IAEA RADIOISOTOPES AND RADIOPHARMACEUTICALS REPORTS No. 2

Cyclotron Based Production of Technetium-99m

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CONTENTS

1. INTRODUCTION

- Efforts and studies to investigate alternative production routes of molybdenum-99 (99Mo) and technetium-99m (99mTc) are ongoing all over the world. The direct production of 99mTc using accelerators is one of the proposed alternatives that utilizes the 100Mo(p,2n)99mTc reaction on highly 100Mo-enriched target material. A Coordinated Research Project (CRP) on Accelerator-based Alternatives to Non-HEU Production of 99Mo/99mTc was initiated with the aim of developing an alternative direct method of production of 99mTc using dedicated high current cyclotrons.

Usable quantities of 99mTc can be produced by the 100Mo(p,2n)99mTc reaction, which has a peak in the cross-section at 15–16 MeV, well within the reach of many commercial cyclotrons. A higher current cyclotron has been used to produce 350 GBq (>9 Ci) of 99mTc, which could supply a large metropolitan area (18 MeV protons, 250μA, 6 h irradiation).

Although an exact estimate is probably not possible at this time, rough estimates put the cost per MBq at about the same level for both generator and direct production methods

2. NUCLEAR DATA AND FACILITES

- 100Mo(p,2n)99mTc
- 100Mo(p,x)99Mo
- 100Mo(d,3n)99mTc
- 100Mo(d,x)99Mo
- 98Mo(d,n)99mTc
- 98Mo(d,p)99Mo
- 98Mo(p,γ)99mTc
- 100Mo(p,2p)99Nb → 99Mo
- 97Mo(d,γ)99mTc
- 100Mo(γ,n)99Mo
- 96Mo(α,p)99mTc
- 97Mo(α,2p)99Mo

The final quality of accelerator produced 99mTc depends on different parameters such as the isotopic composition of the Mo target material, the bombarding proton energy and intensity, the target thickness and the irradiation time. Moreover, the final composition of the produced material is also dependent on post-irradiation processing methods and times (target transportation and chemistry, separation technique of technetium and radio labelling).

IRRADIATION FACILITIES

Variable or fixed energy high current cyclotrons are the most suitable accelerators for the direct production of 99mTc utilizing the 100Mo(p,2n)99mTc reaction. A variety of cyclotrons available on the market or already deployed at research sites and in hospitals can be used for the direct production of 99mTc. The achievable yields, the specific activity and the purity level of the 99mTc are primarily determined by the cross-sections of the main and any side reactions involved in the whole production process.

TARGET MATERIAL REQUIREMENTS

- Levels of 100Mo enrichment at least as high as 99% are needed for good quality production of accelerator 99mTc. Any 100Mo enriched material will contain minor amounts of the other lower mass stable isotopes (92,94,95,96,97,98Mo) on which additional nuclear reactions are induced by the bombarding protons producing unwanted contaminating 9xTc, Ru, Nb and Zr radionuclides through separate reactions.
- long lived Tc isotopes -99gTc, 98Tc and 97gTc
- shorter lived Tc isotopes - 93gTc, 94mTc, 94gTc, 95mTc, 95gTc, 96mTc and 96gTc

TABLE 1. RECOMMENDED SPECIFICATIONS FOR ^{100}Mo TARGET

Isotope	Proposed % isotopic purity to maintain patient dose increase of ~10% compared with pure $^{99m}TcO_4$		
	≤20 MeV[a]	20–22 MeV[b]	22–24 MeV[c]
Mo-92	0.03	0.03	0.03
Mo-94	0.03	0.03	0.03
Mo-95	0.03	0.03	0.03
Mo-96	0.03	0.03	0.03
Mo-97	0.03	0.03	0.03
Mo-98	6.0	0.80	0.25

[a] Maximum increase in patient dose of 10.1% at 20 MeV, 18 h after EOB.
[b] Maximum increase in patient dose of 10.1% at 22 MeV, 18 h after EOB.
[c] Maximum increase in patient dose of 11.0% at 24 MeV, 18 h after EOB.

LIMITATION OF BOMBARDING ENERGIES AND BEAM INTENSITY

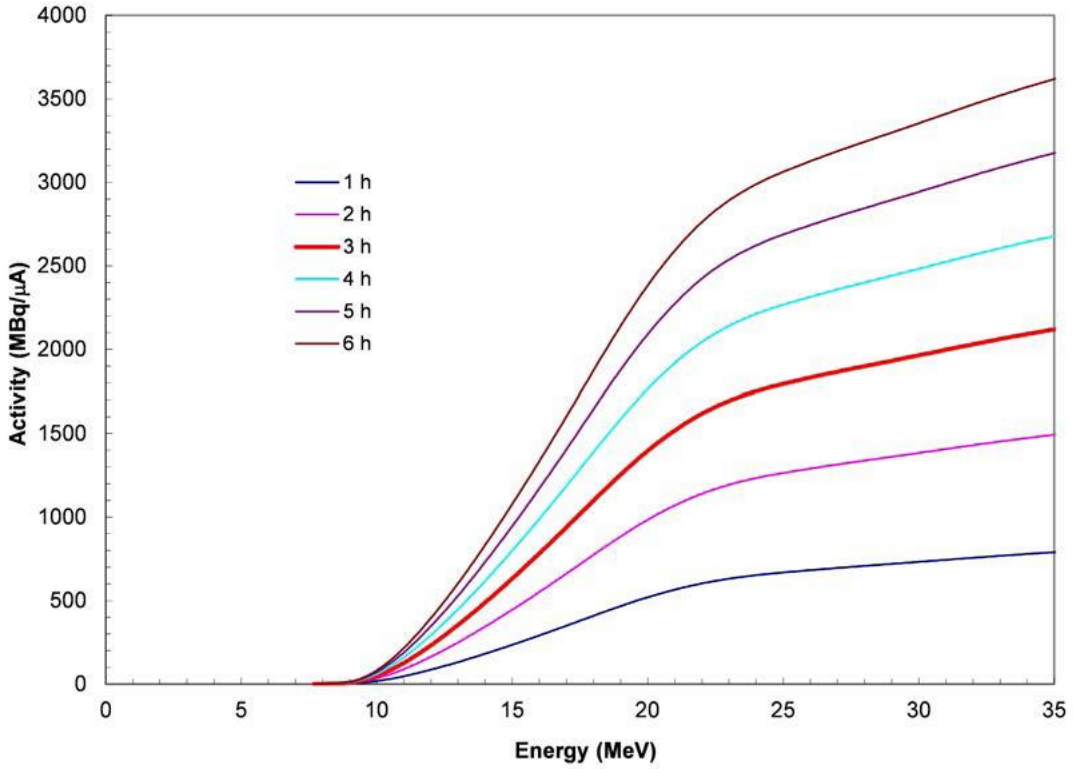

FIG. 1. EOB activity as a function of the bombarding energy and irradiation time.

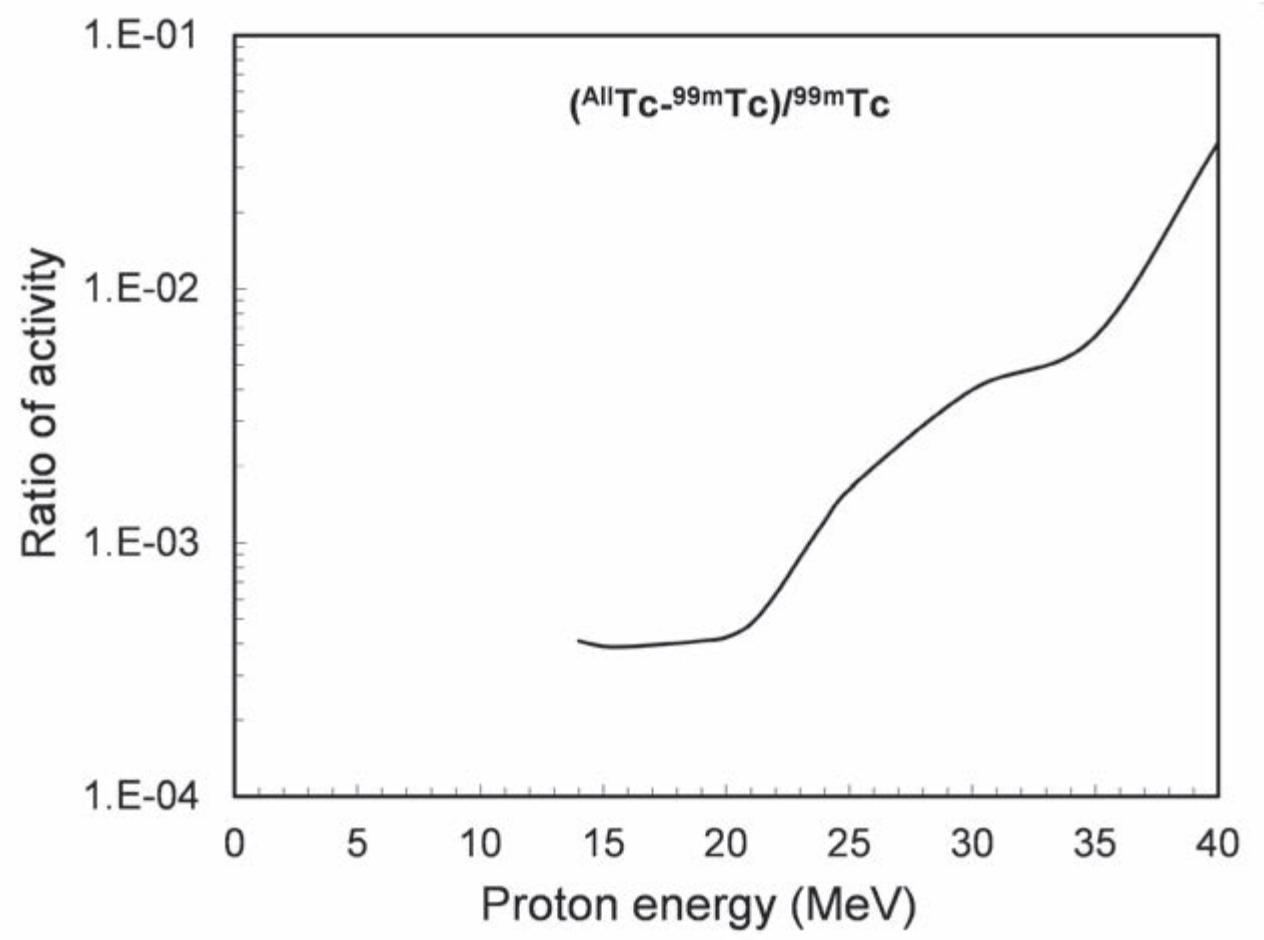

FIG. 2. Relative activity of contaminating Tc as a function of bombarding proton energy after a 3 h irradiation and a 2 h cooling time.

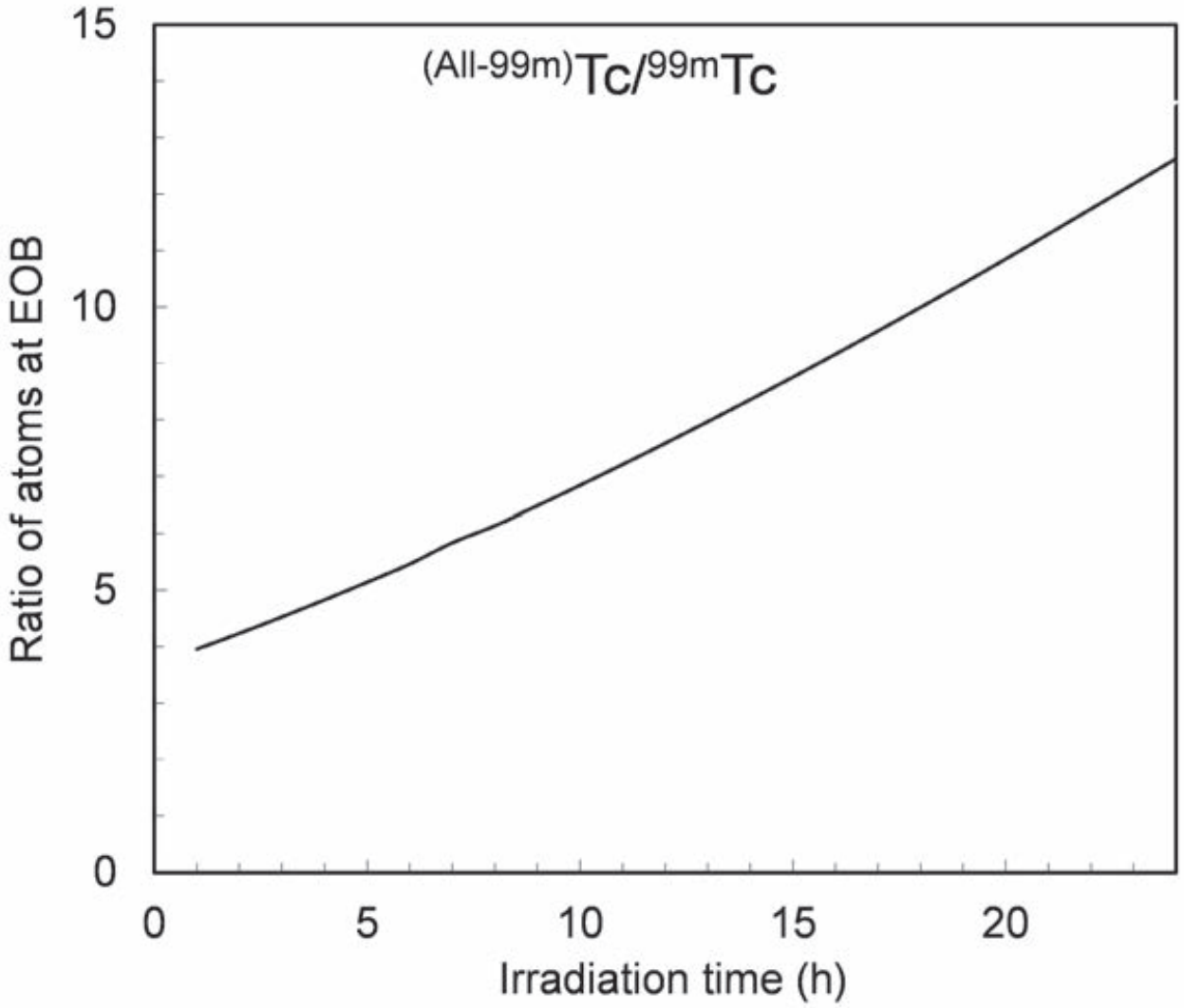

FIG. 3. Ratio of contaminating Tc atoms as a function of bombarding time for a 17 MeV irradiation after a 2 h cooling time.

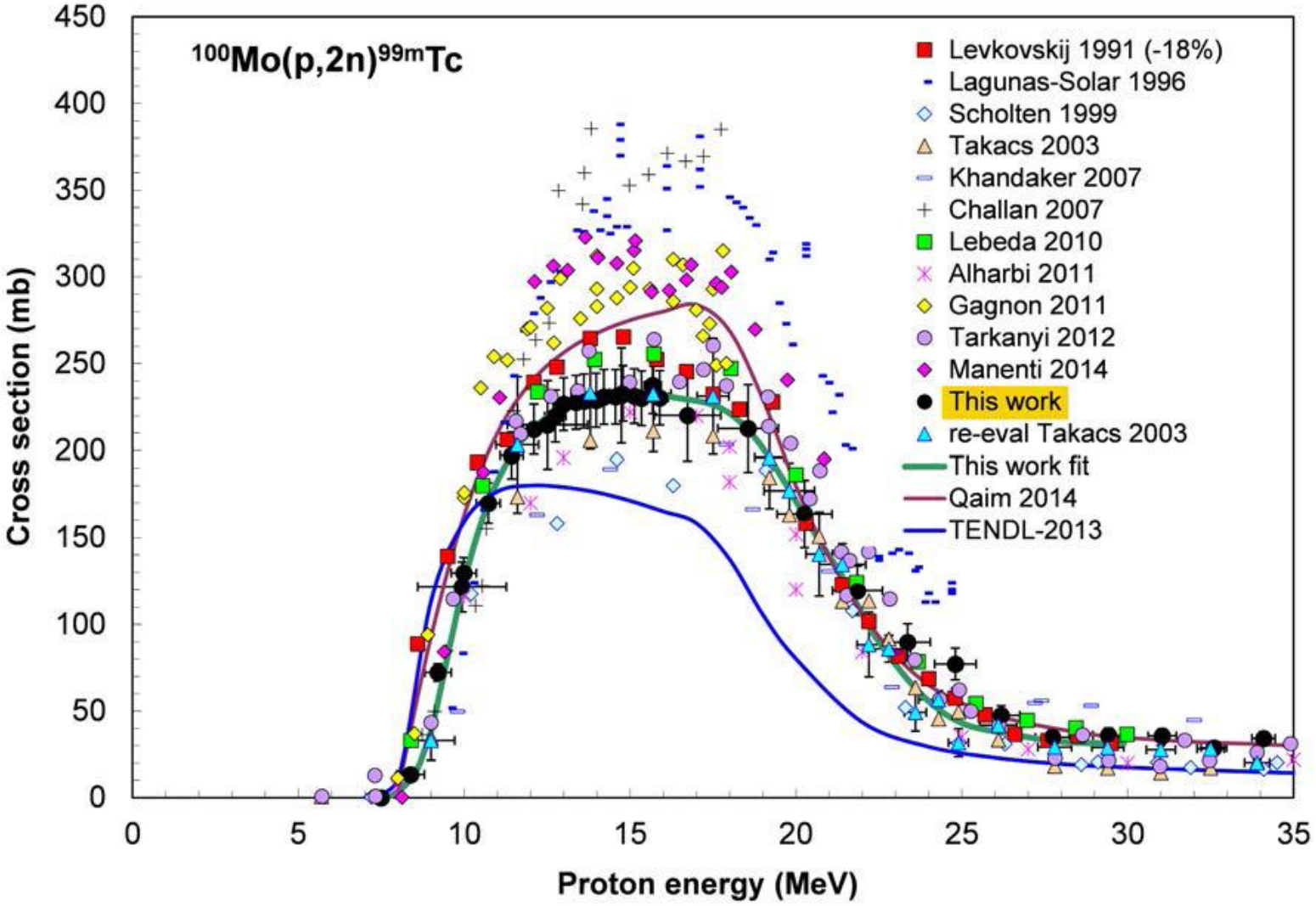

FIG. 5. Experimental cross-section data for the 100Mo(p,2n)99mTc reaction. The newly measured experimental data are represented by the filled black dots.

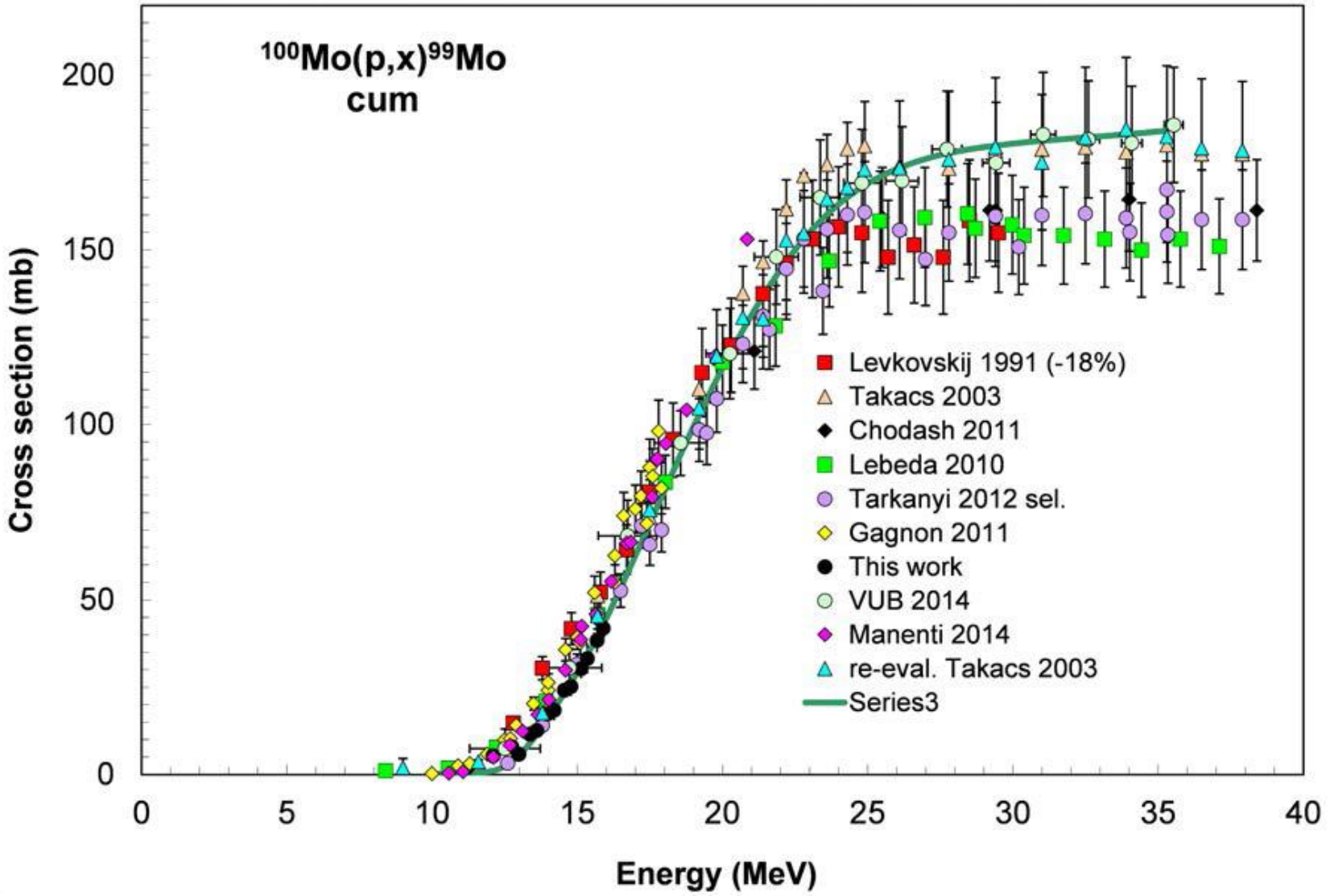

FIG. 6. Experimental cross-sections for the 100Mo(p,x)99Mo reaction. The newly measured experimental data are represented by the filled black dots.

CO-PRODUCTION OF OTHER ISOTOPES

- Depending on the target composition and bombarding beam energy, additional reaction channels can be opened that contribute to the production of Tc radionuclides other than 99Tc as well as stable and/or radioactive isotopes of Mo, Nb, Zr and Ru. As examples, Figs 7–11 show the logarithm of the expected amount of different reaction products after a 3 h and 1 μA irradiation using a 99.5% enriched 100Mo target material as a function of bombarding energy from 15 to 25 MeV.

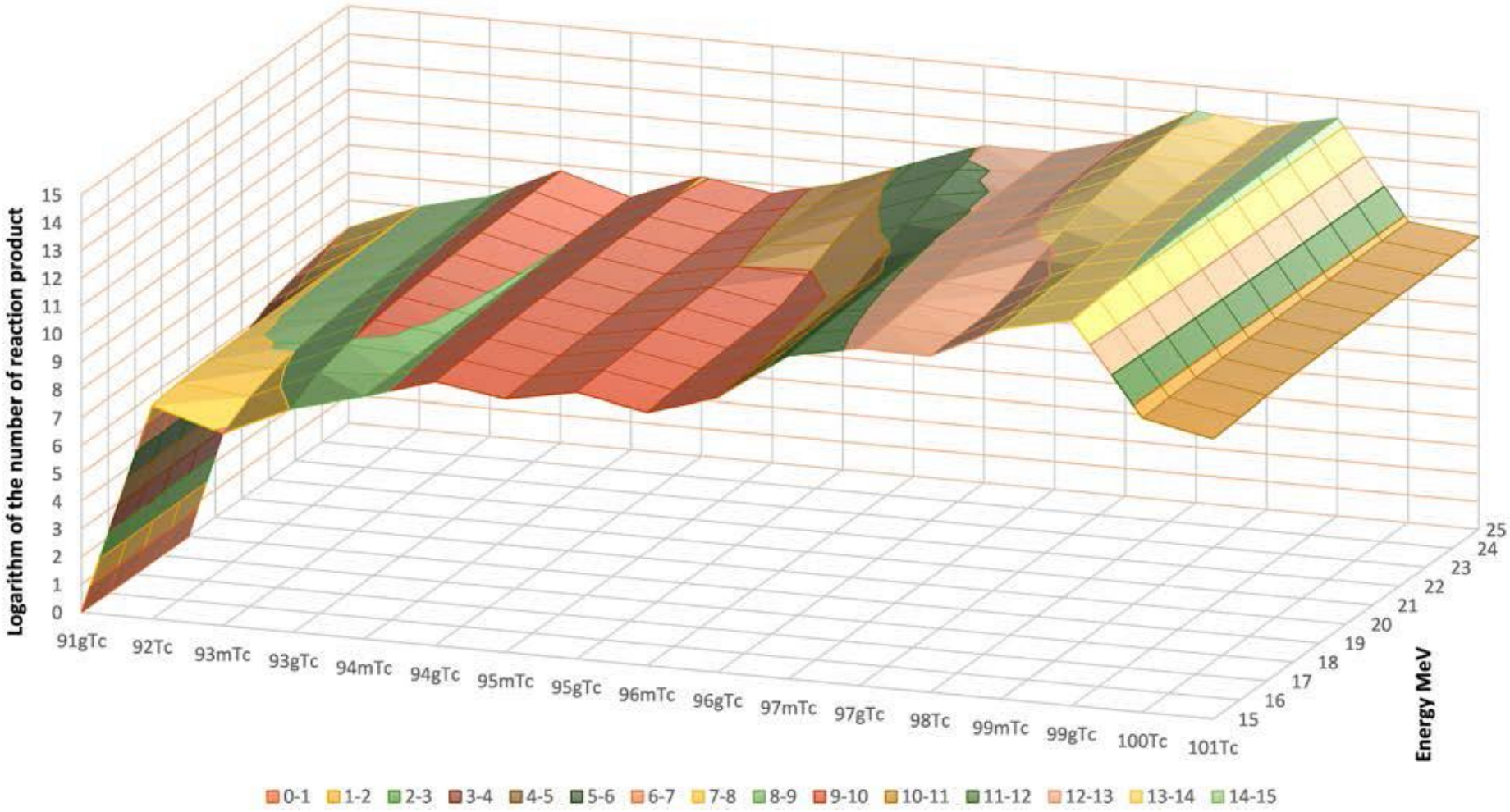

FIG. 7. Production of Tc nuclides as a function of bombarding energy for a 3 h 1 μA irradiation. The vertical axis represents the logarithm of the number of different Tc atoms present in the target at EOB.

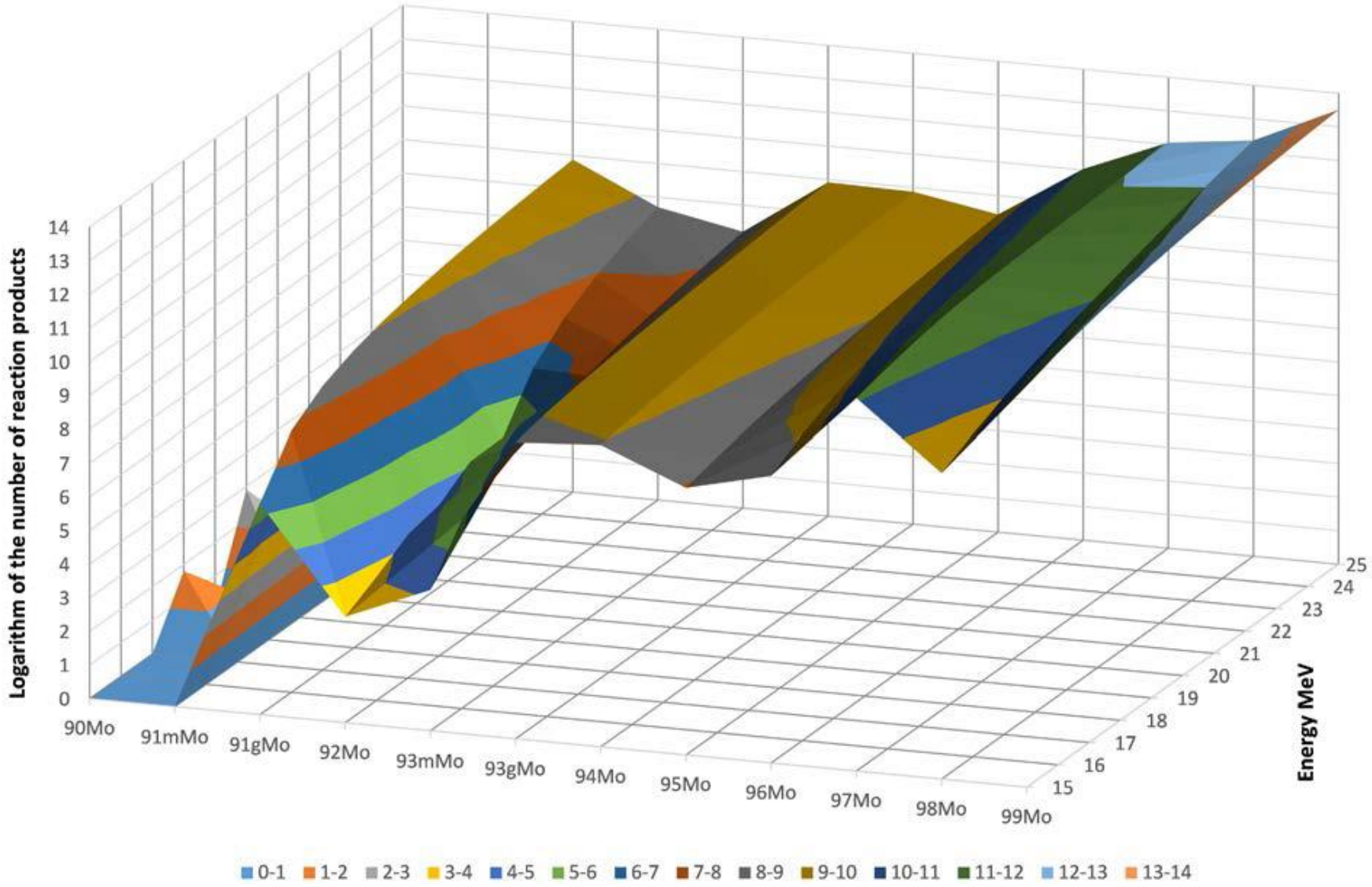

FIG. 8. Production of Mo nuclides as a function of bombarding energy for a 3 h 1 μA irradiation. The vertical axis represents the logarithm of the number of different Tc atoms present in the target at EOB.

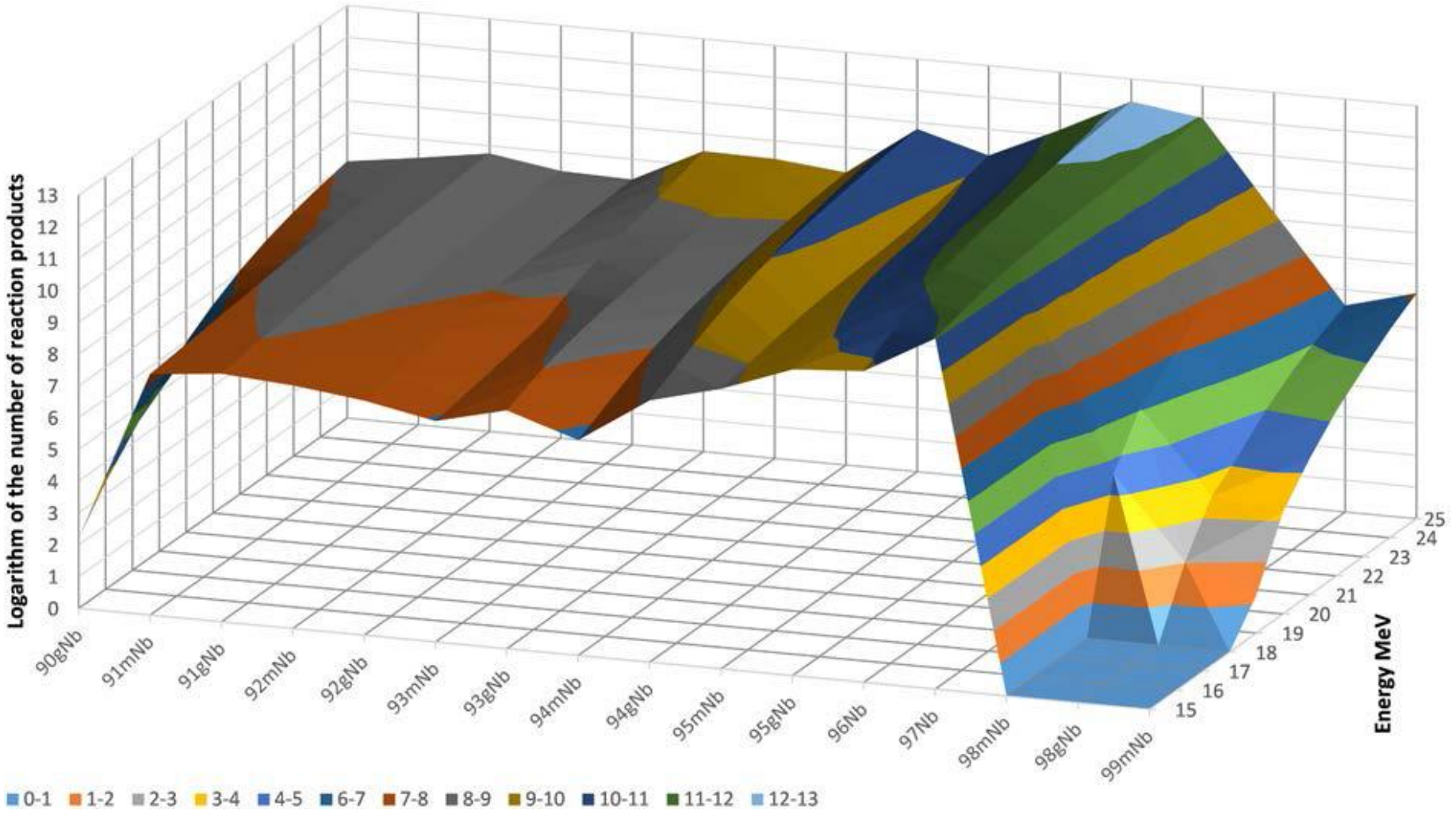

FIG. 9. Production of Nb nuclides as a function of bombarding energy for a 3 h 1 μA irradiation. The vertical axis represents the logarithm of the number of different Tc atoms present in the target at EOB.

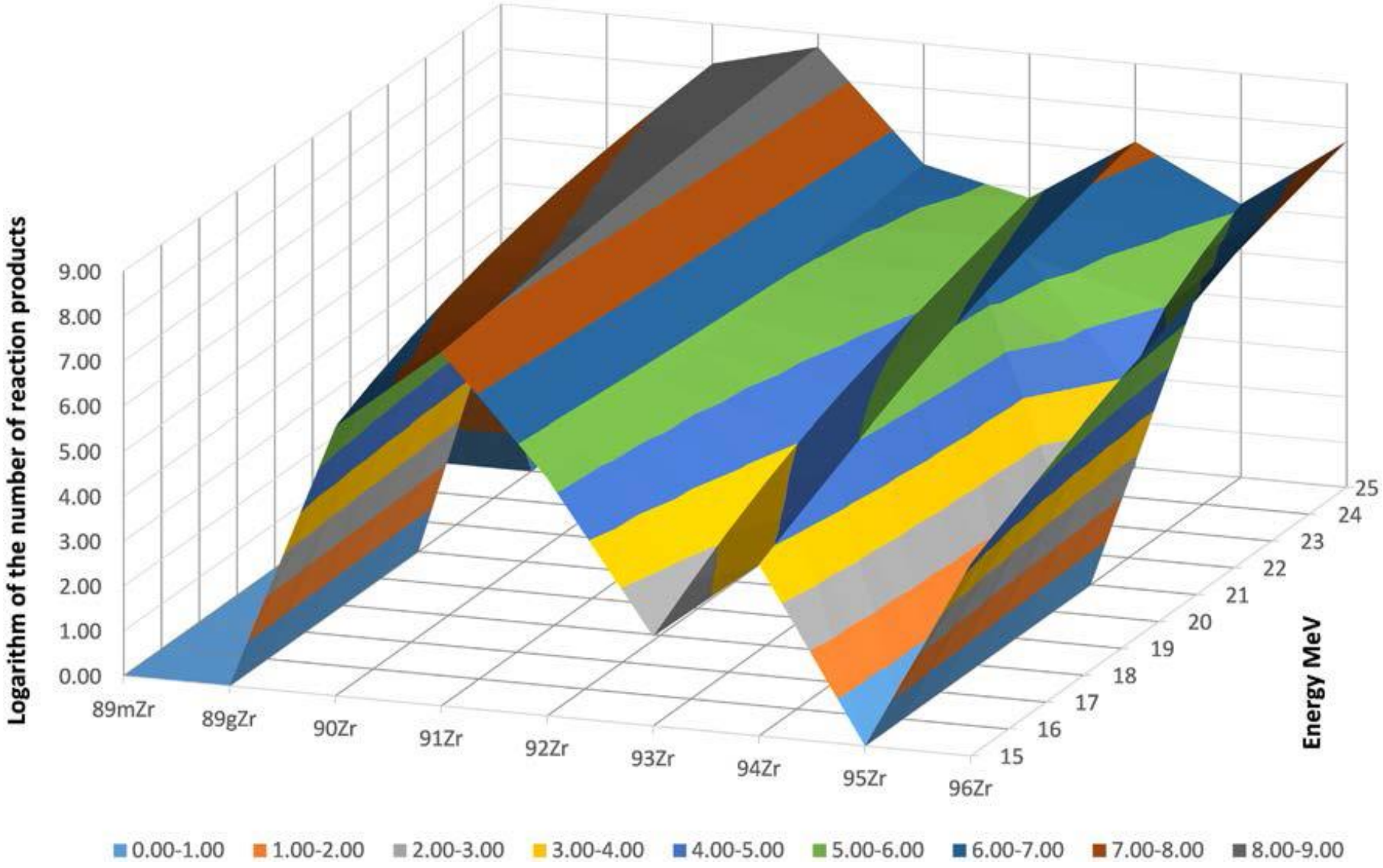

FIG. 10. Production of Zr nuclides as a function of bombarding energy for a 3 h 1 μA irradiation. The vertical axes represent the logarithm of the number of different Tc atoms present in the target at EOB.

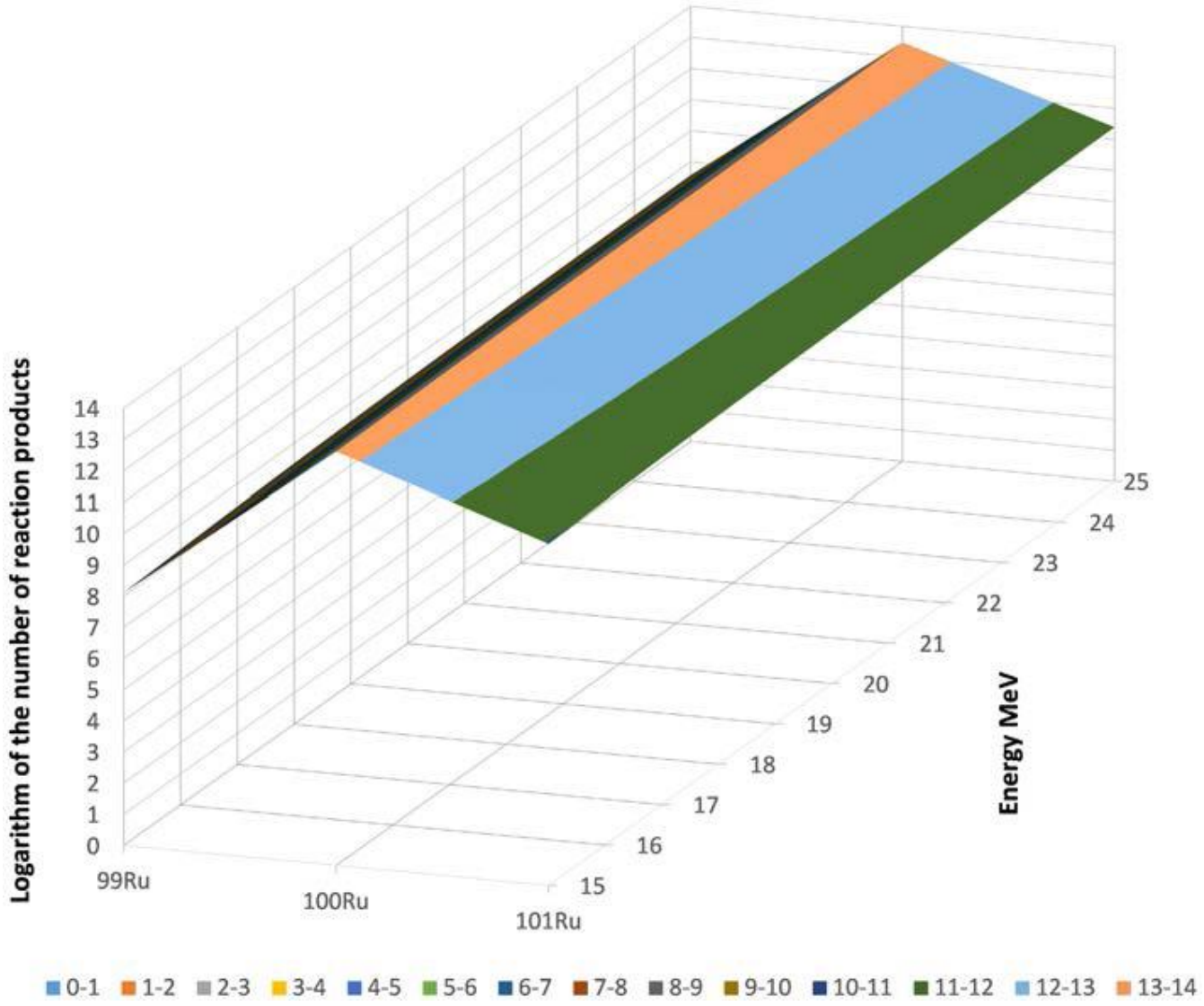

FIG. 11. Production of Ru nuclides as a function of bombarding energy for a 3 h 1 μA irradiation. The vertical axes represent the logarithm of the number of different Tc atoms present in the target at EOB.

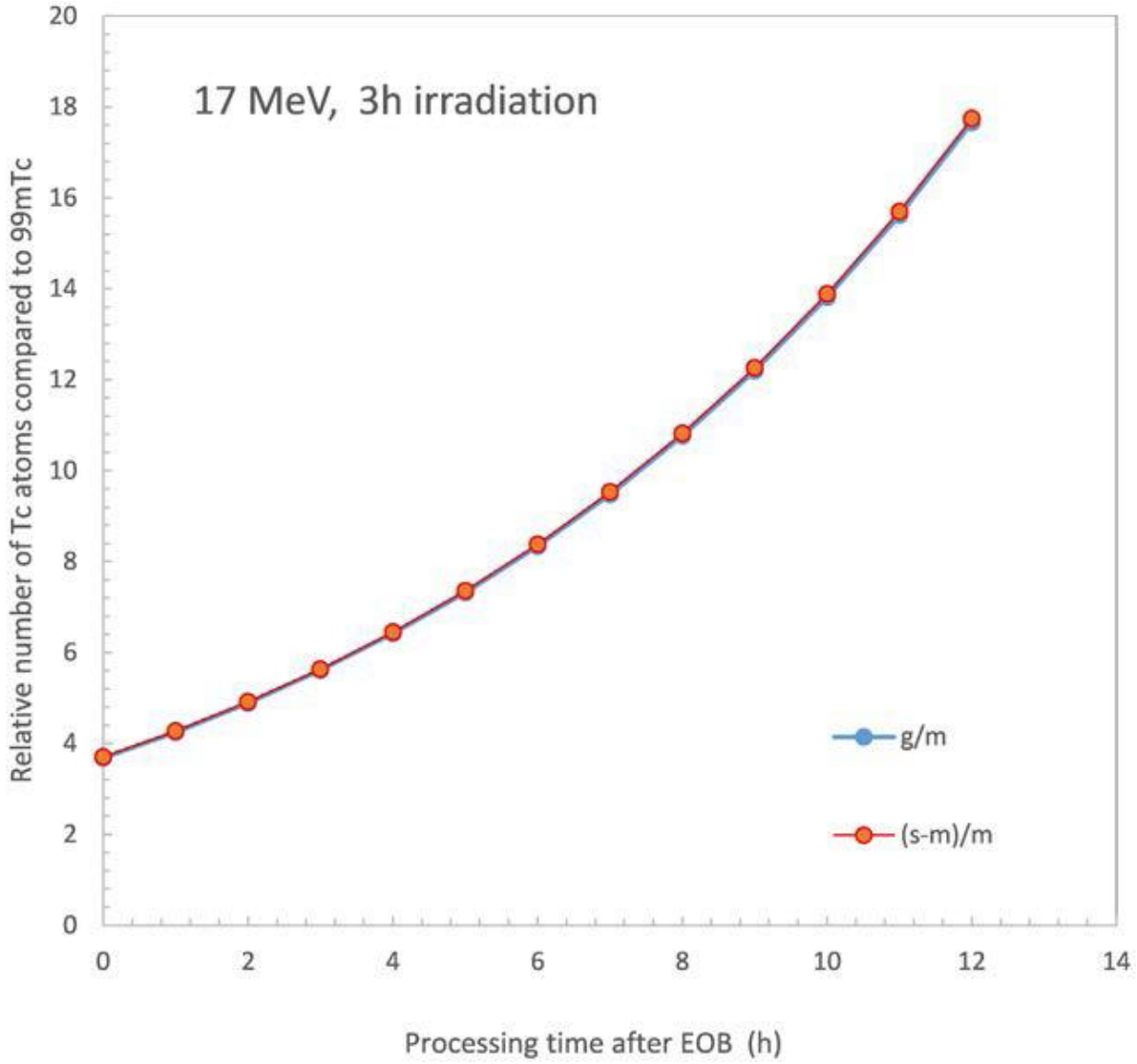

FIG. 12. Time dependence of the Tc radionuclides in the 0 –12 h after EOB (g/m represents the ratio of 99gTc/ 99mTc while (s-m)/m represents (xxTc–99mTc)/ 99mTc for 17 MeV 3h irradiation).

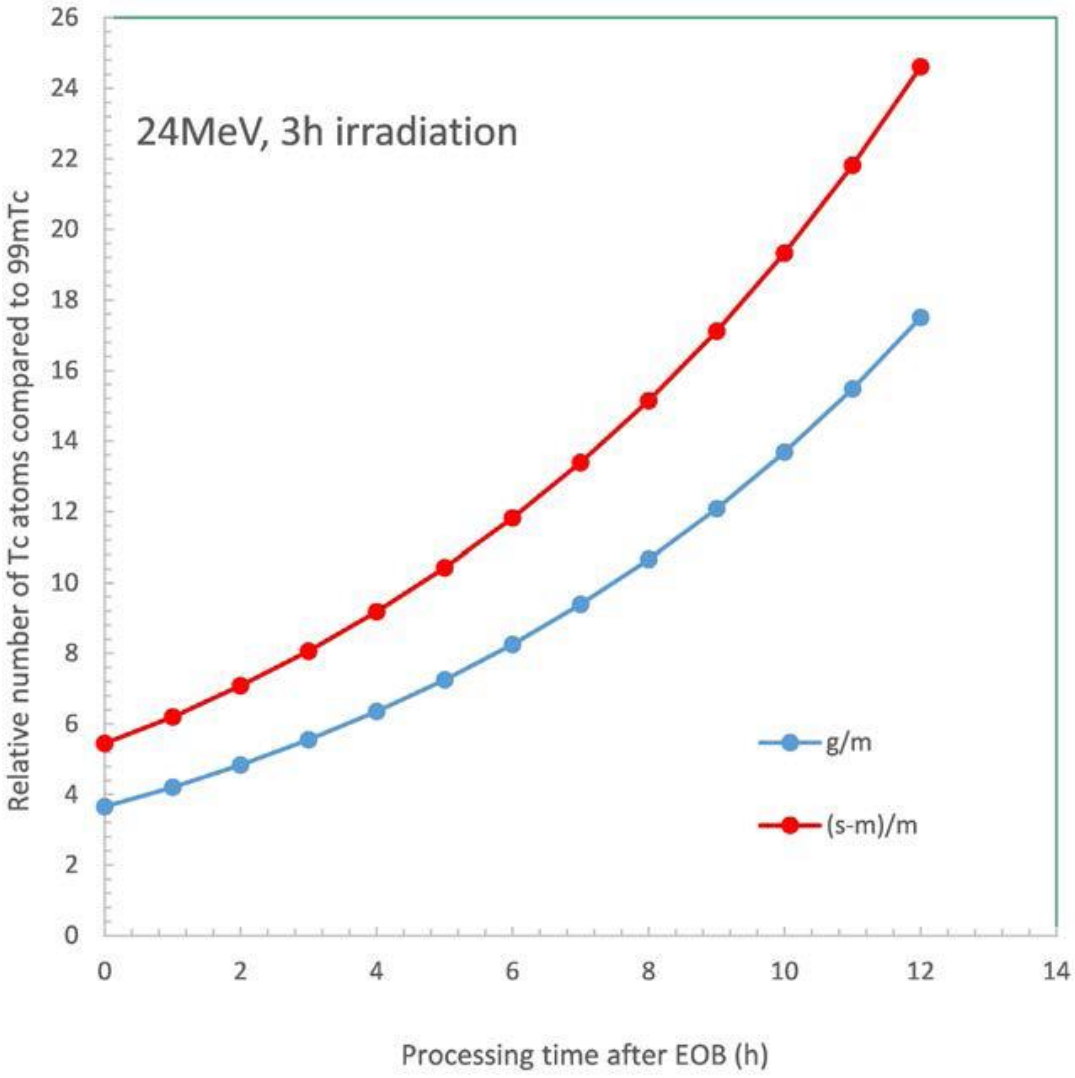

FIG. 13. Time dependence of the Tc radionuclides in the 0–12 h after EOB (g/m represents the ratio of 99gTc/ 99mTc while (s-m)/m represents (xxTc-99mTc)/ 99mTc for a 24 MeV 3 h irradiation).

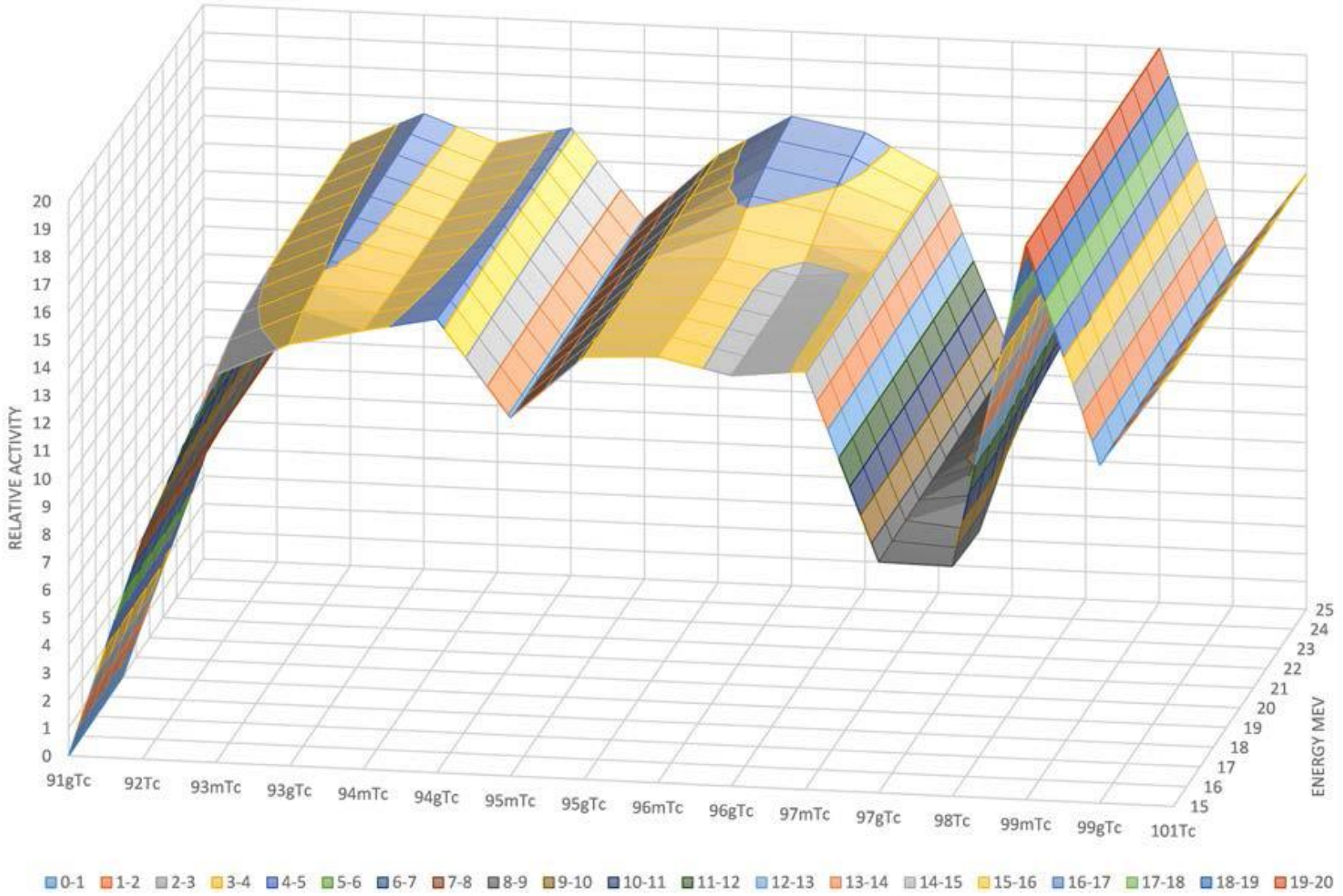

FIG. 14. The relative activity of other co-produced Tc radionuclides compared with 99mTc as a function of bombarding proton energy.

A PRACTICAL APPROACH TO THE ACCELERATOR PRODUCTION OF 99mTc

To provide high quality accelerator produced 99mTc, each site should attempt to:

- Use a proton beam of suitable energy depending on the source material.
- Use the shortest irradiation time possible (to reduce radionuclidic impurities) while meeting the expected needs, taking decay time, labelling time and radiopharmaceutical distribution into account.
- Irradiate targets with the highest beam intensity possible.