Radioisotope production for medicine at DONES

UNIVERSIDAD DE GRANADA

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Investigación industrial en tecnologías y procesos aplicados a IFMIF-DONES para poder evolucionar en el programa de fusión

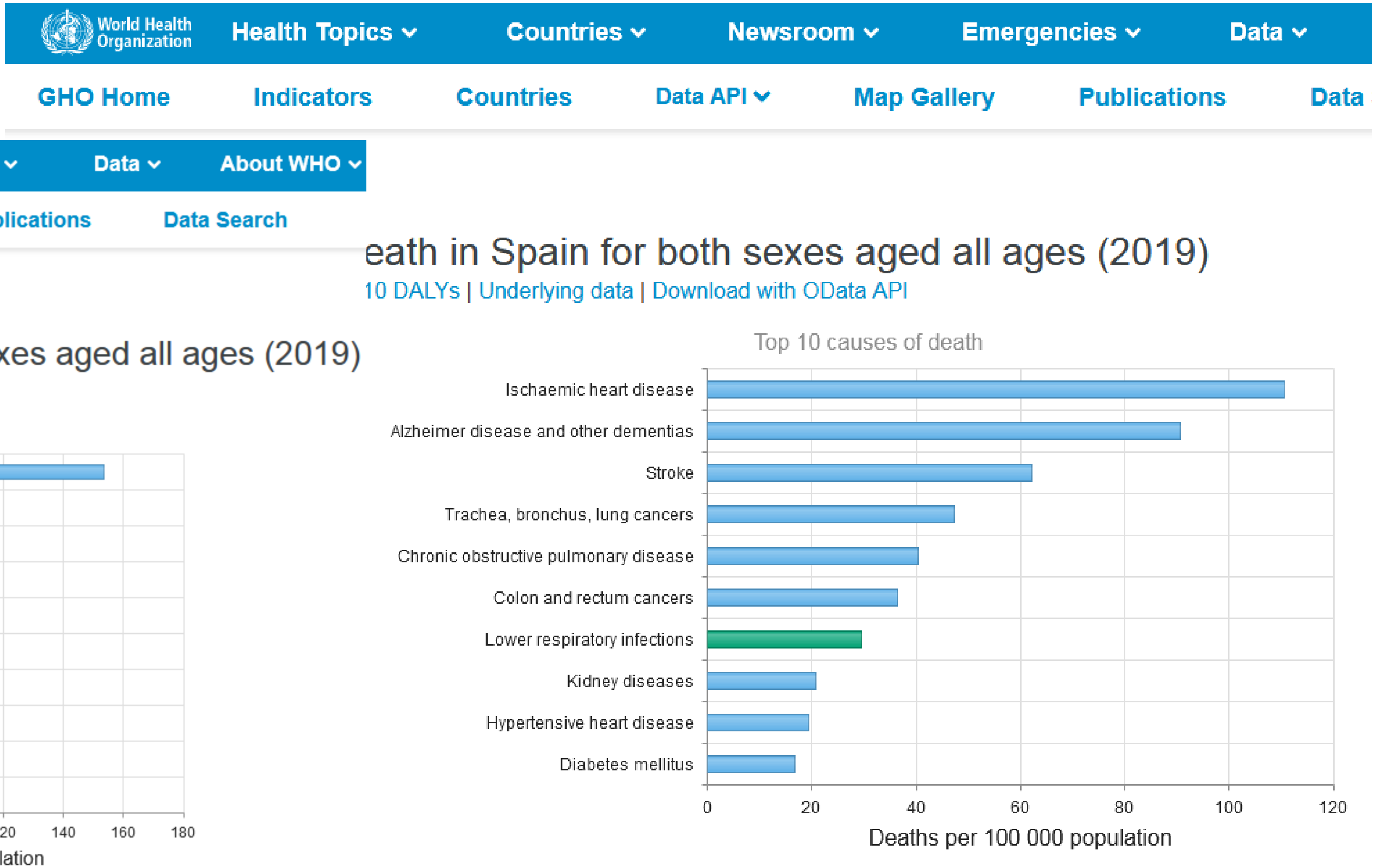
DONES-EVO

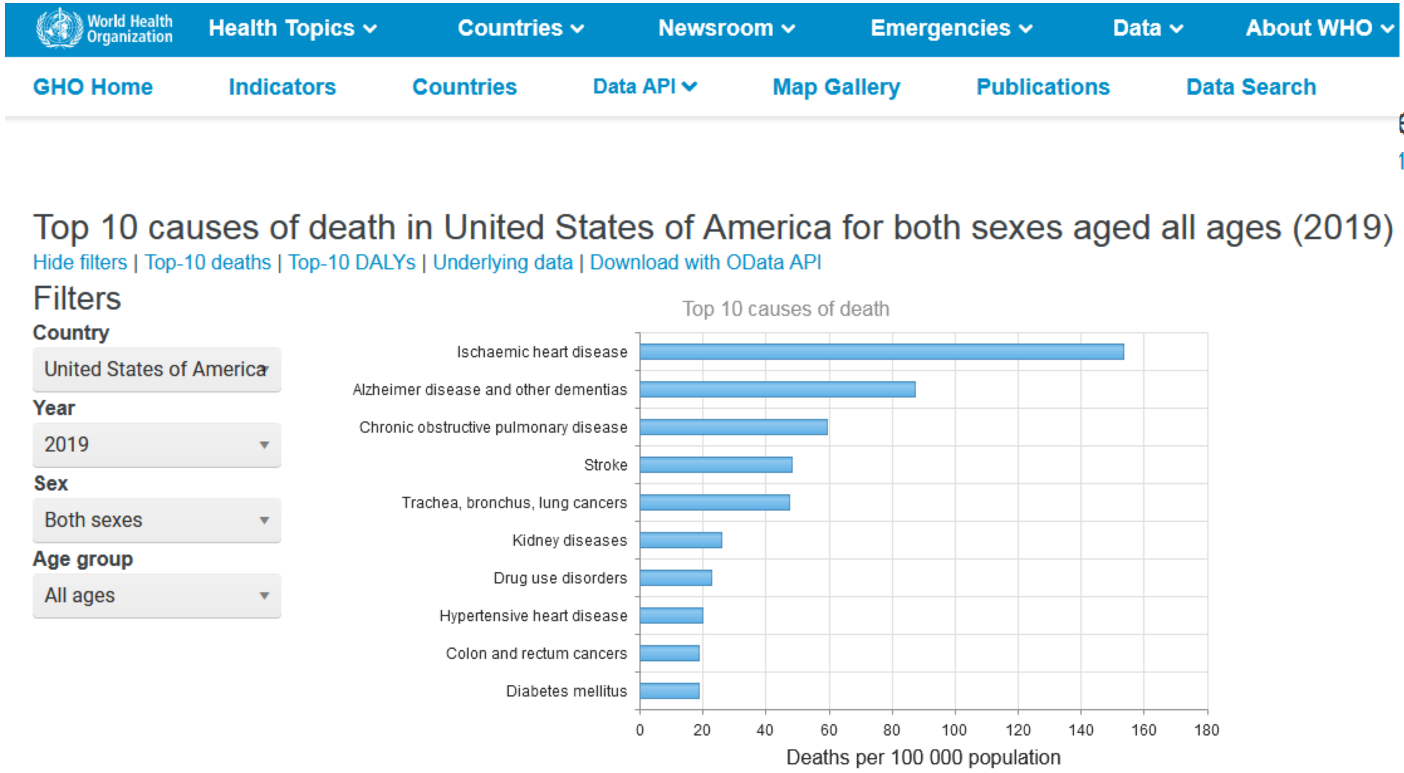
Outline

- **Social justification.**
- **Economic justification.**
- **At DONES every step, from production to patient, is completely new: INNOVATION.**
- Several conventional and new radioisotopes are possible at DONES
- Conventional and new radiopharmaceuticals will be needed.
- Conventional radioisotope could need a new process to get the radiopharmaceutical.
- **This talk is focused on neutron and deuterons and:**
  - **^{99}Mo/^{99m}Tc.**
    - ➢ **80% of all diagnostic medical scans worldwide.**
  - **^{177}Lu.**
    - ➢ **Emergent theranostic (diagnosis and therapy) and in expansion.**

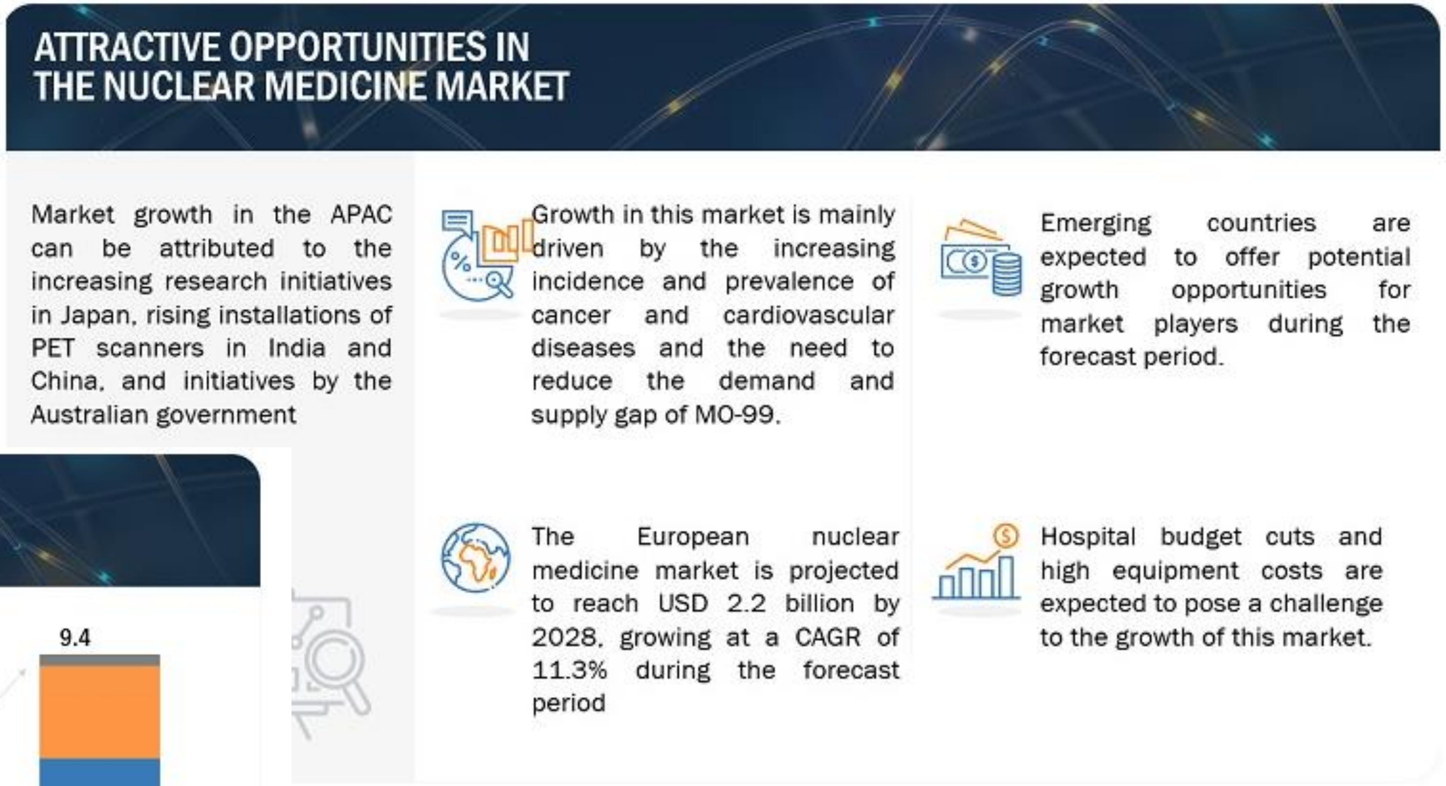
Social justification

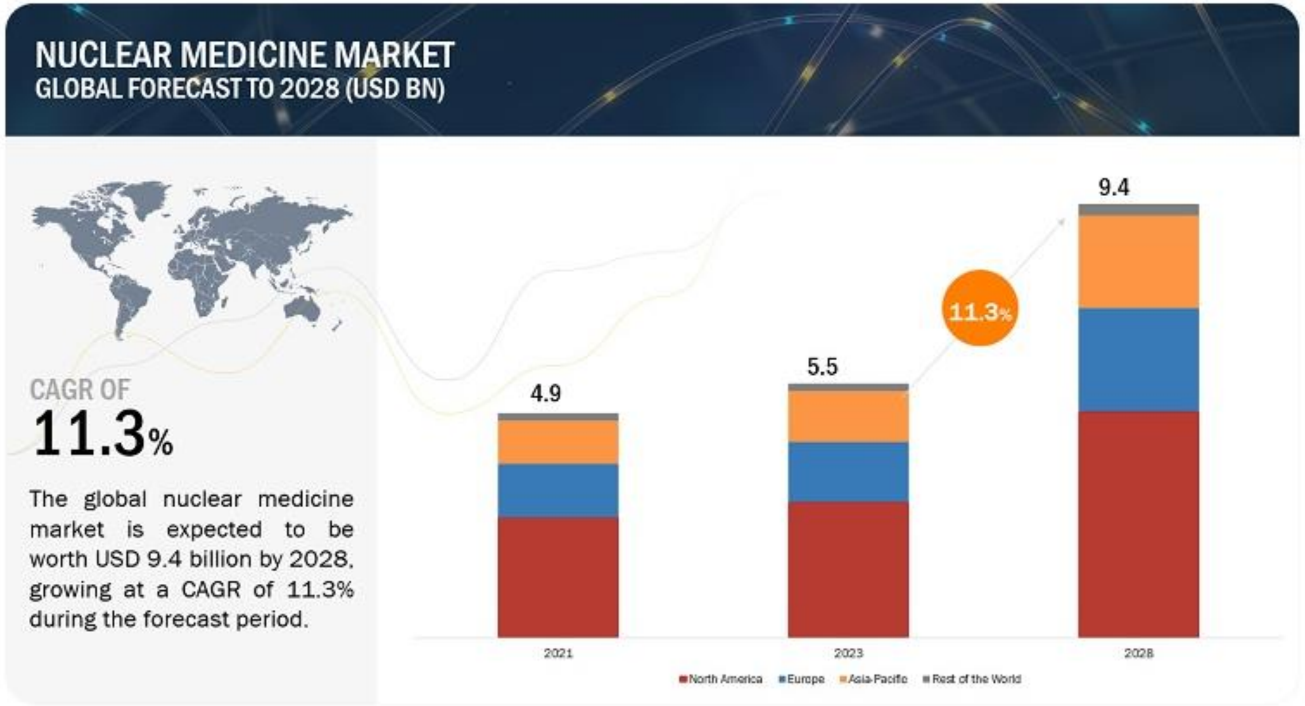
- **Radioisotopes and radiopharmaceutical are key for:**
  - **Diagnosis of cardiovascular and cancer diseases.**
  - **Therapy in cancer.**
  - **PET technique Alzheimer.**





Economic justification





The Mo/Tc is anticipated to account for a major share of the global market for radiopharmaceuticals by 2031

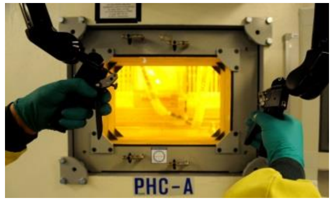
The pathway of radioisotopes: no time to lose

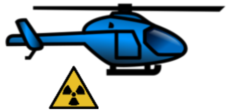
Production

Nuclear Reactors

Cyclotrons

Processing





Hospitals

<u>Innovation at DONES</u>:

Different nuclear reactions.

Nuclear reactors (n,γ) -> DONES ($n,2n$)

Cyclotrons (18p,x) -> DONES (40d,x)

Different contaminations, different experimental setups

<u>Innovation at DONES</u>:

Different processing for conventional radioisotope to radiopharmaceutical.

New radioisotope…

<u>Innovation at DONES</u>:

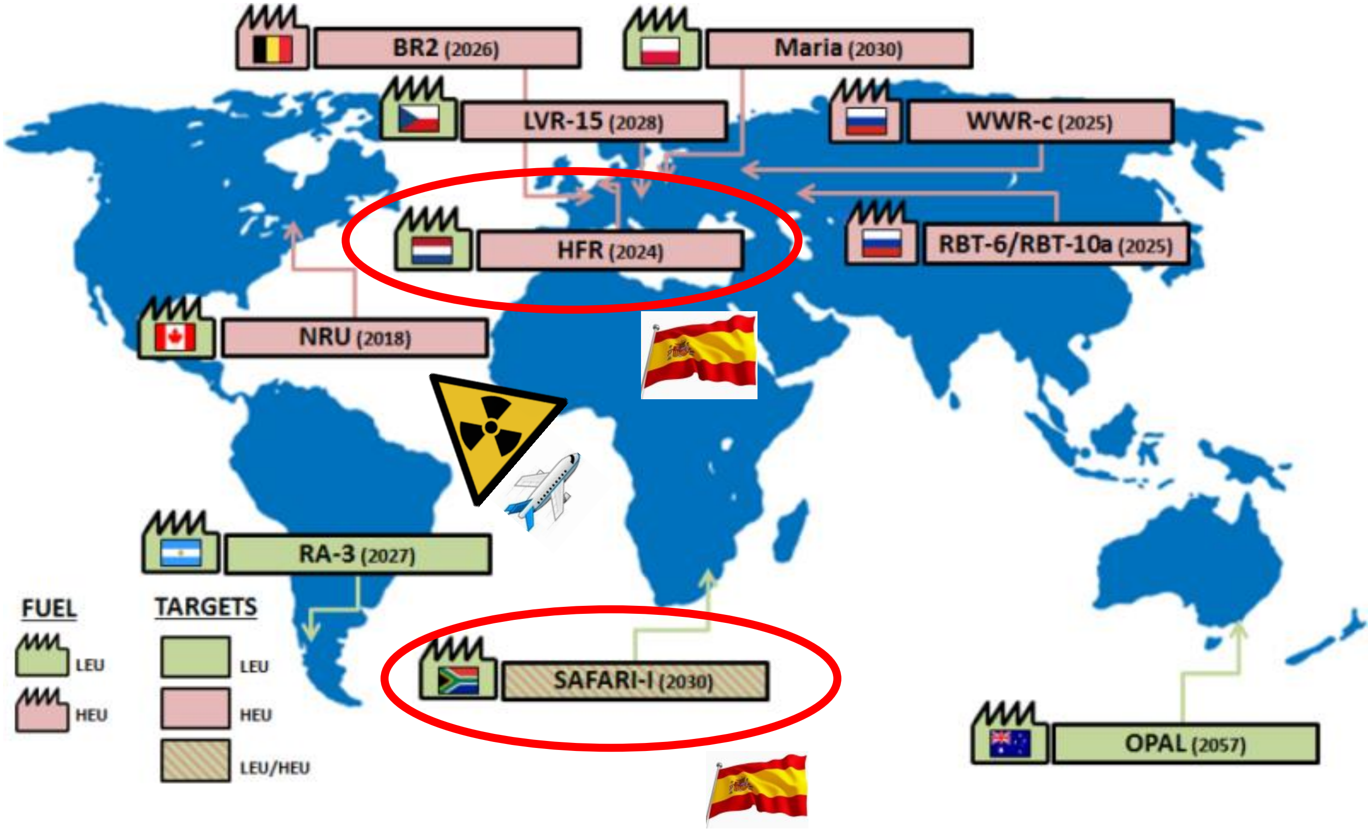
New radiopharmaceuticals and new radioisotopes.

$^{99}Mo/^{99m}Tc$: where is produced at present? Few nuclear reactors

From fission of Uranium (high production)

Or

Neutron capture: $^{98}Mo(n,\gamma)^{99}Mo$ **(medium production)**



The reactor must be designed in advance for producing ^{99}Mo

$^{99}Mo/^{99m}Tc$: Molybdenum world crisis 2009-2010

Unexpected stops at the same period of few nuclear reactors.

Important delays in diagnosis (80% of total!!!).

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Published online 23 October 2008 | Nature | doi:10.1038/news.2008.1186

News

Europe's isotope shortage will continue into 2009

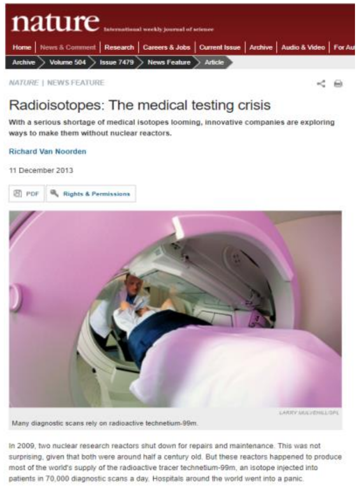
Hospitals forced to use substitute procedures for medical scans.

Paula Gould

A Europe-wide shortage of medical isotopes will continue for at least three months while a Dutch nuclear reactor is repaired. Governments and regulators are now bending their rules concerning the use and transport of radioactive materials so that patients can still undergo diagnostic tests during the supply crisis.

The High Flux Reactor in Petten has been out of action since the end of August (see 'Isotope shortage could delay cancer treatment') after tiny bubbles of gas were found escaping from a pipe into the reactor's cooling system during a routine maintenance inspection. Although the cause of the leak has now been traced

The High Flux Reactor in Petten, the Netherlands, is facing an extended shut-down.
NRG



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NATURE | NEWS FEATURE

Radioisotopes: The medical testing crisis

With a serious shortage of medical isotopes looming, innovative companies are exploring ways to make them without nuclear reactors.

Richard Van Noorden

11 December 2013

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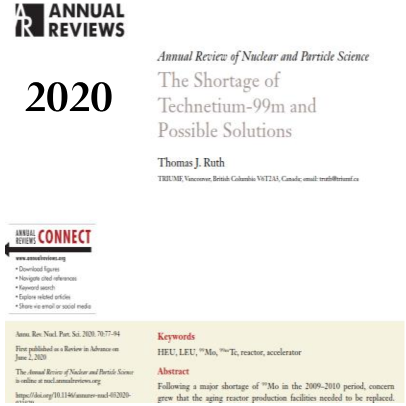
Many diagnostic scans rely on radioactive technetium-99m.

In 2009, two nuclear research reactors shut down for repairs and maintenance. This was not surprising, given that both were around half a century old. But these reactors happened to produce most of the world's supply of the radioactive tracer technetium-99m, an isotope injected into patients in 70,000 diagnostic scans a day. Hospitals around the world went into a panic.

2020



ANNUAL REVIEWS

Annual Review of Nuclear and Particle Science

The Shortage of Technetium-99m and Possible Solutions

Thomas J. Ruth

TRIUMF, Vancouver, British Columbia V6T2A3, Canada; email: truth@triumf.ca

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Keywords

HEU, LEU, ^{99}Mo, ^{99m}Tc, reactor, accelerator

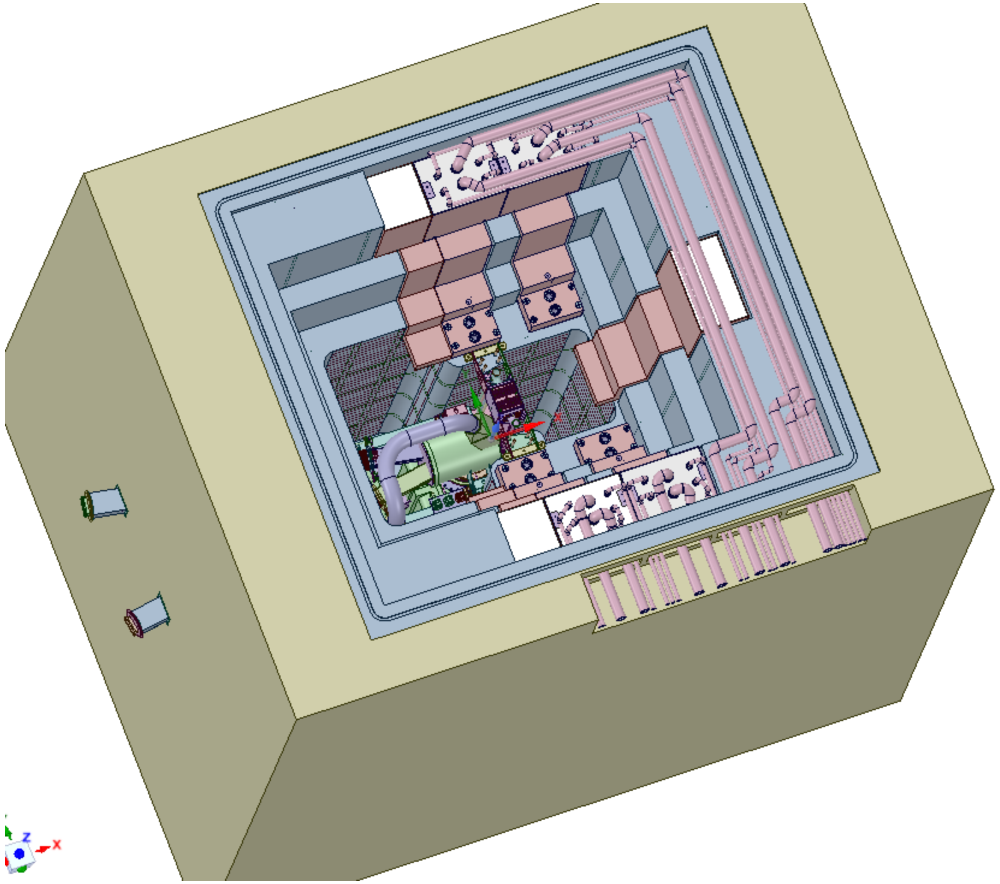
Abstract

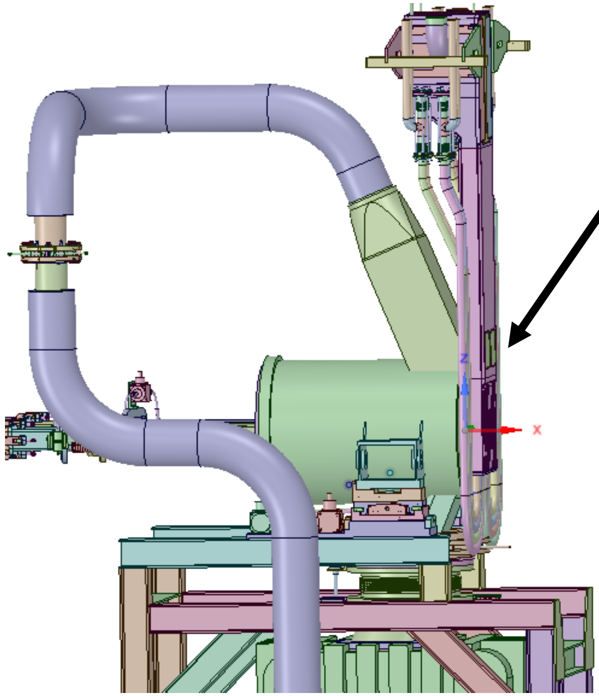
Following a major shortage of ^{99}Mo in the 2009–2010 period, concern grew that the aging reactor production facilities needed to be replaced.

There is a follow-up of the situation of the Mo/Tc by international agencies.

Last small crisis in Spain

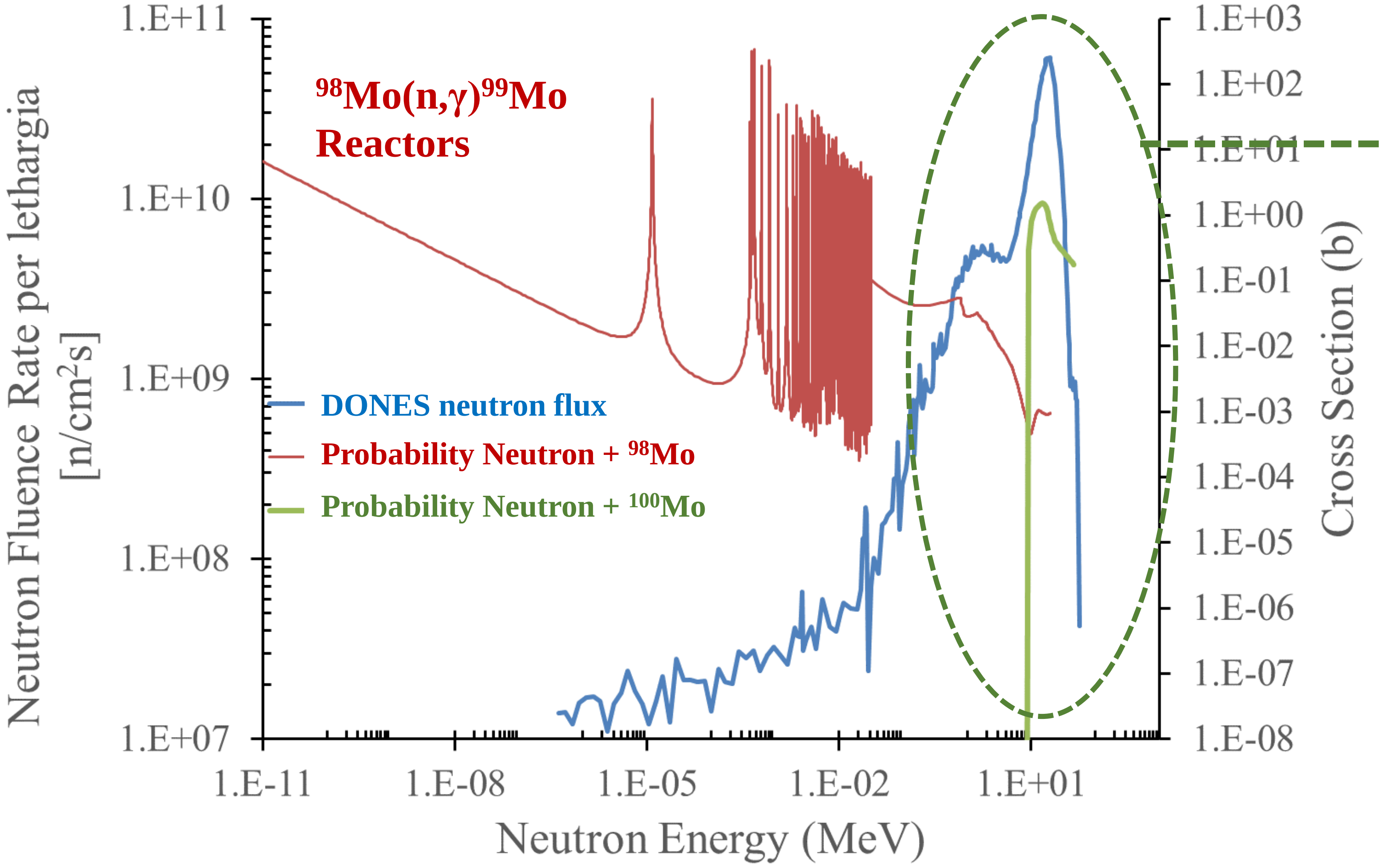
$^{99}Mo/^{99m}Tc$: where at DONES? Test Cell





Best location for production.
Close to the Li jet.

$^{99}Mo/^{99m}Tc$: at DONES different reaction with natural target



$^{100}Mo(n,2n)^{99}Mo$

DONES

$^{99}Mo/^{99m}Tc$: production at DONES

Behind of HFTM	6 irradiation day (GBq/g of Mo)
Shutdown	~ 48,2
5 days decay	~10

Comparable with medium production at nuclear reactors.

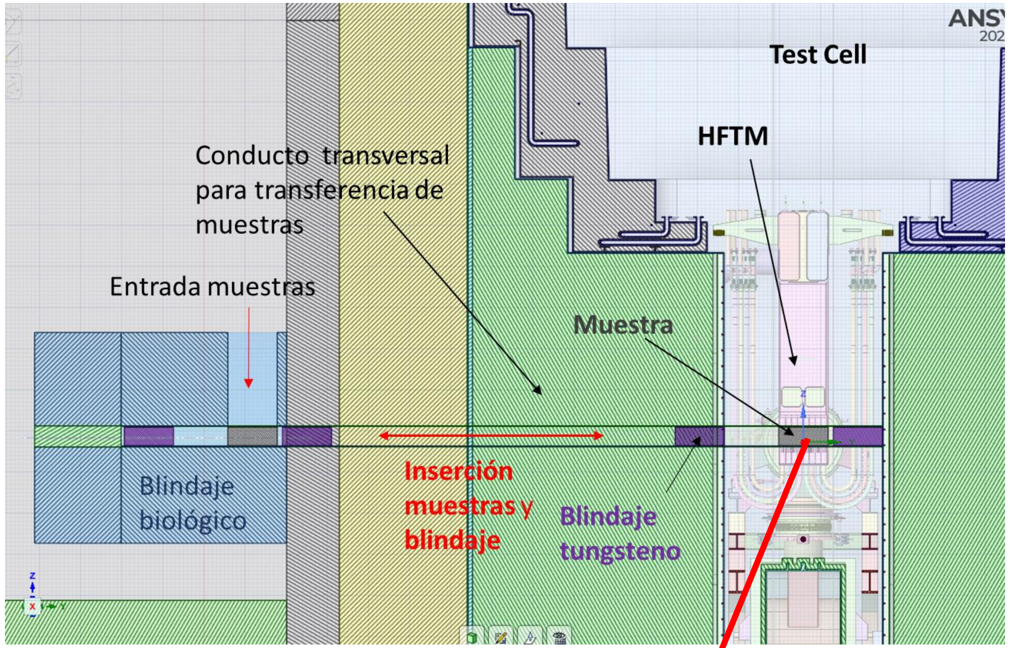
$^{100}MoO_3$ enriched samples, the regional demand of Andalucia could be satisfied, most conservative.

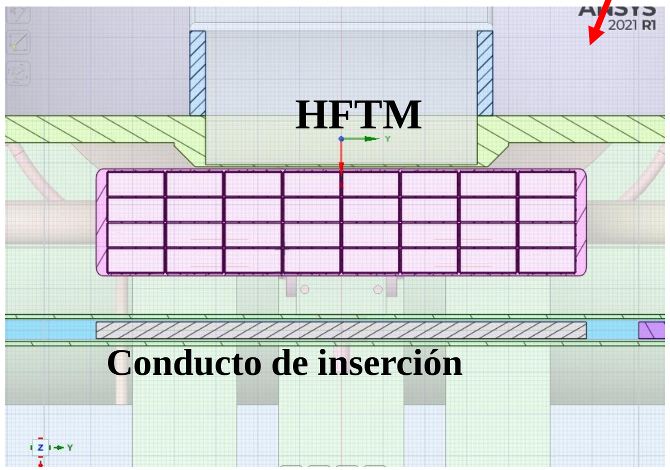
Other radioisotopes could be produced simultaneously.

But in/out device from Test Cell modifies the production…

$^{99}Mo/^{99m}Tc$: in/out device modifies production

Inserción lateral





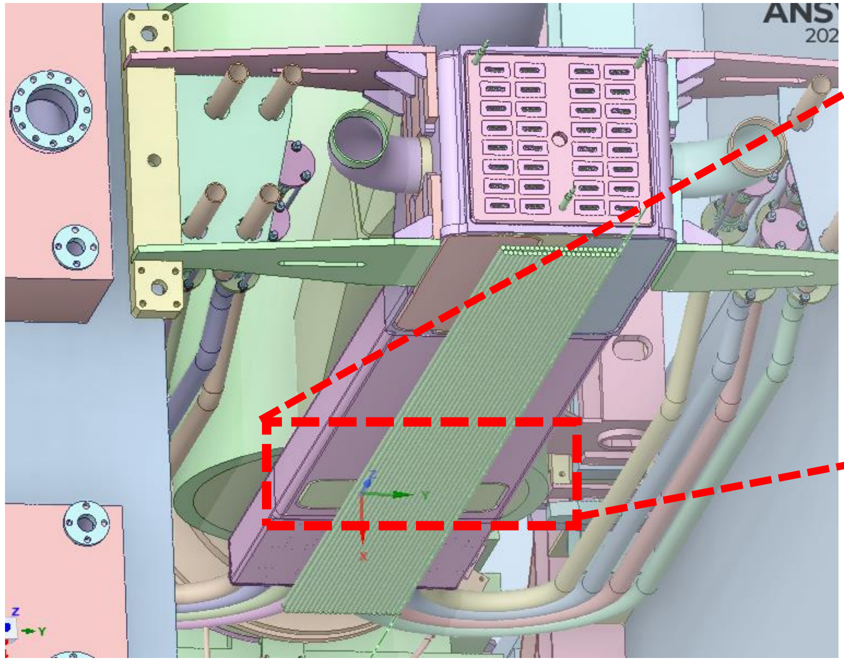
- ✓ Permite insertar muestras automáticamente con periodos programables de tiempo de irradiación
- ✓ Máximo aprovechamiento del área de mayor flujo neutrónico detrás del HFTM
- ✓ Posibilidad de irradiar grandes volúmenes: ~ 100 cm^3.
- ✓ **Ejemplo:** 6 días de irradiación para ^{100}Mo (95%)
  - Producción estimada de ~ 13 TBq de $^{99}Mo/^{99m}Tc$.
  - Cubre las necesidades del **70% de la población de España**

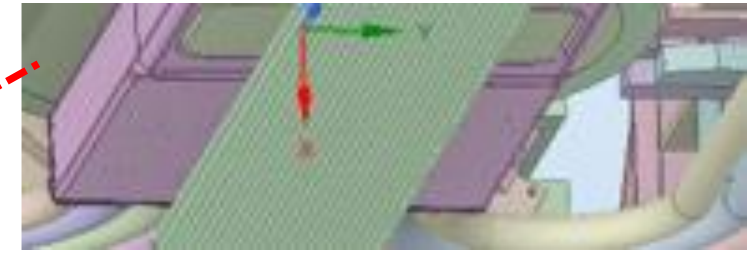
Retos:

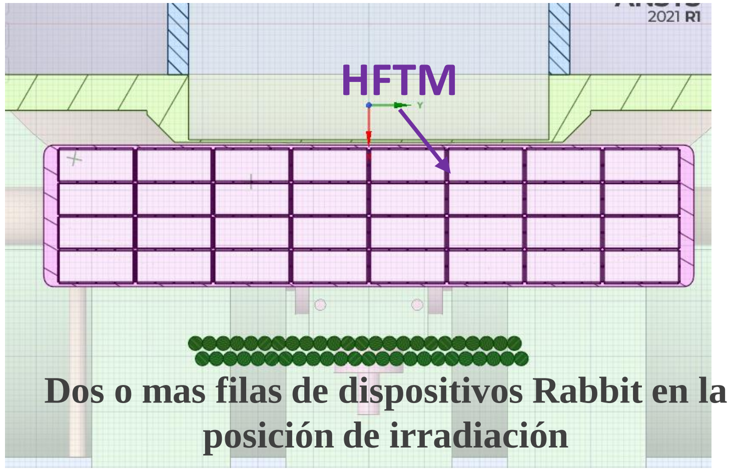
- ✓ Mantener la estanqueidad de la Test Cell
- ✓ Conservar los requisitos de blindaje radiológico de la TC
- ✓ Soportar las extremas condiciones de irradiación

^{99}Mo/^{99m}Tc: in/out device modifies production

Inserción Rabbit ~ STUMM







Sección horizontal

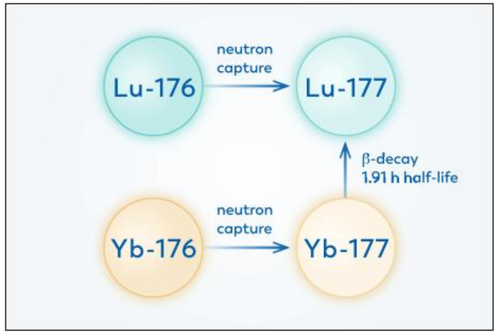
- ✓ No hay cambios de diseño del blindaje de la TC, porque utiliza los tubos que pasan por los PCP.
- ✓ **Ejemplo**: 6 días de irradiación para ^{100}Mo (95%):
  - Producción estimada de ~ 2 TBq de ^{99}Mo/^{99m}Tc.
  - Cubre las necesidades del **100 % de Andalucía.**

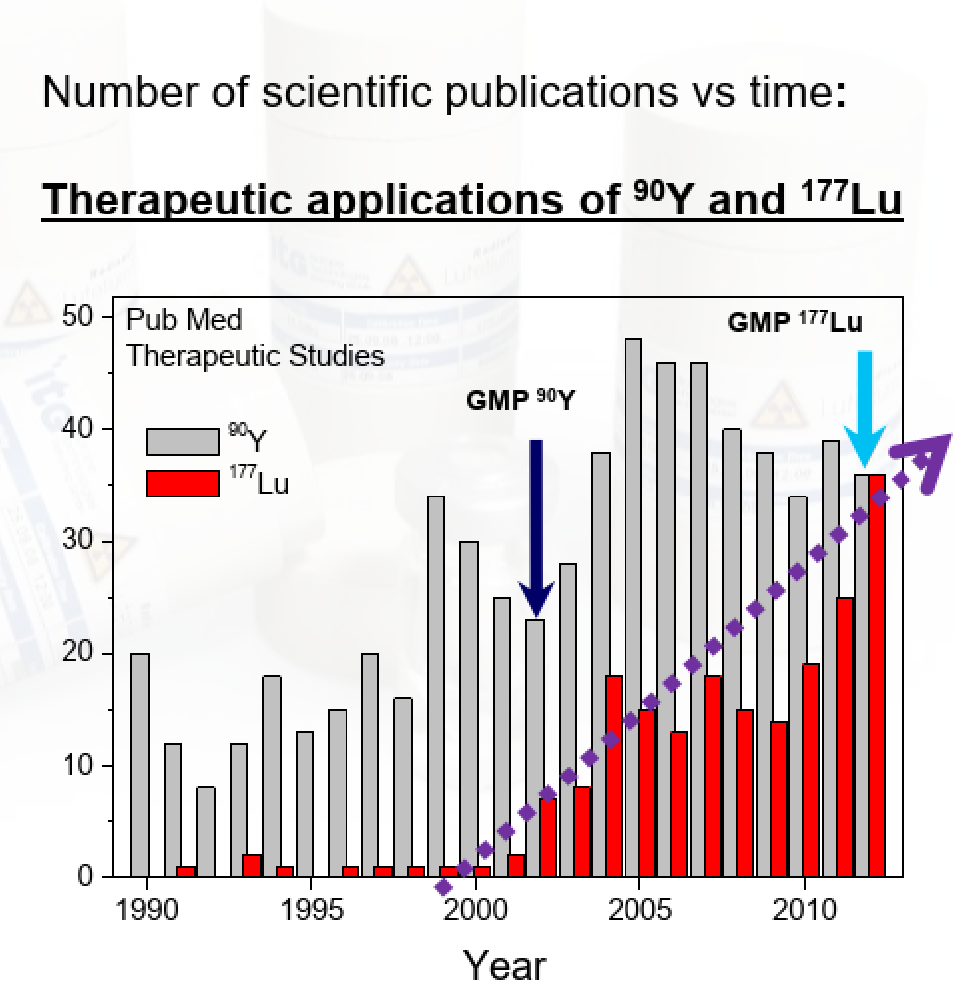
Retos (los mismos):

- ✓ Soportar las extremas condiciones de irradiación
- ✓ Diseñar de los tubos del sistema Rabbit para evitar bloqueos.

^{177}Lu is the most emerging radioisotope

- Theragnostic = diagnosis and therapy.
- Versatile radioisotope and one the most important emergent radioisotopes.
- Currently, ^{177}Lu (6.7 d) is under study for several other tumours with good results.





^{177}Lu: where at DONES?

Not using neutrons (low production at TC)

Using **deuterons** on natural $^{176}Y_2O_3$ target: **innovation.**

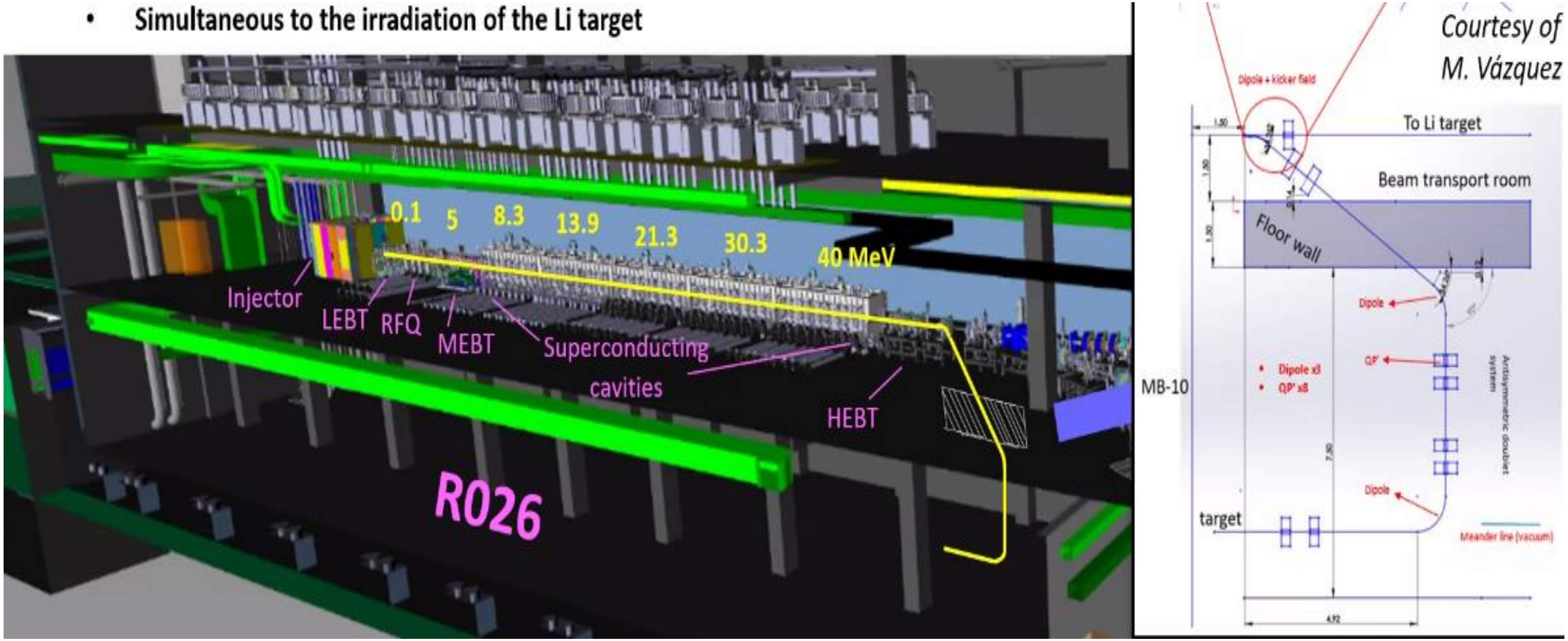
Two reactions produce Lutetium-177 with deuterons:

$$d + {}^{176}Yb \rightarrow n + {}^{177}Lu \ (6.7\ d)$$

$$d + {}^{176}Yb \rightarrow p + {}^{177}Yb \ (1.9\ h) \rightarrow {}^{177}Lu \ (6.7\ d)$$

^{177}Lu: where at DONES?

Possible deuteron beam deflection to R026 at 40 MeV and 1.25 mA



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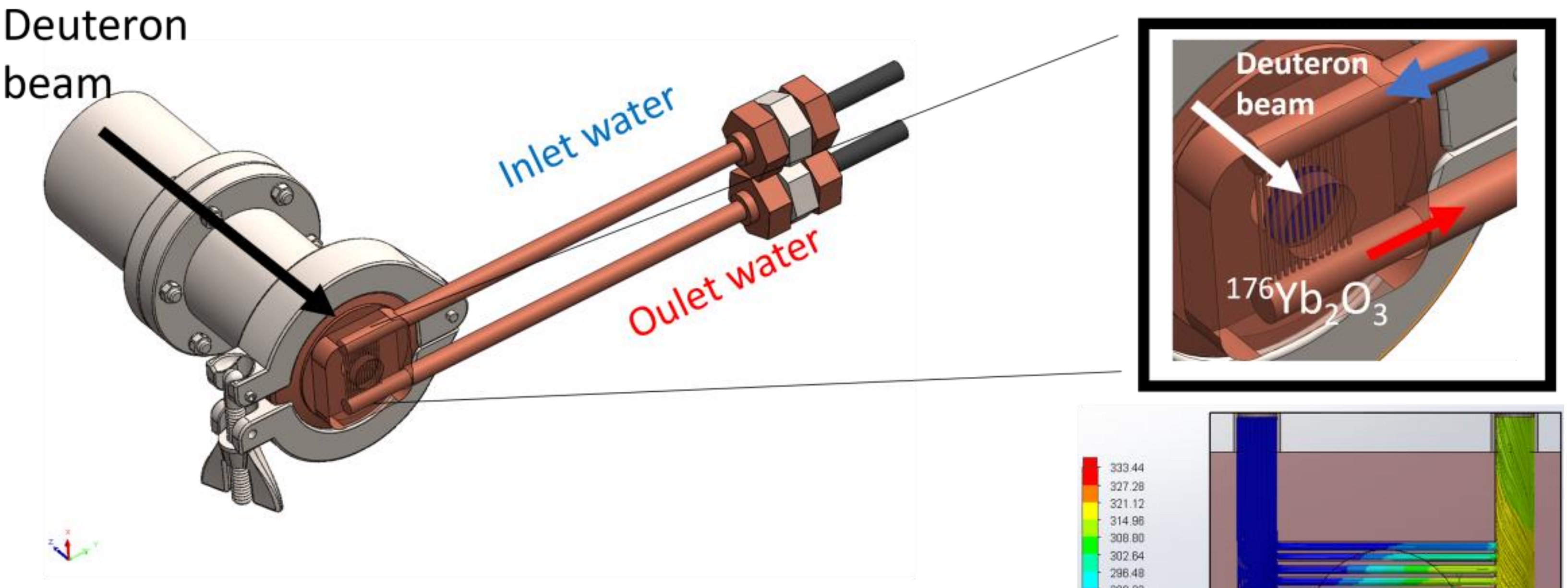
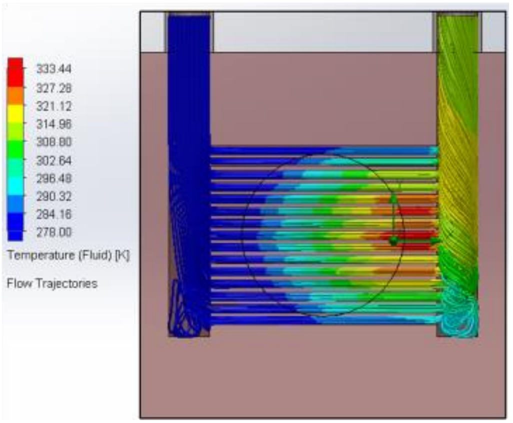
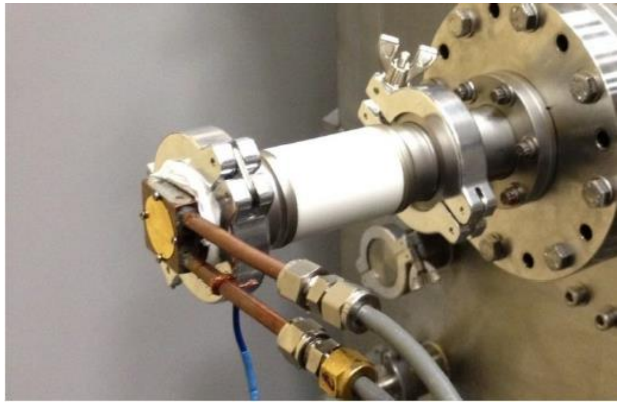
^{177}Lu: innovation in production setup







A realistic device is designed to sustain the power.

^{177}Lu: production at DONES

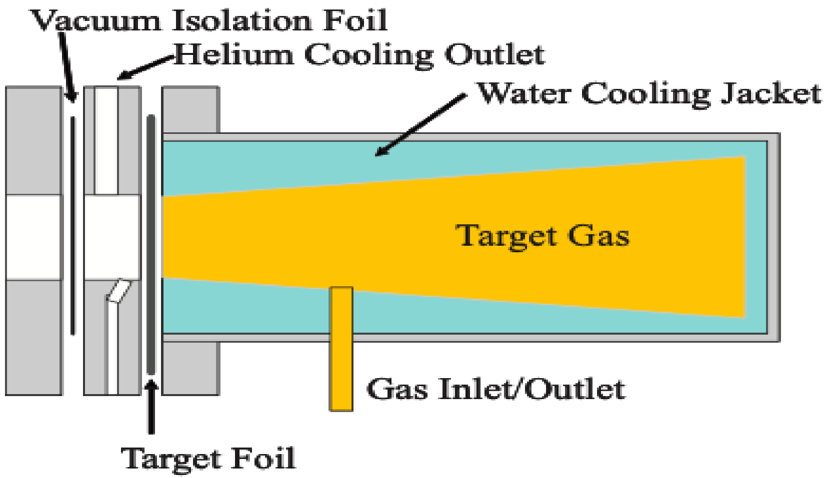
	Specific Activity (GBq/mg)	Days	Reaction
Nuclear Reactors	1,11	7	$^{176}Yb(n,\gamma)^{177}Yb \rightarrow ^{177}Lu$
DONES	1,11	**3**	$^{176}Yb(d,p/n)^{177}Yb \rightarrow ^{177}Lu$

Same production in half of the time!!!

More radioisotopes are under studied

	Vida	Reacción Convencional	Blanco	**Reacción en DONES**	**Aplicación**
^{11}C	20 min	p + ^{14}N	gas	**^{10}B(d,n) baja**	**Multitud de diagnósticos PET**
^{13}N	10 min	p + ^{13}C	sólido	**^{12}C(d,n) baja E**	**Diagnósticos PET en cardiología**
^{15}O	2 min	p + ^{15}N	gas	**^{14}N(d,n) baja E**	**Diagnósticos PET en cardiología**
^{18}F	110 min	p + ^{18}O	líquido	d+^{20}Ne -> α+^{18}F	**Multitud de diagnósticos PET**
$^{68}Ge/^{68}Ga$	270 d / 68 min			**^{69}Ga(d,3n) alta E**	**Diagnósticos PET del cáncer**
^{64}Cu	762 min			**^{63}Cu(d,p) baja E**	**InmunoPET y terapia**
^{89}Zr	78 h			**^{89}Y(d,2n) alta E**	**PET metabólico**
^{44}Sc	4h/58h			**^{44}Ca(d,2n) alta E**	**Gamma-PET**
^{94m}Tc	52 min			**^{92}Mo(d,2n) alta E**	**Gamma-PET**
^{177}Lu	6 d	n + ^{176}Yb		**^{176}Yb(d,p) alta E**	**Terapia del cáncer diversos tumores**
^{90}Y	64 h			**^{89}Y(d,p) baja-alta E**	**Terapia del cáncer por radioembolización**
^{161}Ho	2.5 h			**^{161}Dy(d,2n) alta E**	**Terapia del cáncer por electrones Auger**
^{125}I	59 d			**^{126}Te(d,3n) alta E**	**Terapia del cáncer por electrones Auger**
^{111}In	2.8 d			**^{112}Cd(d,3n) alta E**	**Terapia del cáncer por electrones Auger**
^{195m}Pt	4 d			**^{nat}Pt(d,x) alta E**	**Terapia del cáncer por electrones Auger**

^{18}F: innovation in target designed



Wisconsi Target

	Cyclotron 18 MeV 10 µA			DONES 1.25 mA Wisconsi Updated			DONES 1.25 mA Wisconsi		
	Reacción	Blanco	GBq	Reacción	Blanco	GBq	Reacción	Blanco	GBq
^{18}F	$p+^{18}O \rightarrow n+^{18}F$	$H_2{}^{18}O$ (liq)	**142**	$d+^{20}Ne \rightarrow \alpha+^{18}F$	Ne (gas)	**461**	$d+^{20}Ne \rightarrow \alpha+^{18}F$	Ne (gas)	**150**

Conclusions

- **Production is justified from social and economic point of view.**
- **At DONES every step, from production to patient, is completely new: INNOVATION.**
- **Radioisotopes can be produced without interfering routine operation of DONES**
- **^{99}Mo/^{99m}Tc can be produced at significant quantities (at least Andalucia).**
- **^{177}Lu could be produced in higher quantities than nuclear reactors.**
- **Many radioisotopes could be produced in significant quantities by neutrons and/or deuterons.**

Thank you

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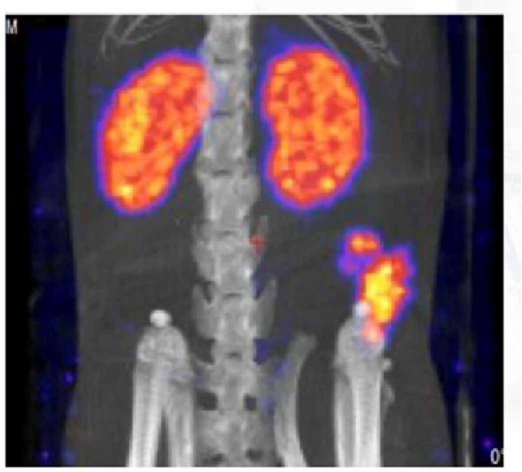
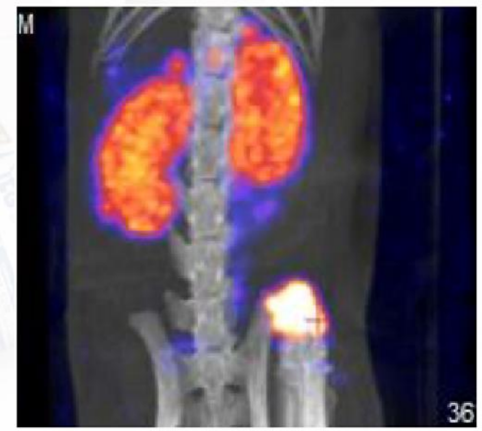
DONES-EVO

^{177}Lu: where is produced? Nuclear Reactors



300 MBq of ^{177}Lu c.a.

Dose to tumor - 35 Gy



300 MBq of ^{177}Lu n.c.a.

Dose to tumor - 70 Gy

Marion de Jong et al.; 2012 ICTR-PHE

"Carrier Added"

Neutrons+Luthetium sample

^{176}Lu(n,γ) → ^{177}Lu + ^{177m}Lu

Higher production.

Lower specific activity.

^{177m}Lu is produced (0.05%), 160 days.

"Non Carrier Added"

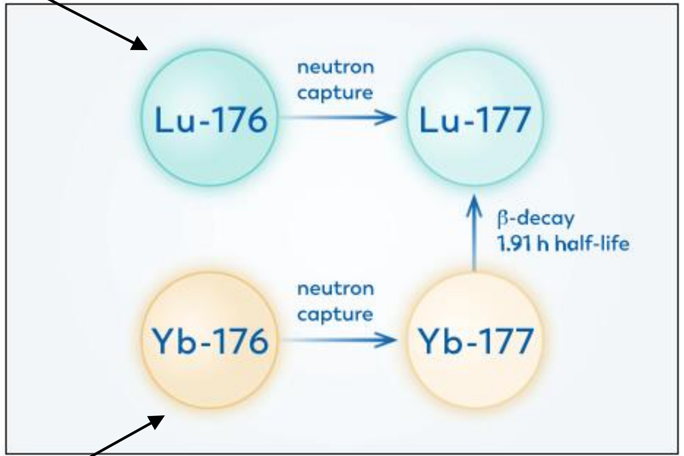
Neutrons+Yterbium sample

^{176}Yb(n,γ)^{177}Yb (1.9 h) → ^{177}Lu (6.7 d))

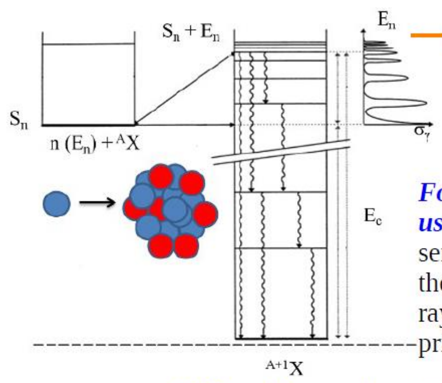
Lower production.

Higher specific activity.

^{177m}Lu is negligible

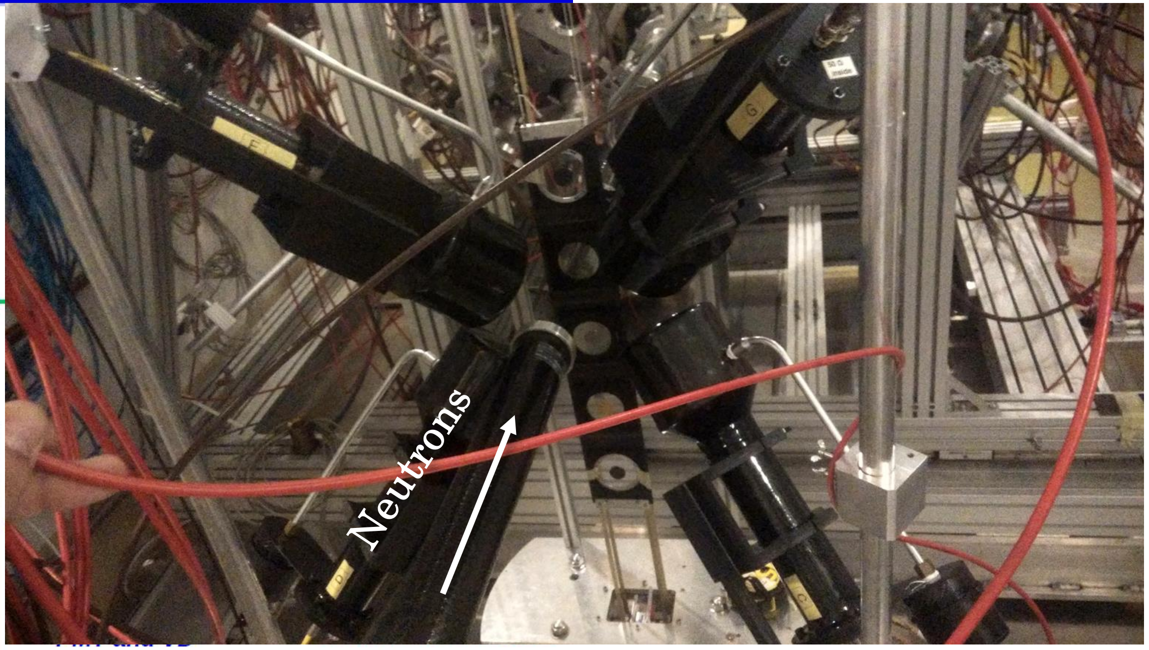


Measure, Experimental Set-Up and ^{176}Yb sample



Sketch of the ***compound cucleus formation when a neutron of energy E_n interacts with ^{A}X nucleus***. The quasi-stationary states on the compound nucleus above the neutron separation energy S_n lead to resonances in the cross section.

Four custom C6D6 scintillation detectors were used, optimized for an extremely low neutron sensitivy. These detectors are positioned at 125° to the beam position to reduce the in beam gamma rays background and minimize the effects of the primary radiation angular distribution [15,16].



The sample is a ***^{176}Yb oxide powder***, (***1.5976 g and 99.43% purity***) ***pressed in a 19 mm Ø quartz and 2mm thickness***.
Kindly ***provided by Richard Henkelmann*** (ITG company) ***and Ulli Koester*** (ILL). This sample will be recycled for radioisotope production at ITG. ***ITG supplies of ^{177}Lu to hospitals***. As mentioned, new routes are of high interest to produce radioisotopes.

Measurement time from ***25/10/2021*** to ***14/11/2021***

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