EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

Addendum to the ISOLDE and Neutron Time-of-Flight Committee

Collection of ^{129m,131m,133m}Xe for the gamma-MRI project: IS691

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Abstract: We request further collections of long-lived ^{129m}Xe, ^{131m}Xe, and ^{133m}Xe isomers (mXe in short) to be used within the EU FET-Open project devoted to a new diagnostic modality (gamma-MRI) using spin-polarized (hyperpolarized) mXe. One of the early milestones of the project is to optimise and evaluate different ways of producing and extracting mXe, including collections at ISOLDE. At the end of 2021 and in 2022 we could test the production of all 3 isotopes of interest, but the yields and level of contaminants were not reproducible and not optimal for the project. Based on the Xe production model that we developed, in 2023 we aim at producing optimised samples. Within this addendum, we request the production of ^{129m,131m,131m}Xe, directly in the GPS target, with a collection at the GLM beamline. mXe will be then collected in thin foils and extracted from them at high temperature in a an UHV chamber coupled to a rest-gas analyser, before being collected in a metallic transport container.

Requested shifts: 18 shifts (split into 2 runs over 1 year)

1 Motivation

Magnetic Resonance Imaging (MRI) is a very powerful technique used commonly in medical diagnosis. Its basis is the Nuclear Magnetic Resonance of atomic nuclei present in the human body combined with mm spatial resolution provided by magnetic field gradients. Most of the time the source of the signal are protons from water present in human tissues, but isotopes of other chemical elements have been used in MRI, as well.
The radionuclide-based SPECT (Single-photon emission computed tomography) and PET (Positron emission tomography) imaging techniques have relatively poor resolution but, they are sensitive to the order of picomolar tracer concentrations. Meanwhile, MRI gives high-resolution anatomical information but suffers from much lower sensitivity to concentration of contrast agent. The combination of both imaging techniques can offer synergetic advantages over either modality alone.
A hybrid MRI/SPECT emerging technique is holding a promise to combine the top resolution of MRI with the high sensitivity of SPECT by recording the asymmetry of the gamma decay from hyperpolarized nuclear states with spin $\geq 1/2$. Long-lived Xenon isomers ^{129m}Xe, ^{131m}Xe and ^{133m}Xe are very good candidates candidates, because stable ^{129}Xe and unstable ^{133}Xe ($T_{1/2}$=5.4 d, I=3/2) have been already extensively used in medical diagnosis and their gamma energies and half-lives are suitable for medical diagnosis, and the spin and decay scheme is favourable for the technique (for more details, see the original proposal P-598 [1]. The final measurements should require only 10 MBq of mXe, whereas for developments (e.g. to optimise polarisation) up to 100 MBq are required. A short introduction to the project can be found in the Master Thesis defended within our team at the end of 2022 [2].

2 ^{129m,131m,133m}Xe yields achieved within P-589

In our original proposal P-589 (IS691) we requested 2 times 3 shifts to optimise the activity and purity of ^{129m,131m,133m}Xe (mXe) samples collected at GLM. The proposal and its shift estimate was based on the asumption that mXe is reproducible and thus the main aim was to implant mXe in several hosts and to work on optimising its extraction from them. The 2021-2022 results presented below come from offline gamma spectroscopy with an efficiency-calibrated Germanium detector (used to estimate yields of ^{129m,131m,133m},133Xe), from current integrator on the GLM or GHM collection ladders (used to estimate total number of ions/s at a given mass, without knowing what they are), in some cases complemented by mass scans in the region of A = 130 (to see relative intensities at different masses).
The September 2021 tests were encouraging. We used a UCx VD7 cold-plasma-line target right after it was used for over 1 week at HIE-ISOLDE. In a several-minute long collections we saw about 1 kBq/s of activity for all 3 isomers ^{129m,131m,133m}Xe and for ^{133}Xe ground state (corresponding to about 10^9 ions/s). This should allow collecting dozens of MBq during 12-24h collections for every isomer. However, ^{129m,131m}Xe consituted only 0.5 % of the total ion current reaching the collection point. For A=133 the beam was 30% of ^{133m}Xe and 60% ^{133}Xe. We interpreted these results as due to stable Xe isotopes (present

at mass 129 and 131, but not 133) in the plasma gas mixture. Therefore, for the next collections we requested gas mixtures without Xe.
In November 2021 we had the possibility for an offline collection. The September target was placed at the MEDICIS-target location and irradiated parasitically. Once the protons stopped for ISOLDE, the target was coupled to the GPS front-end, a gas mixture was used that did not contain Xe, and the target was heated to release the pre-produced mXe. Unfortunately, the target was outgasing a lot, so the heating had to be done very slowly and by the time the beam could be set up and collections could be made, the yield of all Xe isomers was by 1-2 orders of magnitude lower than in September. ^{129m,131m}Xe were released at a rate of 10^7 ions/s and ^{133m}Xe at a rate of 10^6 ions/s, with all of them being about 0.5 % of the total beam. In comparison, ^{133}Xe ground state contributed to almost 100% of the beam at A=133. With such yields, we were not able to achieve MBq activity within a reasonable time. Therefore, we only tested which temperature allowed to extract most mXe from the foils and what total amount of different gases was released from them. The extraction setup made of KF and Swagelok pieces was able to reach 10^{-5} mbar vacuum. However, we saw up to 1 mbar of pressure when the collection foils were heated to 400 degrees, which meant that either the setup developed a leak or the foils contained a lot of contaminants in addition to Xe (they were annealed before implantation, but were exposed to air between implantation and extraction).
Based on the above experience, in 2022 we requested mXe collections with protons on target and without Xe in the cold plasma mixture. We were thus the 1st users of the UCx VD7 cold-plasma-line target that we had already used in 2021. This time the target was used online at GPS and Ar was used in the gas line. The isomer production was higher than offline in November 2021, but not as high as during test collections in September 2021. Altogether, the intensity of mXe and beam purity was changing over time between different short test collections and the main hour-long collections. The activity and beam purity for all collections are presented in Fig. 1 and in more detail in the master thesis of Ilaria Michelon [2]. To understand these changes as a function of time, Ilaria developed a production model based on already calculated Fluka yields of Xe and neighbouring precursors [2]. Most of the observations could be explained with the following experimentally-proven assumptions: (i) all produced and ionised Xe is released within several seconds from the hot target, (ii) Xe precursors (e.g. iodine or cessium) are retained in the target unit, (iii) mXe isomeric ratio is about 70% (i.e. 70% isomer vs 30% gs), (iv) ionisation efficiency is about 10%. Already during this beamtime we were able to produce 28 MBq of ^{129m}Xe, 4 MBq of ^{131m}Xe, and 92 MBq of ^{133m}Xe. ^{129m,133m}Xe samples were then extracted from the foils and used for polarisation. Unfortunately, mXe from the foils and enclosed in the transport vials must have become contaminated with oxygen and/or water vapour, because Rb used for polarisation oxidised. We thus requested another production attempt to use predictions of the production model and to better control the amount of unwanted gases introduced during and/or after collection.
The last mXe collections in 2022 took place at the end of November with a different UCx cold-plasma target unit (MK, with carbon instead of molymbdenum transfer line). Following the production model, we aimed to guarantee optimal conditions for collections of pure high-activity samples: (i) for ^{129m}Xe, sample intensity depended only on proton intensity and not on the time from the beginning of proton bombardement, (ii) ^{131m}Xe

intensity and purify should increase after about 3 days, (iii) ^{133m}Xe was most free from ^{133}Xe ground state at the beginning of beamtime. In spite of the above optimisations, the mXe yield for all 3 isomers fluctuated between 10^7 and 10^8 ions/s and their % in the total beam was changing from several to 20-30% for different test collections over the course of the experiment. During the main collections, up to 1.4×10^8 ^{129m}Xe ions/s were collected (30% of the total beam), resulting in 6.6 MBq of activity before the target broke 1.5 day before the planned end of beamtime. ^{131m}Xe was collected at only 4×10^7 ions/s and thus its longer collection was not attempted. During this beamtime, unlike in previous runs, iodine contamination was clearly above the detection limit (between 10^7 and 10^8 ions/s for 131I and 133I). On a positive note, we upgraded our mXe extraction and collection setup (see Fig. 2), which now consists of only UHV-compatible parts (CF standard), can be baked out for one to several days (allowing to reach 10^{-9} mbar pressure), and includes a Rest Gas Analyser that provides online information on the composition of rest gas and gas released from the implantation foils.
A graphical summary of yields achieved in 2021 and 2022 in short minute-long test collections and a dozen-hour long main collections is presented pin Fig. 1. Since mXe yields and beam purity turned out surprisingly unreproducible, therefore we concentrated on understanding and eliminating the sources of this unreproducibility.

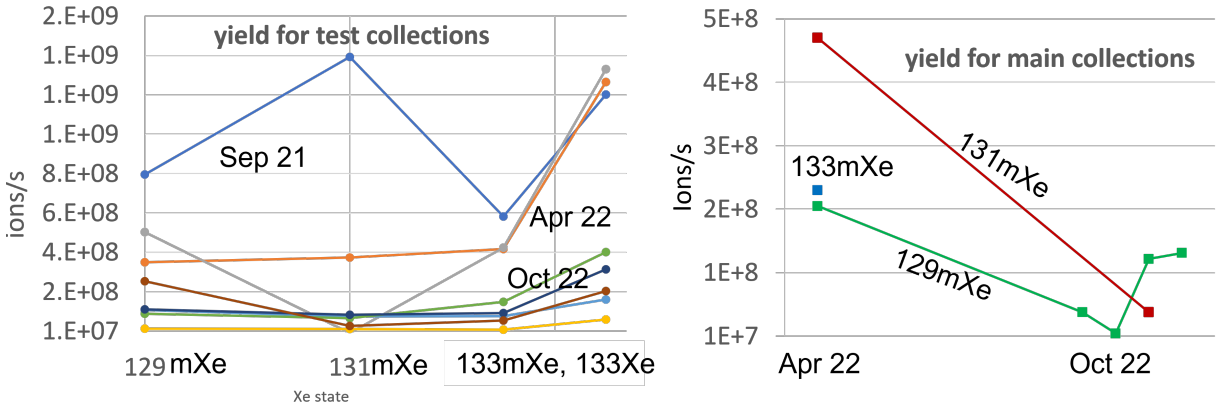

Figure 1: Xenon yields measured during 2021 and 2022 test- and main collections, based on high-resolution gamma spectroscopy performed after the collections.

Seeing the fluctuations in mXe yields, we have concentrated on addressing this problem. Therefore, concerning the chamber used for collections, it was enough to use the main GLM chamber, without connecting a dedicated chamber behind it, as originally planned to ensure high beam purity. The short test collections aimed at characterising the yield were performed in aluminum foils. The main collections aimed at collecting MBqs of mXe for further polarisation were done in pre-annealed gold foils, because it does not oxidise or catch many impurities.
Concerning the mXe extraction and collection setup, in the 2nd half of 2022 we have greatly improved it compared to the earlier version (both are shown in Fig. 2). It can reach even 10^{-9} mbar pressure and we can use it to characterise the contaminants. The

knowledge of the type and level of contaminants helps us to clean the most disturbing contaminants (oxygen and water vapour) right before the polarisation. This is a second reason why we did not develop a dedicated collection chamber. Both setups allowed collecting 70 to 80% of the produced mXe.

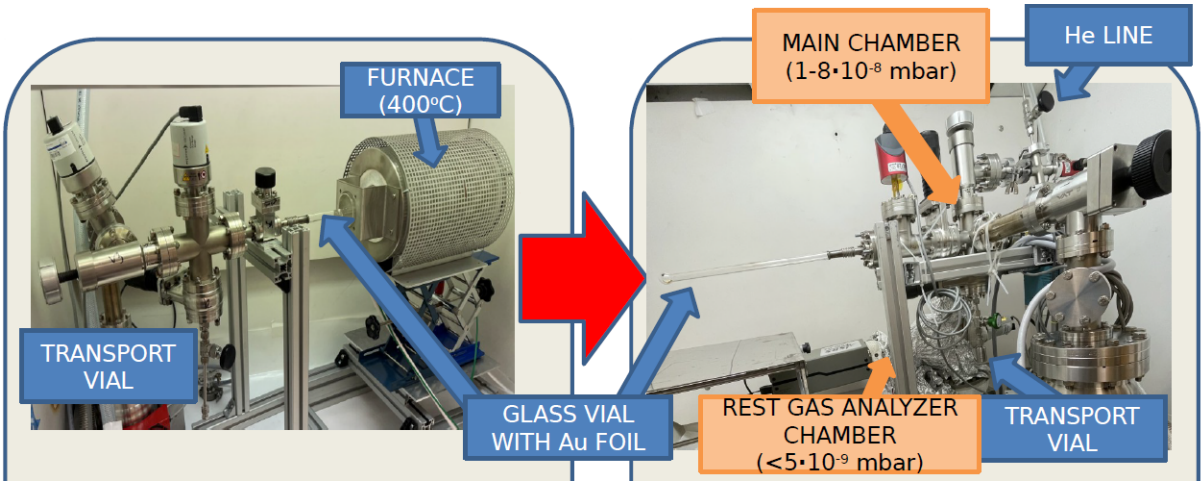

Figure 2: Experimental chambers used to extract and enclose mXe implanted in Au foils. Left: before summer 2022. Right: UHV chamber with Rest Gas Analyser used after summer 2022. From M. Chojnacki.

3 Collections proposed for 2023

Using the upgraded extraction and collection setup, we minimise the amount of oxygen and water vapour and, if needed, we can further clean the collected gas. Therefore, in 2023 we would like to concentrate on assuring a relatively pure and intense production of the longer-lived 129m, ^{131m}Xe with improved reproducibility, to reach up to 50 MBq for each isomer, resulting in 40 MBq of mXe enclosed in the transport vial that should be sufficient for polarisation. If we can reach a yield of 5×10^8 ions/s, equivalent to 1.6 MBq/h for ^{129m}Xe and 1.2 MBq/h for ^{131m}Xe, which were already reached for some test collections and for one ^{131m}Xe main collection in April 2022, then we need about 30h plus 40h (9 shifts) for 1 collection of each isotope.
Seeing that the VD7 ion source gave better yields, we request 2 times 9 shifts to collect sequentially 1 sample of ^{129m}Xe and ^{131m}Xe. We request UCx target with VD7 ion source and no Xe in the gas mixture. We will use GLM implantation chamber to collect mXe in thin gold foils and the upgraded extraction and collection chamber in the chemical laboratory of building 508 to enclose mXe in transport vials.

4 Summary of requested shifts:

2 times 9 shifts in 2023 (production directly at GPS).

5 References:

[1] K. Kulesz, M. Kowalska et al., Proposal to the INTC, CERN-INTC-2021-019/INTC-P-598 (2021)
[2] I. Michelon, Production of metastable Xenon isotopes for a new medical imaging modality, Gamma-MRI, Master Thesis, U Padova (2022), available upon request

Appendix

DESCRIPTION OF THE PROPOSED EXPERIMENT

The experimental setup comprises:

Part of the	Availability	Design and manufacturing
SSP-GLM chamber	☒ Existing	☒ To be used without any modification
sample implantation chamber	☐ Existing	☐ To be used without any modification ☐ To be modified
	☒	☐ Standard equipment supplied by a manufacturer ☐ CERN/collaboration responsible for the design and/or manufacturing
mXe collection chamber	☐ Existing	☐ To be used without any modification ☐ To be modified
	☒	☐ Standard equipment supplied by a manufacturer ☐ CERN/collaboration responsible for the design and/or manufacturing
[insert lines if needed]		

HAZARDS GENERATED BY THE EXPERIMENT hazards generated by the SSP-GLM installation.

Additional hazards:

Hazards	implantation chamber	mXe collection chamber	[Part 3 of experiment/ equipment]
Thermodynamic and fluidic			
Pressure	[pressure][Bar], [volume][l]		
Vacuum	1e-7 mbar		
Temperature		1000 C	
Heat transfer			
Thermal properties of materials			
Cryogenic fluid	LN2 bath, 1 l	LN2 bath 1 l	
Electrical and electromagnetic			
Electricity		20 V, 50 A	
Static electricity			
Magnetic field			
Batteries	☐		
Capacitors	☐		
Ionizing radiation			
Target material [material]			

Beam particle type	^{129m,131m,133m}Xe		
Beam intensity	1e8 particles/s		
Beam energy	60 keV		
Cooling liquids	[liquid]		
Gases	[gas]		
Calibration sources:	□		
• Open source			
• Sealed source	□ [ISO standard]		
• Isotope	^{129m,131m,133m}Xe		
• Activity	¡ 300 MBq	¡ 300 MBq	
Use of activated material:			
• Description	□		
• Dose rate on contact and in 10 cm distance	[dose][mSV]		
• Isotope			
• Activity			
Non-ionizing radiation			
Laser			
UV light			
Microwaves (300MHz-30 GHz)			
Radiofrequency (1-300 MHz)			
Chemical			
Toxic	[chemical agent], [quantity]		
Harmful	[chem. agent], [quant.]		
CMR (carcinogens, mutagens and substances toxic to reproduction)	[chem. agent], [quant.]		
Corrosive	[chem. agent], [quant.]		
Irritant	[chem. agent], [quant.]		
Flammable	[chem. agent], [quant.]		
Oxidizing	[chem. agent], [quant.]		
Explosiveness	[chem. agent], [quant.]		
Asphyxiant	[chem. agent], [quant.]		
Dangerous for the environment	[chem. agent], [quant.]		
Mechanical			
Physical impact or mechanical energy (moving parts)	[location]		

Mechanical properties (Sharp, rough, slippery)	[location]		
Vibration	[location]		
Vehicles and Means of Transport	[location]		
Noise			
Frequency	[frequency],[Hz]		
Intensity			
Physical			
Confined spaces	[location]		
High workplaces	[location]		
Access to high workplaces	[location]		
Obstructions in passageways	[location]		
Manual handling	[location]		
Poor ergonomics	[location]		

Hazard identification:

Average electrical power requirements (excluding fixed ISOLDE-installation mentioned above): [make a rough estimate of the total power consumption of the additional equipment used in the experiment]