Targetry Development at HZDR: Radiometal Production with the TR-Flex Cyclotron

HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

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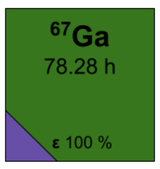
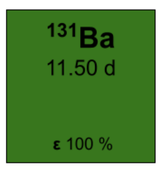
Produced Radionuclides and their Uses

SPECT Radionuclides:

Diagnostics through Single Photon Emission Computed Tomography (SPECT).



γ-lines:
93.3 keV (39 %),
185 keV (21 %),
300 keV (17 %),
i.a.
MAE & CE:
0.99 keV (168 %, AU L),
7.5 keV (61 %, AU K),
84 keV (28 %, CE K),
i.a.

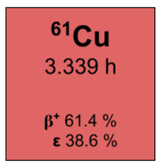


γ-lines:
496 keV (48 %),
124 keV (30 %),
216 keV (20 %),
371 keV (14 %),
i.a.

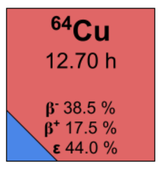
^{131}Ba ✚ ^{223}Ra (α-emitter)
Theranostic Matched Pair

PET Radionuclides:

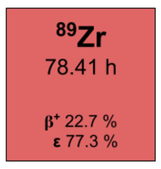
The emitted radiation (β^+-particles, i.e. 511 keV γ-rays) is used for **diagnostics** through Positron Emission Tomography (PET).



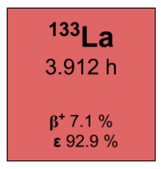
β^+-emission:
$E_{\beta+,mean}$= **499 keV**
γ-lines:
283 keV (12.7 %),
656 keV (10.4 %),
i.a.



β^+-emission:
$E_{\beta+,mean}$= **278 keV**
$E_{\beta-,mean}$= 190 keV
γ-lines:
1346 keV (0.472 %)



β^+-emission:
$E_{\beta+,mean}$= **396 keV**
γ-lines:
909 keV (99 %),
1713 keV (0.75 %)

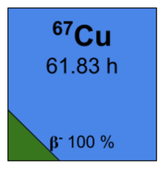


β^+-emission:
$E_{\beta+,mean}$= **463 keV**
γ-lines:
279 keV (2.4 %),
302 keV (1.6 %),
290 keV (1.4 %),
i.a.

$^{61/64}$Cu ✚ ^{67}Cu
Perfect Theranostic Matched Pair

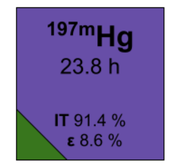
Therapeutic Radionuclides:

Radionuclides that can be used for **therapy** *via* the emission of electrons, i.a. β^--particles, conversion electrons (CE) or Meitner-Auger electrons (MAE).

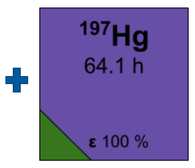


β^--emission:
$E_{\beta-,mean}$= **141 keV**
γ-lines:
185 keV (49 %),
93.3 keV (16 %),
i.a.

MAE & CE:
3.7 keV (78 %, AU L),
8.5 keV (50 %, AU K),
i.a.
γ-lines:
480 keV (1.5%),
Minor γ-lines



MAE & CE:
7.6 keV (71 %, AU L),
150 keV (50 %, CE L),
119 keV (33 %, CE L),
82 keV (20 %, CE K),
i.a.
γ-lines:
134 keV (34%),
279 keV (6.1 %)



MAE & CE:
7.4 keV (119 %, AU L),
63 keV (60 %, CE L),
74 keV (33 %, CE M),
i.a.
γ-lines:
77 keV (19 %)

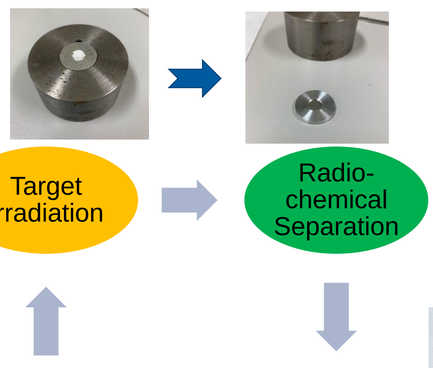
^{133}La ✚ ^{135}La or ^{225}Ac (α-emitter)
(Perfect) Theranostic Matched Pair

Radionuclide properties from IAEA Nuclear Data Services [1].

Irradiation Conditions and Simulations

The Target Cycle:

Three different types of solid targets are used at the HZDR: metallic foils (for ^{89}Zr & $^{197(m)}$Hg), electroplated targets (for $^{61/64}$Cu, ^{67}Cu & ^{67}Ga) and powder targets (for ^{131}Ba & $^{133/135}$La). Due to the high costs of the enriched target materials, usually a recycling strategy is performed (exemption Y for ^{89}Zr, Cs for ^{131}Ba & Au for $^{197(m)}$Hg).

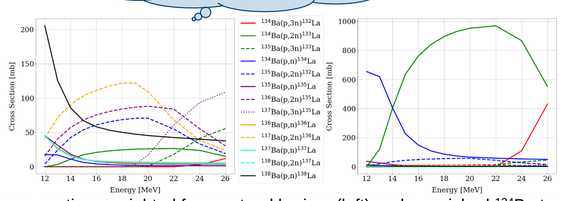


Electrodeposited ^{68}Zn target onto a gold backing for ^{67}Ga production.

Electrodeposited ^{70}Zn target onto a silver backing for ^{67}Cu production.

Au foil on aluminum backing for $^{197m/g}$Hg production.

Electrodeposited ^{62}Ni target onto a gold backing for ^{61}Cu production.



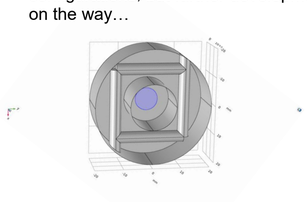
Proton induced cross sections weighted for a natural barium (left) and a enriched ^{134}Ba targets (right) [4].

The TR-Flex Cyclotron:

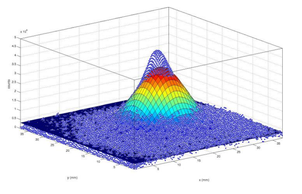
The target irradiations are performed at the TR-Flex Cyclotron, which features a proton energy of 16 – 30 MeV and a current of up to 300 µA.

TR-FLEX Cyclotron: irradiation beam. The solid target stations offers a 90° and a 30° configurations, but further development is on the way…

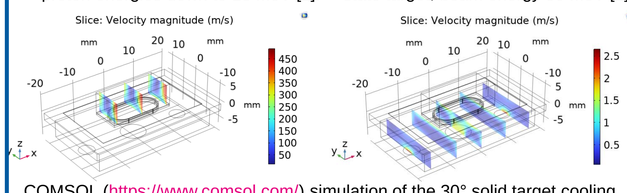
Solid target irradiation configurations: 90° and 30°. The tilted target configuration increases the irradiated area thus improving the cooling of the target.



In-house developed Aluminum degrader allows the irradiation with proton energies down to 13 MeV [2].



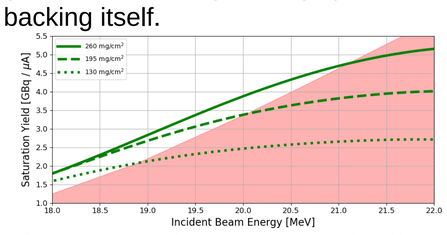
Autoradiographic measurement of an irradiated gold disk at the 90°-solid state target, beam energy 30 MeV [2].



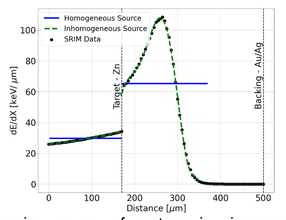
COMSOL (https://www.comsol.com/) simulation of the 30° solid target cooling. The target is cooled on the front with helium (left) and with water on the back (right). The velocity profile of the cooling fluids obtained from the simulation is shown.

Parameter Optimization – Simulations:

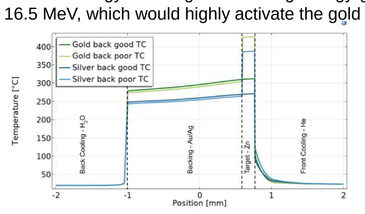
Simulations allow the optimization of the irradiation parameters, i.a. proton beam energy and current, to maximize the radionuclide production. Studies of the backing material are also performed to guarantee the target integrity as well as reducing the activation the backing itself.

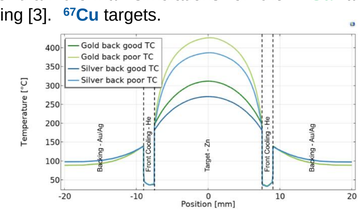


^{61}Cu saturation yield for proton irradiation of a ^{62}Ni target as a function of the incident beam energy. In red, the incident energy resulting in an exiting energy greater than 16.5 MeV, which would highly activate the gold backing [3].

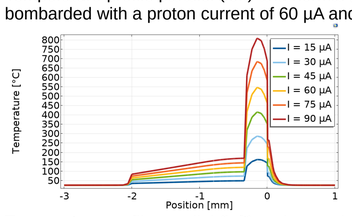


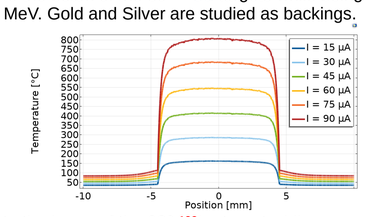
Stopping power of protons in zinc and gold, used as the heat source for the thermal simulations of the ^{67}Ga and ^{67}Cu targets.





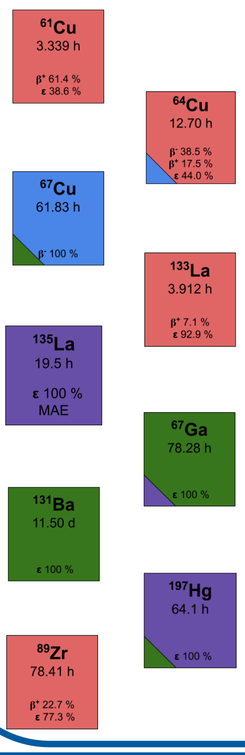
Temperature profile parallel (left) and normal (right) to the beam of the 30° ^{67}Cu targets while being bombarded with a proton current of 60 µA and 16.8 MeV. Gold and Silver are studied as backings.



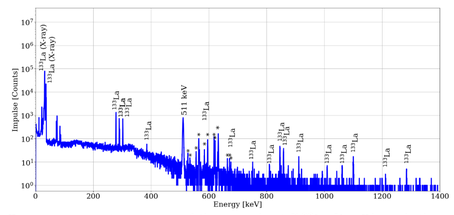


Temperature profile parallel (left) and normal (right) to the beam of the 90° ^{133}La target while being bombarded with 18.7 MeV protons and different currents.

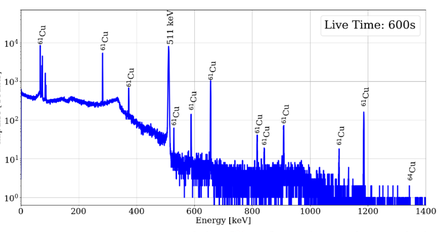
Yields and Product Characterization



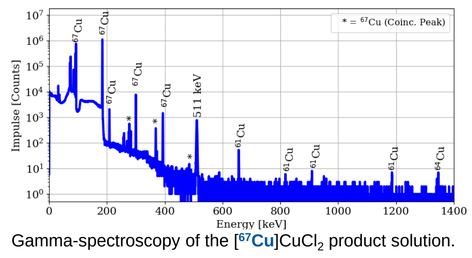
Nuclear Reaction	Irradiation Parameters	Typical Activities @EOP	Typical Saturation Yield @EOB
^{62}Ni(p,2n)^{61}Cu	20.8 – 18.7 MeV, 70 µA, 1 – 2 h	5 – 10 GBq	1300 MBq/µA [3]
^{64}Ni(p,n)^{64}Cu	13.5 MeV, 70 µA, 2 – 2.5 h	20 – 30 GBq	5000 MBq/µA [4]
^{70}Zn(p,α)^{67}Cu	16.8 MeV, 60 µA, 10 – 30 h (in 2/3 days)	400 – 1200 MBq	90 MBq/µA [5,6]
^{134}Ba(p,2n)^{133}La	18.7 MeV, 60 µA, 0.5 – 1 h	1 – 4 GBq	660 MBq/µA [7,8]
^{136}Ba(p,2n)^{135}La	18.7 MeV, 60 µA, 0.5 – 1 h	1 – 2 GBq	800 MBq/µA
^{68}Zn(p,2n)^{67}Ga	19 MeV, 35 µA, 1.5 – 2 h	600 – 1600 MBq	2600 MBq/µA [4]
^{133}Cs(p,3n)^{131}Ba	27.5 MeV, 20 µA, 2 - 4 h	150 – 250 MBq	1200 MBq/µA [4]
^{197}Au(p,n)$^{197m/g}$Hg	13 MeV, 45 µA, 1 – 3 h	250 / 300 MBq	100 / 215 MBq/µA
^{89}Y(p,n)^{89}Zr	11.0 MeV, 35 µA, 1h - 1.5 h	300 – 400 MBq	3000 MBq/µA



Gamma-spectroscopy of the product [^{133}La]$LaCl_3$ solution.



Gamma-spectroscopy of the [^{61}Cu]$CuCl_2$ product solution.



Gamma-spectroscopy of the [^{67}Cu]$CuCl_2$ product solution.

References:

[1] IAEA Nuclear Data Services, https://www-nds.iaea.org/, last accessed on 08.09.2023.
[2] Kreller, M.; Knieß, T.; Preusche, S. *Proceedings of the 22nd International Conf. on Cyclotrons and Their Applications* **2019**, 23-27.
[3] Brühlmann, S.A.; Walther, M.; Kopka, K.; Kreller, M. *EJNMMI radiopharm. chem.* **2024**, 9, 3.
[4] Kreller, M.; Brühlmann, S.A.; Knieß, T.; Kopka, K.; Walther, M. *Instruments* **2024**, 8, 10.
[5] Brühlmann, S.A.; Walther, M.; Kreller, M.; Reissig, F.; Pietzsch, H.-J.; Kniess, T.; Kopka, K. *Pharmaceuticals* **2023**, 16, 314.
[6] Brühlmann, S.A.; Walther, M.; Zhutova, N.; Kopka, K.; Kreller, M. *Radiochim. Acta.* **2025**, 10.1515/ract-2025-0083.
[7] Brühlmann, S.A.; Kreller, M.; Pietzsch, H.-J.; Kopka, K.; Mamat, C.; Walther, M.; Reissig, F. *Pharmaceuticals* **2022**, 15, 1167.
[8] Brühlmann, S.A.; Walther, M.; Blei, M.K.; Mamat, C.; Kopka, K.; Freudenberg R.; Kreller, M. *EJNMMI radiopharm. chem.* **2024** 9, 60.

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DRESDEN concept
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