred mega becquerels (MBq) of activity, beyond which the detector appears to become saturated, making it difficult to detect higher activity levels. In order to improve the sensitivity of the system, a second g-spec detector has been installed at a further distance. This detector is similar to the existing one in front of the window, but it will allow for a greater distance between the detector and the collection foil. Additionally, collimators will be used to increase the activity that can be detected. However, due to the low energy range, it is essential to accurately calibrate the detector efficiency (as detailed in chapter 2.2) to ensure precise and reliable data during the scandium release process.

2.EXPERIMENTAL

2.1 Scandium thermal release from activated ^{nat}Ti and ^{nat}V target materials in mixed particle fields

The thermal release of Sc from metallic foil target materials has been investigated during this work to optimize the process of mass separation of this medically important element at CERN-MEDICIS. Experimental Sc thermal release data were obtained by activating target materials at the CERN High Energy Accelerator Mixed Field Facility, followed by thermal release and analysis in the CERN-MEDICIS Class A laboratories.⁴⁵ After irradiation, each sample was analyzed by γ -spectrometry (HP Ge detector) to quantify the activity of each Sc radionuclide specific to each sample before and after the release experiment. Experiments were conducted with the aim of accurately replicating the conditions present at ISOLDE and MEDICIS. To achieve this, each irradiated sample was positioned inside an ISOL target container, uniformly heated at a constant rate, and then maintained at a predefined temperature for one hour. Subsequently, the target container was cooled, and the sample was extracted for measurement. Dose rate measurements were conducted for each sample before and after release to gather data regarding potential condensation spots in the target container. γ -spectroscopy measurements were then performed again to measure the residual activity in the sample. By comparing the radionuclide activity before and after release, the percentage of released fraction of the Sc radionuclides detectable in each sample was calculated and compared with the estimated theoretical moels.

2.1.1 Radionuclide estimation with ActiWiz

ActiWiz is a software tool developed at CERN that provides fast and accurate assessments of radiological risks associated with various materials used in high energy particle accelerators.⁴⁶ The latest version of the software, ActiWiz 3.6.12/2023-2507, uses a proprietary database of isotope production reactions, based on the evaluated JEFF 3.3 library for neutrons below 20 MeV and on the results of a vast number of FLUKA Monte Carlo simulations for all other reactions.^{47,48} This allows ActiWiz to estimate nuclide inventories for user-defined materials based on arbitrary particle fluence spectra input (neutrons, protons, pions+, pions-, and photons), enabling users to efficiently explore varied compositions and their respective hazards. In addition to its primary function of estimating nuclide inventories, ActiWiz also has many post-processing

options that can be used to analyze the results.⁴⁹ Furthermore, the software was used to calculate the total activity and dose rate per sample, as well as the targeted activity for each radionuclide of interest according to the CHARM activation scenario.

ActiWiz estimations were performed for the Sc activity. The calculations were done in four steps as follows:

1. The fluence spectra (protons, neutrons, pions) were obtained from FLUKA simulations,⁵⁰ see Figure 2.8
2. The sample was defined along with its properties like weight fraction and density, see figure 2.1.

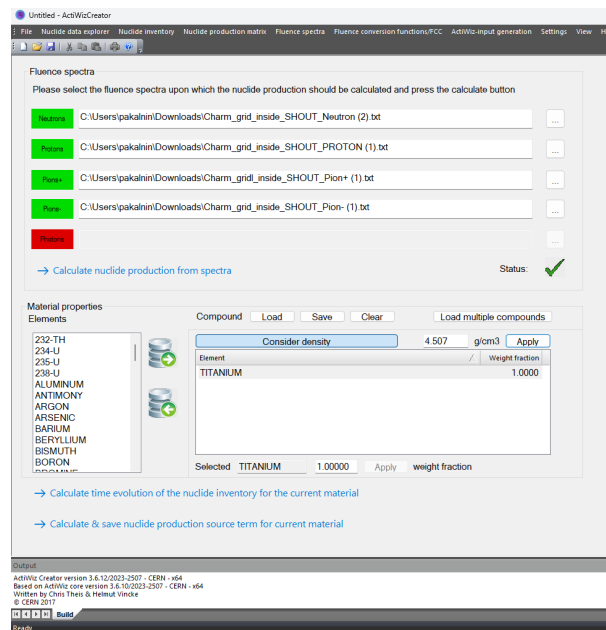


Figure 2.1: ActiWiz Creator window: illustrating material property definition

3. The irradiation / cooling and beam properties were set according to the CHARM parameters, Figure 2.2.

Figure 2.2: ActiWiz Creator window: setting irradiation properties

4. The output generated from the analysis is presented in a text file that showcases the top contributors in terms of activity or dose rate depending on the output requested by ActiWiz, as depicted in Figure 2.3.

 * Irradiation scenario: from fluence spectra
 *
 * 1.) beam intensity: 5E+10 p/s --> prompt dose = 2.99E+07 uSv/h (5.41E+06 uGy/h), irradiation: 432000 s (5 days), cooling: 129600 s (1 day, 12 hours)
 *
 * Selected hazard factor: Activity

TOP CONTRIBUTORS

Top contributors (> 1%) to total specific activity = 2.39E+03 Bq/g +/- 0.99%

Sc-47	51%	1.229967e+03 Bq/g, t1/2 =	289526 s [Source: TITANIUM : 100.00%]
Sc-48	18%	4.308488e+02 Bq/g, t1/2 =	157248 s [Source: TITANIUM : 100.00%]
Sc-44	11%	2.645795e+02 Bq/g, t1/2 =	14292 s [Source: TITANIUM : 100.00%]
Sc-44m	10%	2.488840e+02 Bq/g, t1/2 =	210989 s [Source: TITANIUM : 100.00%]
Sc-46	4%	9.929435e+01 Bq/g, t1/2 =	7.23928e+06 s [Source: TITANIUM : 100.00%]
K-43	1%	2.639063e+01 Bq/g, t1/2 =	79920 s [Source: TITANIUM : 100.00%]

Figure 2.3: ActiWiz Creator window: theoretical top contributors produced in the reaction

2.1.2 Sample preparation

In order to examine the Sc thermal release from metallic foils and the impact of target material structure in MEDICIS mass separation conditions, three types of samples were prepared. These samples comprised of non - embossed ^{nat}Ti (as illustrated in Figure 2.4), embossed ^{nat}Ti (as shown in Figure 3.3), and non-embossed ^{nat}V (for preliminary assessments and similar to Figure 2.4). The samples were produced as compact foil rolls, with non-embossed samples having an average diameter of 0.46 cm and embossed samples having an average diameter of 0.80 cm. The height of all samples was 1.5 cm.

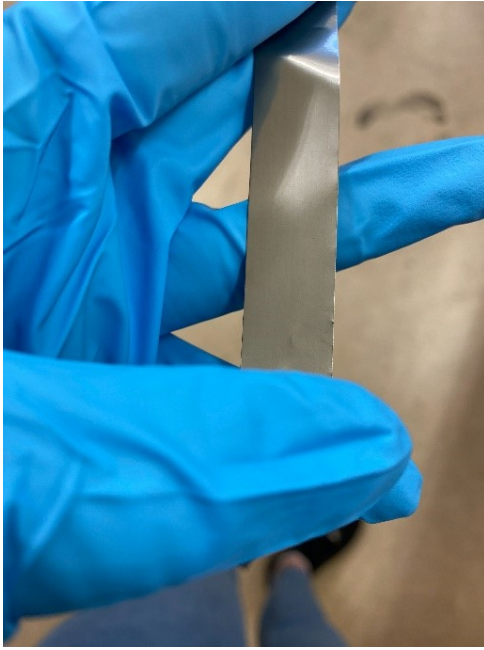


Figure 2.4: Non - embossed ^{nat}Ti foil

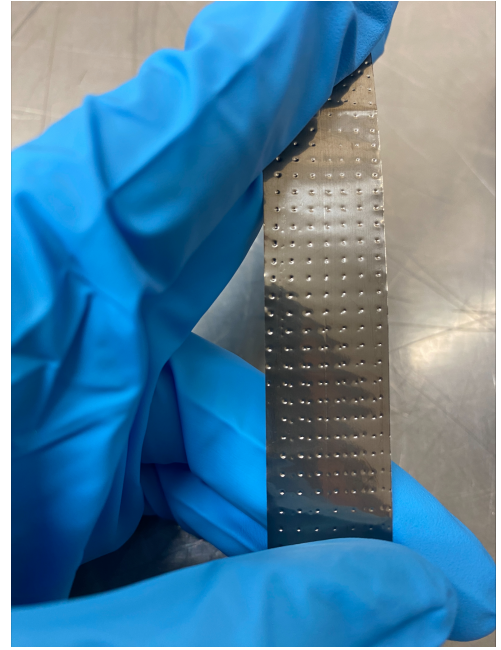


Figure 2.5: Embossed ^{nat}Ti roll

During routine mass separation operations, the foils are embossed to lessen the tightness of the sample roll and to enhance the space between foil layers, which reduces sintering at high temperatures. Therefore, the ^{nat}Ti roll sample types differ from each other in terms of their overall volume. Each roll weighs around 1 g for ^{nat}Ti samples and 3.4 g for ^{nat}V samples. The selection of sample weight was based on the estimated theoretical radionuclide activity (Bq/g of the sample), in line with the irradiation scenarios at the CHARM facility and radiation protection parameters.

2.1.3 Sample activation at CERN-CHARM facility

The CHARM facility at CERN is dedicated to the study of radiation effects on electronic components and benchmarking various material shielding.²⁴ The CHARM facility receives a 24 GeV/c proton beam extracted from the CERN Proton-Synchrotron impinging on a thick copper target. It creates a mixed particle field including secondary neutrons (contribution to the total yield is more than 90%) that were used to activate our samples.

The experimental methodology was followed meticulously, with the samples being inserted into small-scale plastic bags to provide a secure containment environment. Each sample was tagged with a TREC (Traceability of potential Radioactive Equipment at CERN) code and registered in the TREC database for Radiation Protection measurement and traceability purposes. Subsequently, the samples were affixed with cable ties on the CHARM grid door,

ensuring stable placement on the designated hook positioned on the grid. The samples were positioned on the exterior surface of the "cage" door (see Figure 2.6 and 2.7), facilitating a controlled parasite irradiation effect.

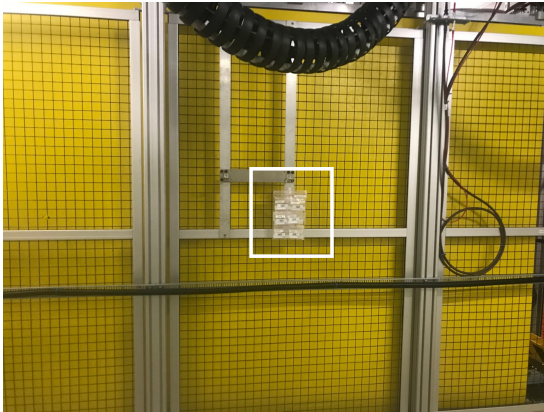


Figure 2.6: Samples placed for activation at CHARM facility "inside grid location"

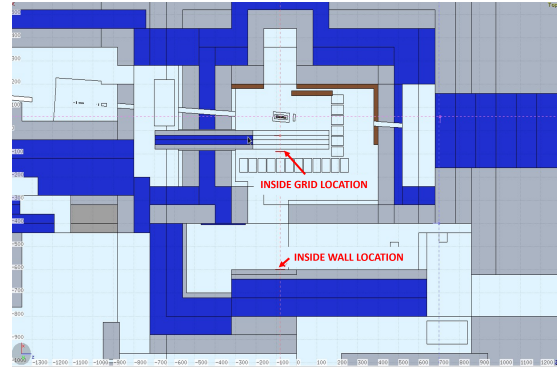


Figure 2.7: CHARM schematic of the sample position labelled as "Inside grid location"

A standard 5 day irradiation followed by 1.5 day cooling time after the end of the beam (EOB) with an average proton beam intensity of 5×10^{10} p/s (protons per second) is typically provided to the users by the CHARM facility. This value was first used to estimate the produced activity from ActiWiz calculations. The particle fluence spectra generated by the $5E10$ p/s primary proton beam onto the CHARM target is shown in Figure 2.8.

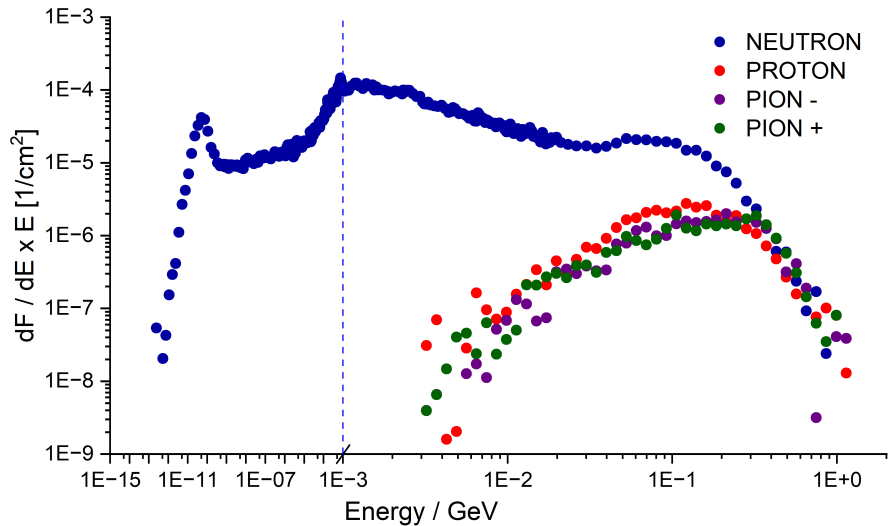


Figure 2.8: Fluence spectra at the grid irradiation location of the CHARM facility used to compute the activity values predicted in the Ti samples

Following every activation, the radionuclide activities were calculated by utilizing the actual average proton beam values and irradiation times that were provided (refer to Table 2.1 for additional information). At CHARM, four batches of Ti and V target material samples were

activated. In the first activation run only embossed titanium samples were used. In the second activation run non- embossed titanium samples were used. In the third activation run vanadium samples were exposed to the CHARM radiation field, and in the fourth activation run all three types of samples were activated.

Table 2.1

Average actual proton beam intensity for each irradiation			
Activation run	Average intensity, p/s	Irradiation time, h	Protons on target
I	6.91×10^{10}	132	3.28×10^{16}
II	6.71×10^{10}	126	3.04×10^{16}
III	6.91×10^{10}	139	3.45×10^{16}
IV	6.64×10^{10}	138	3.29×10^{16}

2.1.4 Gamma-ray spectrometry

The radionuclide activity in each sample was quantified by performing gamma-ray spectrometry measurements after sample activation and just before placing it inside the target container for release. A High Purity Germanium gamma detector from MIRION Technologies (Canberra) SAS was used for the measurements. The detector has an energy range from 3 to 10,000 keV with a relative efficiency of more than 40%, and a resolution of less than 1.2 keV at 122 keV and less than 2.0 keV at 1332 KeV. After the experiments, gamma-ray spectrometry measurements were performed again to determine the residual radionuclide activity in the sample and quantify the released Sc radionuclide activity from each sample. The APEX software (V1.4.1) and the ISOCS (In Situ Object Counting System) modelization²¹ were used for quantitative analysis. Each sample was placed at the same distance from the detector and in the same geometry configuration (see figure 2.9) for relative measurement purposes. Each sample counting was done for a minimum of 15 hours.

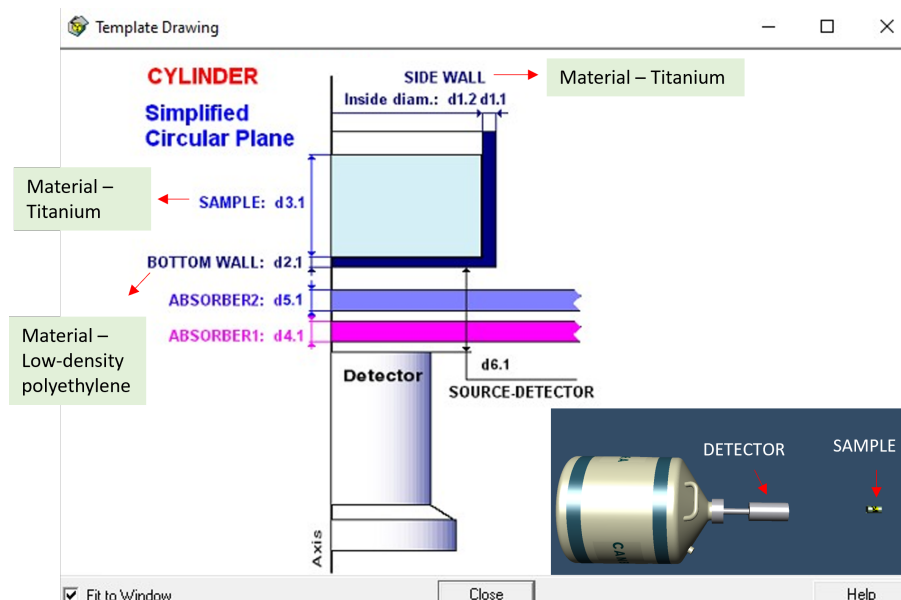


Figure 2.9: Geometry used for gamma - ray spectrometry measurements

2.1.5 Thermal release Set-Up

At CERN-MEDICIS, mass separation is typically carried out at high temperature and low vacuum pressure conditions. The process involves heating the target material up to temperatures as high as 2300°C , with pressure conditions as low as 1×10^{-5} mbar. To release isotopes, the conditions are often close to the target material melting point.²⁰ To achieve this, a specialized ISOL target coupling table (pump stand) is used, which is capable of applying high current of up to 1200 A for heating and obtaining a pressure of down to 1×10^{-7} mbar. The pump stand also features a dedicated gas exhaust system, which helps to trap any potential radioactive gases. A visual representation of the pump stand is shown in Figure 2.10.



Figure 2.10: Set-up for Sc thermal release experiments

For the second part of the experimental setup, a standard ISOL target unit was connected to the pump stand (refer to Figure 2.11).²⁸ This target unit is made up of a target container and an ion source. The target container is a Ta tubular oven that is 2 cm in diameter and 20 cm in length. It is connected to the ion source via a transfer line, which runs perpendicularly between the two. Although no radioactive ions were needed for this particular study, the ion source was still covered by multiple layers of Ta, W, and Mo heat screens. The target container and ion source are mounted on a water-cooled Aluminium base plate and covered by an Al vessel.

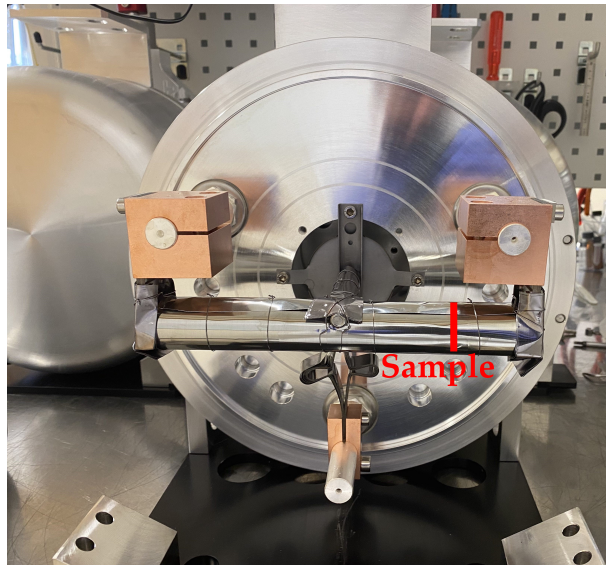


Figure 2.11: ISOL target unit back view

2.1.6 Target calibration using micro optical pyrometer

The target container is heated by resistive current and the heating ramp is correlated to temperature. Prior to the experiment, a temperature calibration was performed (refer to 2.12) on the target container using a micro-optical pyrometer (serial number: MD-8622). This device measures temperature using infrared radiation, without making physical contact with the object. It is particularly useful in measuring high temperatures ranging from 700°C to 3200°C. The optical pyrometer works by comparing the brightness emitted by the target object with that of a reference temperature lamp. The intensity of the lamp is adjusted until it matches the brightness of the target object. The temperature of the object is then determined by analyzing the current passing through the filament of the lamp at the point when both brightness levels are identical. This process involves detecting the thermal radiation emitted by an object and converting it into an electrical signal. The signal is then processed and displayed as a temperature reading, which helps in determining the temperature of the object being measured. The micro-optical pyrometer is very useful in situations where contact with the object is not possible, such as in high-temperature environments.⁵¹

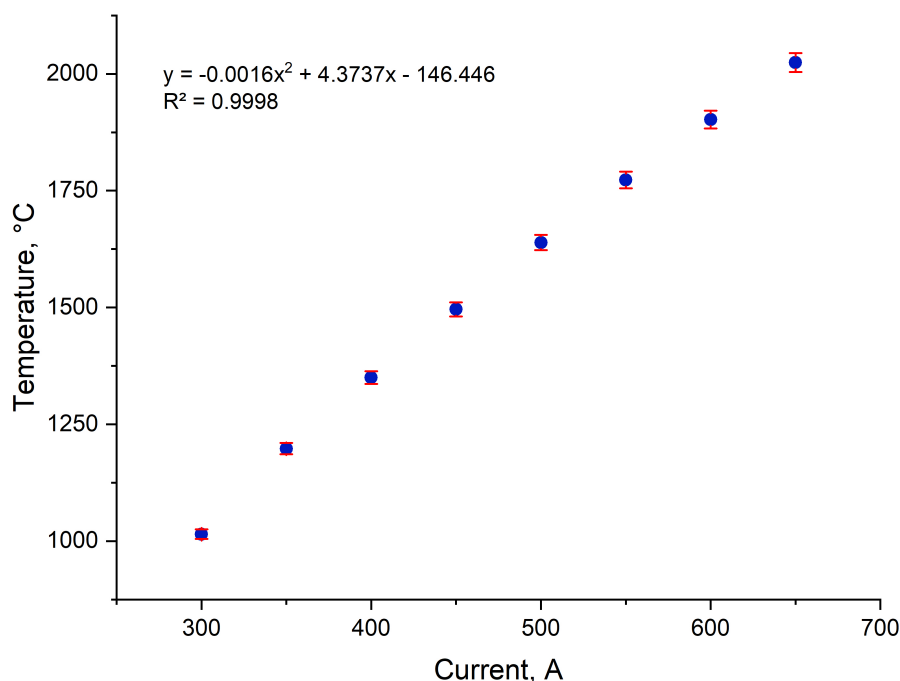


Figure 2.12: Target container (oven) temperature calibration curve

2.1.7 Thermal radionuclide release

In order to prevent the samples from fusing with the Ta container at high temperatures, and to facilitate the safe and easy exchange of samples from the target container, a Ta "boat" was used to hold the samples, see Figure 2.13. Once the samples were loaded onto the Ta boat, the target container was then closed with a Ta cap, and the heat screens were mounted. The samples were placed at the same location and distance within the confines of the target container, matching the calibration location, as shown in Figure 2.11. In order to determine possible contamination and dislocation/condensation of the radioisotopes at different places in the target unit structures, the dose rate of the sample both inside and outside the target container was measured before and after the heating phase. Each sample was then subsequently measured by HPGe gamma spectrometer.

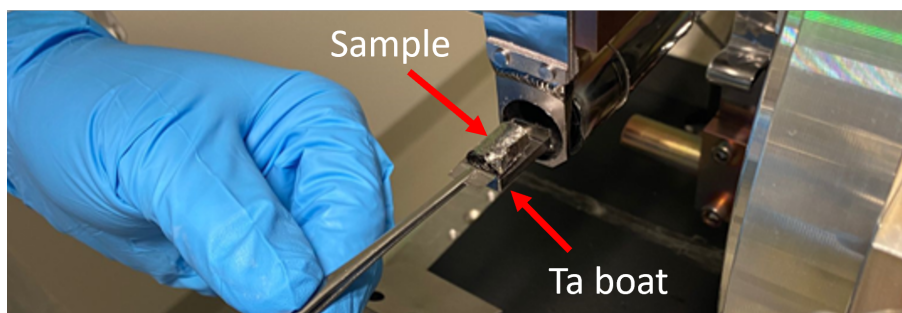


Figure 2.13: ^{nat}Ti foil roll sample in a Ta "boat" after thermal release experiment

After sample loading, the pressure of the system was stabilized to $\leq 2 \times 10^{-6}$ mbar. Once sufficient pressure conditions were reached, each sample underwent a temperature ramp-up process by applying 0.5 A every 25 seconds to the target container. Once the desired temperature was achieved (as an example to reach 1500°C it takes 5 hours of heating), each sample was maintained at the chosen temperature for one hour and cooled down using the same ramp speed of 0.5 A per 25 seconds. These initial pressure conditions and heating speed were chosen to allow for target pressure to stabilize and be kept below 1×10^{-5} mbar even during the heating and out-gassing phase. This way also the mass separation conditions were maintained.

2.1.8 Scandium thermal release experimental calculations

The computation of the relative thermal release of Sc involves the determination of the ratio between the activity measured subsequent to release and the activity measured prior to release, as exemplified by equation 2.1. The initial activity was subjected to decay correction to conform with the date and time of the corresponding sample release study.

$$\text{Ratio } R = \frac{A_A}{A_B} \quad (2.1)$$

where A_A is the activity measured after sample heating and A_B is the activity measured before performing thermal release experiments with the decay correction. The relative uncertainty related to this ratio is expressed as shown in equation 2.2:

$$\Delta R/R = \sqrt{\left(\frac{\Delta A_A}{A_A}\right)^2 + \left(\frac{\Delta A_B}{A_B}\right)^2} \quad (2.2)$$

A reported result with a release of 100%, in the context of counting experiments, signifies that no activity measurable above the Minimum Detectable Activity (MDA) was detected. This uncertainty in counting experiments is generally due to the detection limit (LD), as determined by methods such as the Currie approach. However, gamma spectroscopy relies on the MDA as a threshold value that combines calibration efficiency, nuclear data, measurement time, and detection limit. Therefore, the MDA can be considered a fundamental characteristic of the measurement itself, rather than an uncertainty. It does not stem from a single measurement, but instead relies on estimations involving uncertainties.

Finally, the release is expressed as equation 2.3, on which the relative uncertainty calcu-

lated above is applied:

$$\text{Release} = 1 - \frac{A_A}{A_B} \quad (2.3)$$

2.1.9 Thermal release theoretical estimations

The combination of experimental data and modeling is crucial for obtaining a comprehensive understanding of the release process. As such, complementary calculations have been performed to investigate this phenomenon. The release process can be described as a two-step procedure: firstly, a radionuclide must diffuse within the solid to reach the surface, and secondly, it must desorb from the surface to escape the solid entirely. To estimate the final release, we have employed three semi-empirical expressions presented in,³³ which are based on detailed studies with specifically developed Monte Carlo models. The first expression estimates the Fraction of radionuclides reaching the sample's Surface (FRS), which is entirely determined by the diffusion stage. The second expression aims to estimate the Global Desorption Probability (GDP), which quantifies the likelihood of desorption occurring during the remaining heating time for a radionuclide that has successfully reached the surface. The third expression combines the results from the previous two, yielding an estimation of the Out-Diffusion Fraction (ODF), which corresponds to the release fraction integrated over the heating period. Users are required to provide certain parameters, such as the heating temperature, heating time, and surface-to-volume ratio of the sample. Furthermore, users must input relevant diffusion coefficient and desorption activation enthalpy values. While experimental data for the former is often available, the latter is typically unavailable. In such cases, calculated values and approximations such as sublimation enthalpies⁵² are utilized.

2.2 GR-1+KROMEK detector efficiency calibration

The efficient calibration of the GR-1+ KROMEK (see Figure 2.14) detector is crucial for validating the activity of various novel and innovative radioisotopes collected within the CERN-MEDICIS facility. The accuracy of this calibration process is pivotal in safeguarding against potential contamination in the produced radioisotopes, which is essential for ensuring the safety and efficacy of planned treatments.

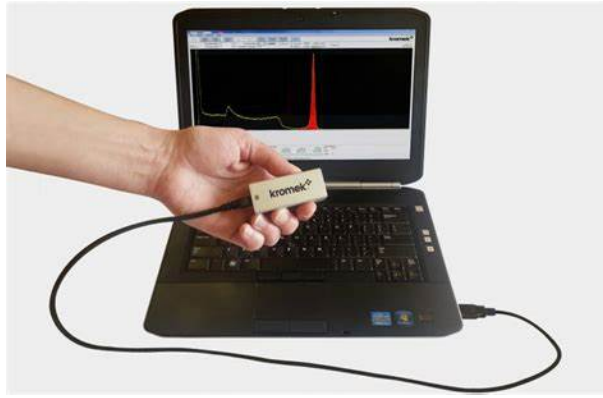
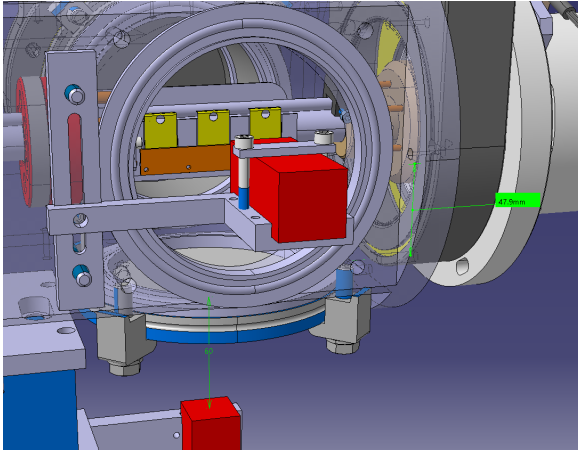


Figure 2.14: CZT GR-1 γ -ray Spectrometer⁴⁴

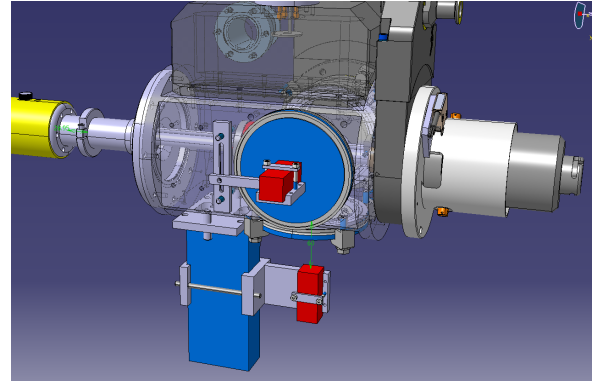
The CZT detector is a small and efficient tool that can detect photon emissions in a range of 30 keV to 3.0 MeV. Detector size is only 10mm x 10mm x 10mm and it weighs 60 grams. All KROMEK GR-1 have a dimension of 25mm x 25mm x 63mm. The detector has a high-energy resolution of less than 2.5% FWHM (full width at half maximum) at 662 keV and low electronic noise of less than 10 keV FWHM. It can process up to 30,000 counts per second, and its differential non-linearity is less than $\pm 1\%$. The detector only uses 250 mW of power and can operate in temperatures between 0°C and 40°C.

2.2.1 Experimental setup configuration

The experimental setup was designed to replicate the real conditions of the measurement on the collection chamber in the CERN-MEDICIS laboratory (see Figure 2.15 and Figure 2.16). The collection chamber comprises of a sample holder that can hold three collection foils. A robotic arm is used to position the foils perpendicularly to the radioactive ion beam. The collection chamber, the collection window, and the GR-1+ detector are shown in bottom side in red (refer to Figure 2.15).



(a) 3D drawing of the KROMEK CZT detector placement: front view



(b) 3D drawing of the KROMEK CZT detector placement: back view

Figure 2.15: 3D drawings of the KROMEK CZT detector placement during mass separation process, source: S.Marzari

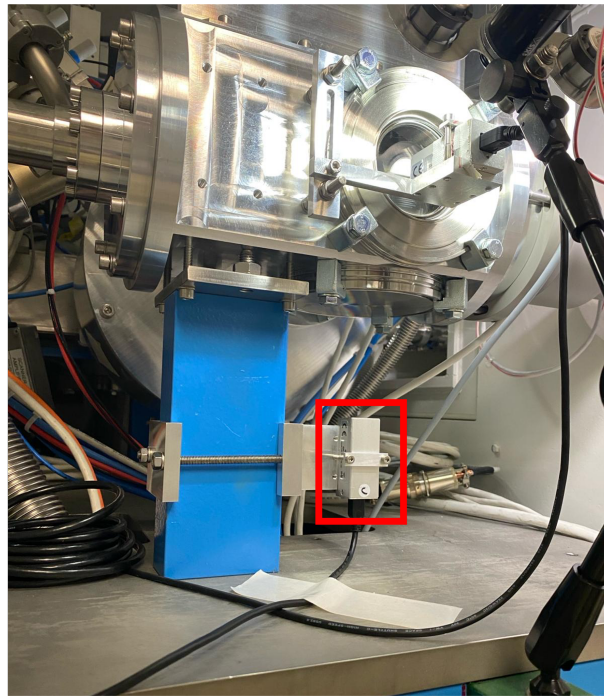


Figure 2.16: Installed KROMEK GR-1+ detector in the collection chamber in CERN-MEDICIS laboratory

The configuration of the experimental setup (see Figure 2.17) consisted of the GR-1+ detector where in front of it was placed 3D printed 50x50 mm tungsten plate (further called as collimator) with density of 4 g/cm^3 and with a 5 mm diameter hole in the middle. Four complete calibrations were performed, each utilizing a collimator at different distances - the initial position without collimator (further called as "empty position"), 5mm, 10mm, and 15mm. The distance between the outer part of the collection chamber flange and the detector was measured to be 9 cm, with the collimator positioned in between the two objects. The sample holder's bottom

was placed at a distance of 4.8 cm from the inner part of the flange. The calibration source was located at the foil position. In this configuration different sources were used (^{60}Co , ^{133}Ba , ^{152}Eu). The activities of the sources, half lives and the γ -ray emissions with the intensities are depicted in Table 2.2

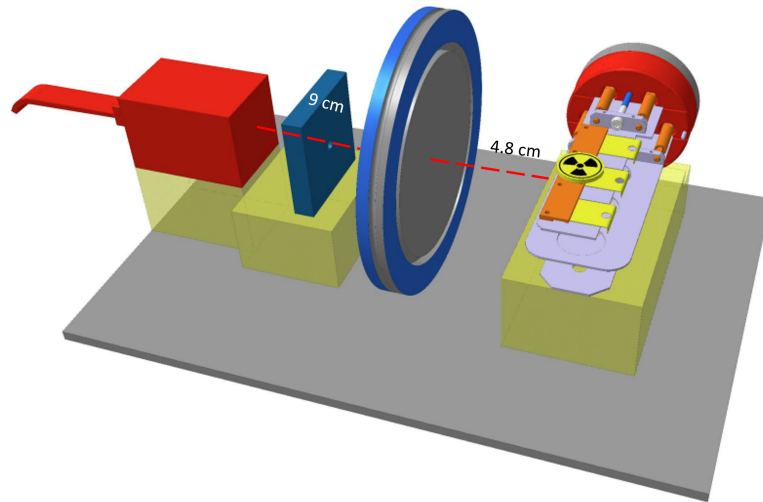


Figure 2.17: Overview of the experimental setup made in 3D CATIA software, source: E. Senbati Fagi

Table 2.2

Properties of selected radioactive sources			
Source	Half life (years)	Activity on 2.04.2024. (Bq)	Energy of γ -emissions (keV) and intensities (%) ⁵³
^{152}Eu	13.5	1.94×10^6	128.78 (28.53%), 244.6974 (7.55%), 344.28 (26.59%), 411.1165 (2.23%), 443.96 (2.82%), 778.9 (12.93%), 964.1 (14.51%), 1085.837 (10.11%), 1112.076 (13.67%), 1408.013 (20.87%)
^{133}Ba	10.6	4.65×10^5	276.3989 (7.16%), 302.8508 (18.34%), 356.0129 (62.05%), 383.8485 (8.94%)
^{60}Co	5.3	1.20×10^5	1173.228 (99.85%), 1332.492 (99.98%)

2.2.2 Operating with CZT detectors: from setup to spectrum analysis

The CZT detector offers a simple operational design. To begin, the detector must be connected to a computer via the USB cable. Multispect Software then identifies the detector, and the setup is prepared for data acquisition and analysis. Upon interaction with the CZT crystal, incident γ -ray photons produce negatively charged electrons and positively charged holes. The latter are collected by the oppositely charged electrodes, leading to a charge pulse. The pre-amplifier detects this charge pulse and generates a voltage pulse, whose height is proportional to the energy deposited by the γ -ray photon. The shaping amplifier then converts the signal into a Gaussian pulse, amplifying it in the process. Finally, the signal is sent to the Multi-Channel Analyzer (MCA), which produces the characteristic spectrum for incoming γ -ray photons. To ensure optimal performance of the CZT detector, it is advisable to allow it to stabilize for at least 5 minutes before initiating data acquisition. Once the detector is stabilized, the user can click the appropriate button in the software to acquire the spectrum. The full spectrum consists of 4096 channels (approximately 3 MeV). The software enables the user to set a Lower Level Discriminator (LLD) no lower than channel 32 to remove the low-energy segment of the spectrum or the noise peak.

2.2.3 Multispect Software

MultiSpect Analysis is a software solution designed specifically for KROMEK range of radiation detectors, allowing for easy connection and setup, and providing tailored analysis functions for the detectors and their applications. An example of the acquired spectrum using MultiSpect Software of ^{152}Eu is shown in Figure 2.18 .

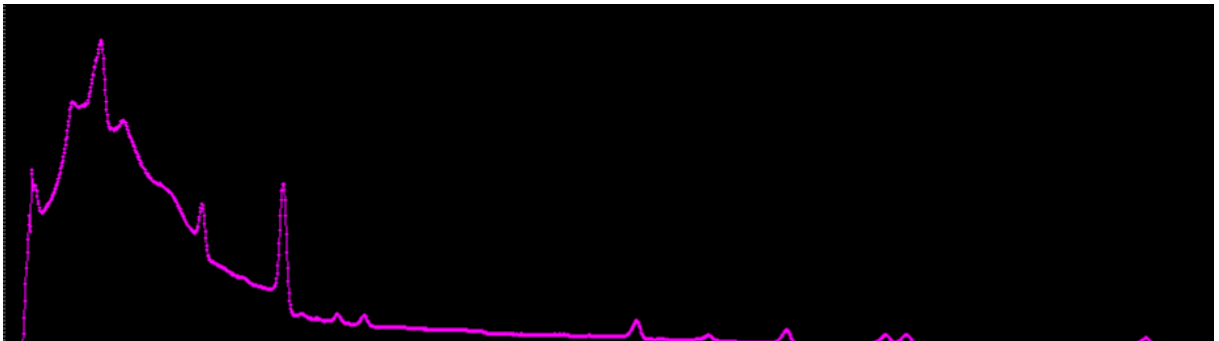


Figure 2.18: Example of ^{152}Eu spectrum using MultiSpect Software

To use MultiSpect Analysis, the user must first assign the appropriate radioisotope to be studied, and then select the energy of the γ -ray emission that corresponds to the peak of the

spectrum to be analyzed. The activity of the radioactive source on the date of calibration, along with its uncertainty, can then be applied into the software. Once this information has been provided, MultiSpect Analysis can calculate the activity on the given day of the measurement and provide information on the efficiency of the radioisotope for the selected energy, as well as the value of its uncertainty. The user can repeat this process for all the energies of the most prominent γ -ray emissions of the radioisotope, thereby obtaining all the efficiency values.

2.2.4 Detector efficiency calculations

The absolute photopeak efficiency of a detector refers to the ratio that exists between the total number of hits detected in the full energy peak(s) and the actual number of gamma-ray photons that are emitted by the source. This detection efficiency is influenced by several factors, including the source activity, the geometry of both the detector and source, as well as the distance separating the source from the detector.⁵⁴ For a given geometry, the detection efficiency for an energy E (keV) is defined by equation 2.4

$$Eff(E) = \frac{N(E)}{I(E) \times t \times A} \quad (2.4)$$

where N is the number of counts (dependent on energy E), I is the intensity of the γ -ray photons at a given energy (dependent on energy E), t is the live time in seconds and A is the Activity in Becquerels of the source reported to the time of the measurement.

3.RESULTS

3.1 Scandium thermal release from activated ^{nat}Ti and ^{nat}V target materials

Two types of ^{nat}Ti foil samples - embossed and non-embossed - were subjected to Sc thermal release experiments. The experimental results obtained were then compared with the theoretical estimations generated by evaluating analytical expressions formulated by F. Ogallar Ruiz.³³ These expressions provide the fraction of Sc that out-diffuses in ^{nat}Ti for a given temperature, sample surface, and volume. In addition to this, the first Sc release experiments from ^{nat}V samples were conducted, and a preliminary Sc thermal release curve was obtained.

3.1.1 Radionuclide production and estimation

The Sc radionuclide inventory and the average activity per sample were determined through γ -ray spectrometry and are presented in Table 3.1 and Table 3.2, respectively. The production of $^{44g/m}\text{Sc}$, ^{46}Sc , ^{47}Sc , and ^{48}Sc radionuclides occurred, with ^{46}Sc and ^{47}Sc being selected for the thermal release study because of their favorable decay half-life and relatively higher activity. However, ^{48}Sc was excluded from the analysis due to the high uncertainties in the γ -ray spectrometry measurements caused by the radionuclide's short half-life.

Table 3.1

Radionuclides produced in ^{nat}Ti sample			
Radionuclide	Avg. activity per sample (Bq)	MDA interval (Bq)	Half-life ($T_{1/2}$)
^{43}Sc	< MDA	$1.41 \times 10^2 - 2.02 \times 10^2$	3.89 h
^{44g}Sc	303 ± 56	$4.26 \times 10^1 - 6.76 \times 10^1$	3.97 h
^{44m}Sc	246 ± 57	$4.44 \times 10^1 - 6.81 \times 10^1$	2.44 d
^{46}Sc	180 ± 19	$2.53 \times 10^1 - 4.67 \times 10^1$	83.79 d
^{47}Sc	1730 ± 190	$7.57 \times 10^1 - 1.02 \times 10^2$	3.35 d
^{48}Sc	496 ± 75	$3.19 \times 10^1 - 4.67 \times 10^1$	43.67 h

Table 3.2

Radionuclide	Avg. activity per sample (Bq)	MDA interval (Bq)	Half-life (T _{1/2})
^{44g} Sc	53.1 ± 12.4	5.09 × 10 ¹ – 5.68 × 10 ¹	3.97h
^{44m} Sc	92.6 ± 21.3	5.24 × 10 ¹ – 5.44 × 10 ¹	2.44d
⁴⁶ Sc	59.5 ± 9.5	3.48 × 10 ¹ – 3.88 × 10 ¹	83.79d
⁴⁷ Sc	304 ± 54	9.12 × 10 ¹ – 9.58 × 10 ¹	3.35d
⁴⁸ Sc	100 ± 14	4.25 × 10 ¹ – 4.71 × 10 ¹	43.67h
⁴⁸ V	107 ± 21	4.35 × 10 ¹ – 4.97 × 10 ¹	15.97d

Comparison of theoretical estimations with ActiWiz and experimentally obtained Sc radionuclide activities for neutron activated ^{nat}Ti samples, showcasing the alignment for ⁴⁷Sc are shown in Figure 3.1 and ⁴⁶Sc in Figure 3.2. The average ratio between the obtained values are 1.09 ± 0.13 for the ⁴⁷Sc and 1.25 ± 0.15 for the ⁴⁶Sc radionuclides. It is noteworthy that the activity per sample for both ⁴⁷Sc and ⁴⁶Sc varies across the samples due to the time gap between irradiation and subsequent γ -ray spectra measurements.

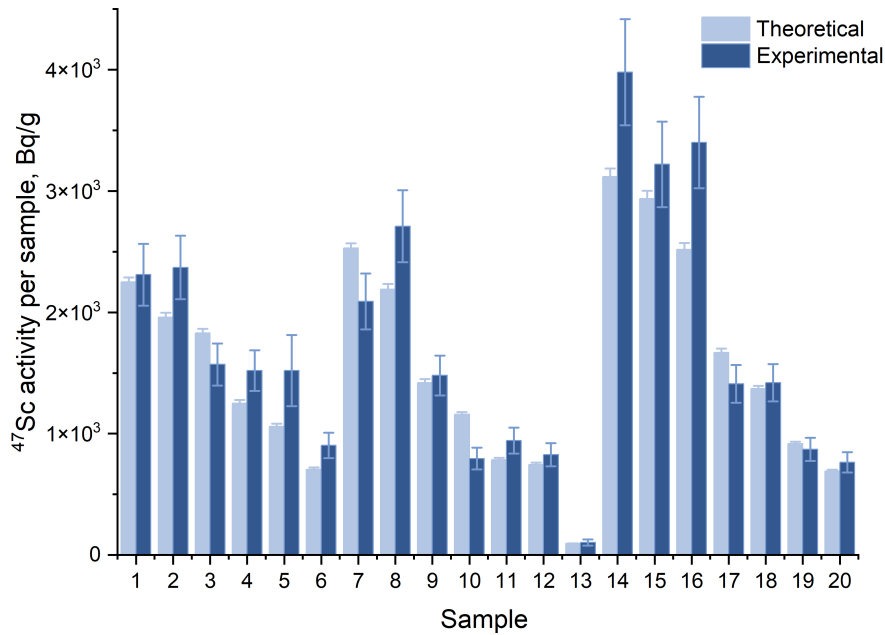


Figure 3.1: ⁴⁷Sc activity per sample given by ActiWiz software versus obtained experimental values with γ -ray spectrometry for ^{nat}Ti samples (the theoretical uncertainties are reported at k=1)

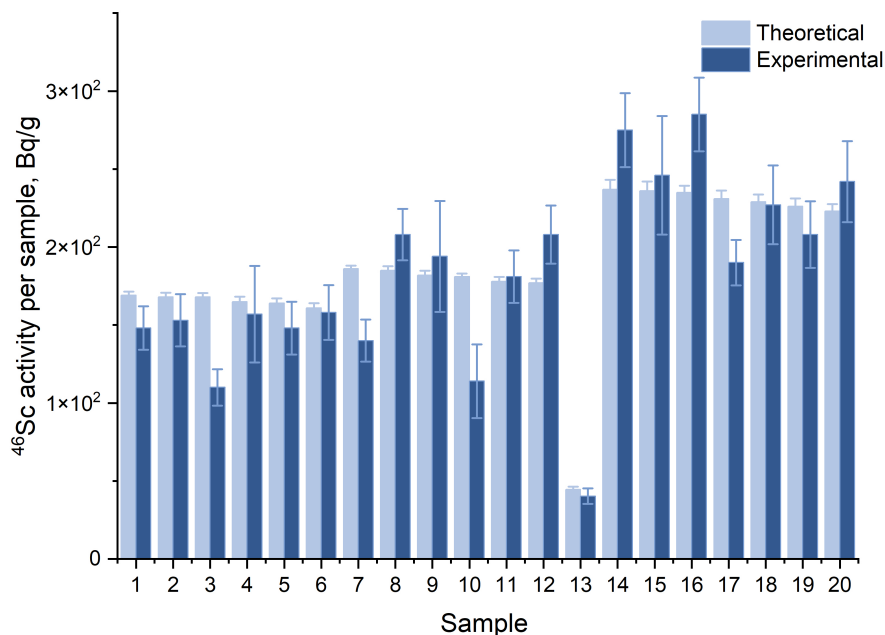


Figure 3.2: ^{46}Sc activity per sample given by ActiWiz software versus obtained experimental values with γ -ray spectrometry for $^{\text{nat}}\text{Ti}$ samples (the theoretical uncertainties are reported at $k=1$)

3.1.2 Sc thermal release from $^{\text{nat}}\text{Ti}$ samples

The experiment aimed to analyze the thermal release of Sc from $^{\text{nat}}\text{Ti}$ foil rolls at different temperatures, with a one-hour hold time at the selected temperature. The temperature selection was based on the typical mass separation conditions and the physical properties of the material, including the melting point. The maximum temperature set was 1550 °C to avoid material melting. However, sintering was observed for a sample studied at 1500 °C, causing the sample to stick to the Ta boat and reducing the release over longer periods of operational time.

The results obtained for the relative thermal release of ^{47}Sc and ^{46}Sc from embossed and non-embossed $^{\text{nat}}\text{Ti}$ samples are illustrated in Figure 3.3 and Figure 3.4. The relative release results for both isotopes were found to coincide for both types of roll samples. It is noteworthy that Sc was not released below 700 °C for both sample types.

The experiment involved heating a sample to a temperature of 1450°C for one hour. It was observed that there was a 100% release of scandium, indicating that the sample was inactive after the heating cycle. In contrast, the non-embossed target material released scandium at lower temperatures, with the maximum release occurring at 1200°C. This is consistent with previous studies conducted by⁵⁵ and⁵⁶. It is important to note that the uncertainties in the results of samples with longer decay time were higher, as the activity remaining in those samples approached the Minimal Detectable Activity (MDA) values.

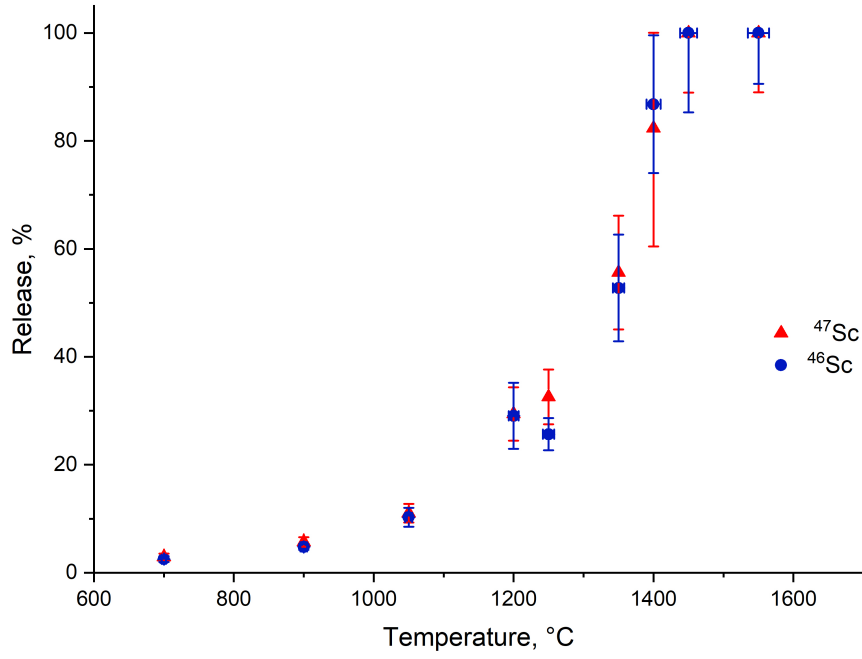


Figure 3.3: ^{47}Sc and ^{46}Sc thermal release from embossed ^{nat}Ti foil samples

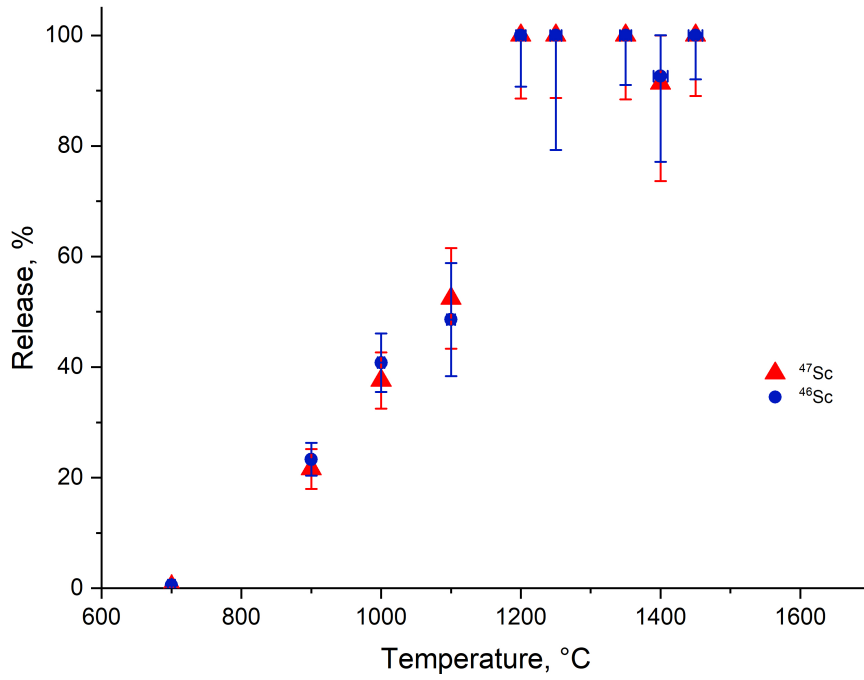


Figure 3.4: ^{47}Sc and ^{46}Sc thermal release from non-embossed ^{nat}Ti foil samples

The release shift to lower temperatures observed in non-embossed target material samples compared to their embossed counterpart raises questions about how surface morphology affects thermal release characteristics. This phenomenon could be due to several factors. Firstly, embossing may lead to a slightly larger specific surface area in the embossed material because of the ductile material stretching and compressing. Theoretical formulas highlight the significance of the surface-to-volume ratio in diffusion and release processes. The larger surface area in

the embossed material could facilitate greater diffusion potential, theoretically promoting faster release. However, the observed release results in Figure 3.3 contradict this expectation and indicate a delayed release for the embossed material. This suggests, that the actual release kinetics are influenced by a combination of factors beyond the specific surface area. During the sample embossing, possible cracks are being produced at the embossing points on a microscale, which would result in deformation of the crystalline matrix of the native titanium oxide layer that possibly could have a notable impact on the release. The embossing process could also alter the diffusion pathways within the bulk material, affecting the rate at which Sc atoms migrate to the surface and are subsequently released. Also the role of heat conduction could contribute in this context. Better heat conduction implies a more powerful driving force for diffusion, potentially leading to an earlier release. In this scenario, isotopes would likely arrive sooner at the surface, influencing the overall release dynamics. Therefore, the interplay between surface topography, diffusion pathways, and heat conduction should be carefully considered to understand the observed release behavior comprehensively.

It is crucial to consider the impact of surface effects and chemical compositions on release dynamics, despite the general trend of higher release with larger surfaces. The increased surface area can result in greater interaction between Sc and surrounding materials and chemical species, thus explaining the less efficient thermal release. As a result, the use of additional tools and equipment may lead to the deposition of contaminants onto the foil surface, stabilizing Sc in a less volatile chemical form. This study did not explore the observed phenomena, but future research will systematically investigate it.

The relative thermal release values of measured Sc radionuclides from both type ^{nat}Ti samples are compiled in Table 3.3 for embossed ^{nat}Ti and in Table 3.4 for non-embossed ^{nat}Ti . All uncertainties are presented as combined values derived from both counting statistics (before and after heating). A relative release sum of ^{46}Sc and ^{47}Sc with their according uncertainties at each temperature are shown to highlight the release pattern of Sc species in general.

Table 3.3

⁴⁶Sc and ⁴⁷Sc relative release from embossed ^{nat}Ti foil samples

Temperature, °C	Release of ⁴⁶ Sc, %	Release of ⁴⁷ Sc, %	Total release of Sc, %
700	2.5 ± 0.5	2.9 ± 0.7	2.7 ± 0.7
900	4.8 ± 0.6	5.7 ± 0.9	5.6 ± 1.0
1050	10.3 ± 1.8	11.0 ± 1.7	10.9 ± 2.9
1200	29.1 ± 6.1	29.4 ± 4.9	29.4 ± 7.4
1250	25.7 ± 3.0	32.6 ± 5.1	31.9 ± 5.8
1350	52.8 ± 9.9	55.6 ± 10.5	54.8 ± 11.0
1400	86.8 ± 12.8	82.3 ± 21.9	83.1 ± 28.0
1450	100.0 ± 14.7	100.0 ± 11.1	100.0 ± 20.4
1550	100.0 ± 9.4	100.0 ± 11.0	100.0 ± 14.5

Table 3.4

⁴⁶Sc and ⁴⁷Sc relative release from non-embossed ^{nat}Ti foil samples

Temperature, °C	Release of ⁴⁶ Sc, %	Release of ⁴⁷ Sc, %	Total release of Sc, %
700	0.57 ± 0.09	0.33 ± 0.05	0.40 ± 0.08
900	23.3 ± 3.0	21.6 ± 3.6	22.0 ± 4.8
1000	40.8 ± 5.3	37.6 ± 5.1	38.5 ± 5.9
1100	48.6 ± 10.2	52.4 ± 9.1	51.6 ± 10.8
1200	100.0 ± 9.3	100.0 ± 11.4	100.0 ± 15.9
1250	100.0 ± 20.7	100.0 ± 11.3	100.0 ± 18.2
1350	100.0 ± 9.0	100.0 ± 11.6	100.0 ± 13.8
1400	92.6 ± 15.5	91.3 ± 17.7	91.4 ± 18.9
1450	100.0 ± 7.9	100.0 ± 11.0	100.0 ± 24.4

A comparative measurement to assess the heating and cooling ramp influence of the released fraction was also performed for a sample at 1400 °C and changing the hold time from 1 h to 0 h. The measurement was done with a non-embossed ^{nat}Ti foil roll resulting in 51.4 ± 10.6 % Sc released. In comparison, the obtained value for the same conditions but with a holding time of 1h was 91.4 ± 18.9 % (see Table 3.4). Because diffusion and effusion are thermally activated processes, the impact of the heating ramp on the released fraction would be non-linearly higher at higher temperatures not only because of the heating time but also the faster diffusion and desorption. The impact of the heating/cooling ramp time on the released fraction suggests the importance of creating the ion beam and setting the separator for isotope collection already at lower target material temperatures while gradually increasing them throughout the process. Keeping the samples at constant high temperatures would maximize the release.⁵⁶ Furthermore, the rapid release may not be suitable for mass separation, because of limited ion source ion load

or ionization efficiency. From the obtained results an optimal release plan, target and ion source unit, and mass separation temperatures can be deducted.

To ensure the integrity of the experiment, dose rate measurements on the target container were conducted both with and without the activated samples within the container. This comprehensive approach aimed to monitor and control potential contamination or condensation effects, to identify any cold spots of the target container. The measurements were taken at six distinct points to facilitate a thorough comparison of results before and after the experiment, with Figure 3.5 providing an illustrative example of the measurements. Point #4 is the target transfer line which was not heated during the experiments and it remained to stay as a cold spot. During mass separation the ion source and transfer line would be heated to $\approx 2000\text{ }^{\circ}\text{C}$ and indirectly heat the target container and prevent adsorption in the transfer line region. Point #5 refers to where the sample was placed each time offering a consistent reference point for analysis resulting in a notable difference in dose rate measurements before and after the heating cycle. Points #1 and #6 represent the ends of the container where the temperature is lower than the central region, leading to an increased chance of condensation.⁵⁷ It can be seen that a certain amount of released radionuclides migrate toward the ends of the target container. The highest condensation is observed at the end, from which the sample exchange is done, because of the removable and target plug and local heat screen assembly.

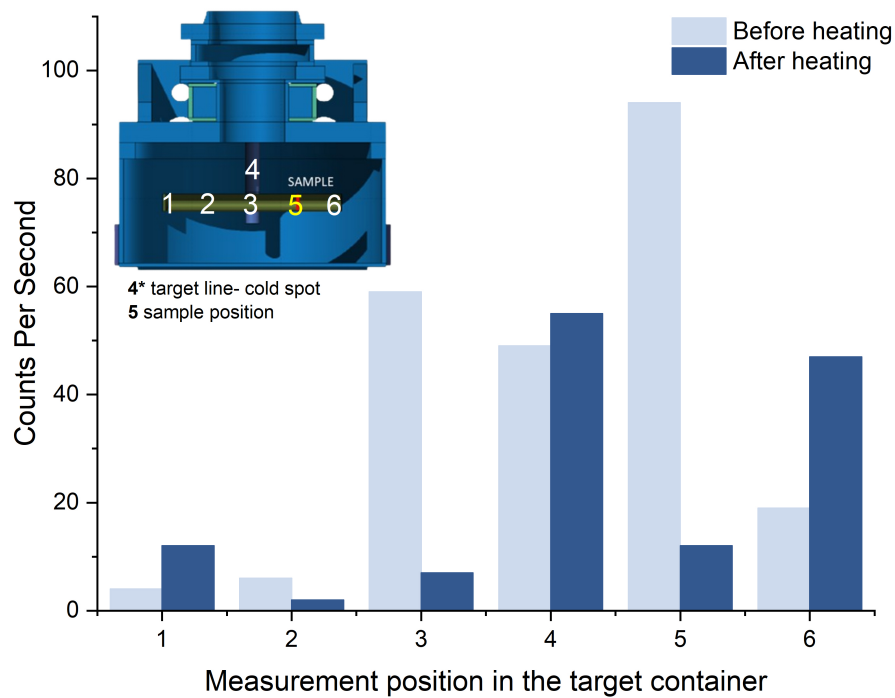


Figure 3.5: Target container dose rate measurements in 6 different locations

3.1.3 Theoretical and experimental result comparison

A comparative analysis was conducted, utilizing the theoretical models outlined in section 2.9, to evaluate and depict the experimental results obtained (refer to Figure 3.6). The heating ramp speed and release during the heating phase applied during the experiments were also taken into consideration. Although the distinction between diffusion and surface effects is not the primary objective, precisely modeling the intricacies of surface effects, both macroscopic and microscopic, presents a considerable challenge. According to the theoretical models, radionuclides migrate to the surface at a much faster rate than they are released, indicating that surface effects are the limiting factor in the thermal release process. It is worth noting that the theoretical model did not account for the Ta environment in which the experiments were conducted (refer to Figure 3.7).

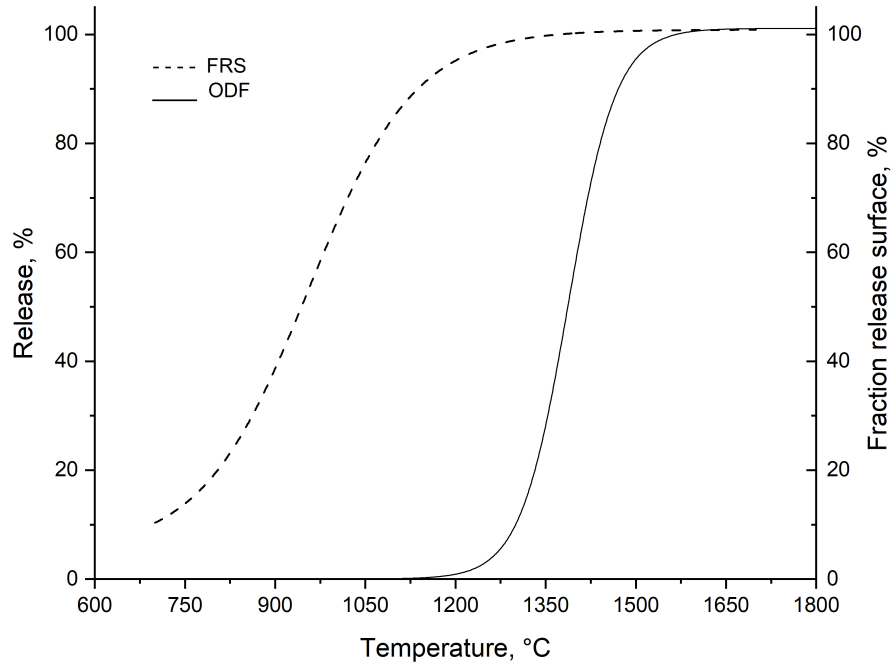


Figure 3.6: FRS and ODF theoretical models for Sc thermal release from ^{nat}Ti foil samples

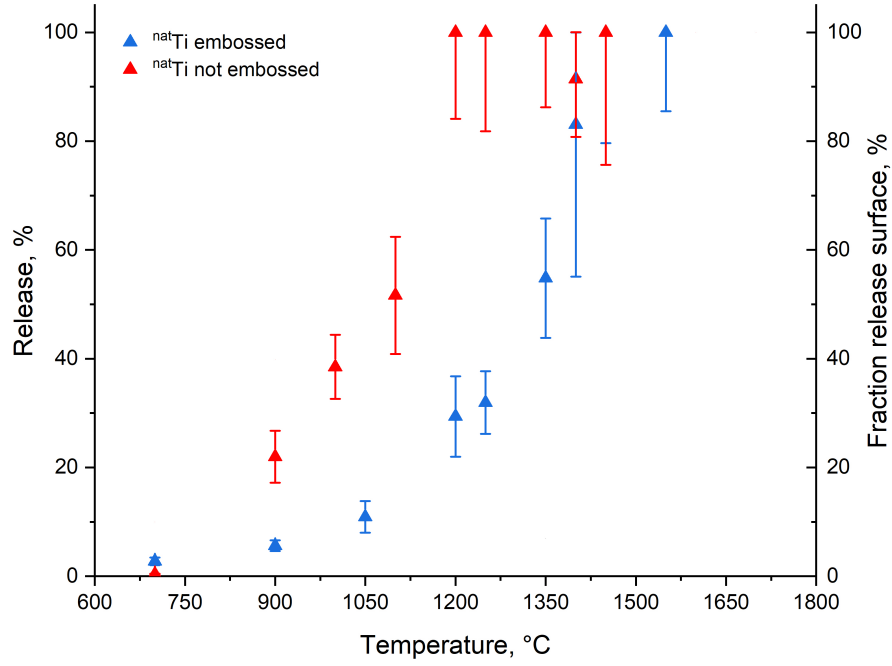


Figure 3.7: Total Sc thermal release from embossed and not embossed ^{nat}Ti foil samples

In examining the thermal release curves, our focus centered on the comparison between experimental and theoretical model data. The theoretical estimations indicated a noteworthy trend: radionuclides exhibit a faster migration to the sample's surface than their release rate suggests. This can be understood by the fact that not all isotopes reaching the surface would eventually be released, as there are mechanisms that can retain them and implies that the release process is more constrained by surface effects rather than diffusion itself. It is important to acknowledge that the desorption enthalpy data used in the theoretical model is sparsely available in the literature, and its reliability comes with a significant level of uncertainty, which unfortunately is not explicitly documented. This uncertainty may have a substantial impact on the estimation of the global desorption probability and, consequently, on the results obtained for the ODF. Reducing the desorption enthalpy of 392.4 kJ/mol⁵⁸ by for example an arbitrary fraction of 5 % in the model would shift the onset of the ODF notably towards lower temperatures. Therefore, one cannot draw consistent conclusions from the theoretical model predictions yet with respect to the behavior of embossed and non-embossed samples. It is also important to mention that ^{nat}Ti and ^{nat}V foils are covered with a native oxide layer that can influence the release from the surface because of chemisorption. To better understand these processes further targeted experiments need to be carried out.

3.1.4 Sc thermal release from ^{nat}V samples

Due to its higher melting point and favorable production cross sections for Sc, ^{nat}V is a promising material for mass separation. In addition, the release of Sc was preliminary studied from activated non-embossed ^{nat}V foil samples. The methodology employed for the ^{nat}Ti samples was replicated in this study. The release study temperature points were selected based on prior mass separation experiments conducted with ^{nat}V foil target materials at MEDICIS.⁵⁷

The thermal release results for ^{46}Sc are shown in Figure 3.8. Only two data points for ^{47}Sc release results were shown and others were discarded due to the high uncertainties from γ spectroscopy measurements obtained due to the low activity produced. Based on previous mass separation experiments and the fact that V has a higher melting point (1910°C) and density than Ti (1668°C), the Sc out-diffusion was expected to happen slower or at higher temperatures.⁵⁹

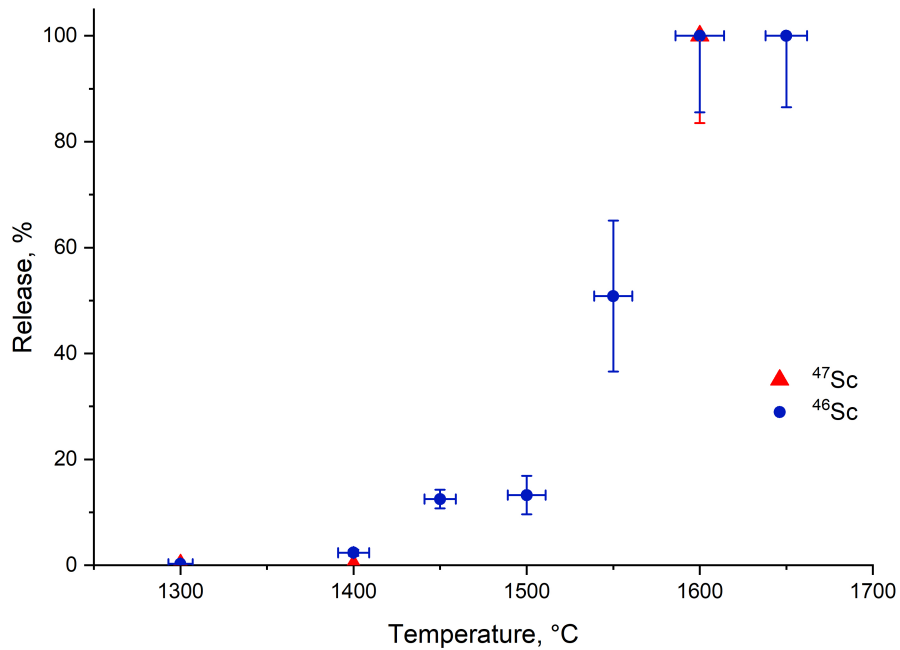


Figure 3.8: ^{46}Sc thermal release from non-embossed ^{nat}V foil samples

As shown in Figure 3.8, there is almost no Sc release below 1450 °C (12.5 ± 1.8), however, 100% release was observed already at 1600 °C (see Table 3.5).

Table 3.5

^{46}Sc and ^{47}Sc relative release from non-embossed ^{nat}V foil samples

Temperature, °C	Release of ^{46}Sc , %	Release of ^{47}Sc , %	Total release of Sc, %
1300	0.27 ± 0.07	0.10 ± 0.03	0.14 ± 0.04
1400	2.4 ± 0.6	0.00 ± 0.23	0.46 ± 0.14
1450	12.5 ± 1.8		
1500	13.2 ± 3.6		
1550	50.8 ± 14.2		
1600	100.0 ± 14.5	100.0 ± 16.5	100.0 ± 23.3
1650	100.0 ± 13.5		

At present, it is not possible to acquire theoretical estimations and curves for Sc diffusion and release from the ^{nat}V sample, owing to the absence of Sc diffusion coefficient data in the ^{nat}V matrix literature. However, a comprehensive understanding of all the processes involved in Sc thermal release can facilitate the derivation of an initial approximation of the diffusion coefficient. The obtained preliminary data can serve as a starting point for determining the first diffusion coefficient for Sc within the V matrix.

The Scandium thermal release studies have yielded successful results, indicating that this release method can be employed in optimizing the mass separation process for other medically important elements at CERN-MEDICIS, such as terbium. Beginning on May 17th, 2024, the author commenced new release studies to optimize the release of radionuclides produced from the irradiation of tantalum target materials such as Tm, Ba, Cs with a special focus on terbium, a difficult-to-extract element. These studies will be the base of the author's PhD thesis in the future.

3.2 KROMEK detector calibration

For the efficiency calibration the sources from the Table 2.2 were used. For the fit of the peaks with the Gaussian shape, two different softwares were used - MultiSpect (version 14.24.3.243) and OriginPro 2024 software.

3.2.1 Precise energy calibration through Gaussian peak fitting with MultiSpect software - case of empty collimator position

Following each measurement, the MultiSpect software was used to analyze the spectra of each source. The software provides two options for analyzing the spectra. The first involves

utilizing the automatically fitted Gaussian peaks values provided by the software. The second, more precise method, involves manually assigning peak fits by selecting the beginning and end of each peak in the spectrum and initiating a Gaussian fit. The latter option is available through the MultiSpect Software, and a visual representation of the process is depicted in Figure 3.9. This process yields the counts for each peak in the γ -ray spectrum, as well as the Sigma of the centroid of the peak.

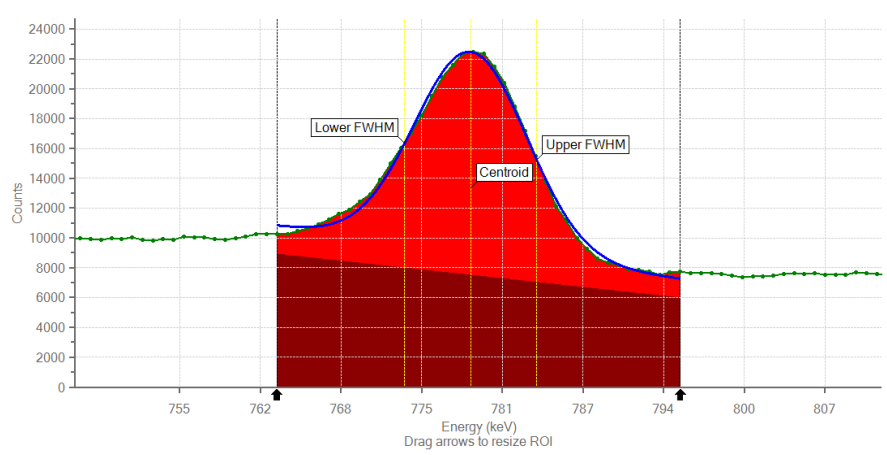


Figure 3.9: Manually assigned peak for Eu-152 with energy of 778.9 keV

Consequently, the efficiency values (see Table 3.6) can be calculated, as all the remaining parameters of equation 2.4 are known.

Table 3.6

Calculated efficiency values for calibration position without collimator

Source	Energy (keV)	Efficiency
^{152}Eu	121.78	$2.32 \pm 0.07 \times 10^{-6}$
^{152}Eu	244.6974	$8.36 \pm 0.28 \times 10^{-6}$
^{133}Ba	276.3989	$8.86 \pm 0.29 \times 10^{-6}$
^{133}Ba	302.8508	$8.72 \pm 0.28 \times 10^{-6}$
^{152}Eu	344.28	$7.94 \pm 0.26 \times 10^{-6}$
^{133}Ba	356.0129	$7.67 \pm 0.25 \times 10^{-6}$
^{133}Ba	383.8485	$7.04 \pm 0.23 \times 10^{-6}$
^{152}Eu	411.1165	$6.39 \pm 0.21 \times 10^{-6}$
^{152}Eu	443.96	$5.72 \pm 0.19 \times 10^{-6}$
^{152}Eu	778.9	$2.72 \pm 0.09 \times 10^{-6}$
^{152}Eu	964.1	$2.47 \pm 0.08 \times 10^{-6}$
^{152}Eu	1085.837	$2.29 \pm 0.07 \times 10^{-6}$
^{152}Eu	1112.076	$2.25 \pm 0.07 \times 10^{-6}$
^{60}Co	1173.228	$2.10 \pm 0.06 \times 10^{-6}$
^{60}Co	1332.492	$1.79 \pm 0.06 \times 10^{-6}$
^{152}Eu	1408.013	$1.62 \pm 0.05 \times 10^{-6}$

Subsequently, the efficiency curve can be generated using MultiSpect software, showcas-

ing the efficiency as a function of the energy, see Figure 3.10a, however, as the energy radius ranging from 80 to 500 keV holds significant importance in the context of medical applications, the efficiency curve needs to be optimised by using Gaussian function fit to make a better fit for the low energies as well as more data points for more precise efficiency curve, see Figure 3.10b.

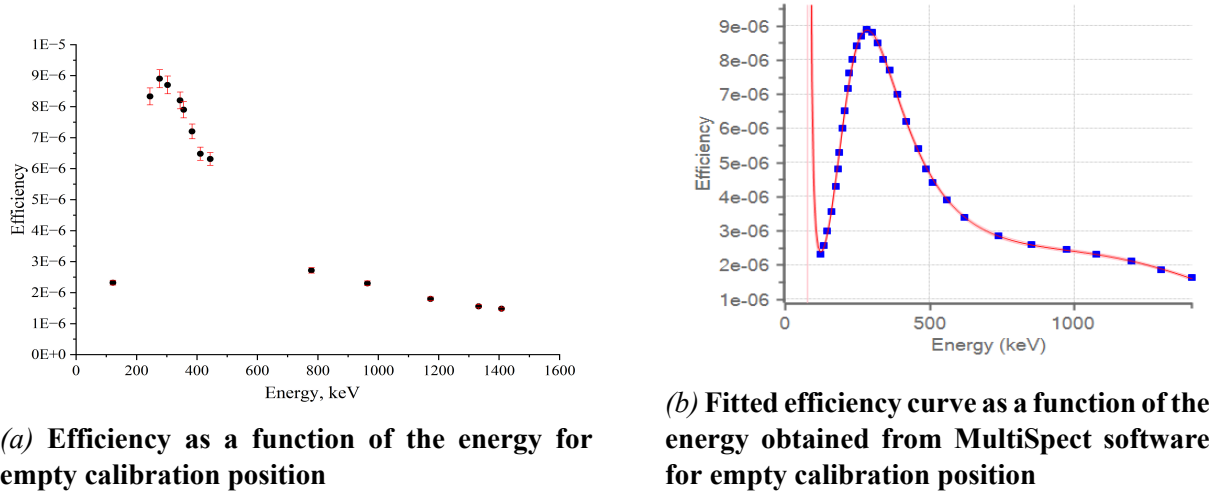


Figure 3.10: Comparison of efficiency data obtained experimentally and by MultiSpect software

The activity of a radioactive source can be determined by utilizing Equation 3.1, which is essentially Equation 2.4 solved for the activity. By virtue of the efficiency curves and live times obtained during the efficiency calculation for each energy, the counts of each peak and intensities of γ -ray emissions have been determined for every radioactive source (as illustrated in Table 2.2).

$$A = \frac{N}{E \cdot I \cdot t} \quad (3.1)$$

From this information, the activity corresponding to each γ -ray emission energy can be calculated. The activity of the source is subsequently determined by computing the plain average of the activities of the γ -ray emissions with the strongest emissions for each radioisotope, see Figure 3.11 for example of ^{152}Eu spectrum.

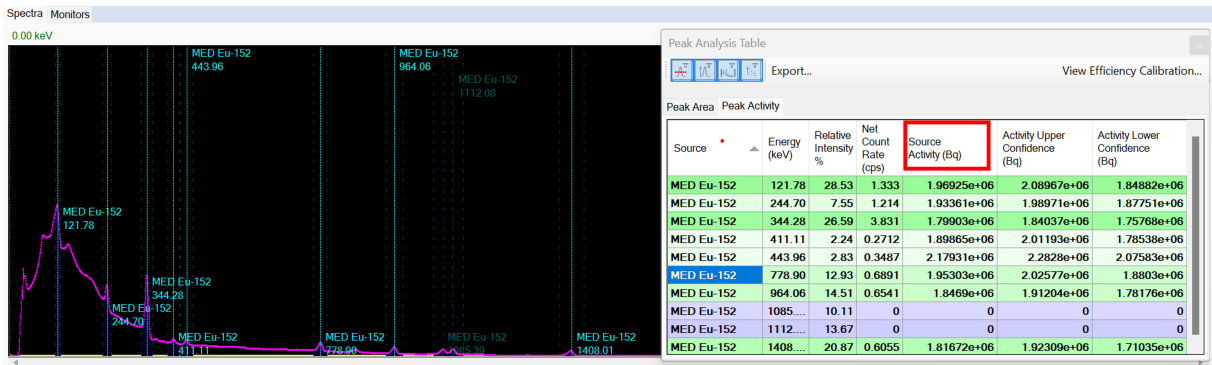


Figure 3.11: Obtained source activity for ^{152}Eu using the generated efficiency curve

In Table 3.7 the comparison between the calculated activities after performing the fit of the efficiency curve using the efficiency data from MultiSpect and the actual activity of the sources is presented. The presented table summarizes the calculated activities of various radioactive sources measured at specific gamma-ray energies, alongside their expected activities. The calculated activities are derived from experimental measurements, while the expected activities are based on known or assumed values. The differences between the calculated and expected activities are also provided, expressed as percentages.

Table 3.7
Calculated efficiency values for calibration position without collimator

Source	Energy (keV)	Calculated activity (Bq)	Source activity, Bq	Difference (%)
^{152}Eu	121.78	1.96×10^6	1.94×10^6	1.1
^{152}Eu	244.6974	1.93×10^6		0.6
^{152}Eu	344.28	1.79×10^6		7.7
^{152}Eu	411.1165	1.89×10^6		2.6
^{152}Eu	443.96	2.17×10^6		10.5
^{152}Eu	778.9	1.95×10^6		0.6
^{152}Eu	964.1	1.84×10^6		5.2
^{152}Eu	1408.013	1.81×10^6		6.7
^{133}Ba	276.3989	4.57×10^5	4.65×10^5	1.7
^{133}Ba	302.8508	4.49×10^5		3.4
^{133}Ba	356.0129	4.41×10^5		5.2
^{133}Ba	383.8485	4.48×10^5		3.7
^{60}Co	1173.228	1.13×10^5	1.20×10^5	5.8
^{60}Co	1332.492	1.12×10^5		6.6

The calculated activities generally align well with the expected activities for most of the examined gamma-ray energies across different sources. However, slight discrepancies are observed, as indicated by the differences expressed as percentages. These discrepancies range

from as low as 0.6% to as high as 10.5%. The activities calculated for most energy levels of ^{152}Eu demonstrate a close match with expected activities, with differences generally below 2.6%. However, at higher energies, such as 443.96 keV and 1408.013 keV, the differences increase to 6.7% and 10.5%, respectively. This deviation may be attributed to factors such as measurement uncertainties, calibration errors, or variations in source decay characteristics. Similarly, for ^{133}Ba , the calculated activities exhibit good agreement with expected values, with differences ranging from 1.7% to 5.2%. While these discrepancies are relatively small, they suggest potential areas for improvement in calibration procedures or measurement techniques. Regarding ^{60}Co , the calculated activities also demonstrate reasonable agreement with expected values, with differences of 5.8% and 6.6% for the measured energies. Although these differences are slightly higher compared to the other sources, they still fall within an acceptable range, considering inherent uncertainties in measurement systems and techniques.

3.2.2 Energy calibration using Gaussian peak fitting with MultiSpect and Origin Pro software for 5 mm, 10 mm, and 15 mm collimator positions

In the previous section, the methodology for calculating the detector efficiency under ideal conditions was presented. However, when a collimator is used, an additional factor is incorporated, rendering the calibration of efficiency more challenging. Consequently, the use of MultiSpect software for peak fitting is no longer sufficient. The method for calculating the detector efficiency is described in section 3.2.1. However, it should be noted that when applying collimators of varying sizes, the efficiency curve generated from experimental data points was not ideal. To address this issue, the OriginPro software was utilized to obtain a better Gaussian fit. This allowed for a more accurate representation of the detector efficiency under differing collimator sizes.

The results of this analysis, which are illustrated in Figure 3.12, suggest that gamma line intensity is inversely proportional to the thickness of the collimator. This means that thicker collimator lead to a decrease in gamma line intensity, which in turn reduces the detector efficiency. Therefore, it is crucial to perform precise calibration of the detector to ensure the accuracy of the results obtained.

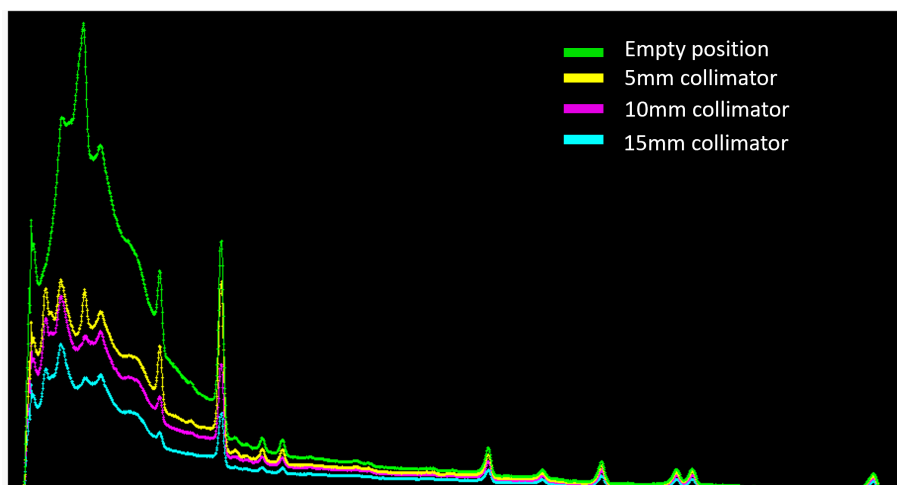


Figure 3.12: Comprehensive gamma spectra for all the calibrations performed

An attempt was made to fit a Gaussian curve to the experimental data using MultiSpect software. However, due to the limited number of data points and the wide range of values, the Gaussian fitting did not accurately represent the underlying distribution. An example of 10mm collimator efficiency fit using Multispect software is shown in Figure 3.13

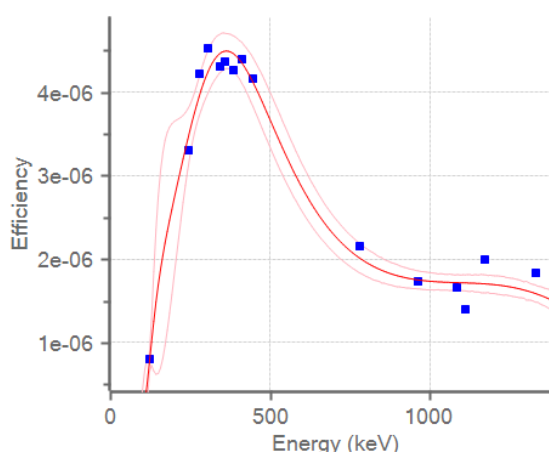


Figure 3.13: Efficiency curve fitted using MultiSpect software for 10mm collimator

However, due to certain inherent limitations in the software, it was unable to provide accurate results of Gaussian fitting. The Origin software was used to create a more accurate Gaussian curve based on experimental data points, particularly in the low energy range. This is because many of the radionuclides used in medical applications (especially therapeutic and SPECT) have a low energy range, such as ^{47}Sc which has a gamma line at 159.38 keV. The reason for this was that the experimental data, owing to the collimator used, was not ideal and required a more accurate fitting. By using Origin software, the experimental data points were accurately fitted to a Gaussian curve, and this allowed for more data points to be extracted and added into the MultiSpect software. This, in turn, led to an improved efficiency curve. A detailed

comparison between the experimental values and the fitted ones can be seen in figure 3.14.

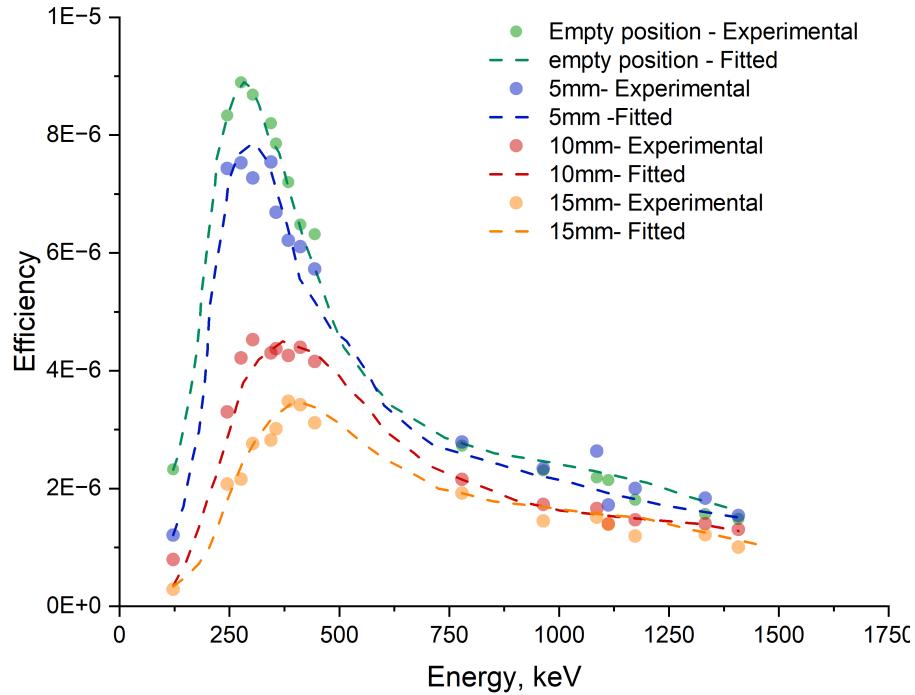


Figure 3.14: Experimental data comparison with fitted curves of all the calibrations done

After fitting in Origin software, efficiency for each of the energy depending from the collimator thickness was calculated (see Table 3.8).

Table 3.8

Fitted efficiency values for all of the calibration positions				
Energy (keV)	Efficiency 0 mm	Efficiency 5 mm	Efficiency 10 mm	Efficiency 15 mm
121.78	2.32×10^{-6}	1.21×10^{-6}	3.53×10^{-7}	3.35×10^{-7}
244.6974	8.36×10^{-6}	7.00×10^{-6}	2.83×10^{-6}	1.79×10^{-6}
276.3989	8.86×10^{-6}	7.70×10^{-6}	3.64×10^{-6}	2.37×10^{-6}
302.8508	8.72×10^{-6}	7.86×10^{-6}	4.13×10^{-6}	2.73×10^{-6}
344.28	7.94×10^{-6}	7.23×10^{-6}	4.34×10^{-6}	3.17×10^{-6}
356.0129	7.67×10^{-6}	7.08×10^{-6}	4.59×10^{-6}	3.31×10^{-6}
383.8485	7.04×10^{-6}	6.47×10^{-6}	4.46×10^{-6}	3.50×10^{-6}
411.1165	6.39×10^{-6}	5.54×10^{-6}	4.39×10^{-6}	3.46×10^{-6}
443.96	5.72×10^{-6}	5.14×10^{-6}	4.30×10^{-6}	3.38×10^{-6}
778.9	2.72×10^{-6}	2.61×10^{-6}	2.15×10^{-6}	1.92×10^{-6}
964.1	2.47×10^{-6}	2.22×10^{-6}	1.69×10^{-6}	1.67×10^{-6}
1085.837	2.29×10^{-6}	2.12×10^{-6}	1.56×10^{-6}	1.56×10^{-6}
1112.076	2.25×10^{-6}	1.92×10^{-6}	1.53×10^{-6}	1.54×10^{-6}
1173.228	2.10×10^{-6}	1.91×10^{-6}	1.49×10^{-6}	1.51×10^{-6}
1332.492	1.79×10^{-6}	1.70×10^{-6}	1.38×10^{-6}	1.24×10^{-6}
1408.013	1.62×10^{-6}	1.51×10^{-6}	1.28×10^{-6}	1.00×10^{-6}

The efficiency of gamma-ray detection systems is affected by various parameters, including energy and positional dependencies, as well as material thickness. Higher gamma-ray ener-

gies are associated with increased probabilities of interactions such as Compton scattering and pair production, leading to decreased detection efficiency. Similarly, an increase in the distance between the gamma-ray source and detector causes attenuation and geometric effects, resulting in a reduction in detection efficiency. The effect of material thickness on detection efficiency is also crucial to consider. Introducing a 5 mm material layer reduces efficiency across all energy levels, with a more pronounced decrease at higher energies due to increased attenuation and scattering effects. A further reduction in efficiency is observed with a 10 mm material thickness, accentuating attenuation and scattering effects, particularly at lower energies. The efficiency is found to be significantly lower with a 15 mm material thickness, highlighting the cumulative impact of attenuation and scattering on detection sensitivity.

After collecting additional data points through the Origin software, these data were subsequently incorporated into the MultiSpect Software for further analysis. Within MultiSpect, a Gaussian fitting algorithm was once again applied to the efficiency values. This iterative process allowed for the generation of a refined efficiency curve, see Figure 3.15.

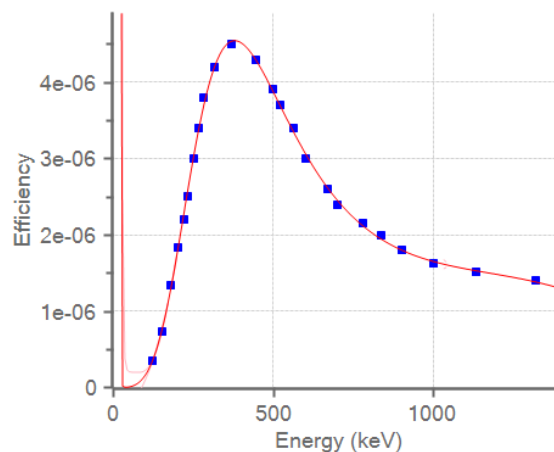


Figure 3.15: Example of the final efficiency curve obtained with 10mm collimator

The MultiSpect software was utilized to input all the efficiency values, which were then used to generate efficiency curves for various collimator thicknesses. These efficiency curves will play a crucial role in the real-time monitoring of the implanted activity.

3.2.3 On-Line monitoring of the implanted activity

The positioning of KROMEK in front of the windows (see Figure 2.15a) facilitates real-time monitoring of the initial kBq and enables the adjustment of temperature for isotope extraction at the onset of collection. However, this placement leads to detector saturation at activity levels

ranging from several tens to one hundred MBq, depending on the measured isotope. As a result, tracking activity levels above these thresholds becomes unfeasible. To address this limitation, a new detector has been installed below the collection chamber (see Figure 2.15b), positioned at a greater distance than the window-mounted detector, allowing for the measurement of higher activities.

Every year, around April, the CERN-MEDICIS facility restarts operations after a break period from December. During one of the first runs this year, ^{224}Ra was collected. Its decay chain involves radioactive ^{220}Rn , ^{216}Po , ^{212}Pb , ^{212}Bi , ^{212}Po , or ^{208}Tl , ultimately leading to stable ^{208}Pb . The cumulative radiation emitted during this decay chain is 400% α , 200% β .

During this collection, the activity of ^{212}Pb was measured using the newly installed KROMEK and compared to the KROMEK placed in front of the window. After initially detecting activity with the KROMEK detector placed in front of the window, it was switched to a new one. As shown in figure 3.16, the detected activity followed the expected trend, indicating successful KROMEK calibration.

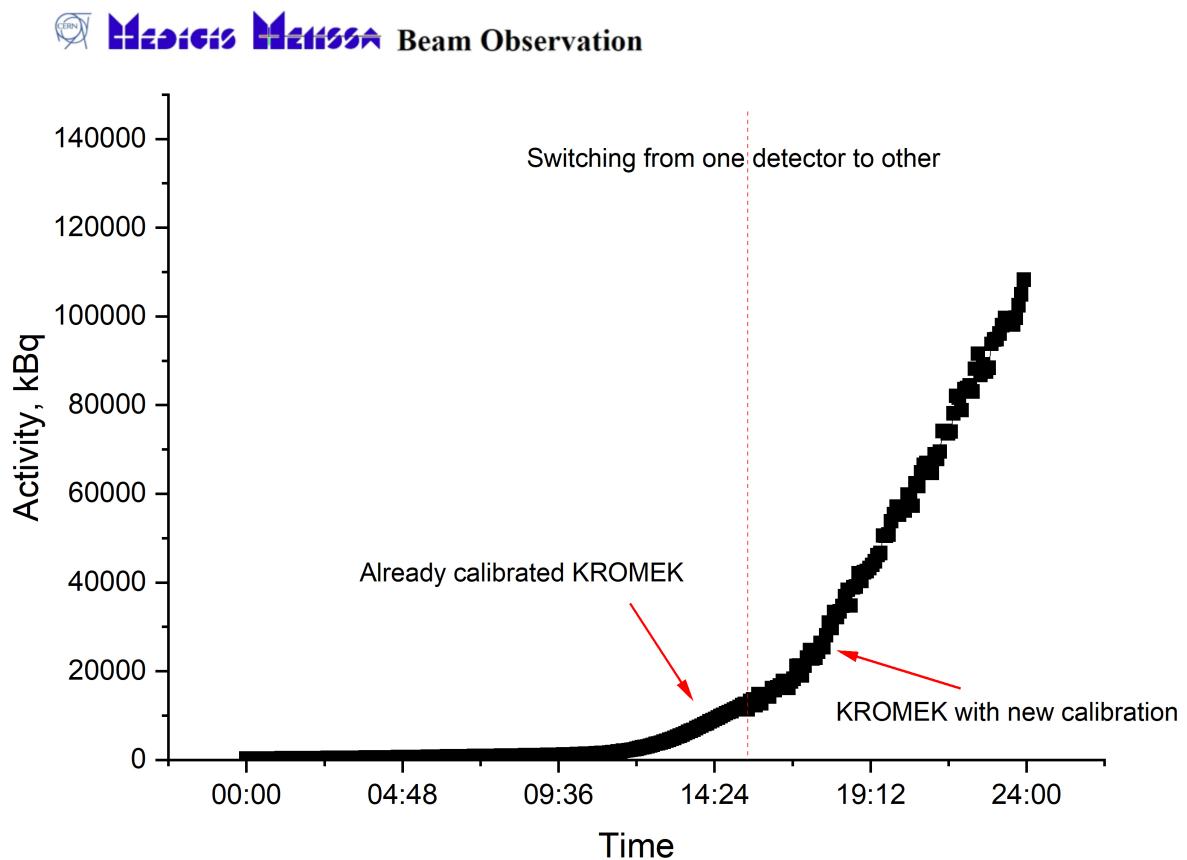


Figure 3.16: On-line monitoring of the ^{212}Pb implanted activity using both KROMEK detectors

CONCLUSIONS

1. The relative Sc radionuclide thermal release pattern from metallic ^{nat}Ti foil and ^{nat}V samples in the MEDICIS and ISOLDE mass separator target unit and Ta environment was systematically studied. Full Sc release within one hour after reaching the set temperature was achieved at 1200°C for non-embossed ^{nat}Ti , and 1450°C for embossed ^{nat}Ti foil samples respectively. In contrast to the expected, the Sc radionuclide relative release of embossed metallic ^{nat}Ti foils was shifted towards higher temperatures to achieve the same released fraction.
2. The first preliminary results for Sc release from ^{nat}V foil samples are presented, showing full (100%) Sc release at 1600 °C within 1 hour of reaching the temperature.
3. The theoretical Activiz and mathematical model estimations, used in this study, were in very good agreement with the obtained experimental data for ^{nat}Ti . The obtained preliminary results from experimental Sc release from ^{nat}V foils can serve as a benchmark for theoretical model improvements for V materials.
4. The starting radionuclide activities in these release experiments, however, should be chosen to maintain them well above the minimal detectable activity levels throughout the whole release experiment, to decrease the uncertainties and therefore increase the experiment output.
5. The efficiency of gamma-ray detection systems is influenced by factors such as energy and positional dependencies, as well as material thickness, with higher energies and greater distances leading to decreased detection efficiency, and thicker material layers exacerbating attenuation and scattering effects, thus emphasizing the importance of carefully considering these parameters for optimal system performance.

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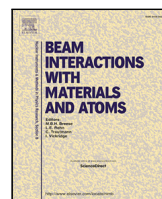
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Scandium thermal release from activated ^{nat}Ti and ^{nat}V target materials in mixed particle fields: Investigation of parameters relevant for isotope mass separation

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ABSTRACT

Scandium (Sc) has gained significant interest in nuclear medicine due to its ^{43}Sc , $^{44\text{g/m}}\text{Sc}$, and ^{47}Sc radioactive isotopes being suitable for cancer diagnostics and therapy, offering a promising avenue for theranostics. Various production methods, including irradiation of enriched or naturally abundant calcium (Ca), titanium (Ti), and vanadium (V) materials with different particle beams, have been investigated to produce ^{43}Sc , $^{44\text{g/m}}\text{Sc}$, and ^{47}Sc . However, challenges persist in achieving high molar activity and radiochemical purity for medical applications. The physical isotope mass separation technique presents an alternative, obviating the need for enriched target materials by inherently isolating Sc isotopes during the separation process. Despite recent advancements in Sc mass separation at different facilities, efficiency and yield remain sub-optimal for medical dose production. This study aims to systematically investigate the thermal release kinetics of Sc radionuclides from activated natural titanium foils in tantalum (Ta) environments of ISOL (Isotope Separation On-Line) target units. By elucidating the combination of target material structure and temperature conditions, enhanced release parameters were identified. Maximum Sc release from a non-embossed ^{nat}Ti foil samples was achieved at 1200 °C, for embossed ^{nat}Ti foil samples at 1450 °C and for ^{nat}V foil samples at 1600 °C, within an hour of reaching the set temperature. These findings offer insights into optimizing the mass separation process to improve the efficiency in Sc radionuclide production for medical applications.

1. Introduction

Scandium (Sc) is an element of interest in nuclear medicine because of three radioactive isotopes with decay properties suitable for cancer diagnostics and therapy — theranostics [1]. The advantage of Sc radionuclides is their application in “matched pair” radiopharmaceutical production, where the chemical drug structure is identical both for diagnostic and therapeutic agents [2]. ^{43}Sc ($T_{1/2} = 3.891(12)$ h [3]) is a positron (β^+) emitter that holds great potential for immuno-PET (Positron Emission Tomography) and macro-molecular imaging studies, making it valuable for extended PET examinations [4]. $^{44\text{g}}\text{Sc}$ ($T_{1/2} = 4.042(25)$ h [3]) is another promising β^+ emitter for PET and has already been translated to successful in-human proof of concept studies conducted in clinical setting [5,6]. ^{47}Sc ($T_{1/2} =$

$3.3492(6)$ d [3]) is a β^- emitter with a 159.4 keV (68.3%) gamma-ray emission that would be suitable for therapeutic applications and single-photon emission computed tomography (SPECT) imaging [7]. ^{47}Sc shows potential for use in radio-immunotherapy of tumors by being attachable to monoclonal antibodies (MAb) and conjugates [8]. Nevertheless, the supply of these radionuclides is currently limited due to costly enriched target materials, their enrichment, availability and efficient production capabilities, accessible only at nuclear reactors or medium to high energy cyclotron centers.

To produce ^{43}Sc , $^{44\text{g/m}}\text{Sc}$, and ^{47}Sc , the irradiation of enriched calcium (Ca) and titanium (Ti) or naturally abundant metallic materials, such as natural calcium, (^{nat}Ca), titanium (^{nat}Ti) and vanadium (^{nat}V) has been investigated using neutrons, proton, deuteron and alpha beams [9]. In the context of enriched material, it is crucial

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to emphasize that the enrichment levels must be meticulously optimized to mitigate impurities that could compromise the radionuclide purity of the final sample. Although cost-efficient, the irradiation of natural target materials is accompanied by challenges arising from the presence of other naturally occurring isotopes and the involvement of various nuclear reaction pathways. For instance, the direct production of $^{44g/m}\text{Sc}$ in ^{nat}Ti occurs through various nuclear reactions, including $^{47}\text{Ti}(p, \alpha)$, $^{48}\text{Ti}(p, n\alpha)$, $^{49}\text{Ti}(p, 2n\alpha)$, and $^{50}\text{Ti}(p, 3n\alpha)$ [10]. At the same time the long-lived ^{46}Sc ($T_{1/2} = 83.79$ d, $E_\gamma = 889$ keV; 1120 keV) is produced via the $^{47}\text{Ti}(p, 2p)$, $^{48}\text{Ti}(p, 2pn)$, $^{49}\text{Ti}(p, 2p2n)$, $^{49}\text{Ti}(p, \alpha)$ and $^{45}\text{Ti}(p, 2p3n)$ nuclear reactions [11]. Notably, the reactions with ^{48}Ti are the primary pathways because of its significant prevalence of 73.8% [12] in natural titanium [13]. Various routes to produce the therapeutic ^{47}Sc are documented, such as employing reactors, cyclotrons, or electron linear accelerators. The main nuclear reactions for ^{47}Sc production are $^{47}\text{Ti}(n, p)$, $^{48}\text{Ti}(p, 2p)$, and $^{48}\text{Ca}(p, 2n)$ and again suggest the necessity to use enriched target materials to obtain sufficient radionuclide yield [14,15]. However, ^{46}Sc and ^{48}Sc co-production cannot be fully avoided. ^{47}Sc can also be produced with ^{nat}V target irradiation with protons (^{50}V , 0.250% and ^{51}V , 99.750%) [16]. Recent study [16] showed that ^{47}Sc can be produced with a non-detectable amount of ^{46}Sc , however, the production yield is severely decreased. The attractiveness of utilizing natural Ti and V target materials is underlined by their cost-effectiveness, widespread availability and achievable yield with a considerable number of medium-energy cyclotrons in Europe and Worldwide. But it also results in the generation of a diverse array of radionuclides, including Ti, Ca, V and long-lived Sc isotopes. Some of these isotopes are unsuitable for nuclear medicine and cannot be removed with chemical post-processing methods [17]. Another method for Sc radionuclide production could be by using inverse kinematics, where heavy ions, such as Mo, Zn, Ti or V could be impinged on light gas targets and the reaction products caught on a catcher foil. It offers a promising alternative method by allowing precise control over reaction parameters, optimizing yields and minimizing unwanted byproducts [18,19]. Although this route allows for more exotic reaction pathways, the final product still could contain long-lived Sc impurities. Furthermore, a more complex cyclotron, ion source and target system with the possible enriched source material is required to maximize medical Sc radionuclide production yield.

An alternative method for the production of high molar activity, radiochemical pure and medically suitable Sc radionuclides involves the development of a mass separation process. With the mass separation technique, the necessity for utilizing an enriched target material is obviated, as the various isotopes of Sc are inherently isolated during the separation process [20]. MEDICIS (MEDical Isotopes Collected from ISOLDE) facility at CERN (European Organization for Nuclear Research) is specifically designed for the production by mass separation of high-purity novel radionuclides for medical applications [21]. The mass separation method is adapted from ISOLDE (Isotope Separator OnLine DEvice) facility, but the isotopes are produced and mass separated in a batch mode [22]. The radionuclides of interest are produced through the irradiation of thick natural targets with 1.4 GeV protons delivered by the CERN Proton Synchrotron Booster (PSB) [23]. This process allows for the efficient production of the targeted radionuclides in clinically relevant activities. CERN-MEDICIS has successfully produced several radiolanthanides, including samarium (Sm), terbium (Tb), thulium (Tm), and actinium (Ac), which have gained significant attention for targeted radionuclide therapy. These elements share a similar therapeutic potential with ^{177}Lu , a lanthanide already in use in clinical applications [24,25]. Recently at MEDICIS, the medical Sc radionuclides have been produced and mass-separated from irradiated cyclotron-compatible ^{nat}Ti and ^{nat}V target materials. Although high molar activity and radiochemical purity were obtained, the mass separation efficiency and yield are still unsatisfactory for medical dose activity production [26]. Due to the refractory Sc properties, high

adsorption enthalpy with tantalum (Ta) ISOL (Isotope Separation On-Line) target unit structures, batch mode experiment limitations, and difficulties in extracting Sc radionuclides from the target units, the conditions for Sc radionuclide release dynamics from metallic ^{nat}Ti and ^{nat}V foils within ISOL target units are not yet fully understood. Multiple studies in radionuclide release from irradiated ISOL target units with various target materials during mass separation have been done at ISOLDE before, however, sufficient post-analysis of the target materials after irradiation was not possible due to the high radiological risks and hazards [27–29]. A study of Sc radionuclide release from 5 μm Ti foil also has been performed, but the impact of thicker foils or multiple layers was not investigated [30].

The objective of this study was to systematically investigate the thermal release kinetics of Sc radionuclides from activated ^{nat}Ti metallic foil rolls in a Ta environment and ISOL target units. Specific focus was placed on understanding the impact of target material structure and temperature conditions on radionuclide release. By studying these factors, the project aimed to study the mechanisms governing Sc release during the mass separation process within the ISOL target unit. By advancing the understanding of these mechanisms, the research outcome paves the way for optimized Sc production via mass separation with high separation efficiency and yield. The study was done in similar conditions as routine radionuclide mass separation done at the CERN-MEDICIS facility. An ISOL-type target unit containing a Ta target container was used and subjected to the same heating method and vacuum conditions, reaching temperatures of 1650 °C. Theoretical estimations were done to estimate radionuclide production in target materials and to identify the possible limiting factors during thermal release. A proof of concept for the methodology to study MEDICIS and ISOLDE-produced radionuclide release kinetics and behavior from various target materials and structures is presented. This work also aims to complement radionuclide release studies in case of fire accidents for radiation protection purposes and provide a way to benchmark theoretical codes. Preliminary results for ^{46}Sc and ^{47}Sc release from activated ^{nat}V foils are also presented.

2. Materials and methods

2.1. General overview

The Sc thermal release data have been experimentally obtained by activating target materials at the CERN High energy AcceleRator Mixed field facility (CHARM) facility [31] followed by thermal release and analysis in class A labs. After irradiation, each sample was analyzed by γ spectrometry, allowing for the quantification of each Sc radionuclide activity specific to each sample before and after the release experiment. Within this experimental framework, each irradiated sample was positioned one by one inside an ISOL target container, always at the same position. The samples were uniformly heated at a constant rate, and then maintained at a pre-defined temperature for one hour. Subsequently, the target container was subjected to a cooling phase, and the sample was then extracted to be measured. Dose rate measurements were conducted for each sample before and after the release, aiming at gathering data regarding potential condensation spots in the target container. γ spectroscopy measurements were performed again to measure the residual activity in the sample. By comparing the radionuclide activity before and after release, a percentage of released fraction of the Sc radionuclides detectable in each sample was calculated and compared with the estimated theoretical data.

2.2. Radionuclide estimation with ActiWiz

The ActiWiz software (version: 3.6.12/2023-2507) is a tool developed at CERN that enables swift assessments of the radiological risks associated with diverse materials employed in high energy particle accelerators [32]. For this purpose, ActiWiz employs a proprietary

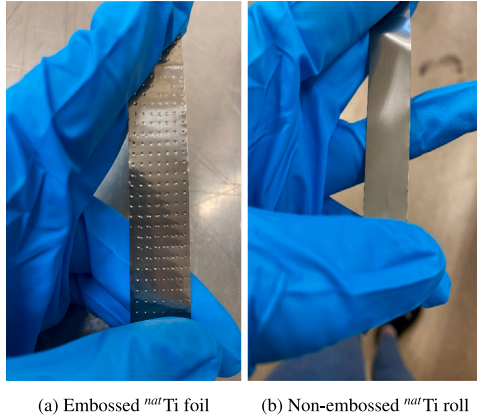


Fig. 1. ^{nat}Ti foils used in roll preparation for thermal release studies and mass separation.

database of isotope production reactions that for neutrons below 20 MeV is based on the evaluated JEFF 3.3 library and for all other reactions utilizes the results of a vast number of FLUKA Monte Carlo simulations [33,34]. It allows for the estimation of nuclide inventories as a function of particle type and energy for user-defined materials using arbitrary particle fluence spectra (neutrons, protons, pions+, pions- and photons) as input. From the results, the users can explore varied compositions and their respective hazards efficiently. ActiWiz has many post-processing options that can be used to analyze the results [35]. The ActiWiz software was used to calculate the total activity and dose rate per sample as well as the targeted activity for each radionuclide of interest according to the CHARM activation scenario.

2.3. Sample preparation

To study Sc thermal release from metallic foils and target material structural impact in MEDICIS mass separation conditions, three different type of samples were prepared : embossed ^{nat}Ti (see Fig. 1(a)), non-embossed ^{nat}Ti (see Fig. 1(b)) and non-embossed ^{nat}V (for preliminary tests and similarly to Fig. 1(b)). The samples were prepared in the form of compact foil (0.25 μm ,) rolls with average diameter of 0.46 cm for non embossed samples, 0.80 cm for embossed samples and height 1.5 cm.

For routine mass separation operation, the foils are embossed to reduce the tightness of the sample roll and increase the space between foil layers which reduces the sintering of layers at high temperatures. Therefore the ^{nat}Ti roll sample types differ from one another by their overall volume. Each roll weighs approximately 1 g for ^{nat}Ti and 3.4 g for ^{nat}V samples. The selection of sample weight was based on estimated theoretical radionuclide activity (Bq/g of the sample) according to the irradiation scenarios at CHARM facility and radiation protection aspects.

2.4. Sample activation at the CHARM facility at CERN

The CHARM facility at CERN is dedicated to the study of radiation effects on electronic components and benchmarking various material shielding [36]. The CHARM facility receives a 24 GeV/c proton beam extracted from the CERN proton-synchrotron impinging on a thick copper target. It creates a mixed particle field including secondary neutrons (contribution to the total yield is more than 90%) that were used to activate our samples. A standard 5 day irradiation followed by 1.5 day cooling time after the end of the beam (EOB) with an average proton beam intensity of 5E10 p/s (protons per second) is typically provided by the CHARM facility. This value was first used to estimate the produced activity from ActiWiz calculations. The simulated particle

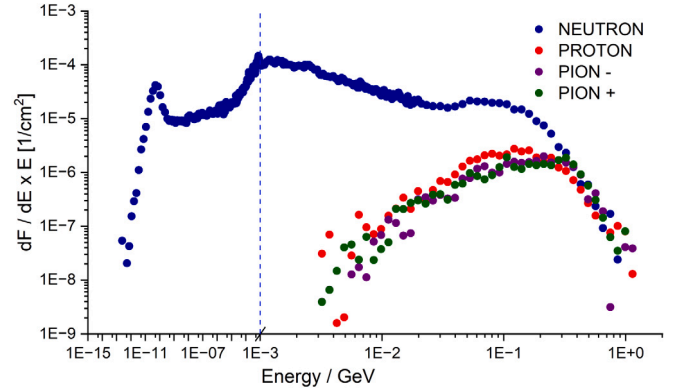


Fig. 2. Fluence spectra (in lethargy representation) at the grid irradiation location of the CHARM facility used to compute the activity values predicted in the Ti samples.

Table 1

Average actual proton beam intensity for each irradiation.

Activation run	Average intensity, p/s	Irradiation time, h	Protons on target
I	6.91 E10	132	3.28 E16
II	6.71 E10	126	3.04 E16
III	6.91 E10	139	3.45 E16
IV	6.64 E10	138	3.29 E16

fluence spectra generated by the 5E10 p/s primary proton beam onto the CHARM target is shown in Fig. 2.

After each activation, the actual average proton beam values and irradiation times were used to estimate more precisely the radionuclide activities (see Table 1). In total four ^{nat}Ti and ^{nat}V target material sample batches were activated at CHARM. In the first activation run only embossed ^{nat}Ti samples were used. In the second activation run non- embossed ^{nat}Ti samples were used. In the third activation run ^{nat}V samples were exposed to the CHARM radiation field, and in the fourth activation run all three types of samples were activated.

2.5. Gamma-ray spectrometry

Gamma-ray spectrometry measurements were performed after the sample activation just before placing each sample inside the target container for release to precisely quantify the radionuclide activities in each sample. The measurements were done with a High Purity Germanium (HPGe) γ -ray detector from MIRION Technologies (Canberra) S.A.S. (energy range from 3 to 10 000 keV with relative efficiency of more than 40%, resolution at 122 keV: < 1.2 keV and at 1332 KeV: < 2.0 keV) [37]. After the Sc release experiments, γ -ray spectrometry measurements were performed again to determine the residual radionuclide activity in the sample and quantify the released Sc radionuclide activity from each sample. The quantitative analysis was performed using the APEX software (V1.4.1) and the ISOCS (In Situ Object Counting System) modelization [38]. For relative measurement purposes, each sample was placed at the same distance from the detector and in the same geometry configuration. Each sample was measured for at least 15 h.

2.6. Thermal release set-up

Isotope mass separation at MEDICIS typically is done at temperatures up to 2300 °C and in vacuum conditions of less than 1E-5 mbar pressure. Often the conditions for release of isotopes are close to the target material melting point [26]. Therefore a specialized ISOL target



Fig. 3. Set-up for Sc thermal release experiments.

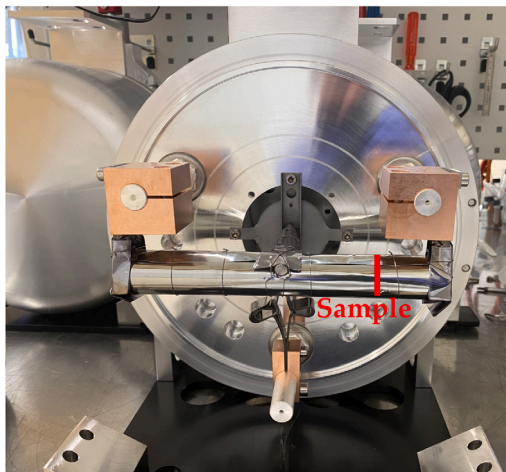


Fig. 4. Opened ISOL target unit back view.

coupling table (pump stand) having the possibility to apply high current (up to 1200 A) for heating and obtain pressure down to $1\text{E}-7$ mbar was used and is shown in Fig. 3. The pump stand has a dedicated gas exhaust system for any potential radioactive gas trapping.

As the second part of the experimental set-up, a standard ISOL target unit was coupled to the pump stand (see Figs. 3 and 4) [39]. The target unit consists of a target container - Ta tubular oven of 2 cm diameter and 20 cm length - and ion source - hollow Re metallic tube. The target container is perpendicularly connected to the ion source via a transfer line. Since no radioactive ions were needed for this study, the ion source was not heated. The target container and ion source are covered with multiple layers of Ta, W, and Mo heat screens. The target container and ion source are mounted on a water-cooled Al base plate and covered with an Al vessel.

The target is heated by resistive current and the heating ramp by current is correlated to temperature. Five current-regulated (± 0.1 A) power supplies were used. Before the experiment, a temperature calibration on the target container was done with a micro-optical pyrometer (see Fig. 5).

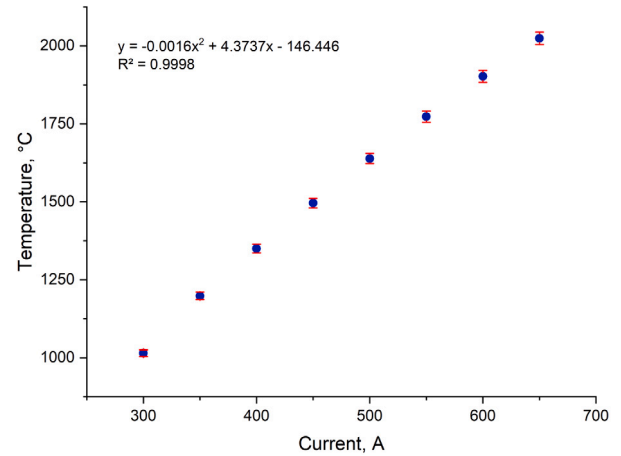
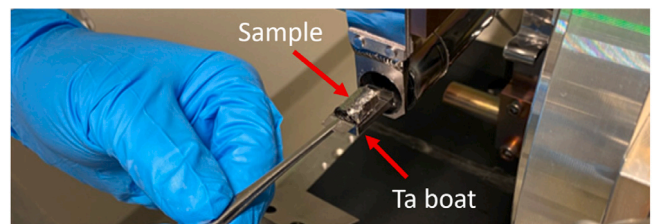


Fig. 5. Target container (oven) temperature calibration curve.

Fig. 6. ^{nat}Ti foil roll sample in a Ta “boat” after thermal release experiment.

2.7. Thermal radionuclide release

To prevent sample fusing with Ta container at high temperatures and allow for a safe and simple exchange of samples from the target container, the samples were placed on a Ta “boat” (see Fig. 6). Once the sample was loaded, the target container was closed with a Ta cap, and the heat screens were mounted. The samples were placed at the same place and distance within the confines of the target container, matching the calibration location (see Fig. 4). The dose rate of the sample and outside the target container with and without the sample was measured before and after the heating phase to determine possible contamination and condensation of the radioisotopes at different places of the target unit structures. Each sample was then subsequently measured by HPGe γ -ray spectrometer (see Section 2.5).

After sample loading, the pressure of the system was stabilized to $\leq 2\text{E}-6$ mbar. Once sufficient pressure conditions were reached, each sample underwent a temperature ramp-up process by applying 0.5 A every 25 s to the target container. Once the desired temperature was achieved (as an example to reach 1500 °C it takes 5 h of heating), each sample was maintained at the chosen temperature for one hour and cooled down using the same ramp speed of 0.5 A per 25 s. These initial pressure conditions and heating speed were chosen to allow for target pressure to stabilize and be kept below $1\text{E}-5$ mbar even during the heating and out-gassing phase. This way also the mass separation conditions were maintained.

2.8. Sc thermal release experimental calculations

The calculation of the relative thermal release of Sc involves the ratio between the activity measured after release and before release, as described in Eq. (1). Decay correction was applied to the initial activity to align with the date and time of the corresponding sample release study.

$$\text{Ratio } R = \frac{A_A}{A_B}, \quad (1)$$

where A_A is the activity measured after sample heating and A_B is the activity measured before performing thermal release experiments with the decay correction. The relative uncertainty related to this ratio is expressed as shown in Eq. (2):

$$\Delta R/R = \sqrt{\left(\frac{\Delta A_A}{A_A}\right)^2 + \left(\frac{\Delta A_B}{A_B}\right)^2} \quad (2)$$

A result reported with 100% release signifies that no activity above the Minimum Detectable Activity (MDA) was measurable. Typically the uncertainty of counting experiments originates from the detection limit (LD) as determined by approaches like the Currie method. However, in the case of gamma spectroscopy the MDA is used as a threshold value which combines the detection limit, calibration efficiency, nuclear data and measurement time [40]. As such it can be considered to be a fundamental characteristic of the measurement itself rather than an uncertainty. It does not directly stem from a single measurement but instead relies on estimations involving uncertainties.

Finally, the release is expressed as Eq. (3), on which the relative uncertainty calculated above is applied:

$$\text{Release} = 1 - \frac{A_A}{A_B} \quad (3)$$

2.9. Thermal release theoretical estimations

The integration of experimental data with modeling allows for a more comprehensive understanding of the release process, which is why complementary calculations have been carried out in this respect.

The release process can be understood as a two-step procedure. For a radionuclide to be released, it must first undergo diffusion within the solid to reach its surface. Subsequently, it must desorb from the surface to escape the solid entirely. To estimate the final release, we have employed the three semi-empirical expressions formulated in [41], based on detailed studies with specifically developed Monte Carlo models. The first of them provides an estimation of the Fraction of Radionuclides reaching the sample's Surface (FRS). This quantifiable parameter is entirely determined by the diffusion stage. The second aims to estimate the so-called Global Desorption Probability (GDP), which quantifies the likelihood of desorption occurring during the remaining heating time for a radionuclide that has successfully reached the surface. The third expression combines the results from the previous two, yielding an estimation of the Out-Diffusion Fraction (ODF), which corresponds to the release fraction integrated over the heating period.

These expressions necessitate user-provided parameters, including heating temperature, heating time, and the surface-to-volume ratio of the sample, which was determined from the foil dimension measurements before preparing the roll. Additionally, users are required to input the relevant diffusion coefficient and desorption activation enthalpy. While experimental data for the former is often accessible, experimental data for the latter is typically unavailable, relying instead on calculated values and, at times, approximations such as sublimation enthalpies [42]. In our study, we have adopted diffusion coefficient parameters from [43] and sourced the desorption activation enthalpy from [44].

3. Results and discussion

Sc thermal release experiments were performed on two different types of ^{nat}Ti foil samples — embossed and non-embossed. Obtained experimental results were compared with the theoretical estimations obtained through the evaluation of the analytical expressions formulated and described by F. Ogallar Ruiz [41]. These calculations give the out-diffused fraction of Sc in ^{nat}Ti for a given sample surface, volume, and temperature. The first Sc release experiments from ^{nat}V samples were performed and a preliminary Sc thermal release curve was obtained.

Table 2
Radionuclides produced in ^{nat}Ti sample.

Radionuclide	Avg. activity per sample (Bq)	MDA interval (Bq)	Half-life ($T_{1/2}$)
^{43}Sc	<MDA	1.41E2–2.02E2	3.89 h
^{44g}Sc	303 ± 56	4.26E1–6.76E1	3.97 h
^{44m}Sc	246 ± 57	4.44E1–6.81E1	2.44 d
^{46}Sc	180 ± 19	2.53E1–4.67E1	83.79 d
^{47}Sc	1730 ± 190	7.57E1–1.02E2	3.35 d
^{48}Sc	496 ± 75	3.19E1–4.67E1	43.67 h

Table 3
Radionuclides produced in ^{nat}V sample.

Radionuclide	Avg. activity per sample (Bq)	MDA interval (Bq)	Half-life ($T_{1/2}$)
^{44g}Sc	53.1 ± 12.4	5.09E1–5.68E1	3.97 h
^{44m}Sc	92.6 ± 21.3	5.24E1–5.44E1	2.44 d
^{46}Sc	59.5 ± 9.5	3.48E1–3.88E1	83.79 d
^{47}Sc	304 ± 54	9.12E1–9.58E1	3.35 d
^{48}Sc	100 ± 14	4.25E1–4.71E1	43.67 h
^{48}V	107 ± 21	4.35E1–4.97E1	15.97 d

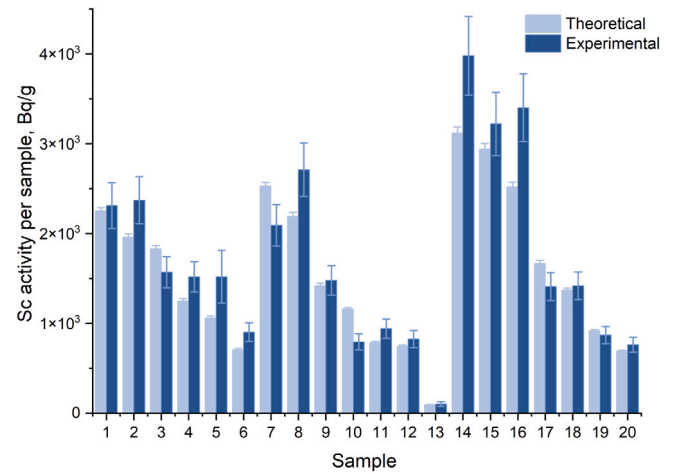


Fig. 7. ^{47}Sc activity per sample given by ActiWiz software versus obtained experimental values with γ -ray spectrometry for ^{nat}Ti samples (the theoretical uncertainties are reported at $k = 1$).

3.1. Radionuclide production and estimation

The produced Sc radionuclide inventory and the average activity per sample were measured with γ -ray spectrometry and are shown in Tables 2 and 3. $^{44g/m}\text{Sc}$, ^{46}Sc , ^{47}Sc and ^{48}Sc radionuclides were produced from which ^{46}Sc and ^{47}Sc were used in the thermal release study because of their favorable decay half-life and relatively higher activity. ^{48}Sc was discarded from the analysis because of the high uncertainties obtained from γ -ray spectrometry measurements due to the short half-life of the radionuclide.

Comparison of theoretical estimations with ActiWiz and experimentally obtained Sc radionuclide activities for neutron activated ^{nat}Ti samples, showcasing the alignment for ^{47}Sc are shown in Fig. 7 and ^{46}Sc in Fig. 8. The average ratio between the obtained values are 1.09 ± 0.13 for the ^{47}Sc and 1.25 ± 0.15 for the ^{46}Sc radionuclides. It is noteworthy that the activity per sample for both ^{47}Sc and ^{46}Sc varies across the samples due to the time gap between irradiation and subsequent γ -ray spectra measurements.

3.2. Sc thermal release from ^{nat}Ti samples

The thermal release of Sc from ^{nat}Ti foil rolls was conducted at various temperatures with a one-hour hold time at the chosen temperature. The selection of temperatures was chosen by the typical mass

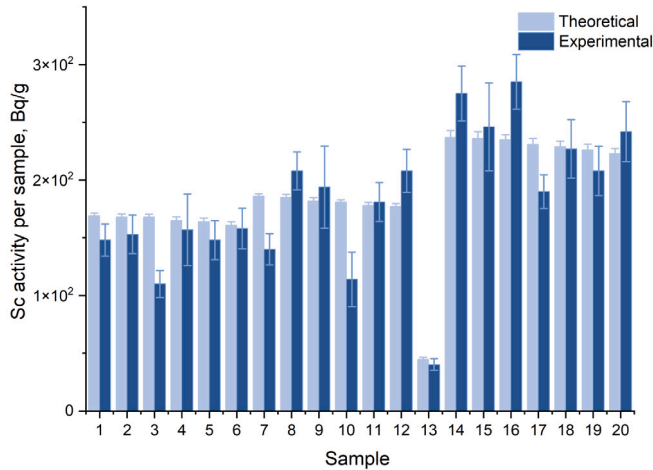


Fig. 8. ^{46}Sc activity per sample given by ActiWiz software versus obtained experimental values with γ -ray spectrometry for ^{nat}Ti samples (the theoretical uncertainties are reported at $k = 1$).

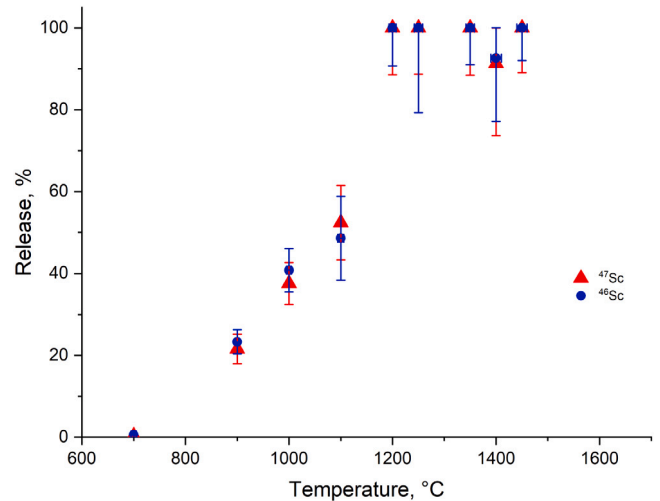


Fig. 10. ^{47}Sc and ^{46}Sc thermal release from non-embossed ^{nat}Ti foil samples.

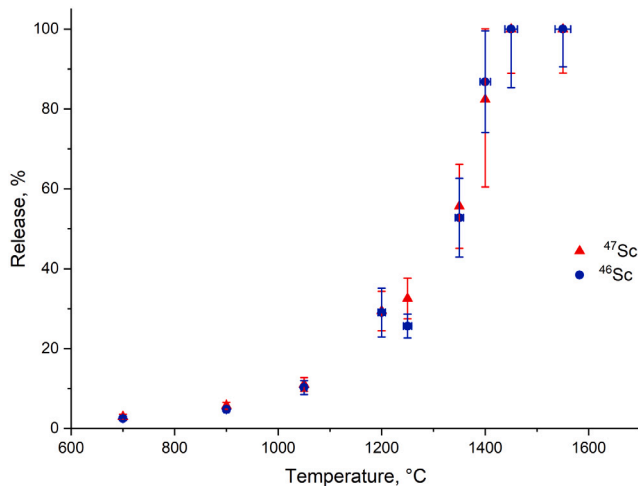


Fig. 9. ^{47}Sc and ^{46}Sc thermal release from embossed ^{nat}Ti foil samples.

separation conditions and physical properties of the material, including considerations such as the melting point. The upper limit was set at 1550 °C to prevent material melting. There was no melting of the material observed for a sample studied at 1500 °C, however, there was a subtle occurrence of sintering, and the sample stuck to the Ta boat. The sintering may be at the source of reduced release over longer periods of operational time during mass separation.

The experimentally obtained relative thermal release results for ^{47}Sc and ^{46}Sc from embossed and non-embossed ^{nat}Ti samples are shown in Figs. 9 and 10. The ^{47}Sc and ^{46}Sc relative release results coincide with each other for both types of roll samples. For both sample types, no release of Sc was observed below 700 °C.

After 1 h at the peak temperature of 1450 °C, 100% scandium release was observed, signifying the complete absence of activity in the sample after the heating cycle. Conversely, for the non-embossed target material, the same release results are shifted to lower temperatures, showcasing the maximum Sc release already at 1200 °C which is in good agreement with previously published studies by [45,46]. It is important to highlight that the uncertainties obtained for samples with longer decay time after the sample activation are notably higher because the activity remaining in the samples closely approached the Minimal Detectable Activity (MDA) values.

The observed release shift to the lower temperatures for the non-embossed target material samples compared to its embossed counterpart raises intriguing questions about the impact of surface morphology on thermal release characteristics. This phenomenon could be attributed to several factors. Firstly, the embossing may lead to a slightly larger specific surface area in the embossed material because of the ductile material stretching and compressing. The derived theoretical formulas emphasize the significance of the surface-to-volume ratio in diffusion and release processes. The larger surface area in the embossed material could facilitate greater diffusion potential, theoretically promoting faster release. However, the observed release results in Fig. 9 contradicts this expectation and indicates a delayed release for the embossed material. This suggests, that the actual release kinetics are influenced by a combination of factors beyond the specific surface area. During the sample embossing, possible cracks are being produced at the embossing points on a microscale, which would result in deformation of the crystalline matrix of the native titanium oxide layer that possibly could have a notable impact on the release. The embossing process could also alter the diffusion pathways within the bulk material, affecting the rate at which Sc atoms migrate to the surface and are subsequently released. Also the role of heat conduction could contribute in this context. Better heat conduction implies a more powerful driving force for diffusion, potentially leading to an earlier release. In this scenario, isotopes would likely arrive sooner at the surface, influencing the overall release dynamics. Therefore, the interplay between surface topography, diffusion pathways, and heat conduction should be carefully considered to understand the observed release behavior comprehensively. While larger surfaces generally result in higher release, it is essential to consider the impact of surface effects and chemical compositions on release dynamics. The increased surface area might also increase the interaction between Sc and the surrounding materials and chemical species, explaining the less efficient thermal release. Therefore the additional use of tools and equipment can lead to contaminant deposition into the foil surface, which can stabilize Sc in a less volatile chemical form, such as ScC and Sc_2O_3 [47]. The observed phenomena was not a part of this study and will be further systematically investigated in a future study.

The relative thermal release values of measured Sc radionuclides from both type ^{nat}Ti samples are compiled in Table 4 for embossed ^{nat}Ti and in Table 5 for non-embossed ^{nat}Ti . All uncertainties are presented as combined values derived from both counting statistics (before and after heating). A relative release sum of ^{46}Sc and ^{47}Sc with their according uncertainties at each temperature are shown to highlight the release pattern of Sc species in general.

Table 4
 ^{46}Sc and ^{47}Sc relative release from embossed ^{nat}Ti foil samples.

Temperature, °C	Release of ^{46}Sc , %	Release of ^{47}Sc , %	Total release of Sc, %
700	2.5 ± 0.5	2.9 ± 0.7	2.7 ± 0.7
900	4.8 ± 0.6	5.7 ± 0.9	5.6 ± 1.0
1050	10.3 ± 1.8	11.0 ± 1.7	10.9 ± 2.9
1200	29.1 ± 6.1	29.4 ± 4.9	29.4 ± 7.4
1250	25.7 ± 3.0	32.6 ± 5.1	31.9 ± 5.8
1350	52.8 ± 9.9	55.6 ± 10.5	54.8 ± 11.0
1400	86.8 ± 12.8	82.3 ± 21.9	83.1 ± 28.0
1450	100.0 ± 14.7	100.0 ± 11.1	100.0 ± 20.4
1550	100.0 ± 9.4	100.0 ± 11.0	100.0 ± 14.5

Table 5
 ^{46}Sc and ^{47}Sc relative release from non-embossed ^{nat}Ti foil samples.

Temperature, °C	Release of ^{46}Sc , %	Release of ^{47}Sc , %	Total release of Sc, %
700	0.57 ± 0.09	0.33 ± 0.05	0.40 ± 0.08
900	23.3 ± 3.0	21.6 ± 3.6	22.0 ± 4.8
1000	40.8 ± 5.3	37.6 ± 5.1	38.5 ± 5.9
1100	48.6 ± 10.2	52.4 ± 9.1	51.6 ± 10.8
1200	100.0 ± 9.3	100.0 ± 11.4	100.0 ± 15.9
1250	100.0 ± 20.7	100.0 ± 11.3	100.0 ± 18.2
1350	100.0 ± 9.0	100.0 ± 11.6	100.0 ± 13.8
1400	92.6 ± 15.5	91.3 ± 17.7	91.4 ± 18.9
1450	100.0 ± 7.9	100.0 ± 11.0	100.0 ± 24.4

A comparative measurement to assess the heating and cooling ramp influence of the released fraction was also performed for a sample at 1400 °C and changing the hold time from 1 h to 0 h. The measurement was done with a non-embossed ^{nat}Ti foil roll resulting in $51.4 \pm 10.6\%$ Sc released. In comparison, the obtained value for the same conditions but with a holding time of 1 h was $91.4 \pm 18.9\%$ (see Table 5). Because diffusion and effusion are thermally activated processes, the impact of the heating ramp on the released fraction would be non-linearly higher at higher temperatures not only because of the heating time but also the faster diffusion and desorption. The impact of the heating/cooling ramp time on the released fraction suggests the importance of creating the ion beam and setting the separator for isotope collection already at lower target material temperatures while gradually increasing them throughout the process. Keeping the samples at constant high temperatures would maximize the release [46]. Furthermore, the rapid release may not be suitable for mass separation, because of limited ion source ion load or ionization efficiency. From the obtained results an optimal release plan, target and ion source unit, and mass separation temperatures can be deduced.

To ensure the integrity of the experiment, dose rate measurements on the target container were conducted both with and without the activated samples within the container. This comprehensive approach aimed to monitor and control potential contamination or condensation effects, to identify any cold spots of the target container. The measurements were taken at six distinct points to facilitate a thorough comparison of results before and after the experiment, with Fig. 11 providing an illustrative example of the measurements. Point #4 is the target transfer line which was not heated during the experiments and it remained to stay as a cold spot. During mass separation the ion source and transfer line would be heated to ≈ 2000 °C and indirectly heat the target container and prevent adsorption in the transfer line region. Point #5 refers to where the sample was placed each time offering a consistent reference point for analysis resulting in a notable difference in dose rate measurements before and after the heating cycle. Points #1 and #6 represent the ends of the container where the temperature is lower than the central region, leading to an increased chance of condensation. It can be seen that a certain amount of released radionuclides migrate towards the ends of the target container. The highest absolute count rate is observed at the end, from which the sample exchange is done, because of the removable target plug and local heat screen assembly, suggesting the highest radionuclide condensation.

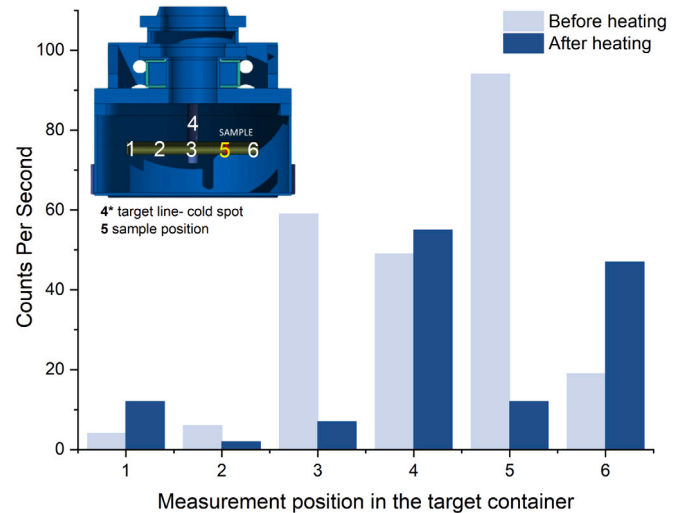


Fig. 11. Target container dose rate measurements in 6 different locations.

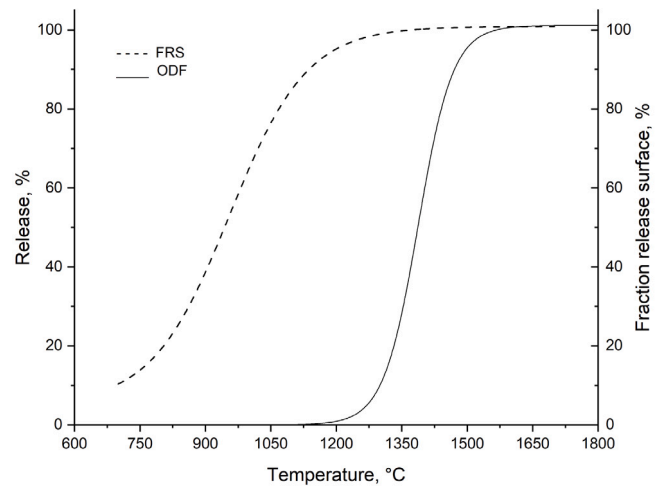


Fig. 12. FRS and ODF theoretical models for Sc thermal release from ^{nat}Ti foil samples.

3.3. Theoretical and experimental result comparison

Comparative analysis using the theoretical models described in Section 2.9 were performed (see Fig. 12) to assess and describe the obtained experimental results, see Fig. 13, by also taking into account the heating ramp speed and release during the heating phase applied during the experiments. While distinguishing between diffusion and surface effects is not the primary goal, accurately modeling the complexities of surface effects, both macroscopic and microscopic, poses a significant difficulty. The theoretical models suggest that radionuclides migrate to the surface much faster than they are released, hinting at surface effects being the limiting factor in the thermal release process. It is noteworthy that the theoretical model did not consider the Ta environment in which the experiments were conducted.

In examining the thermal release curves, our focus centered on the comparison between experimental and theoretical model data. The theoretical estimations indicated a noteworthy trend: radionuclides exhibit a faster migration to the sample's surface than their release rate suggests. This can be understood by the fact that not all isotopes reaching the surface would eventually be released, as there are mechanisms that can retain them and implies that the release process is more constrained by surface effects rather than diffusion itself. It is important to acknowledge that the desorption enthalpy data used in the theoretical model

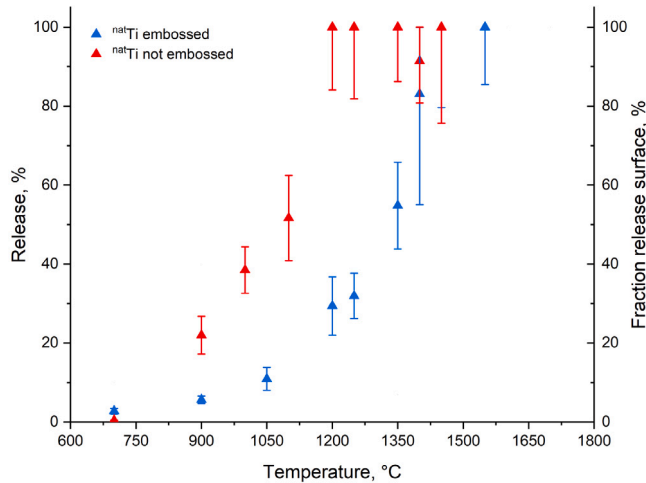


Fig. 13. Total Sc thermal release from embossed and not embossed ^{nat}Ti foil samples.

is sparsely available in the literature, and its reliability comes with a significant level of uncertainty, which unfortunately is not explicitly documented. This uncertainty may have a substantial impact on the estimation of the global desorption probability and, consequently, on the results obtained for the ODF. Reducing the desorption enthalpy of 392.4 kJ/mol [44] by for example an arbitrary fraction of 5% in the model would shift the onset of the ODF notably towards lower temperatures. Therefore, one cannot draw consistent conclusions from the theoretical model predictions yet with respect to the behavior of embossed and non-embossed samples. It is also important to mention that ^{nat}Ti and ^{nat}V foils are covered with a native oxide layer that can influence the release from the surface because of chemisorption. To better understand these processes further targeted experiments need to be carried out.

3.4. Sc thermal release from ^{nat}V samples

^{nat}V has a higher melting point (1910 °C) than ^{nat}Ti (1668 °C). Moreover, the cross-section (see ref [26]) values for the production of Sc-47 and Sc-44 are in the same order of magnitude for both materials at the energy available at CERN-MEDICIS. Therefore ^{nat}V is a promising material for mass separation and the release of Sc-47 was already investigated at MEDICIS from activated non-embossed ^{nat}V foil samples. The same methodology was used, as described for the ^{nat}Ti samples. The release study temperature points were chosen according to previous mass separation experiments with ^{nat}V foil target materials at MEDICIS [26].

The thermal release results for ^{46}Sc are shown in Fig. 14. Only two data points for ^{47}Sc release results were shown and others were discarded due to the high uncertainties from γ spectroscopy measurements obtained due to the low activity produced. Based on previous mass separation experiments and the fact that V has a higher melting point (1910 °C) and density than Ti (1668 °C), the Sc out-diffusion was expected to happen slower or at higher temperatures [48].

As shown in Fig. 14, there is almost no Sc release below 1450 °C ($12.5 \pm 1.8\%$), however, 100% release was observed already at 1600 °C (see Table 6).

Currently, obtaining theoretical estimations and curves for Sc diffusion and release from the ^{nat}V sample is not possible due to the absence of Sc diffusion coefficient data in the ^{nat}V matrix within the literature. However, with a comprehensive understanding of all the processes involved in the Sc thermal release, it would be possible to derive an initial approximation of the diffusion coefficient. The obtained preliminary data serves as a starting point for determining the first diffusion coefficient for Sc within the V matrix.

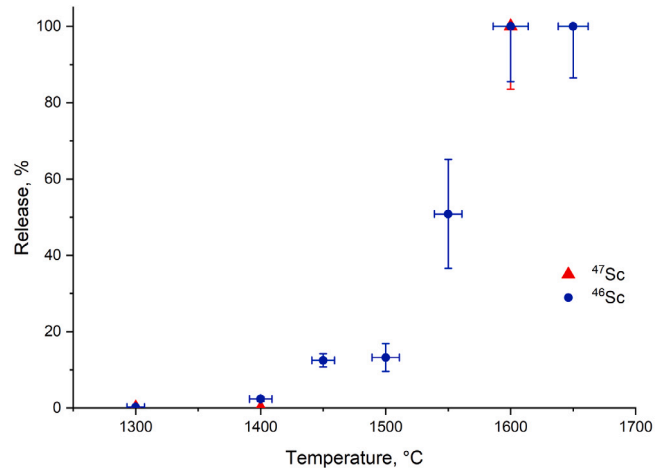


Fig. 14. ^{46}Sc thermal release from non-embossed ^{nat}V foil samples.

Table 6

^{46}Sc and ^{47}Sc relative release from non-embossed ^{nat}V foil samples.

Temperature, °C	Release of ^{46}Sc , %	Release of ^{47}Sc , %	Total release of Sc, %
1300	0.27 ± 0.07	0.10 ± 0.03	0.14 ± 0.04
1400	2.4 ± 0.6	0.00 ± 0.23	0.46 ± 0.14
1450	12.5 ± 1.8		
1500	13.2 ± 3.6		
1550	50.8 ± 14.2		
1600	100.0 ± 14.5	100.0 ± 16.5	100.0 ± 23.3
1650	100.0 ± 13.5		

4. Summary and conclusions

The relative Sc radionuclide thermal release pattern from metallic ^{nat}Ti foil and ^{nat}V samples in the MEDICIS and ISOLDE mass separator target unit and Ta environment was systematically studied. Full Sc release within one hour after reaching the set temperature was achieved at 1200 °C for non-embossed ^{nat}Ti , and 1450 °C for embossed ^{nat}Ti foil samples respectively. In contrast to the expected, the Sc radionuclide relative release of embossed metallic ^{nat}Ti foils was shifted towards higher temperatures to achieve the same released fraction. The underlying mechanism of this observation will be investigated in future studies. The first preliminary results for Sc release from ^{nat}V foil samples are presented, showing full (100%) Sc release at 1600 °C within 1 h of reaching the temperature.

The theoretical Activiz and mathematical model estimations, used in this study, were in very good agreement with the obtained experimental data for ^{nat}Ti . The obtained preliminary results from experimental Sc release from ^{nat}V foils can serve as a benchmark for theoretical model improvements for V materials.

This study has broader implications, and the methodology and findings of this study not only advance our understanding of Sc release in MEDICIS mass separation conditions but also pave the way for other isotope release studies from ISOL target materials, such as Tb radionuclides from metallic Ta foil target materials as well as build up an experimental database and benchmark theoretical diffusion and release model developments. The starting radionuclide activities in these release experiments, however, should be chosen to maintain them well above the minimal detectable activity levels throughout the whole release experiment, to decrease the uncertainties and therefore increase the experiment output.

CRedit authorship contribution statement

E. Mamis: Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Data curation,

Conceptualization. **P. Kalnina**: Writing – review & editing, Writing – original draft, Visualization, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **C. Duchemin**: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **L. Lambert**: Writing – review & editing, Supervision, Investigation, Conceptualization. **N. Conan**: Supervision, Investigation. **M. Deschamps**: Supervision, Investigation. **A. Dorsival**: Supervision, Investigation. **R. Froeschl**: Supervision, Methodology, Investigation, Conceptualization. **F. Ogallar Ruiz**: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **C. Theis**: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **H. Vincke**: Writing – review & editing. **B. Crepieux**: Resources, Methodology, Investigation, Conceptualization. **S. Rothe**: Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. **E. Pajuste**: Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **T. Stora**: Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Maģistra darbs „CERN-MEDICIS isotope mass separation process optimization: the case of scandium for release study and on-line monitoring of the implanted activity” izstrādāts LU Ķīmijas fakultātē.

Ar savu parakstu apliecinu, ka pētījums veikts patstāvīgi, izmantoti tikai tajā norādītie informācijas avoti un LUISā iesniegtā darba elektroniskā kopija atbilst izdrukai un/vai e-studijās iesniegtai darba elektroniskai versijai.

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