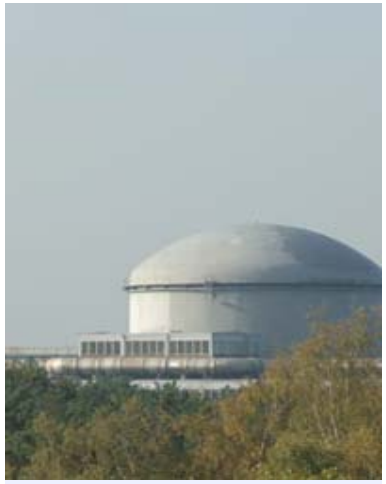

Production of Radioisotopes in the BR2 Reactor :

Past Performances and Future Prospects

Bernard Ponsard

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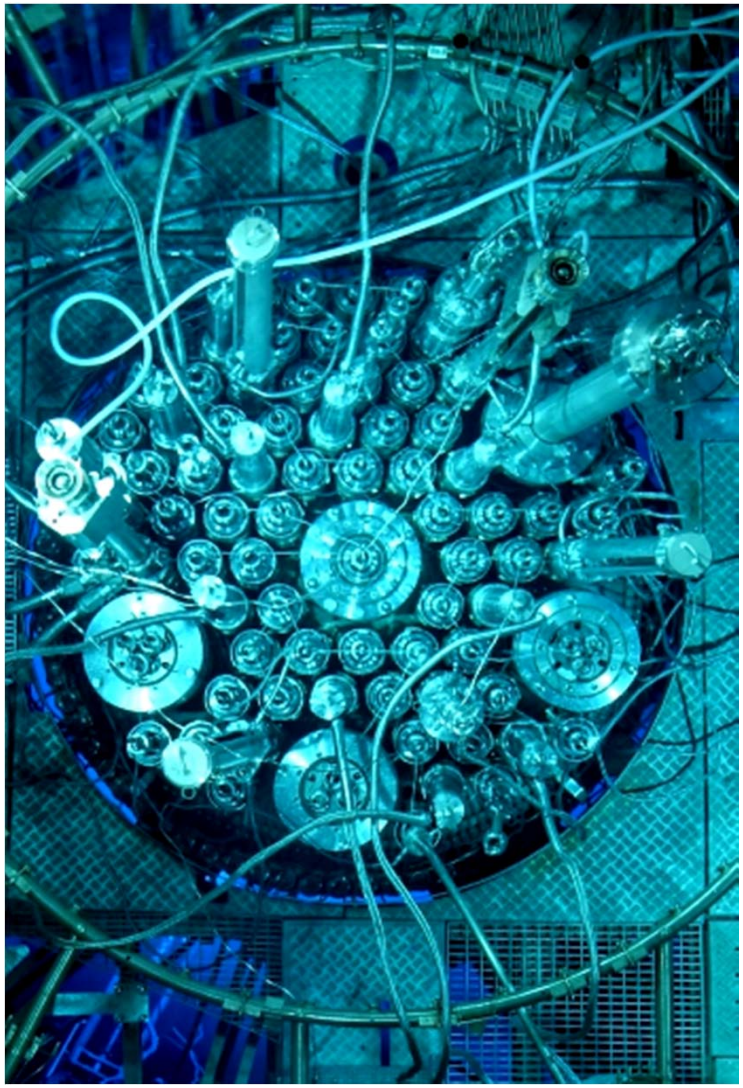
Content

- Introduction
- The BR2 High-Flux Reactor
- Radioisotopes for Diagnosis
  - ^{99}Mo supply
  - ^{99}Mo/^{99m}Tc by fission
- Radioisotopes for Therapy and Palliation
  - ^{177}Lu, ^{188}W/^{188}Re, ^{117m}Sn, ^{153}Sm, ^{89}Sr, ^{192}Ir, ^{90}Y, …
- Radioisotopes for Industrial applications
  - ^{192}Ir, ^{75}Se, ^{203}Hg, …
- Conclusions



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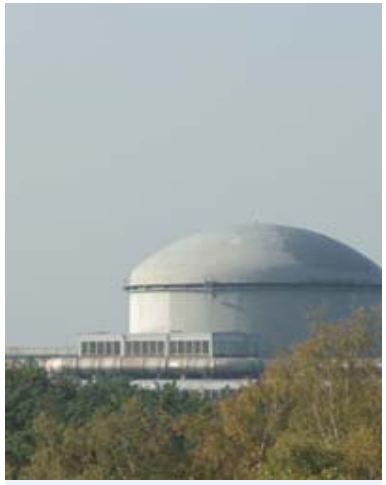
Introduction



- The **BR2 reactor** is a multipurpose **100 MW_{th}** High-Flux 'Materials Testing Reactor' operated since 1961 (first criticality) by the Belgian Nuclear Research Centre (SCK•CEN) to perform various **research** (materials, fuel) and **commercial** programs.
- The commercial activities such as **radioisotope production** and **silicon doping** have been actively developed since the early 1990's to generate additional revenues and **to reduce BR2's financial dependence** on Government funding.
- An important maintenance program is in place to operate the BR2 reactor on a **safe and reliable way**. The beryllium matrix of the reactor has been replaced in the period February 2015 – June 2016 to provide an operating lifetime extension **until 2026**, at least.

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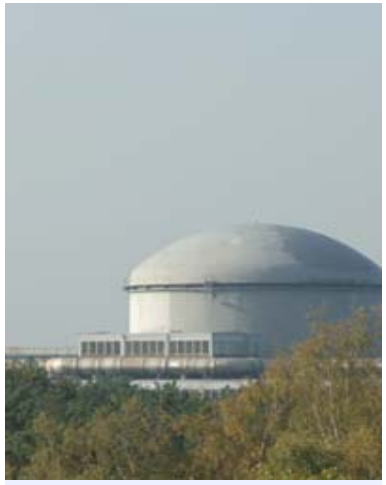
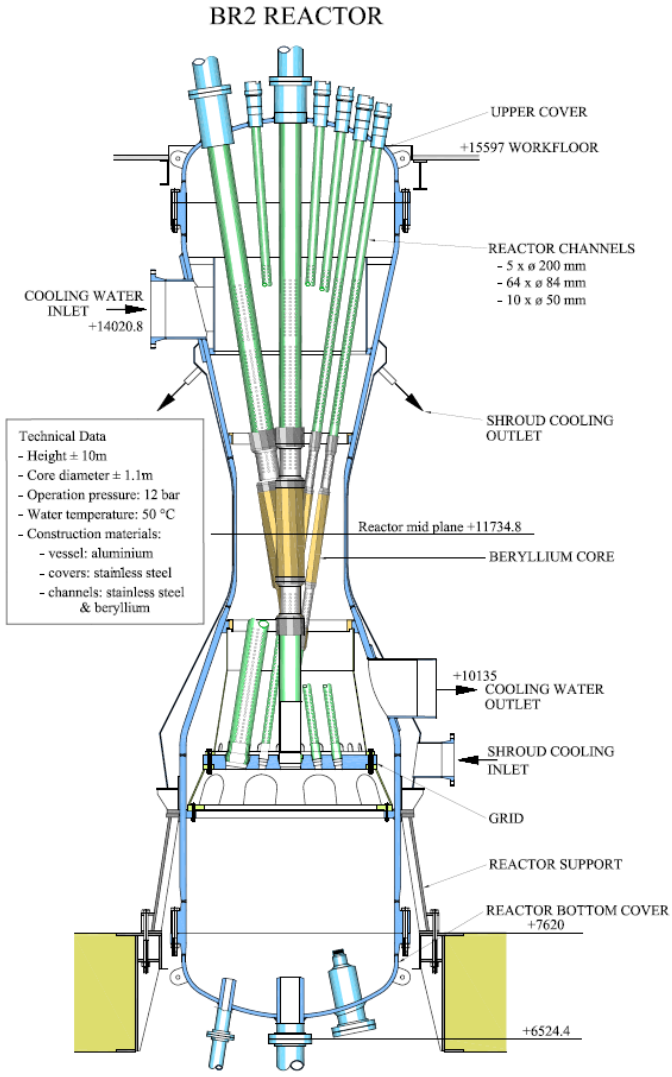
The BR2 Reactor



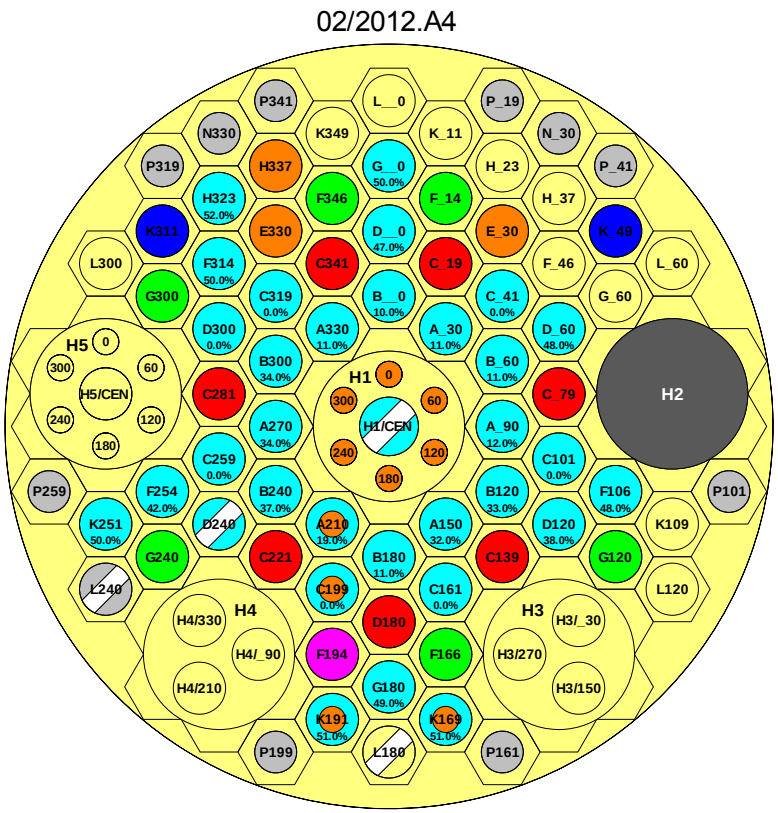
- **Reactor type**
  - High Flux Materials Testing Reactor
  - Pressurized, light water
  - Be matrix, compact core
  - HEU fuel (93% ^{235}U)
  - LEU conversion project in place
  - In operation since 1963
  - Refurbishments:
    1979-1980 _1995-1997 _ 2015-2016
- **Aluminium pressure vessel**
  - Geometry : hyperboloid of revolution
  - Easy access to the top and bottom
  - Diameter : 1 to 2 m
  - Height : 8.6 m
- **Very compact core**
  - Diameter : 1.05 m
  - Height : 0.91 m

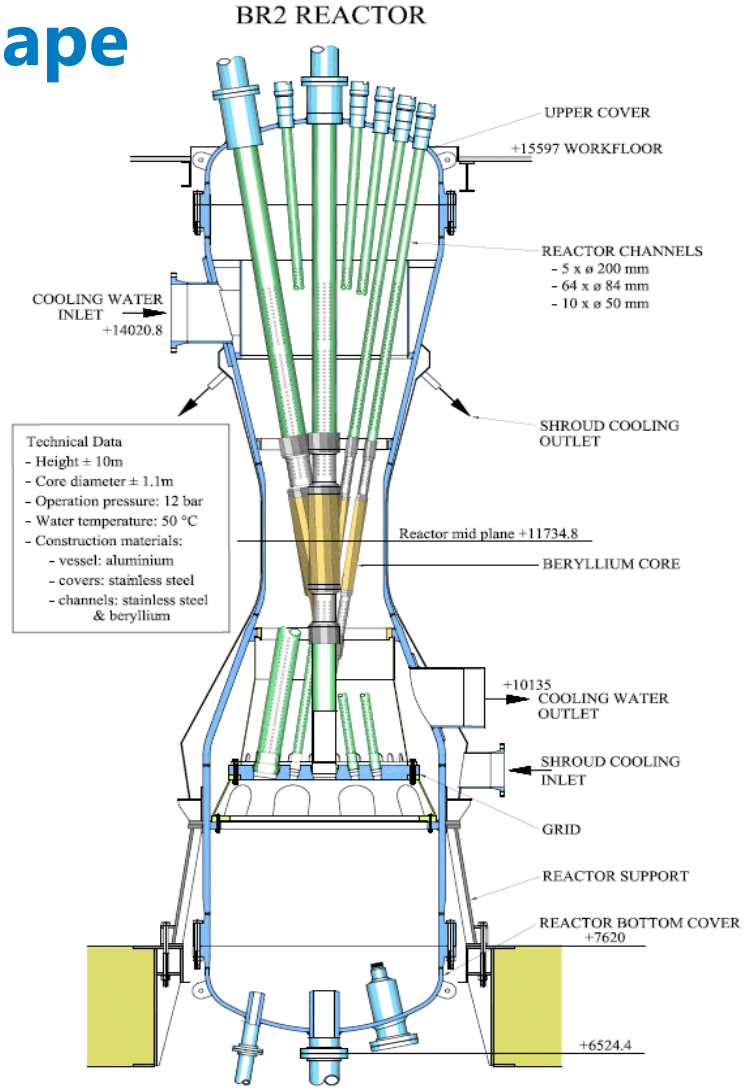
100 MW



The BR2 Reactor

Unique shape





Typical configuration

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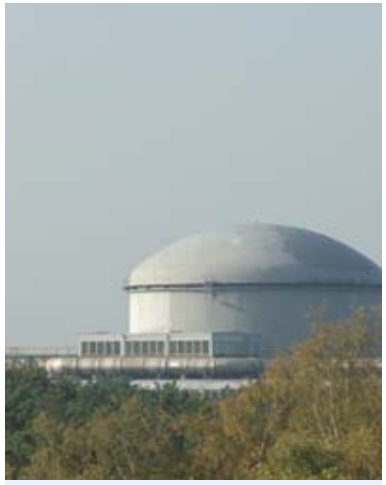
The BR2 Reactor



- **Operating power :** 55 – 100 MW_{th}
- **Operating cycle :** 21 – 28 days
- **Operating regime :** 6 cycles per year, i.e. 190 days per year
- **Moderators :** Beryllium and Light water
- **Primary coolant :** Light water @ 12 bars
- **Water temperature :** 40 - 45 °C
- **Flow rate :** 6 500 m^3/h
- **Fuel :** HEU (Highly Enriched Uranium); 93% U-235
- **Control rods :** Hafnium
- **Neutron fluxes :**
  - **Thermal (E_n < 0.5 eV)** : up to 1.0 x 10^{15} $n/cm^2.s$
  - **Epithermal (E_n ~ 5 eV)** : up to 4.2 x 10^{13} $n/cm^2.s$
  - **Fast (E_n > 100 keV)** : up to 6.0 x 10^{14} $n/cm^2.s$

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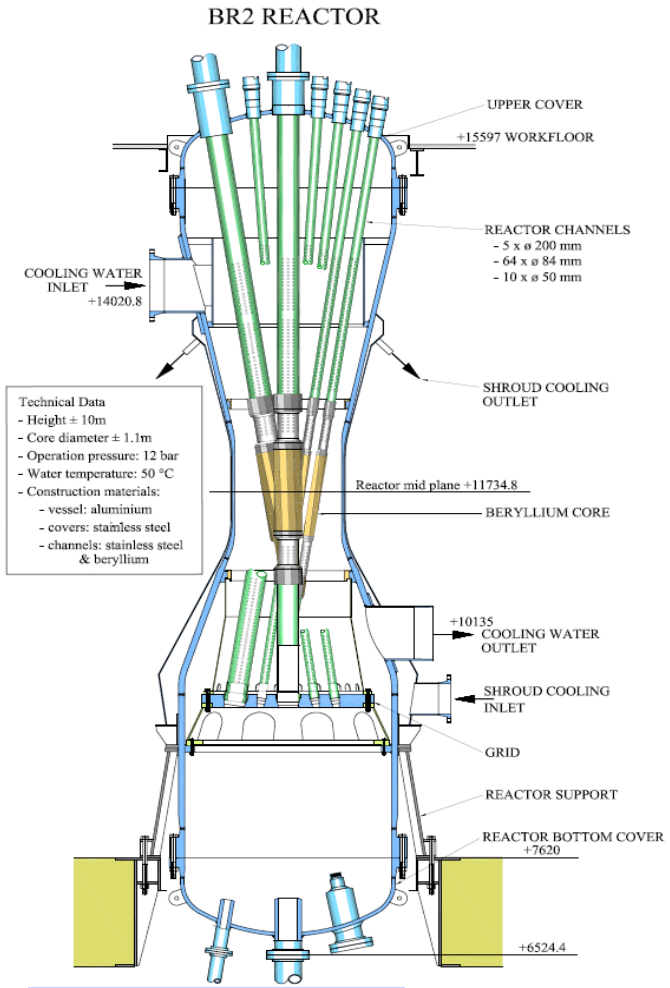
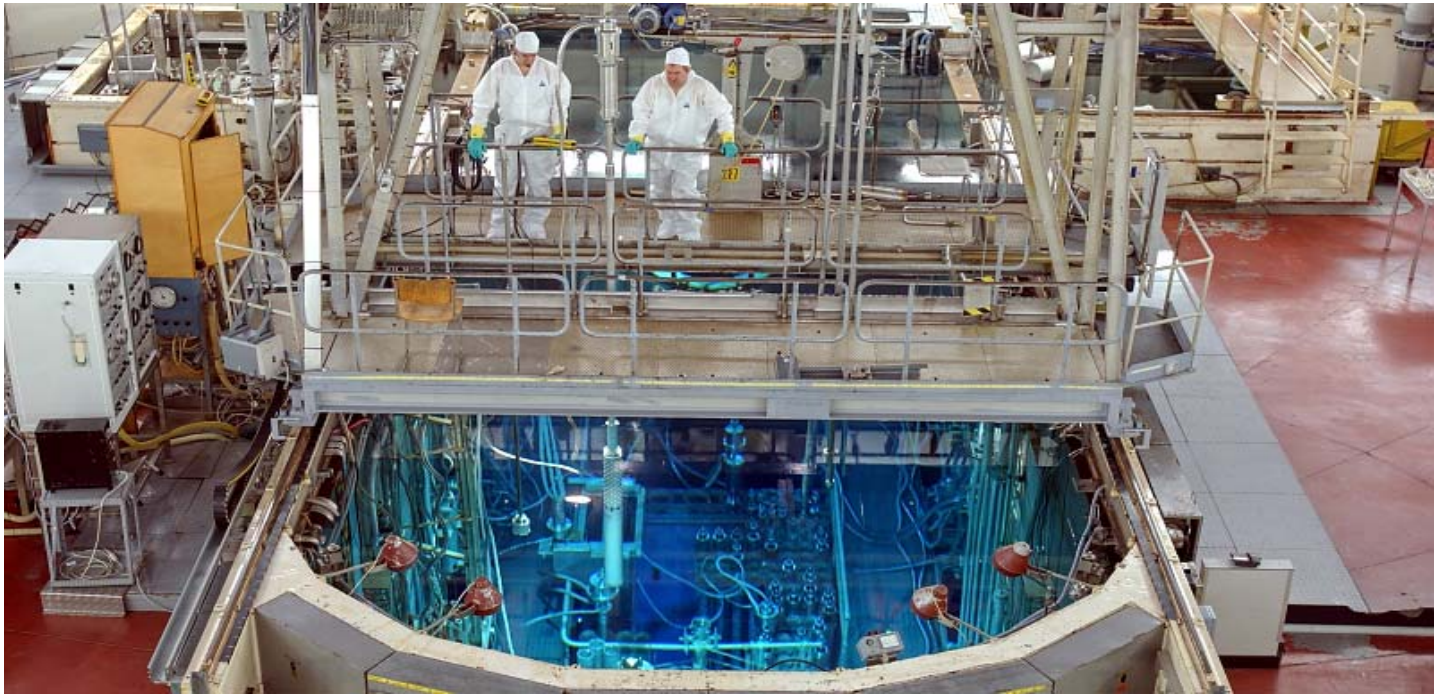
The BR2 Reactor



- The BR2 reactor is a major player in the production of radioisotopes worldwide:
  - High neutron fluxes (thermal up to e+15 n/cm².s and fast up to 6 e+14 n/cm².s), large irradiation volumes, very flexible, … but limited by its operating regime (140 – 190 operating days per year).



100 MW

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Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

Mo-99/Tc-99m Generator

- The worldwide supply of Mo-99 relies on a **limited number** of research reactors and processing facilities.
- Its production is **essential for nuclear medicine** as Tc-99m, obtained from Mo-99/Tc-99m generators, is used in about **80% of diagnostic** nuclear imaging procedures.
- These applications represent approximately **30 million** examinations worldwide per year.
- Therefore, a weekly Mo-99 production of about **9.000 Ci '6-day'** calibrated is required to supply **North America** (53%), **Europe** (23%), **Asia** (20%) and the **rest of the world** (4%).
- Given the short half-lives of Mo-99 (66 hours) and its daughter Tc-99m (6 hours), a **regular supply of Mo-99/Tc-99m** generators to hospitals or central radiopharmacies is required.

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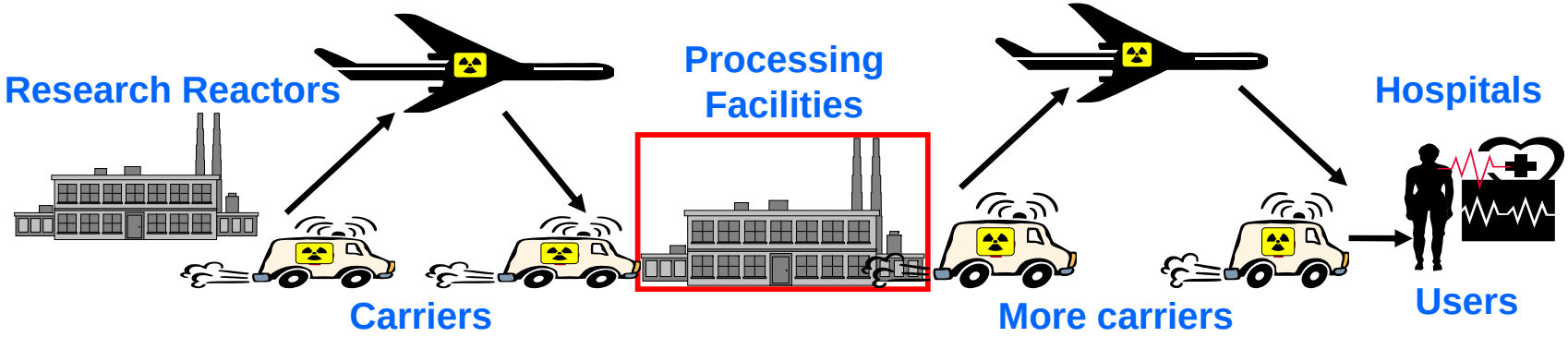
Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

- The **supply chain** consists of :
  - uranium **target manufacturers**
  - **research reactors** for target irradiation
  - **processing facilities** to dissolve the irradiated targets and extract Mo-99
  - Mo-99/Tc-99m **generators manufacturers**
  - **radiopharmacies** to elute Tc-99m from the generators and prepare radiopharmaceutical doses to be injected to the patients for diagnosis
  - **transport companies** to ship the produced activities to the different participants involved in the supply chain.

From the producers to the users … No time to lose …



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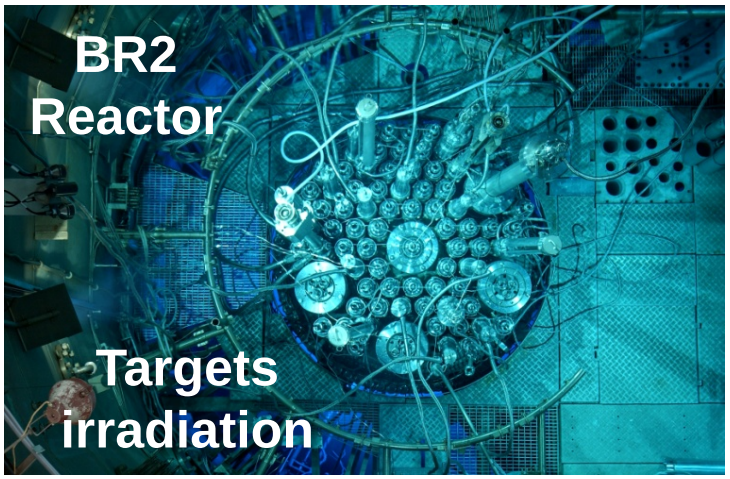
Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

Targets manufacture



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Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

OPERATIONS INVOLVED	TIME SCALE	EVOLUTION OF THE MO-99 ACTIVITY
IRRADIATION IN THE REACTOR	150 HOURS	1000 Ci Mo-99 'EOI'/ target
UNLOADING FROM THE REACTOR …	12 HOURS	
LOADING CONTAINERS	4 HOURS	
SHIPMENT CONTAINERS	4 HOURS	810 Ci / target
PROCESSING IRRADIATED TARGETS	12 HOURS	640 Ci bulk Mo-99
SHIPMENT BULK Mo-99	12 HOURS	
MANUFACTURE and DELIVERY GENERATORS	12 HOURS	500 Ci Mo-99
USE IN HOSPITALS	120 HOURS	120 Ci Mo-99 '6-DAY'

Production of Mo-99/Tc-99m in the BR2 Reactor

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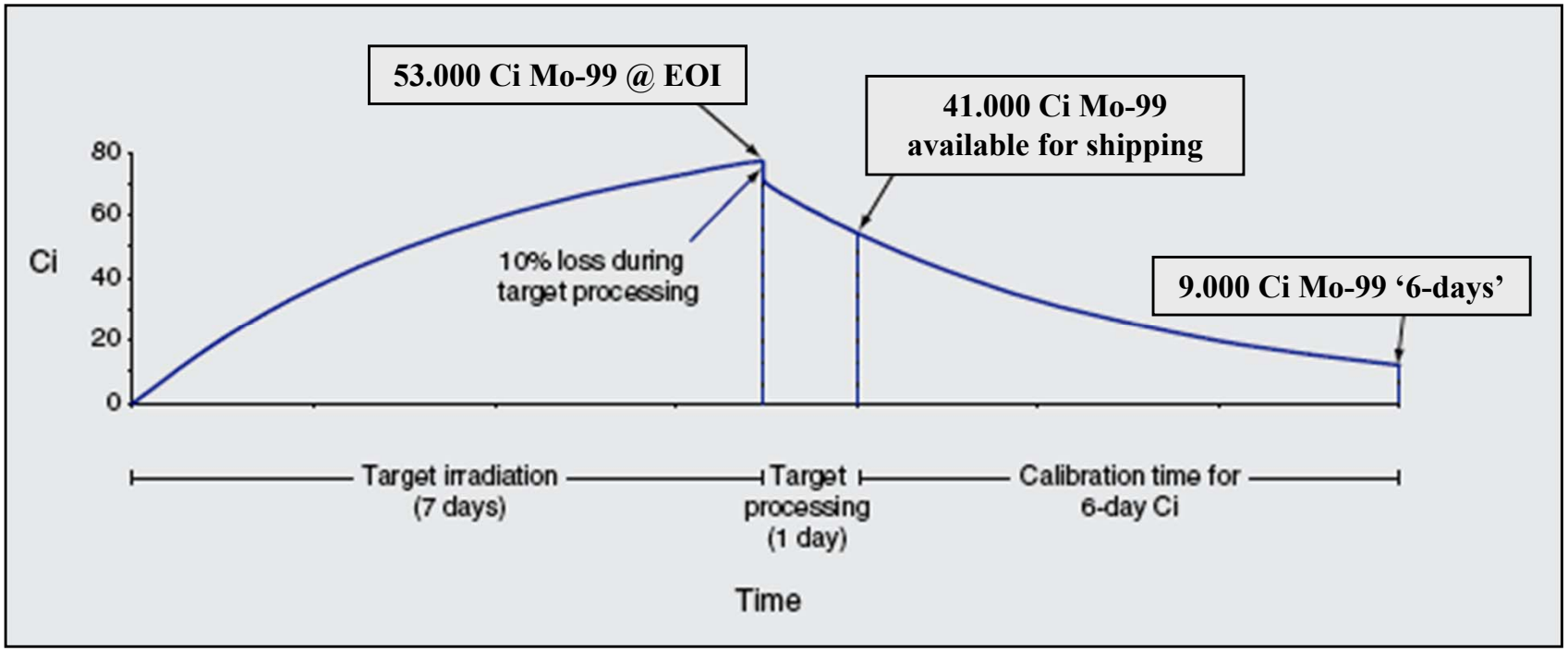
Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

The **"6-day Ci"** is a unit of measure that takes the Mo-99 decay rate into account, the losses during shipments and processing, and represents an average amount of Mo-99 that would be available for use 6 days after processing

Mo-99 Global Demand

About 9.000 Ci Mo-99 '6-day' calibrated per week !!!

Or about 468.000 Ci Mo-99 '6-days' calibrated per year !!!



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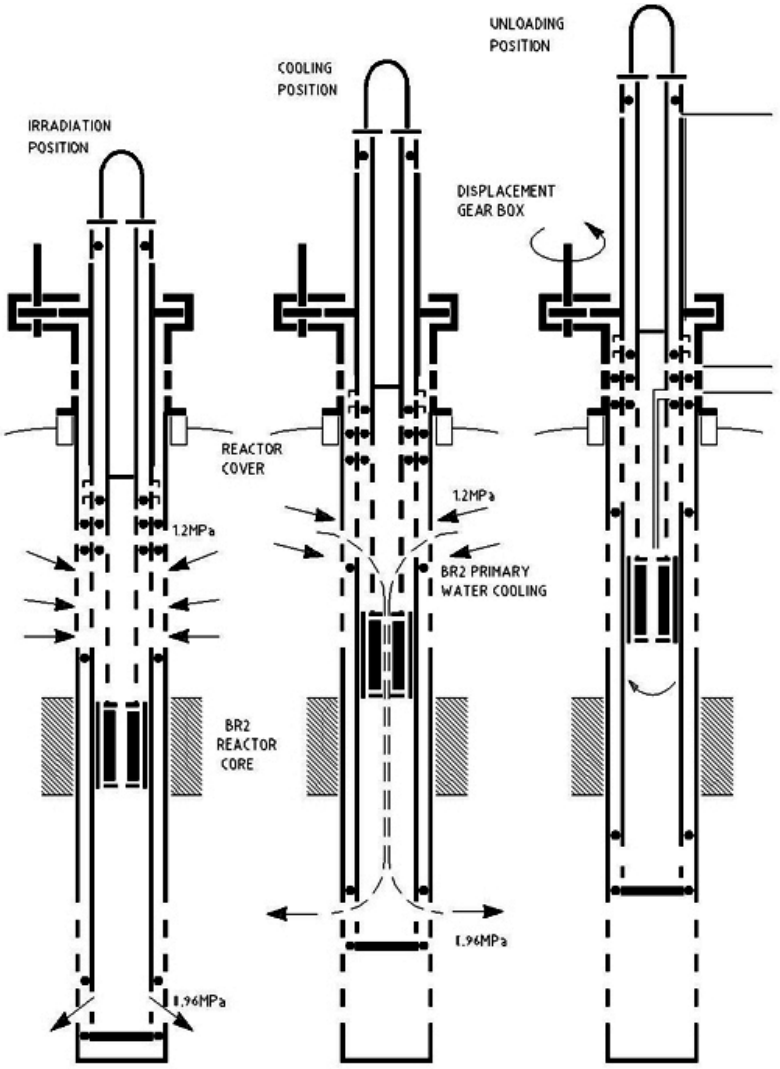
Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

- BR2 has the **largest irradiation capacity** in the world for the production of Mo-99 !!!
- The **6 PRF** (Primary Reloadable water-cooled device for Fissile targets) **irradiation devices** are routinely loaded in BR2 reflector channels.
- They provide a total simultaneous irradiation capacity of **75 HEU targets**.
- These targets are cooled by the **primary reactor water** and loaded/unloaded during the reactor operation.
- Irradiation capacity = **65%** of the global Mo-99 demand in peak, i.e. **25%** in average.



Irradiation Devices

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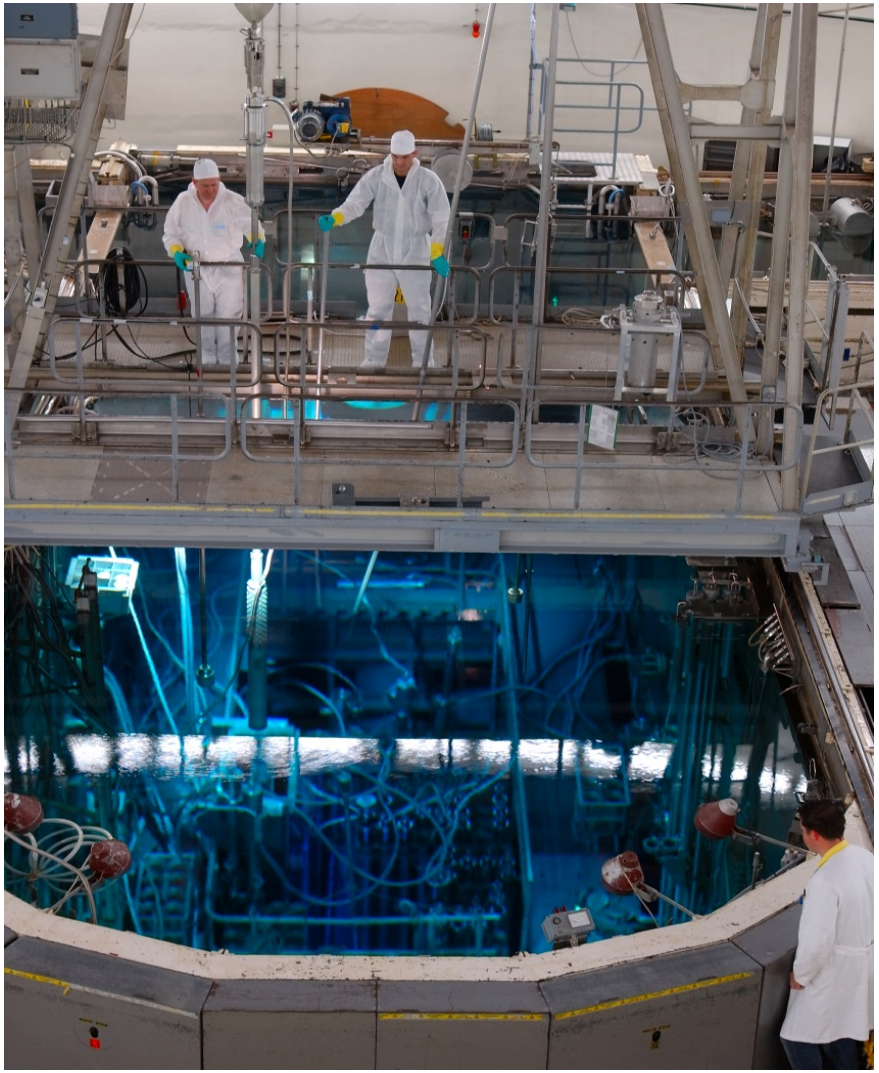
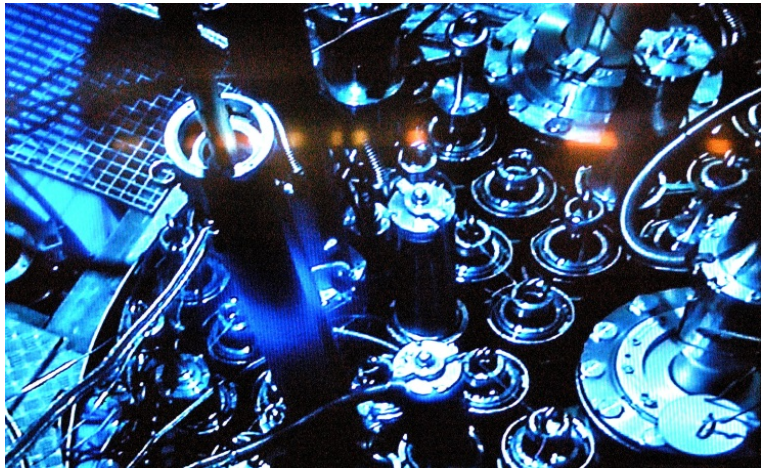
Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

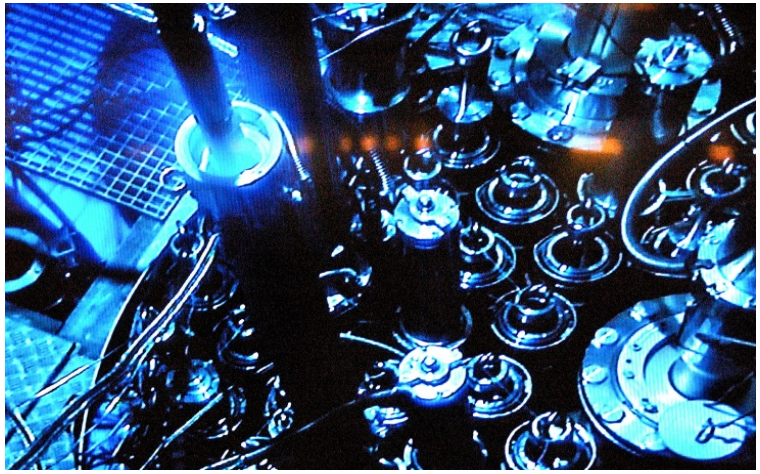
From U-235

To Mo-99





Targets unloading



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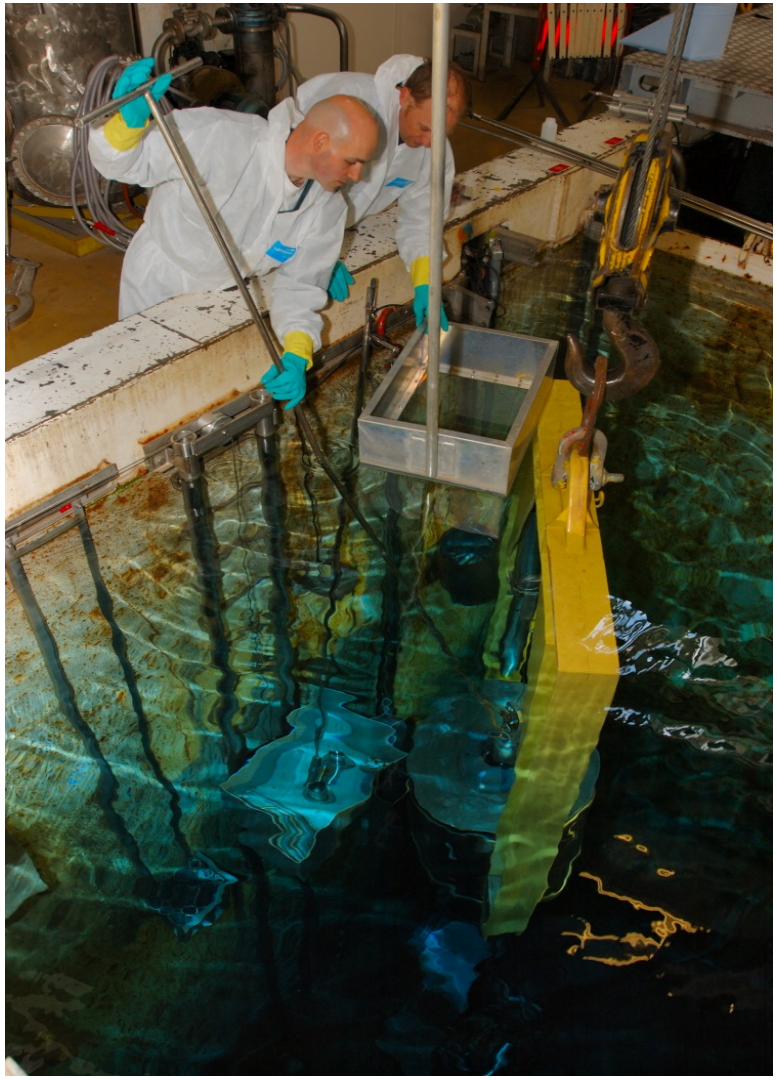
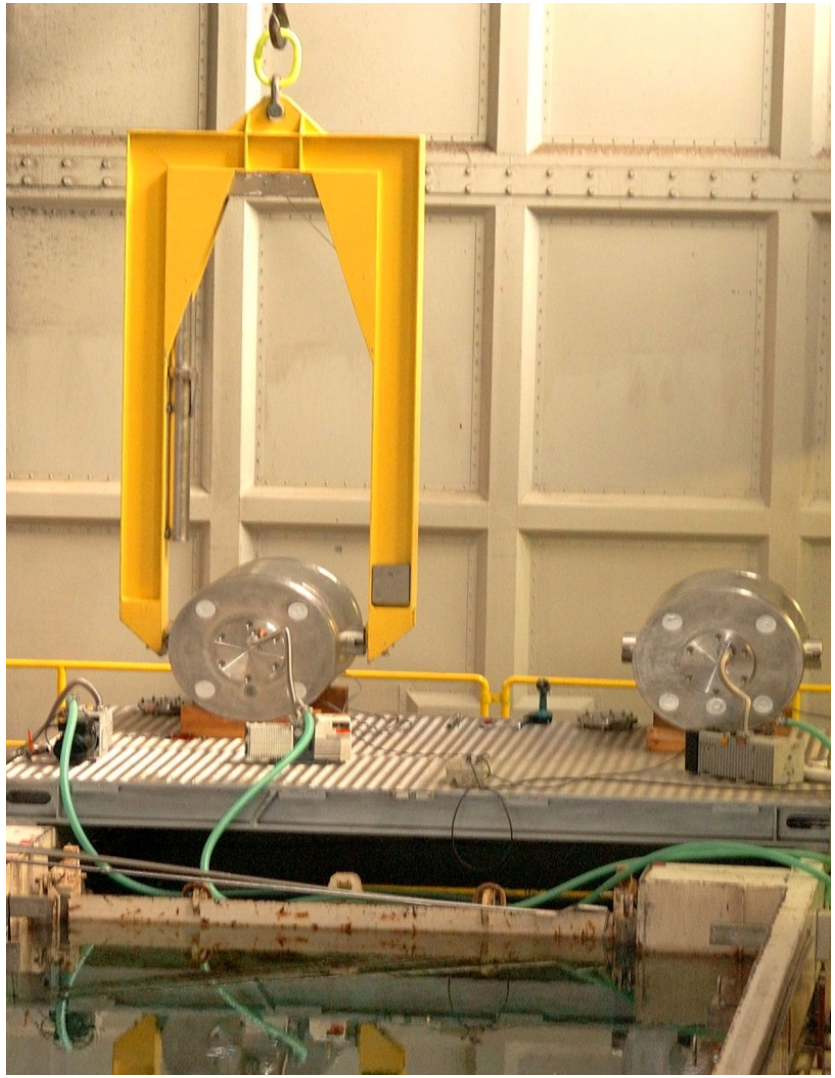
From U-235

To Mo-99





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Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

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Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

From U-235

To Mo-99

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Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

From U-235

To Mo-99

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Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m

From U-235

To Mo-99

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From U-235

To Mo-99

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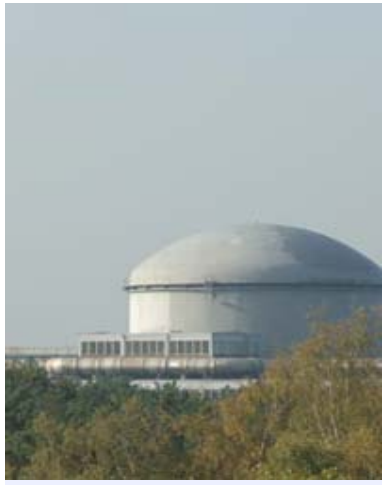

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- The BR2 reactor is member of the **AIPES** Reactors & Isotopes Working Group which has the task to secure the global supply of Mo-99.
  - **Ten reactors** are represented in the AIPES R&I WG: **BR2** (Belgium), **HFR** (Netherlands), **SAFARI** (South Africa), **MARIA** (Poland), **LVR-15** (Czech Republic), **OPAL** (Australia), **RA-3** (Argentina), **FRM-II** (Germany; currently not irradiating targets for Mo-99), **NRU** (Canada; no routine production from November 2016), **OSIRIS** (France; shutdown) and **JHR** (France; under construction).
  - **Six processors** are represented in the AIPES R&I WG: **IRE** (Belgium), **MALLINCKRODT** (NL), **ANSTO Health** (Australia), **NTP** (South Africa), **CNEA** (Argentina) and **CNL/NORDION** (Canada; no routine production from November 2016).

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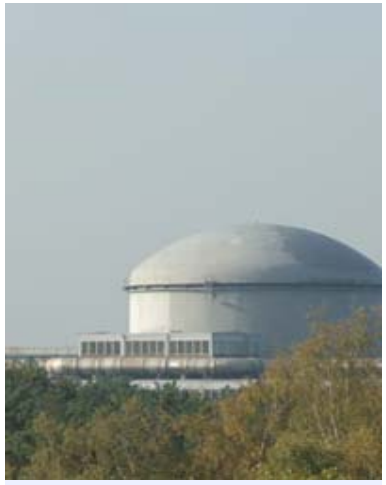
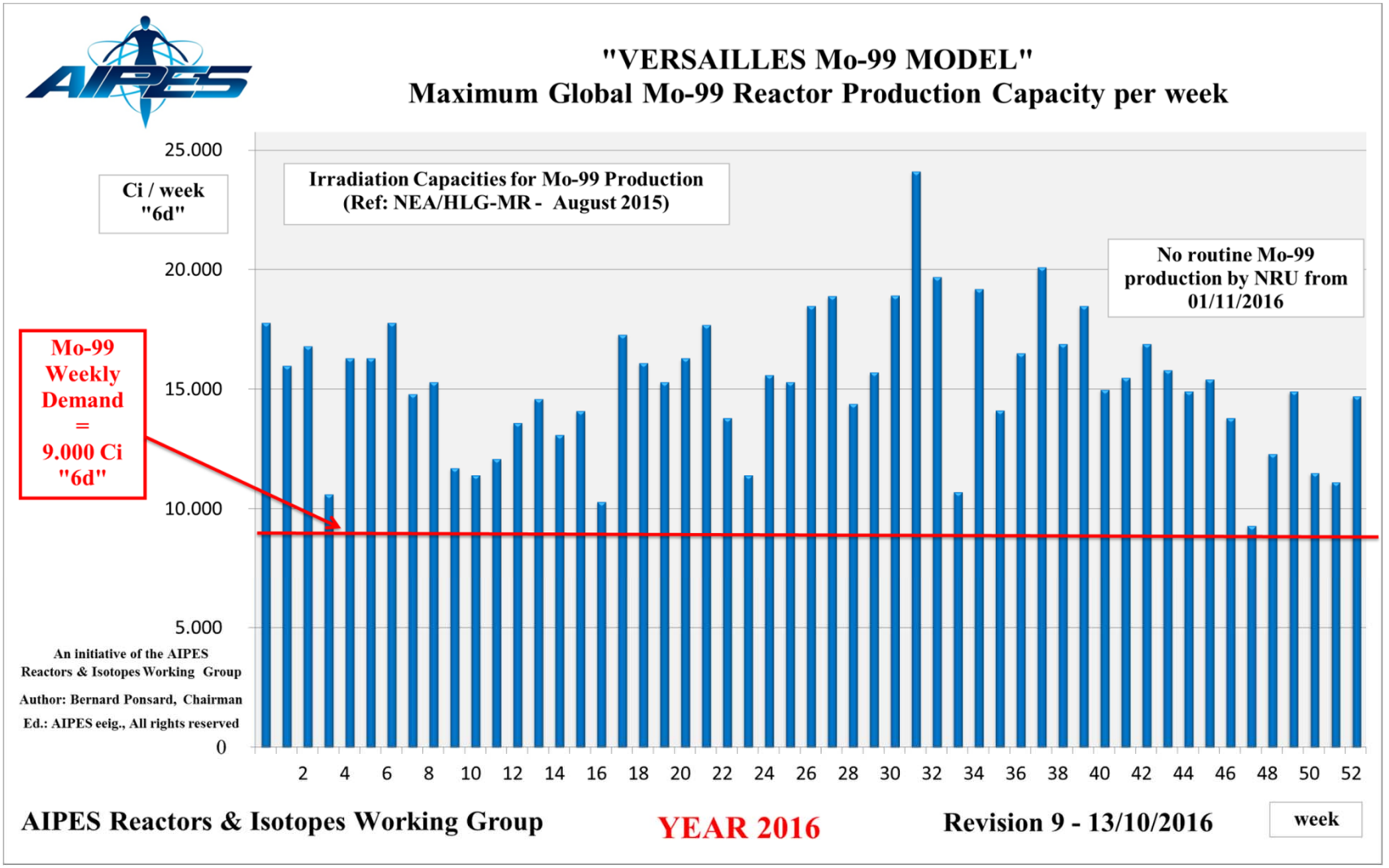
Radioisotopes for Diagnosis: Production of Mo-99/Tc-99m





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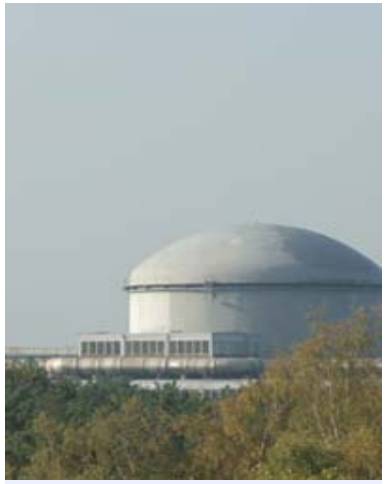
Radioisotopes for Therapy and Palliation: Production of Lu-177, Sm-153, …



- The **BR2 Reactor** is not only producing Mo-99.
- **Dedicated irradiation devices** allow the routine production of various radioisotopes for **therapy** and **palliation treatments**:
  - I-131 and Xe-133 in the PRF irradiation devices (... Mo-99)
  - Ir-192, Sr-89, W-188/Re-188, … in RA25 irradiation baskets
  - Lu-177, Re-186, Sm-153, Er-169, Y-90, …in DG thimbles
  - Sn-117m, Cu-67, ... in RH15 irradiation baskets
- Currently, SCK is **not performing any chemical process** on target material irradiated in the BR2 reactor in the frame of the production of radiopharmaceuticals.
- **Special efforts** are expected to be made in the near future by SCK to develop the production of new radioisotopes, including **chemical processing** for some of those.

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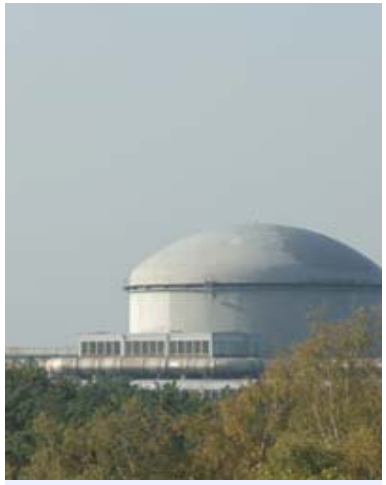
Radioisotopes for Therapy and Palliation: Production of Lu-177, Sm-153, …

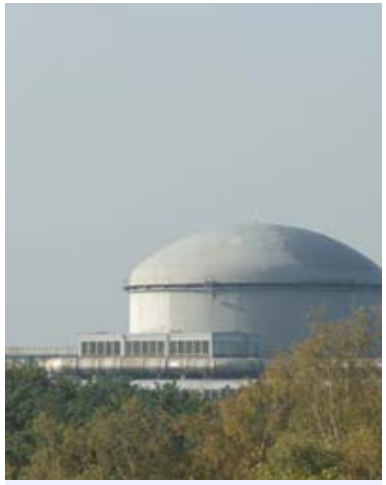


- The BR2 reactor is routinely producing **Ir-192** ($T_{1/2}$=74.2 d), for curietherapy and several radioisotopes for metastatic bone pain palliation as **Re-186** ($T_{1/2}$=3.8 d), **Sm-153** ($T_{1/2}$=46.7 h), **Y-90** ($T_{1/2}$=64 h) and **Sr-89** ($T_{1/2}$=50.5 d).

- The BR2 reactor is also routinely producing the very attractive **Lu-177** ($T_{1/2}$=6.7 d) for targeted therapy of small tumours (prostate, …) and metastatic bone pain palliation by both direct and indirect routes.
  - **Direct route**: $^{176}Lu\ (n_{th}, \gamma)\ ^{177}Lu$; yield = 35 Ci/mg at "EOI"
  - **Indirect route**: $^{176}Yb\ (n_{th}, \gamma)\ ^{177}Yb \rightarrow\ ^{177}Lu$;
    yield = 110 Ci/mg at "EOI"

- Furthermore, reactor operators have collaborated on several occasions to secure the supply of additional radioisotopes that have become more interesting such as **W-188/Re-188** and **Sn-117m** (**$T_{1/2}$**= 13.6 d), especially with the HFIR reactor at Oak Ridge National Laboratory (ORNL, USA).

Radioisotopes for Industrial Applications: Production of Ir-192, …



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- The BR2 reactor is **not only** producing medical radioisotopes.
- BR2 is a major producer of **Ir-192** worldwide.
- **Ir-192** is one of the most widely used sealed sources for Non Destructive Testing (NDT) applications and is produced by $^{191}Ir(n,\gamma)^{192}Ir$ reaction on natural or Ir-191 enriched iridium discs.
- **Ir-192** decays with a half-life of **74.2 days** to stable Pt-192 and emits **beta particles** at a maximum energy of 672 keV (46%) and **gamma rays** at energies of 604, 468 and 308 keV.
- BR2 is able to achieve high Ir-192 specific activities in the range of **500** to **1500 Ci/g at "EOI"** in a full cycle irradiation of 21 to 28 days.

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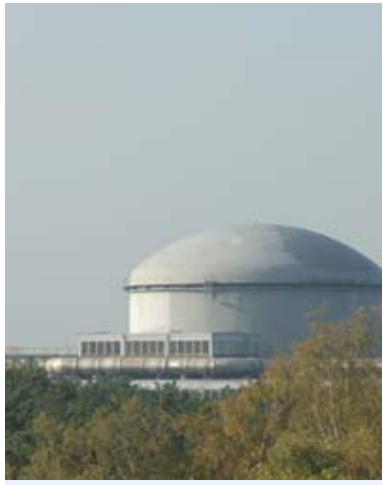
Radioisotopes for Industrial Applications: Production of Ir-192, …



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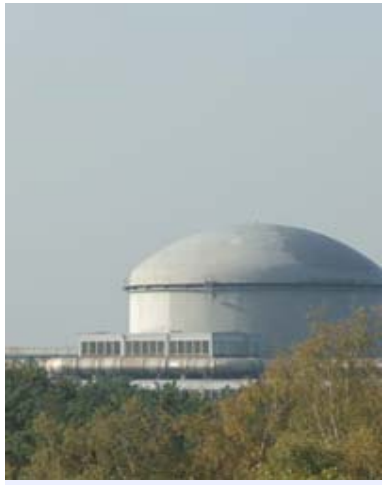

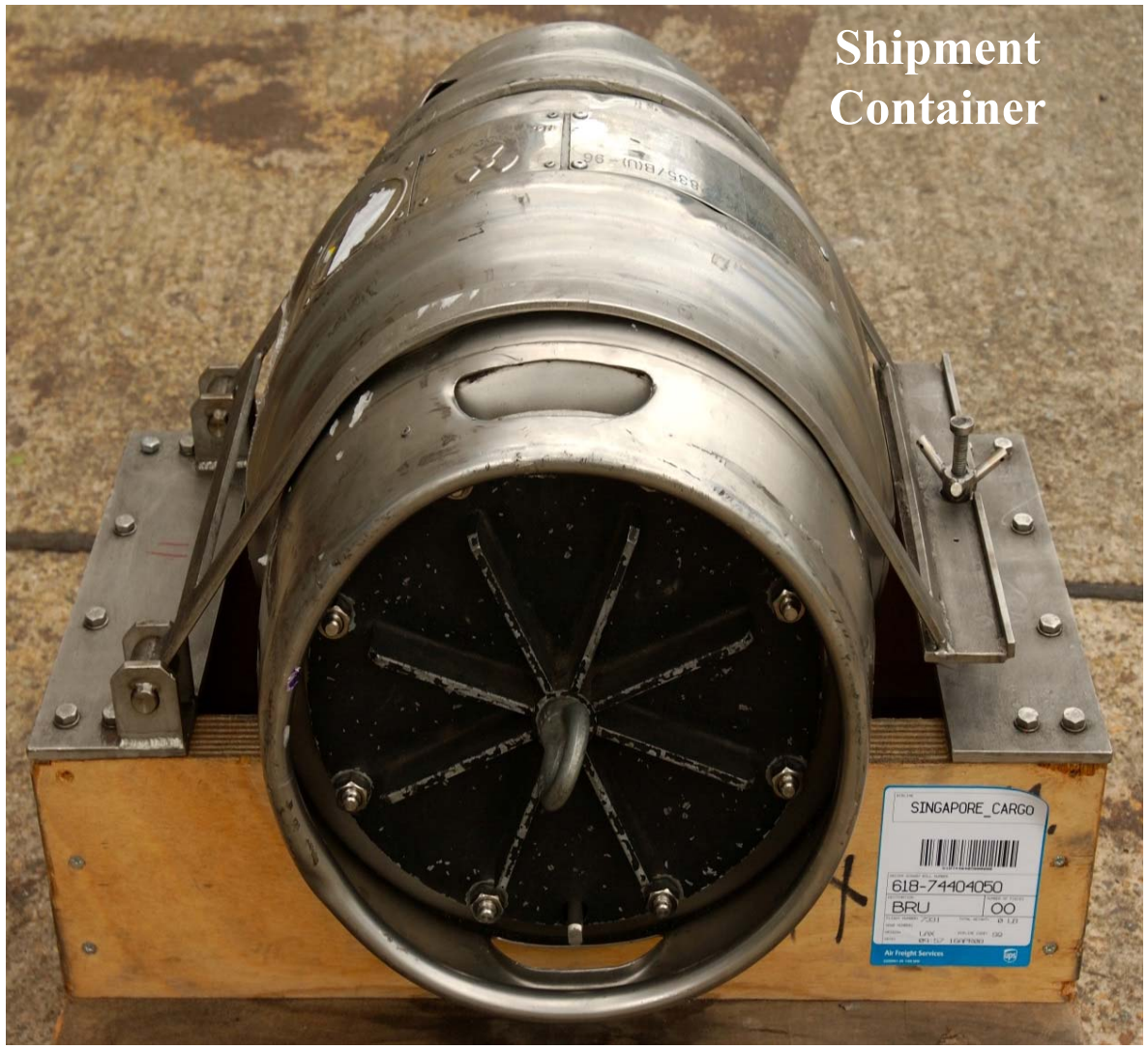

10 kCi ^{192}Ir

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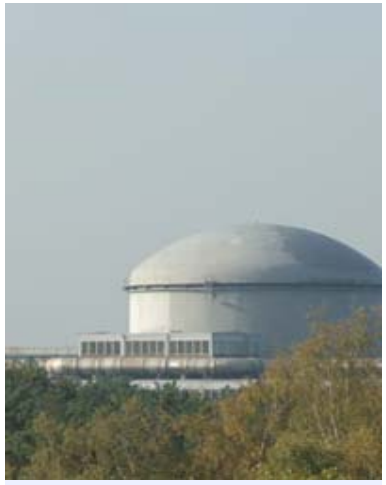
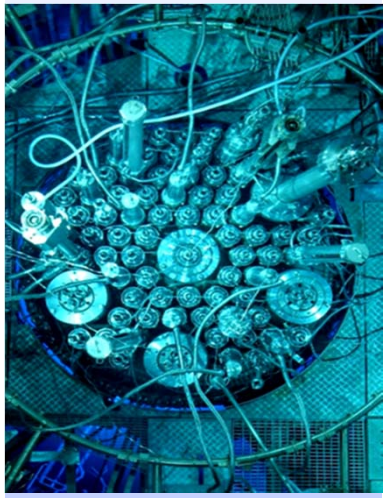
Radioisotopes for Industrial Applications: Production of Se-75, …





- The production of **Se-75** (γ rays : 66 – 401 keV) – in complementarity to Ir-192 (γ rays : 308 – 604 keV) – for NDT applications is under development.
- Several irradiations have been already performed in the BR2 reactor and provided **encouraging results**.
- The availability of **very high thermal neutron fluxes** (in the range of e+15 n/cm².s) and the use of highly (98%) **enriched Se-74** target material (very high cost price) are mandatory for this kind of production.
- **Se-75** versus Ir-192 has **several advantages** as increased contrast and image quality, lesser radiation for users, softer gamma rays, smaller steel wall thickness investigations, …

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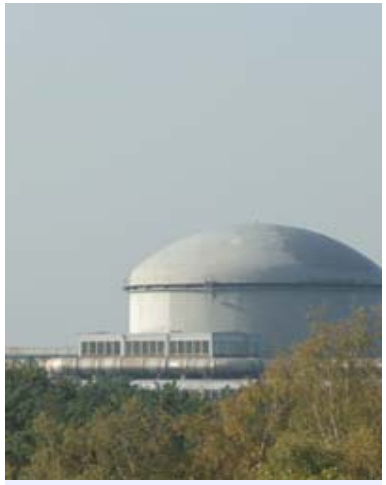
Conclusions



- The **BR2 reactor** is a **major facility** for the global production of radioisotopes for nuclear medicine and industry.
- Serious efforts have been made to perform all BR2's commercial activities (production of 'Radioisotopes' and 'Neutron Transmutation Doped Silicon') in accordance with a **'Quality System'** that has been certified to the requirements of the "**EN ISO 9001: 2008** – Quality Systems – Model for **Quality Assurance** in production, installation and servicing".
- The production of several new radioisotopes is currently investigated as the β^- emitters **Ho-166** and **Y-90** microspheres for liver cancer treatment.
- The production of radioisotopes for **alpha therapy** is also under investigation (**Ra-223**, …).

PONSARD B.

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