EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

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

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

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Abstract: We request the collection of long-lived ^{129m}Xe, ^{131m}Xe, and ^{133m}Xe isomers (mXe in short) to be used within a recently funded 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. Within the present proposal, we request the production of ^{129m,131m,131m}Xe, directly in the GPS target, or in a parasitic mode in the MEDICIS target behind the HRS target or in the new ISOLDE Irradiation Station (ISIS) behind the GPS the targets. mXe will be then collected in a holder placed behind the GLM collection chamber, which will be moved to the GLM/GHM fume hood for the preparation of a pure sample of mXe. This pure mXe sample will be then transported to the classified type B laboratory at HEPIA in Geneva, authorised to handle radioactive open and shielded sources, for further manipulation and hyperpolarisation optimisation.

Requested shifts: 6 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 (see fig. 1) is favourable for the technique. Zheng et al. [1] reported in 2016 on the proof-of concept results for such a technique. In 2017, within a small, but an interdisciplinary group of specialists from different fields of research (CERN, UCM, HES-SO, UNIGE), we have initiated a project to explore whether such an approach can be turned into a real technology. The initial resources, including a CERN Medical Applications Grant, have allowed us to enlarge the group of collaborators (RS2D and KULeuven) and bid successfully for a 3-year project within the EU Future and Emerging Technology program (starting in April 2021). Optimisation of mXe production and extraction, addressed in the present proposal, is one of the first milestones of this EU gamma-MRI project (for which the CERN team is responsible).

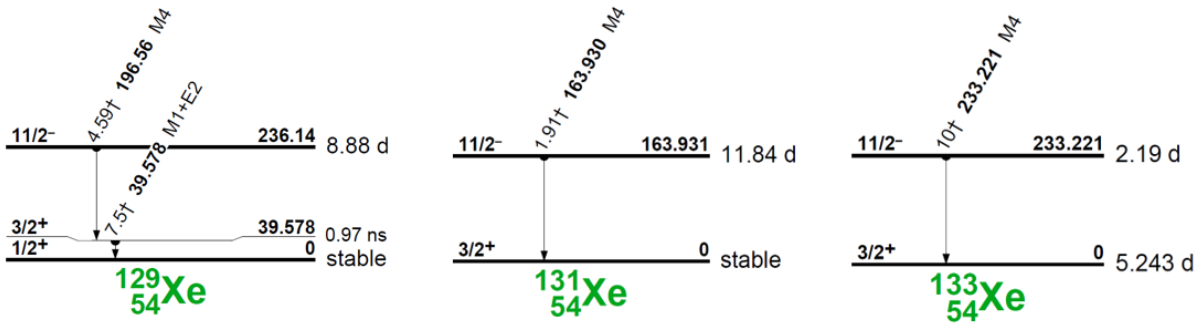

Figure 1: Radioactive decay schemes of the selected isomers: ^{129m}Xe, ^{131m}Xe, ^{133m}Xe.

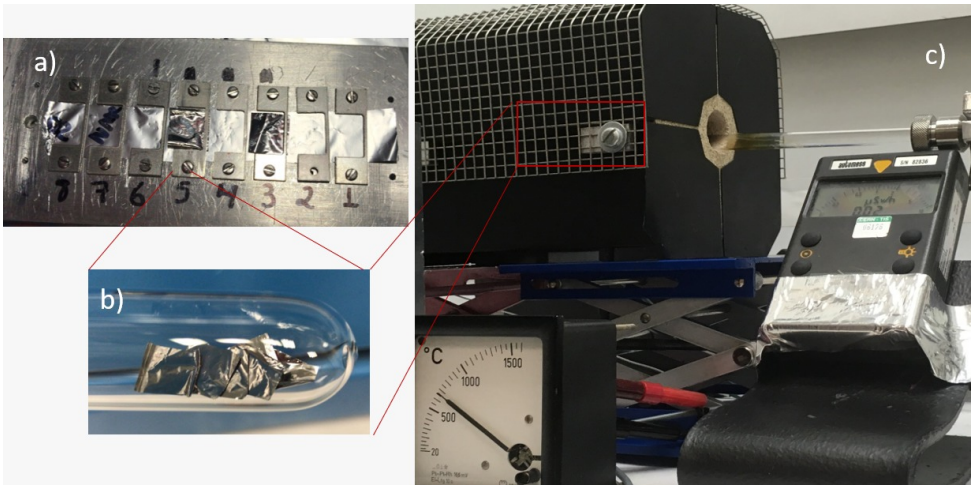

Figure 2: 133mXe production and extraction at ISOLDE in 2018: a) the plate with Ta, Ti, Nb, Al, and C foils irradiated with 133mXe in the GLM chamber; b) one type of the irradiated foils before mXe extraction inside an oven; c) oven-based extraction setup for mXe (also shown: measured temperature and activity).

2 Previous collection at ISOLDE

In July and August 2018, following our letter of Intent I-205 [2], two campaigns took place to produce and collect ^{131,133m}Xe at ISOLDE, using the GPS frontend and GLM beamline. The first campaign with a thorium carbide (ThC) target and cold plasma ion source aimed to collect ^{131m}Xe and ^{133m}Xe onto two tantalum foils. Online and offline gamma spectroscopy revealed that while ^{133m}Xe release from ThC target was good, ^{131m}Xe was not present in the beam and only short lived contaminants were collected (which led to a very high, hundreds MBq, activity at the collection point, which decayed within a day) [3]. The second campaign involved a uranium carbide (UCx) target and cold plasma ion source. Unfortunately, ^{131m}Xe was also not visible among the short-lived contamination. On the other hand, ^{133m}Xe was again successfully produced and implanted into several foils (see fig. 2, top) . Different implantation materials were tested, including tantalum, titanium, niobium, carbon and aluminum to optimize the efficiency of mXe extraction, following previous Xe extraction studies [4]. Gamma-spectroscopy on the foils showed that the the total activity at mass 133 was between 80 – 280 MBq collected on each foil during 1 – 2 h with up to 1.37 μA proton current, which is sufficient for tests of mXe hyperpolarization. Gamma spectroscopy showed that most of this activity corresponds to ^{133m}Xe isomeric and ^{133}Xe ground states, whose gamma lines were over an order of magnitude stronger than that of the contaminants. With the isobaric ratio of 70%, determined also via our offline gamma spectroscopy measurements, this would correspond to an upper limit for 133mXe yield in the range of 1e9 ions/s. The beam contaminants included several A=133 isobars, and possibly A=131 isobars too, but with an activity in the kBq range or lower. After heating the foils in an oven, gamma-spectroscopy of the extracted beam gave the mXe extraction rate from the foils of about 20%. Unfortunately, a high pressure of other gases was registered during the mXe extraction process, when the foils were heated to high temperatures. This situation was most probably due to the fact that the foils, after

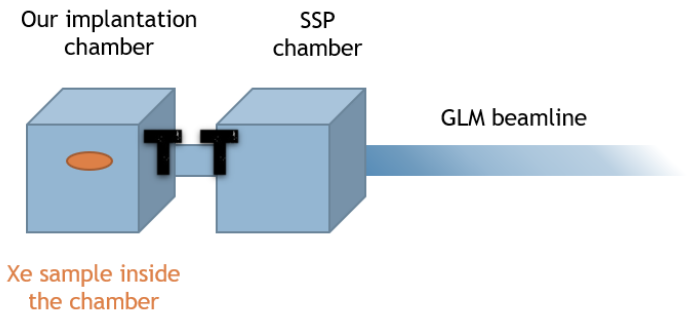

Figure 3: Schematic overview of the implantation setup.

the irradiation in the GLM chamber, were exposed to air for the duration of the transfer to the extraction chamber in bldg. 508. Foil-handling under vacuum, which we plan for this proposal, should remedy this problem. The 2018 campaigns allowed us to gain the first experience with mXe production and extraction at ISOLDE. They also opened the question why 131mXe was not visible among the mass 131 beam implanted into the foils. As no protons have been available since 2018, the extraction of mXe produced at ISOLDE could not have been optimised. Our 2019 experimental run instead used mXe produced at the Institute Laue-Langevin reactor and let us characterise this way of producing mXe. It also allowed us to observe a small but consistent hyperpolarisation signal [3].

3 Proposed experimental setup and procedures

Collection of mXe at GLM
We would like to collect ^{129,131,133m}Xe in a small tailor-made chamber connected behind the main GLM collection chamber (see Fig. 3). We would like to further investigate the possible methods of handling mXe implantation and extraction processes — in order to establish the most efficient and safe way of producing pure mXe in the future. We, therefore, propose to implant mXe in ice or in thin metal foils (with and w/o the use of potassium salt coating). In the first case we will use the existing bio chamber previously involved in isotope collections in ice for biological PAC experiments. The activity collected at the mXe decay line will be monitored with one of the ISOLDE gamma detectors.
This implantation chamber will be easily decoupled from the vacuum pumps, from the LN2 connection when working with water, and from the GLM chamber, while being vacuum tight. This decoupled, but air-evacuated, chamber will be moved to the GLM/GHM fume hood and will be connected to another chamber (Fig. 4, in which mXe should be collected via the standard approach of freezing it on the walls of a glass container immersed in a LN2 bath (an approach we also used in 2018 and 2019 experiments). Once the chambers are coupled together (with the valve between still closed), the collection chamber will be evacuated and then filled with He at 1 bar pressure. When the valve between the chambers is opened both chambers will be in inert He atmosphere and in the collection chamber the collection point will be immersed in the LN2, so that mXe can be frozen but not He.
The implanted metal or C sample will be heated to 800 – 1000 degrees centigrade (as in 2018). Water will be heated to about 50 centigrade, so that mXe solubility becomes much lower than in the cold water and most of it can escape from the liquid [5]. The mXe

released from the metal or water sample will be collected in the glass vial that is part of the collection chamber, which will be immersed in a LN2 bath.
Finally, the valve above the glass vial will be closed and the LN2 bath will be removed. Such an enclosed vial with mXe under under He atmosphere can be safely transported to the class B laboratories of the HEPIA school in Geneva, where the Xe hyperpolarisation setup is located.

mXe hyperpolarization at HEPIA

The primary goal of the experiments to be performed at HEPIA will be to optimise the hyperpolarization of mXe using the spin-exchange optical pumping (SEOP) and to monitor it by the degree of gamma-decay asymmetry in orthogonal planes[6]. The polarization setup that we have already used in 2019 [7], shown in Fig.5), resembles a conventional SEOP setup for stable ^{129}Xe: the infra-red laser system for optical pumping of a Rb vapour, the static magnetic field necessary for the choice of the orientation axis, and the heating system providing thermal optimum for SEOP process. In addition, the polarisation vial is surrounded by gamma detectors. More details about the experiment's principles can be found in [6, 7, 3]. The mXe will be transferred to the polarisation cell which contains Rb, the cell will be heated to vaporise rubidium. The polarising laser will polarise atomic spins of Rb, via the optical pumping process, and this polarisation will be transferred to Xe nuclei via a spin-exchange process. The degree of nuclear orientation (or *spin alignment*, precisely speaking) will be monitored by the degree of asymmetry of gamma radiation spatial distribution registered between gamma detectors located parallel and perpendicular to the magnetic field. The aim of the experiments will be to optimise the degree of this asymmetry.

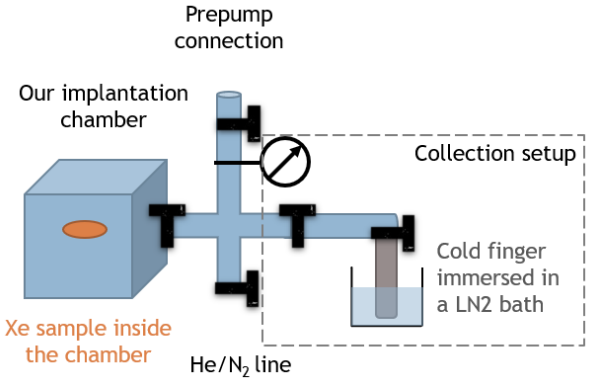

Figure 4: Schematic overview of the collection setup.

4 ISOLDE production details and shift estimate

^{129m,131m,133m}Xe can be produced at ISOLDE from UCx and molten PbBi targets, see Table below. The upper limit for the yield of ^{133m}Xe in a UC target was determined during our 2018 campaign (the isomeric ratio was 70%). If we assume a similar isobaric ratio for the other two Xe isotopes (due to the same spin and similar excitation energy of the isomer), we obtain the numbers quoted below. If the production yield is similar to those for ^{133m}Xe in 2018, then we should collect about 200 MBq activity of ^{129,131,133m}Xe during about 1.5-2 h each when working with single implantation sample in the chamber. Tests of different implantation samples will require to multiply this time by 6, leading to about 1 shift needed for each isotope and 3 shifts in total. In 2021, 1 run will be devoted to the collection into ice and another one to multiple implantations in metal foils, leading

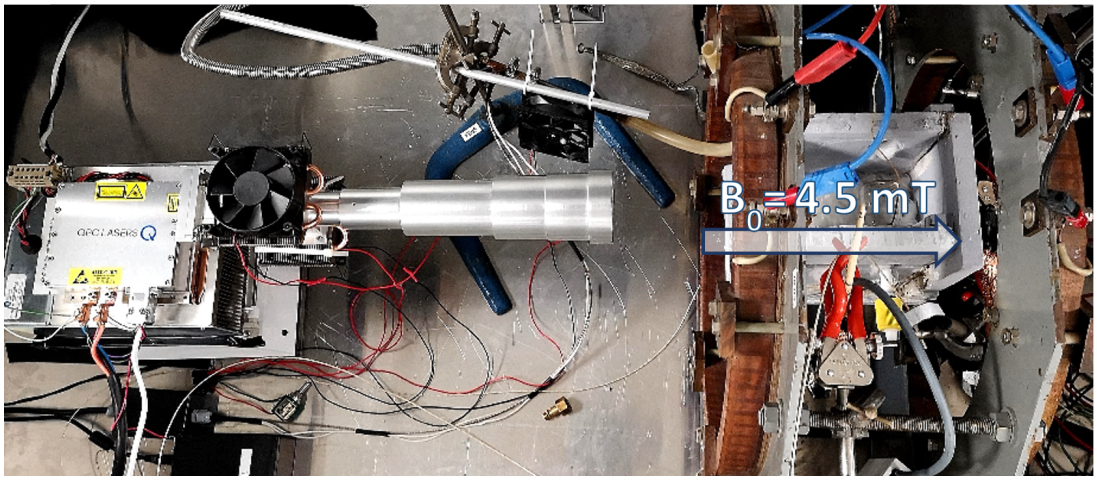

Figure 5: A scheme (top) and a picture (bottom) of the polarizer with detectors: (a) laser diode array with the telescopic lenses; (b) a pair of Helmholtz coils; (c) an insulating oven accommodating the pumping cell; and a set of four detectors consisting of three GAGG:Ce scintillating crystals (d) and a $LaBr_3$:Ce scintillating crystal (e) coupled to SiPM photosensors.

to 6 shifts of access to protons in total. In 2022 and 2023 the approach proved to be the most suitable will we applied.

THE YIELD OF XENON ISOTOPES FROM SELECTED TARGETS				
ISOTOPE	YIELD FROM			REFERENCE
	PbBi	UC	ThC	
^{129}Xe(gs+m)	8e8	-	-	Isolde yield database
^{131}Xe(gs+m)	2.5e8	-	-	Isolde yield database
^{133}Xe(gs+m)	6e7	-	-	Isolde yield database
^{129m}Xe	-	5.6e9	-	upper estimate using 70% isomeric ratio
^{131m}Xe	-	1.8e9	-	upper estimate using 70% isomeric ratio
^{133m}Xe	-	1e9	-	upper estimate in 2018 campaign

Since our collection chamber will be mounted at the GLM beamline, the Xe isotopes should be extracted from a GPS target. Direct irradiation at GPS and online extraction are one possibility. Two other options, which provide more scheduling flexibility is to irradiate a MEDICIS target behind the HRS target, or make use of the New ISOLDE Irradiation Station (ISIS) behind the GPS target. In these two cases a suitable cold target is irradiated when not all protons are taken by the main ISOLDE user, the target is later moved and coupled to the GPS frontend, mXe are extracted, mass separated in the GPS magnet, and guided to the GLM beamline.

5 Summary of requested shifts:

2 times 3 shifts in 2021 (production directly at GPS or in parasitic mode behind HRS or GPS targets). Once the best method of extraction is determined, we will come back with an addendum for 2022 and 2023.

References

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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,133mXe		
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,133mXe		
• 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]