

Production of Copper-64 via laser-driven proton acceleration exploiting Double-Layer Targets for therapeutic applications

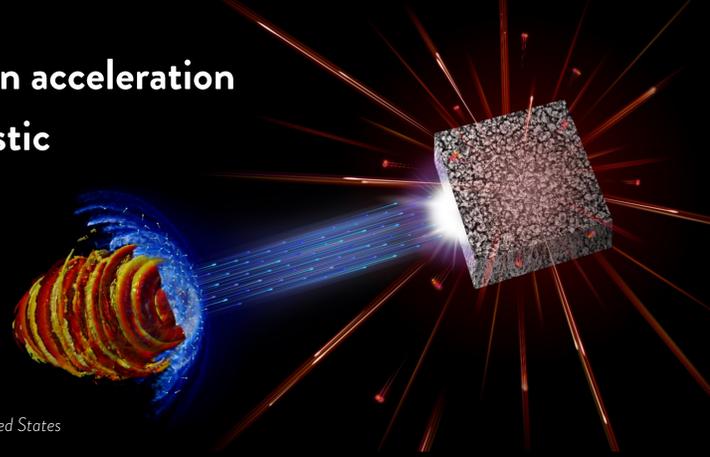
F. Mirani¹, A. Maffini¹, A. C. Giovannelli^{1,2,3}, A. Formenti^{1,4} and M. Passoni¹

¹Department of Energy, Politecnico di Milano, Milano, Italy

²Center for Proton Therapy, Paul Scherrer Institute, Villigen, Switzerland

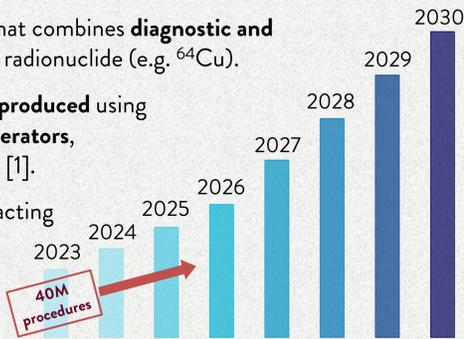
³Department of Physics, ETH-Hönggerberg, Zurich, Switzerland

⁴Accelerator Technology and Applied Physics Division, Lawrence Berkeley National Laboratory, Livermore, CA, United States



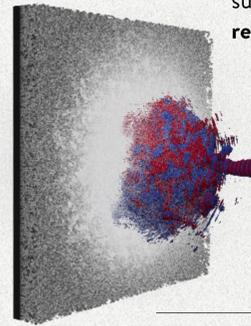
1 BACKGROUND

- Radioisotopes play a crucial role in nuclear medicine for both diagnostic and therapeutic purposes [1].
- The demand for radioisotopes will increase up to 5% annually in the next years.
- Radiotheranostics is a novel approach that combines diagnostic and therapeutic applications using the same radionuclide (e.g. ⁶⁴Cu).
- Radioisotopes for nuclear medicine are produced using nuclear reactors and conventional accelerators, mostly cyclotrons (3–30 MeV, 10s μA) [1].
- Laser-driven ion acceleration [2] is attracting interest as a promising alternative for radioisotope production (potentially compact & cost effective) [3].



2 MOTIVATIONS & GOALS

- Radioisotopes production is a demanding application in terms of particle fluxes and energies.
- Exploit advanced Double-Layer Targets (near-critical carbon foam layer [4] + dense substrate) to enhance the acceleration process and mitigate the laser requirements for challenging applications [5,6].

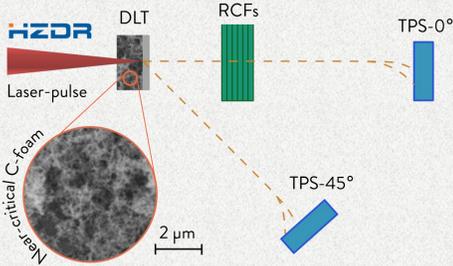


Starting from experimental data [7], assess the applicability of laser-driven proton sources to the production of ⁶⁴Cu for pre-clinical and clinical studies [8].

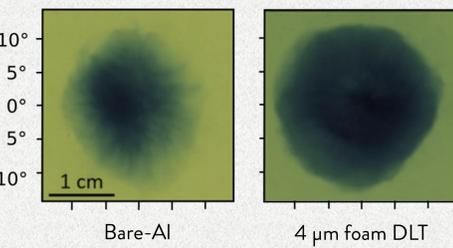
- ≈ 5 MBq for pre-clinical studies with mice.
- ~100 MBq for clinical studies.

3 LASER-DRIVEN PROTON ACCELERATION: COMPARISON BETWEEN EXPERIMENT & PIC

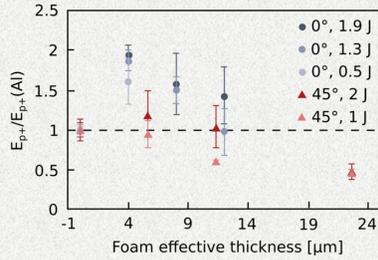
- Experimental scheme [7]*:



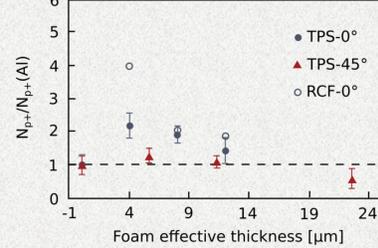
- Angular divergence from RCFs:



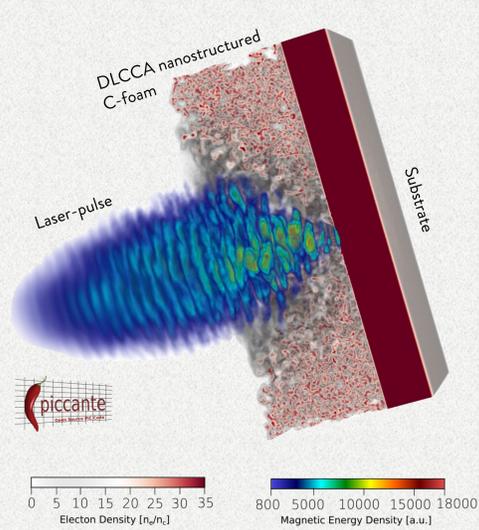
- Maximum energy enhancement:



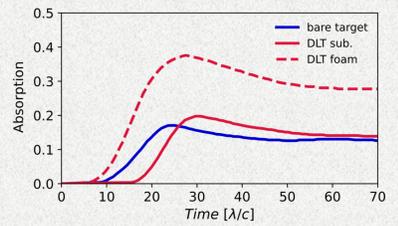
- Proton number enhancement:



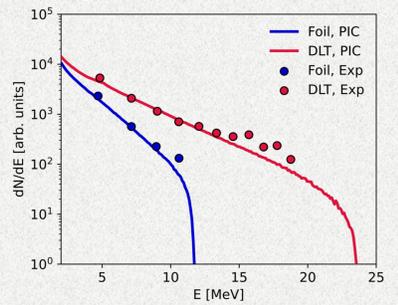
- 3D Particle-In-Cell snap-shot:



- 3D-PIC laser energy absorption:



- Comparison between PIC & RCF:

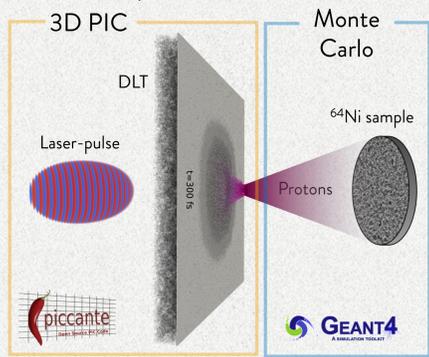


* Laser parameters: 150 TW laser power, 30 fs pulse duration, 2.8 μm FWHM focal spot size, 16 normalized laser intensity (a₀), normal incidence to the target surface.
Target parameters: 1 n_c average density C-foam, 1.5 μm Al-substrate thickness.

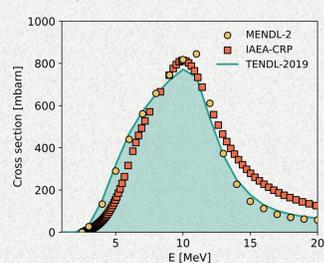
- Energy enhancement of ~2 for the maximum energy (11.6 → 23.5 MeV) and 2.2 for the number of accelerated protons.
- Agreement between experimental and PIC results. → Input for ⁶⁴Cu activity estimation.

4 ⁶⁴Cu ACTIVITY WITH A 150 TW LASER

- ⁶⁴Cu production scheme:



- ⁶⁴Ni(p, n)⁶⁴Cu cross section (σ):

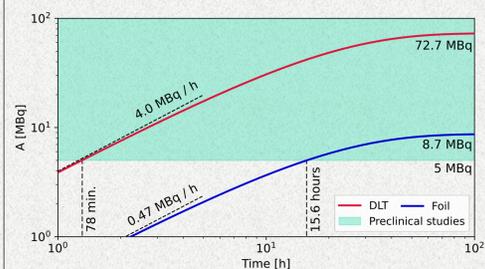


- Production yield of ⁶⁴Cu (Y) retrieved with Monte Carlo for both single-layer target and DLT.

- Activity (A) during irradiation (t):
 $A = RR \cdot N_p \cdot Y \cdot (1 - e^{-\lambda t})$ *

- 78 min. irradiation required with DLTs and 150 TW laser for pre-clinical studies.

* Repetition rate RR = 10 Hz, Number of protons per shot N_p = 2.6 × 10¹⁰, Decay constant λ = 0.055 h⁻¹



5 ⁶⁴Cu ACTIVITY ESTIMATION WITH MODEL

- Analytical formula for production yield of ⁶⁴Cu in a semi-infinite converter:

$$Y = \frac{N_{Cu}}{N_p} = \frac{N_{Av}}{M} \rho \int_0^\infty f(E_p) \int_0^{E_p} \frac{\sigma(E)}{S_p(E)} dE dE_p \approx Y_{max} \exp\left(\frac{\omega^2 - 4E_0 T_e}{T_e^2}\right)$$

* ...with some approx. & model presented in []...

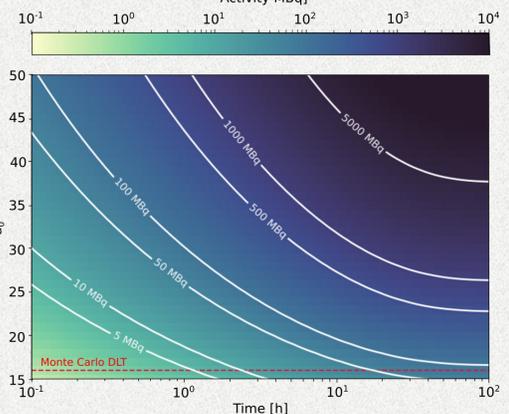
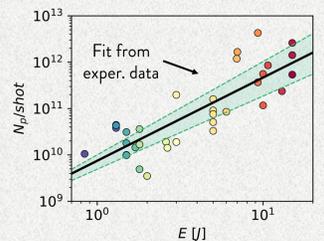
- Retrieve A as a function of the irradiation time and a₀ between 15 – 50 (0.7 – 17.5 J).

- For a₀ = 20 – 50:
✓ pre-clinical studies achievable in minutes irradiation;
✓ clinical studies achievable in ~1 hour irradiation or more.

- Rep. rate = 10 Hz kept fixed. → Advances in targetry required.

* a/s ~ Gaussian function, f ~ exponential function of temperature T_p, electron temperature T_e ~ T_p → Y_{max} = 2.0 × 10⁻³, ω = 4.38 MeV, E₀ = 10.25 MeV

- Number of protons:



7 REFERENCES

[1] IAEA. Copper-64 radiopharmaceuticals: Production, quality control and clinical applications. No. 7 in radioisotopes and radiopharmaceuticals series. Vienna (2022).
[2] A. Macchi, et al. Rev Mod Phys 85.2 (2013): 751.
[3] Z. Sun. AIP Adv. 11.4 (2021).
[4] A. Maffini, et al. Appl. Surf. Sci. 599 (2022): 153859.
[5] M. Passoni, et al. PPCF 62.1 (2019): 014022.
[6] F. Mirani, et al. Phys. Rev. Appl. 19.4 (2023): 044020.
[7] I. Prencipe, et al. New J. Phys. 23.9 (2021): 093015.
[8] A. Maffini, et al. Front. Phys. 11 (2023): 1223023.

8 CONCLUSIONS

- Laser-driven proton sources can be adequate to produce ⁶⁴Cu isotopes for pre-clinical studies.
- To this aim 100s TW – PW class lasers and advanced DLTs are required.
- Advancing target delivery system and laser technology could unlock their use for clinical purposes.

ACKNOWLEDGEMENTS & CONTACTS



To the publication...



www.ensure.polimi.it

francesco.mirani@polimi.it