Triangle Universities Nuclear Laboratory (TUNL)

A US Department of Energy Center of Excellence in Nuclear Physics, Durham, NC, USA

Cross Section Measurements of Photonuclear Reaction Pathways Towards Promising Medical Radioisotopes

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Workshop for Applied Nuclear Data Activities (WANDA 2022)

Duke UNIVERSITY NCCentral UNIVERSITY NC STATE UNIVERSITY THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Cancer: Statistics, types, and treatments

- When the orderly process of cell multiplication breaks down, and abnormal or damaged cells grow and multiply when they shouldn't, tumors are formed. These tumors can be cancerous or benign;
- Cancerous tumors can spread into, or invade, nearby tissues and can travel to distant places in the body to form new metastatic tumors

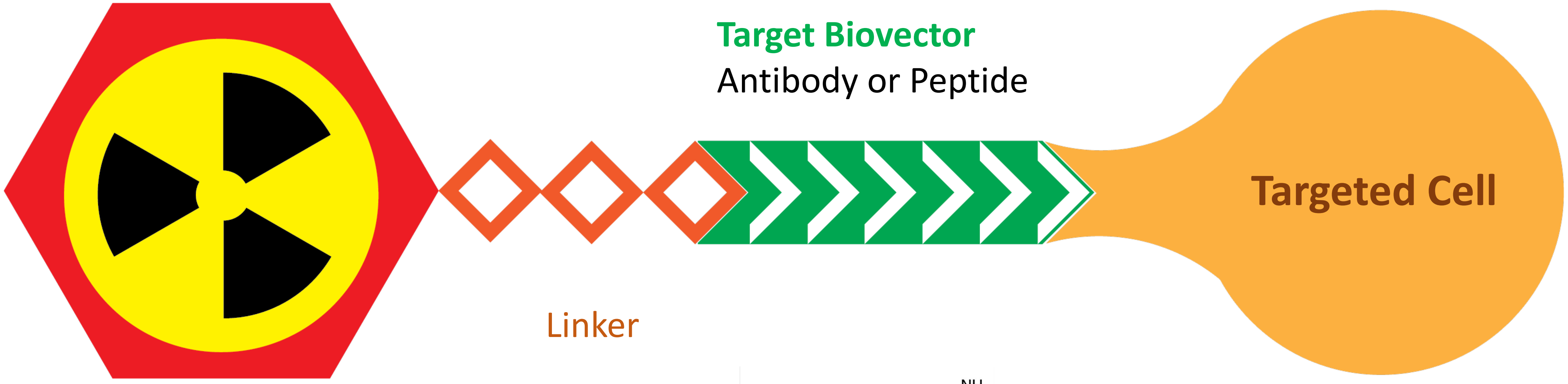
Cancer is among the leading causes of death and the yearly world-wide cases are expected to be nearly 30 million by year 2040

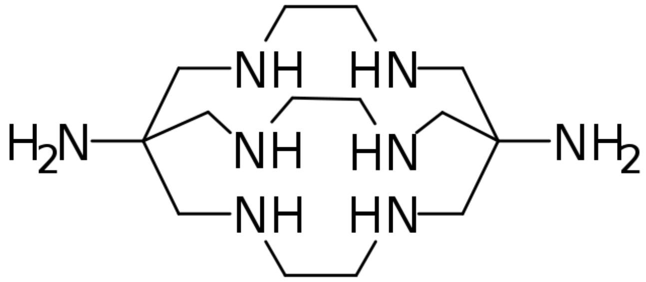
Types of Cancer	Treatment Description	Comments
Localized	**Surgical** Excision	Collateral damage, trauma due to removal of suspicious growth as well as nearby tissue
	Brachytherapy, Internal Surgical Radiotherapy	Long term radiation therapy. Typically limited to single treatments
	Ion Beam ablation of target tissue	"image-guided" tumor therapy – reduced side effects
Localized & Metastasized	Intravenous **Chemotherapy**	Severe damage to **ALL** tissues and biological systems. Goal: kill the cancer before killing the patient
	Intravenous **Targeted Radionuclide Therapy** (TRT)	R&D in isotopes and delivery methods for highly localized, tumor specific therapy – reduced side effects

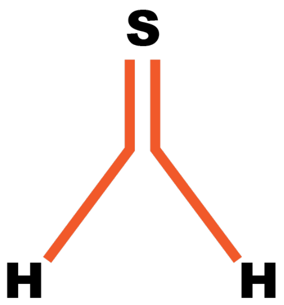
Delivering the radionuclide to the targeted cell

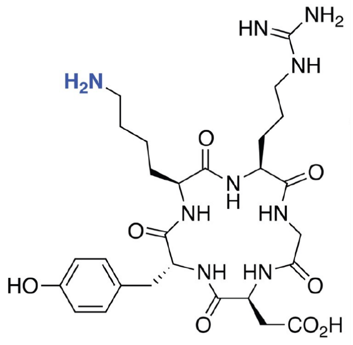
Chelator

organic chemical that bonds with radionuclide metal ions and produces a chelate compound

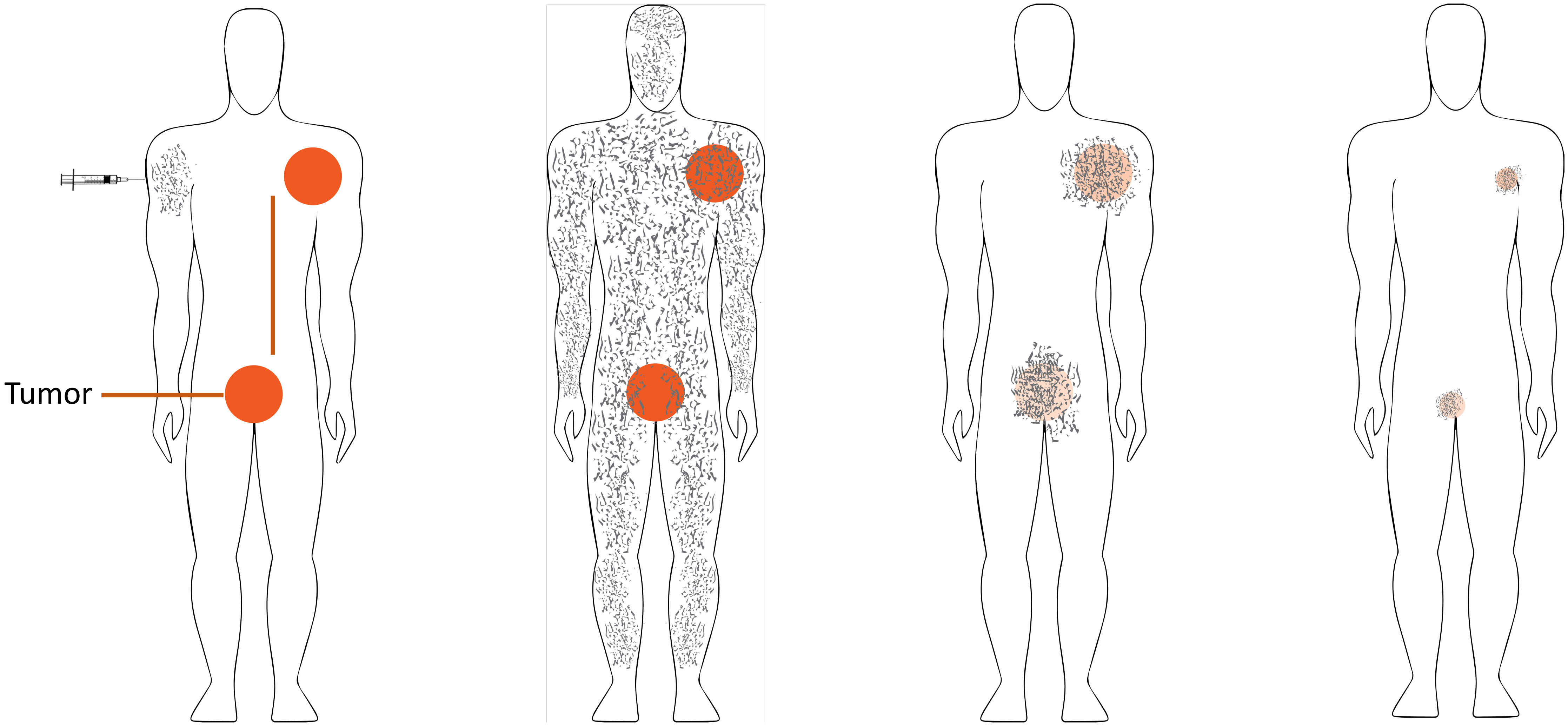






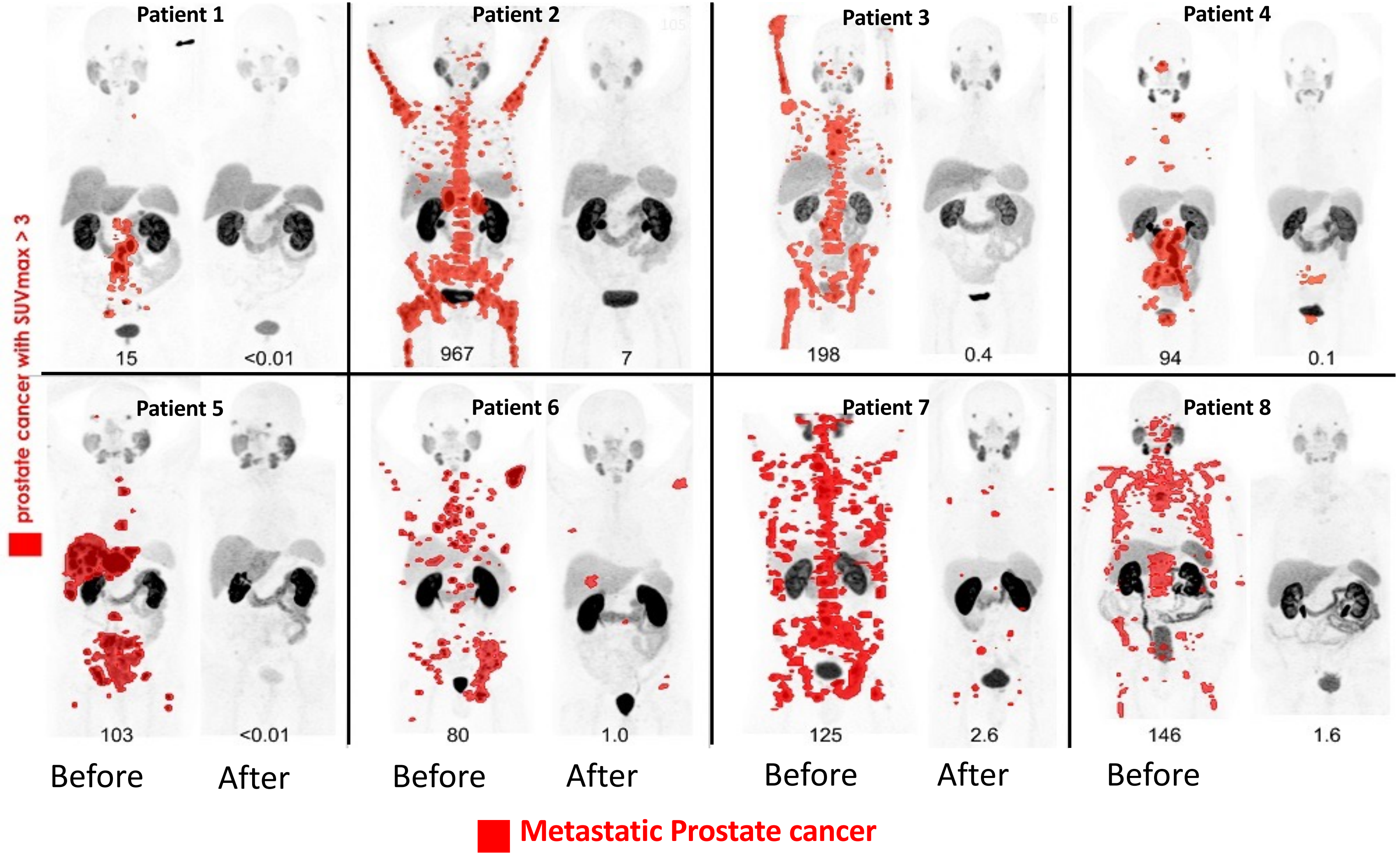


Targeted Radionuclide Therapy



1. The targeted radioligand is administrated; **2.** distributes in the whole body; **3.** Localizes and Concentrates in Target Tissue; **4.** Selectively deliver cytotoxic doses of radiation

How well it works!

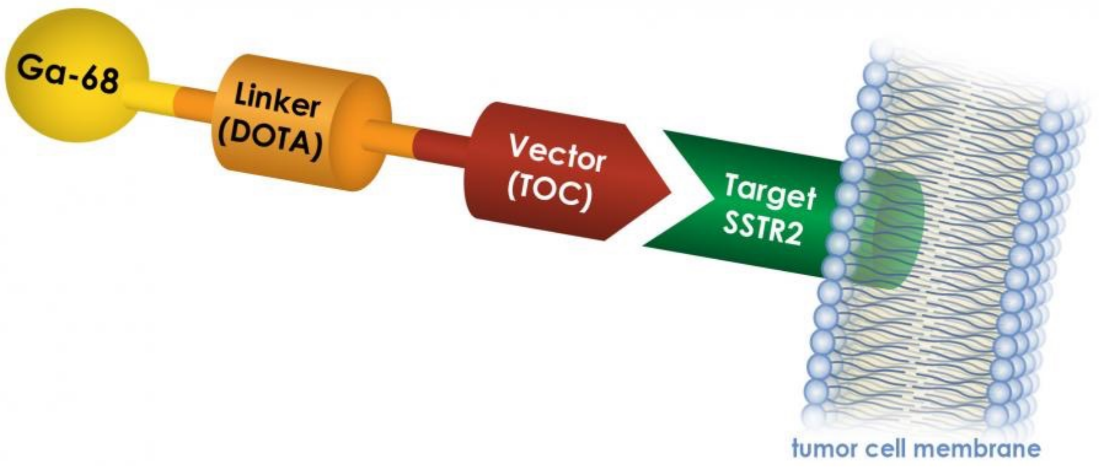


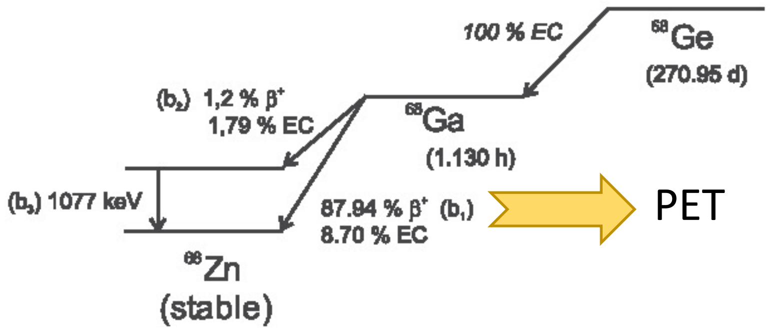
•Images **before** and **after** **radiopharmaceutical treatment** with Lu-177 PSMA617 theranostic in 8 patients with metastatic prostate cancer who **exhausted standard treatment options**

Hoffman, et al. JNM 2018

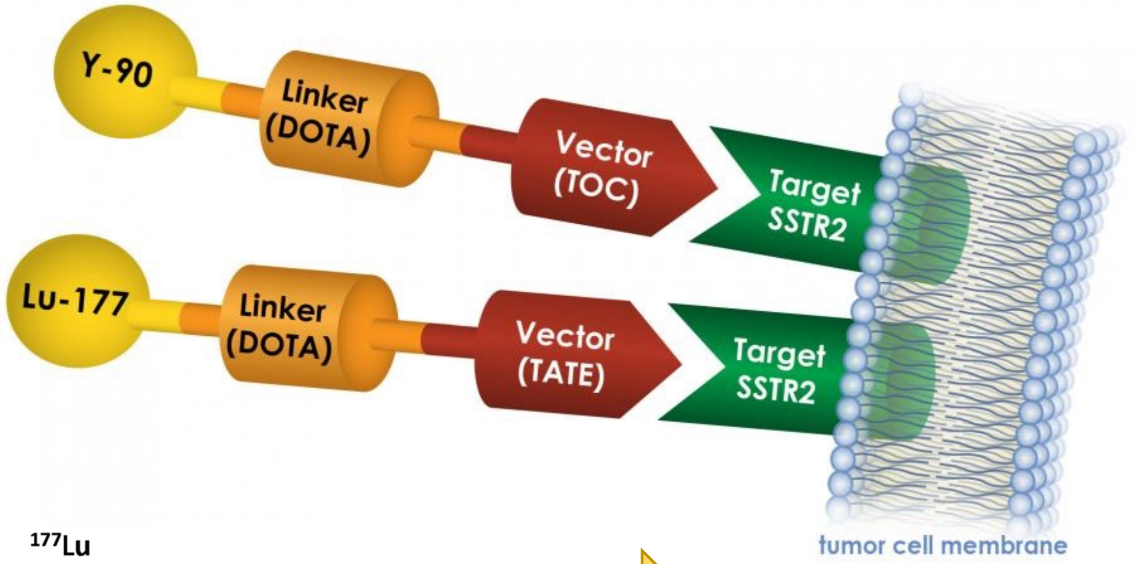
therapeutics and diagnostics = theranostics

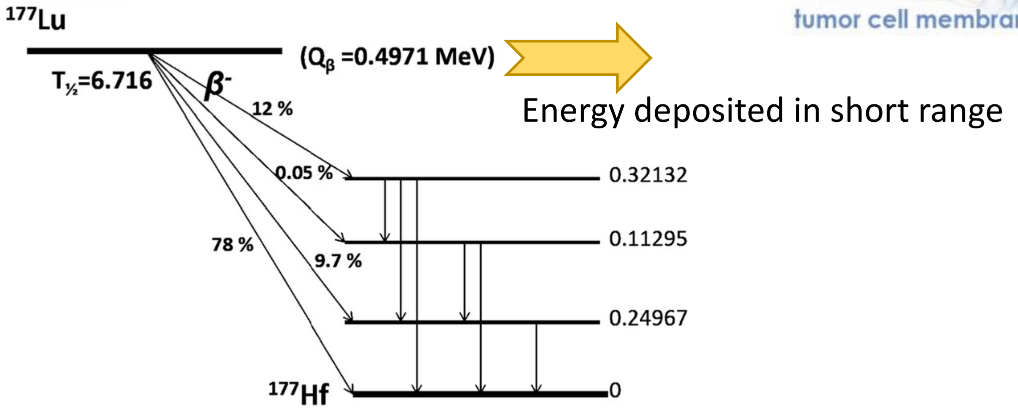
DIAGNOSTICS





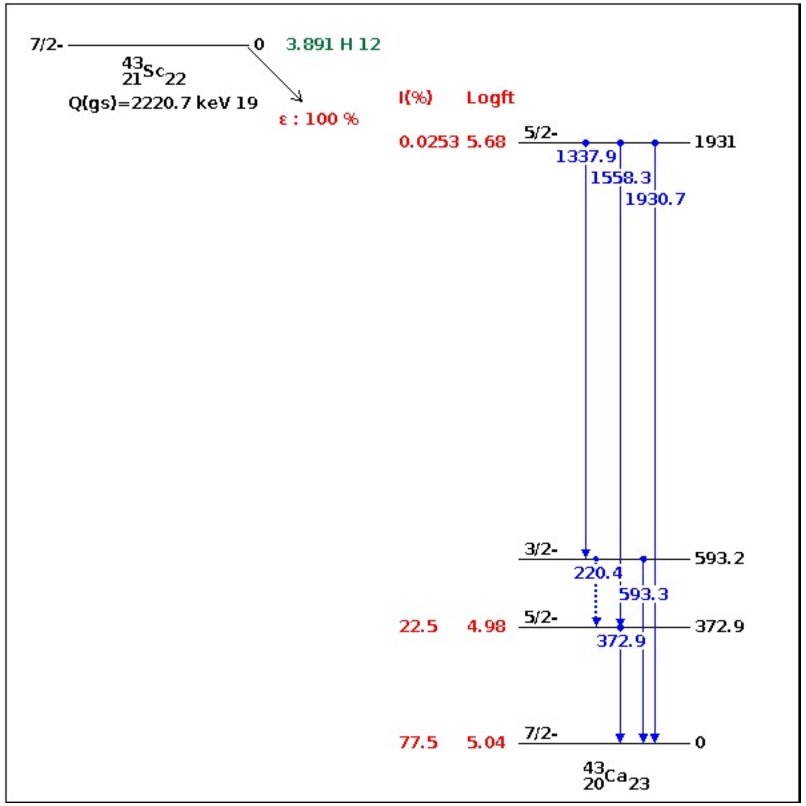
THERAPEUTICS





Not all theranostics are equally!

In case of ^{68}Ga and ^{177}Lu, they are two different elements. The chemical behavior of ^{68}Ga may be different than ^{177}Lu



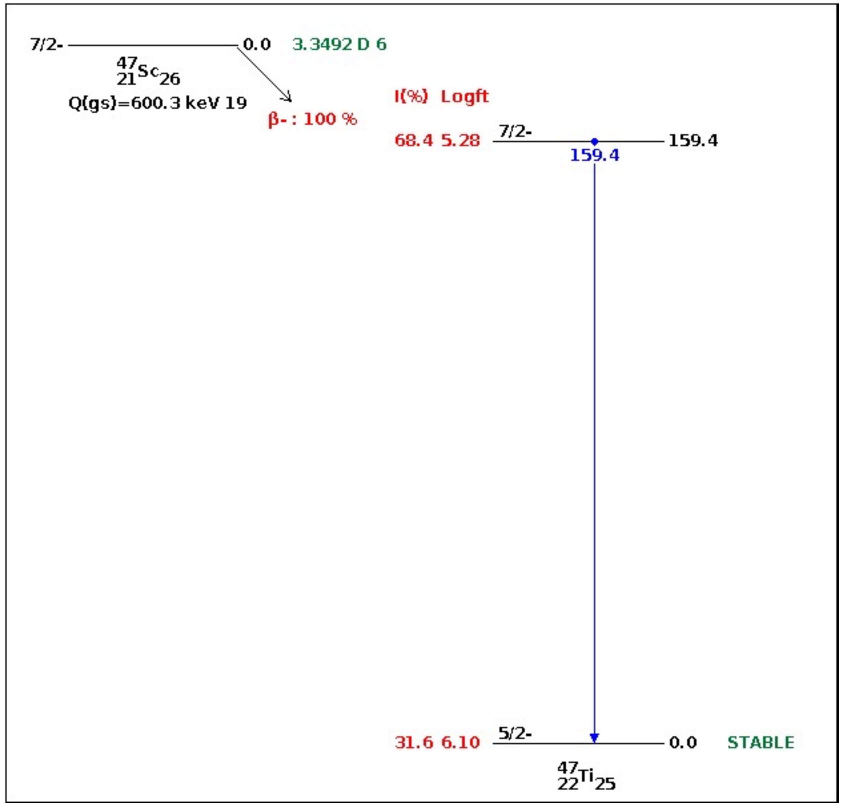
43Sc / 47Sc

diagnostic / **thera**peutic

Similar chemistry

β+ / β-

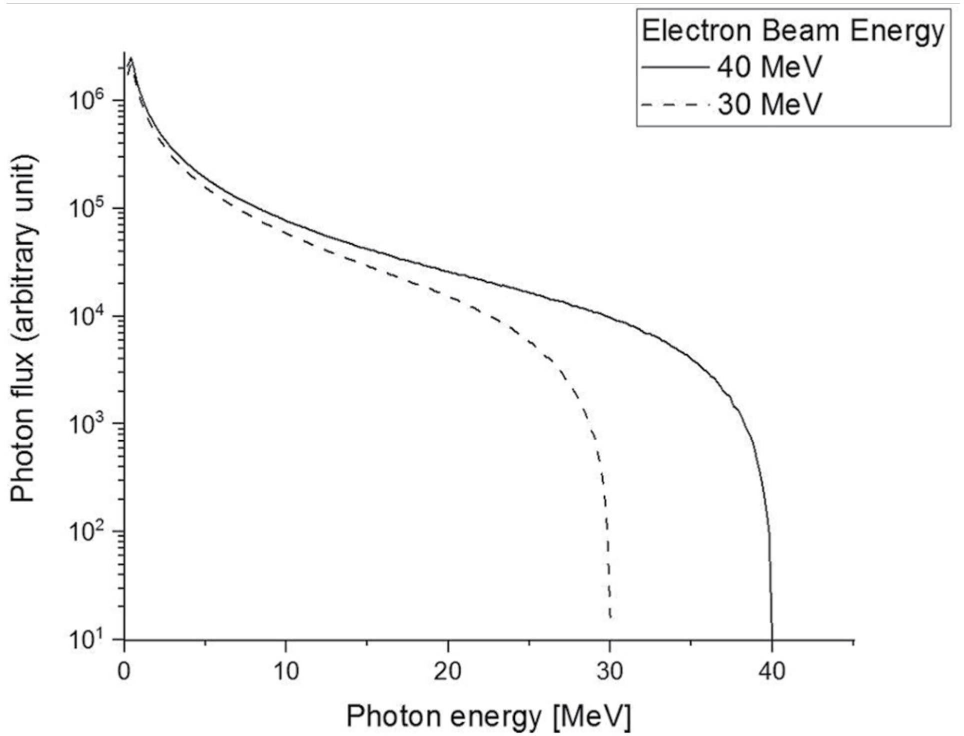
3.8 H / 3.35 d



Advantages of similar chemistry with same element of diagnostic and therapeutic agent

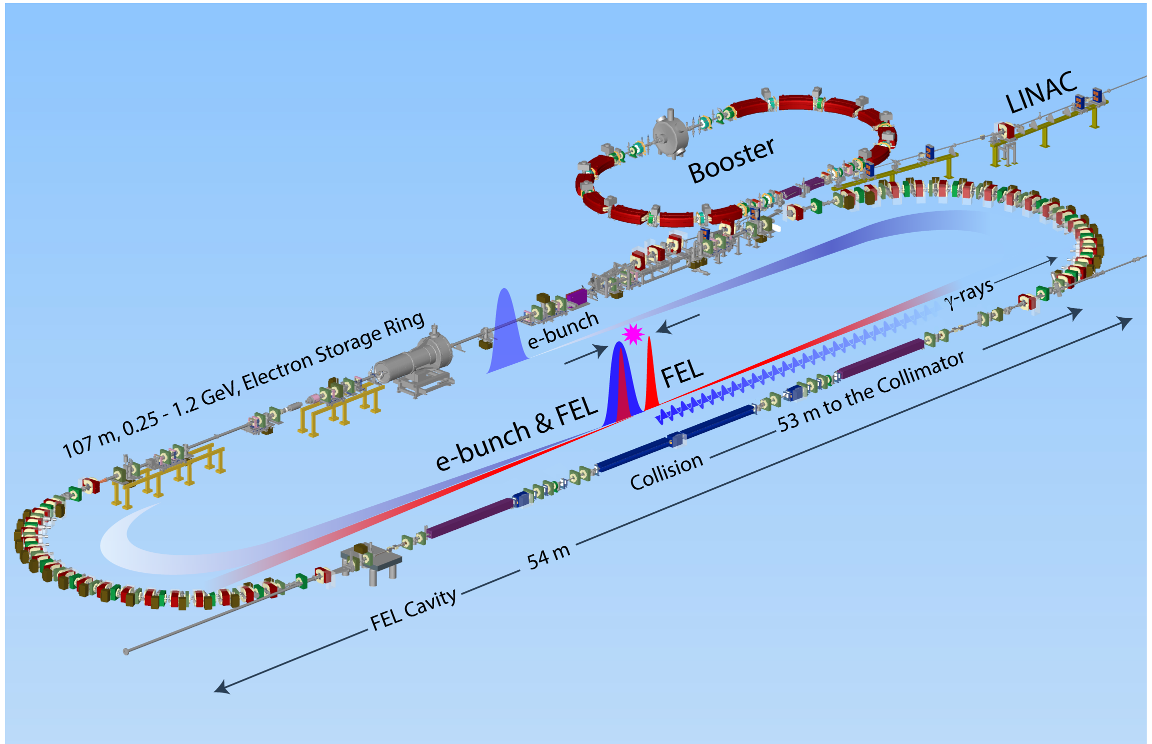
Radionuclide production using high-energy photons

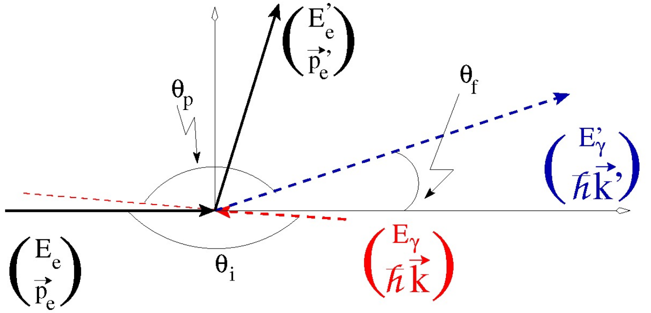
- Isotopes of interest are produced using Bremsstrahlung photons via photonuclear reactions such as (γ,n), (γ,p), (γ,α), (γ,np), … (Facilities: LEAF @ ANL)



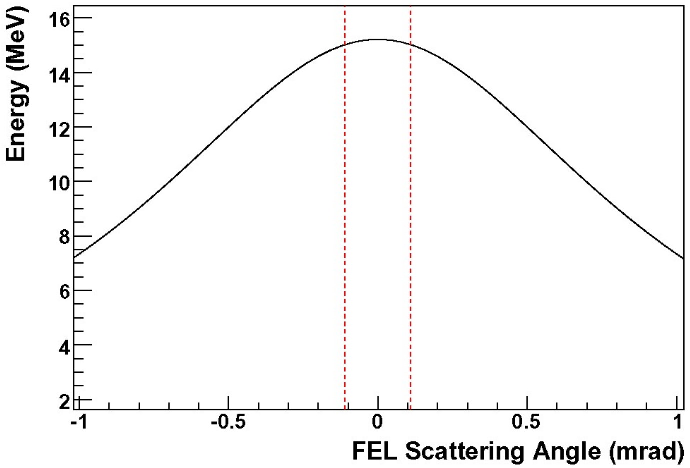
- **In order to quantify the production yields, we must correctly know the probability (cross-section) of all possible photonuclear reactions leading to the production of a particular isotope from a given parent sample**
- **These cross section must be known as a function of photon energy**

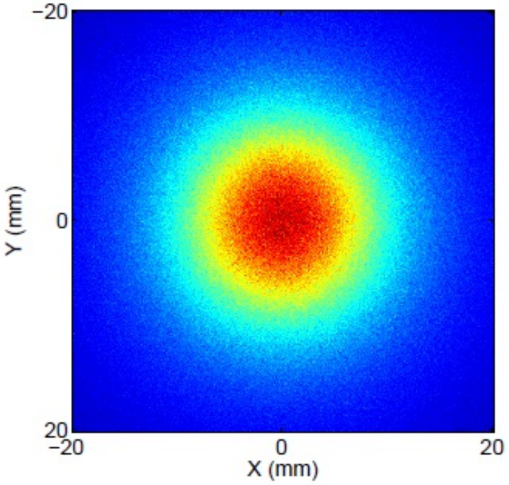
High Intensity Gamma Ray Source (HIGS)





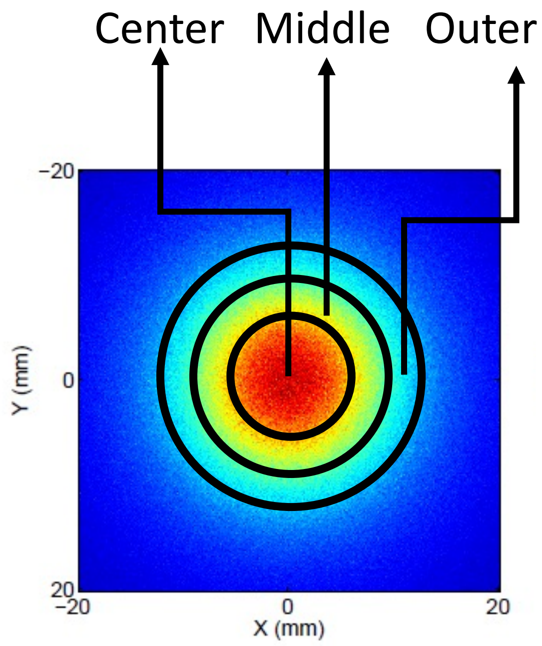
$$E_\gamma = \frac{4\gamma^2 E_\lambda}{1 + \gamma\theta_f + 4\gamma^2 E_\lambda / E_e}$$



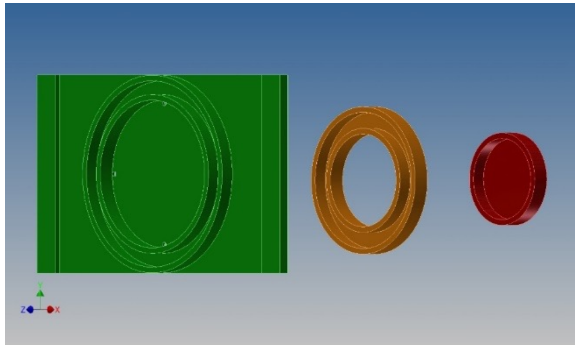


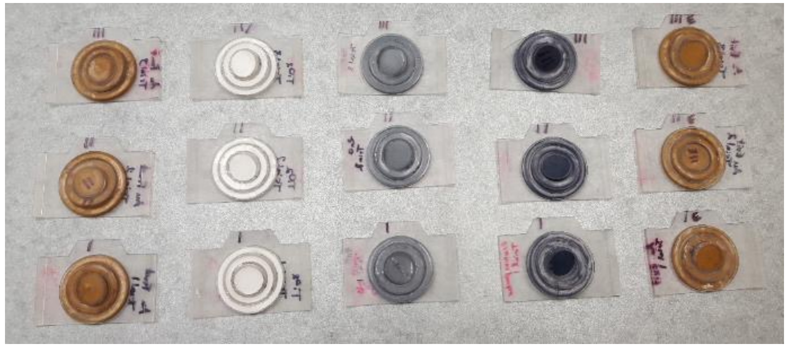
The measurement plan

- We need to measure cross section as a function of energy
- If we did one energy setting at a time, it would require a lot of beam time
- Use energy-spatial distribution of the beam to measure cross sections at multiple energies at one energy setting of irradiation



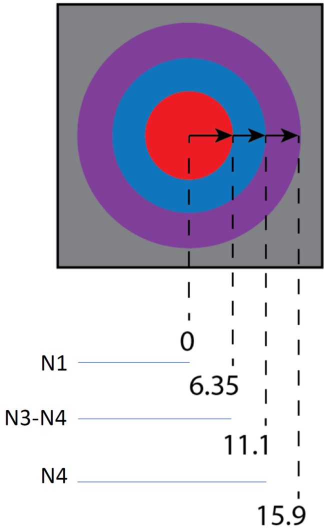
- **Target samples fabricated to match three different energy regions of the beam**
- **Multiple target samples mounted in a stack**

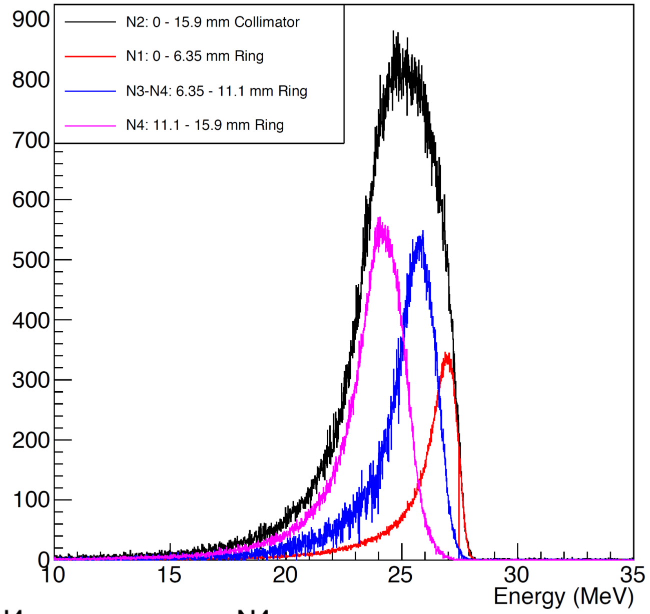


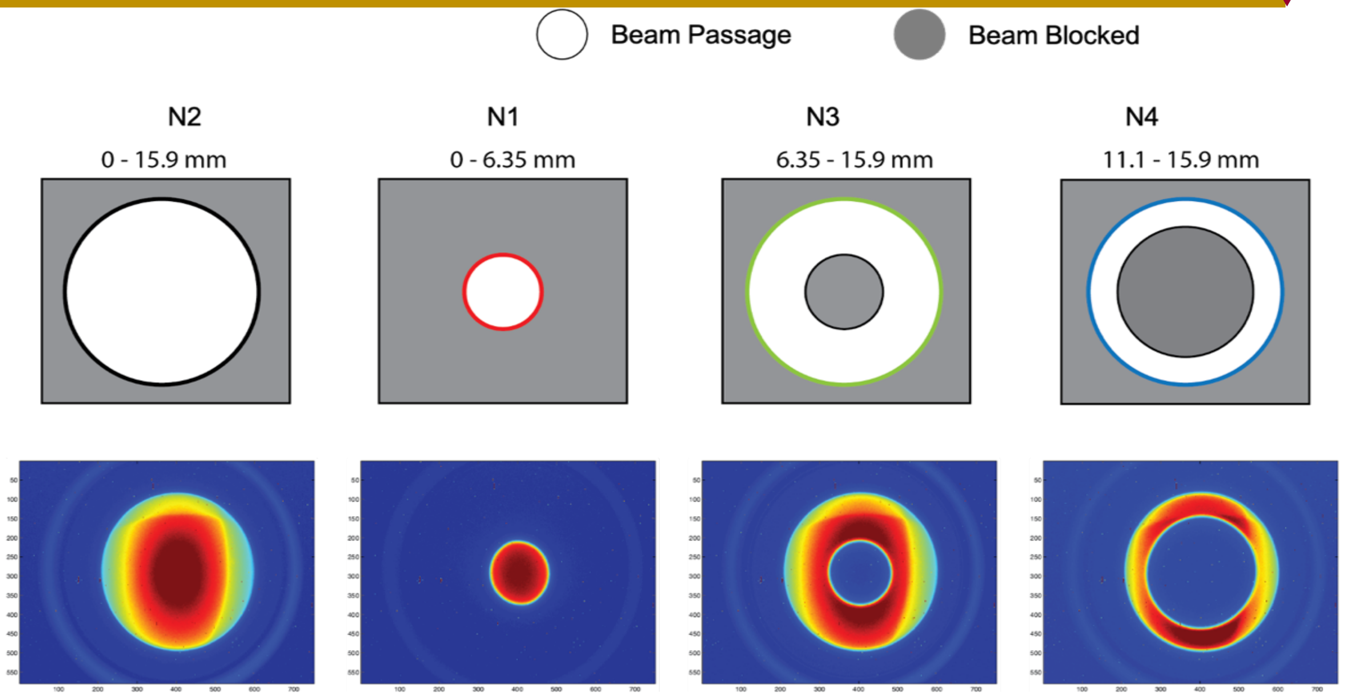


The Concept Test

From four measured spectra, three ring energies can be constructed

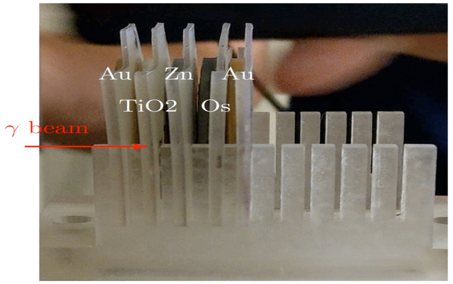




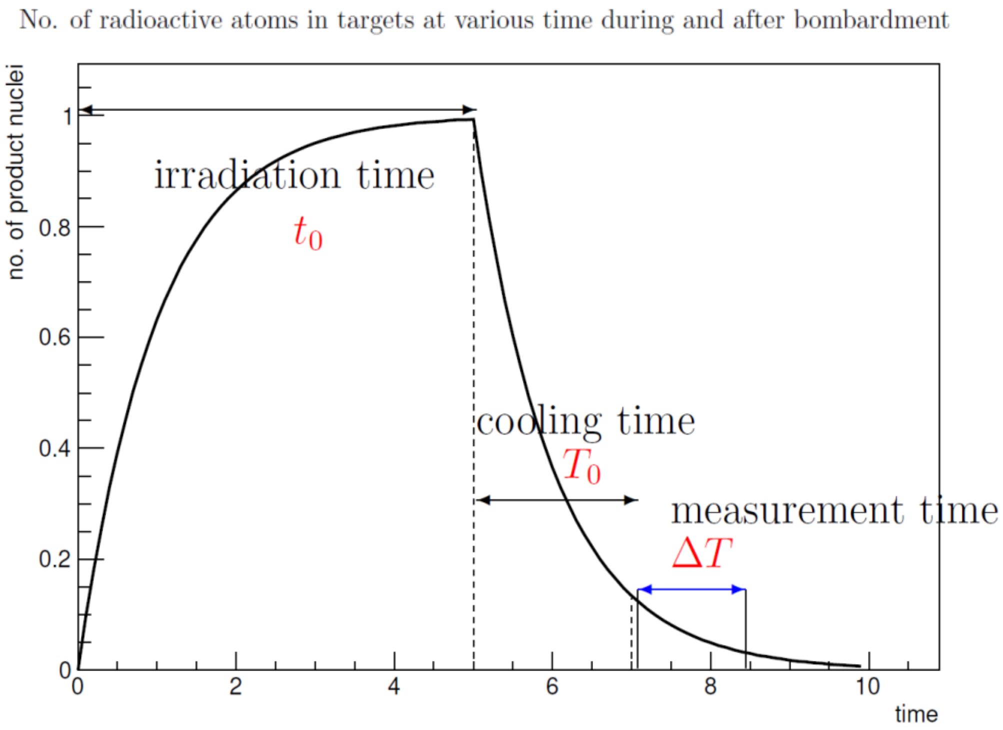


	N1 N3	N3-N4		N4
Rings	**0 – 6.35**	**6.35 – 11.1**	**11.1 – 15.9**	**6.35 – 15.9**
Meas. Flux %	18%	37%	45%	81%
Siml. Flux %	20%	35%	45%	80%
Meas. Energy	27.0	25.8	24.1	24.9
Siml. Energy	27.1	26.1	24.5	25.6
Meas. dE	0.66	1.6	2.4	
Siml. dE	0.52	1.8	2.2	

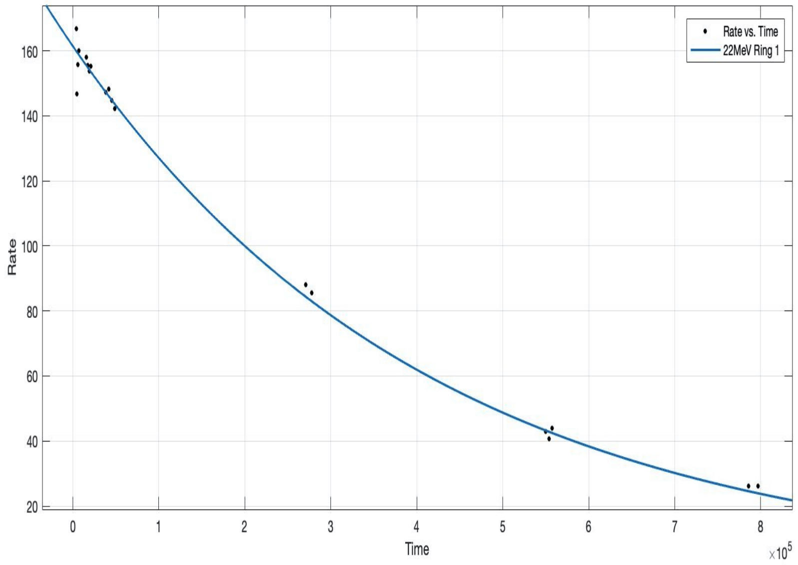
- The concept of multiple energy measurements in a single irradiation works



The Measurement Cycle



The counting stations



The radioactive decay counting

Primary and secondary isotopes of interest

Target	Reaction	Product	Observed
^{48}Ti	(γ,p)	^{47}Sc	YES - NCCU
	(γ,pn)	^{46}Sc	NOT seen - NCCU
^{68}Zn	(γ,p)	^{67}Cu	YES
	(γ,pn)	^{66}Cu	**NO (short half-life)**
^{77}Se	(γ,p)	^{76}As	NO data taken
^{78}Se	(γ,pn)	^{77}As	
^{187}Os	(γ,p)	^{186}Re	NO (too weak)
^{189}Os	(γ,p)	^{188}Re	YES
^{190}Os	(γ,p)	^{189}Re	YES
^{196}Pt	(γ,p)	^{195}Ir	Complicated analysis
	(γ,n)	^{195m}Pt	YES
^{197}Au	(γ,pn)	^{195m}Pt	Complicated analysis
	(γ,n)	^{196}Au	YES
^{162}Dy	(γ,p)	^{161}Tb	NO data taken
	(γ,pn)	^{160}Tb	

Target	Product isotope	Reaction(s)
^{nat}Zn	^{62}Zn	^{64}Zn(γ,2n)
	^{63}Zn	^{64}Zn(γ,n) ^{66}Zn(γ,3n)
	^{65}Zn*	^{66}Zn(g,n) ^{67}Zn(γ,2n) ^{68}Zn(γ,3n)
	^{69}Zn	^{70}Zn(γ,n)
^{nat}Os	^{191}Os	^{192}Os(γ,n)
	^{185}Os	^{186}Os(γ,n) ^{187}Os(γ,2n) ^{188}Os(γ,3n)
^{nat}Pt	^{197}Pt	^{198}Pt(γ,n)
	^{194}Ir*	^{195}Pt((γ,p) ^{196}Pt((γ,pn) ^{198}Pt((γ,p3n)
^{197}Au	^{194}Au	^{197}Au(γ,3n)

An example: Production of ^{47}Sc from $^{nat}Ti(\gamma,X)$ reaction

Isotope	Photonuclear Reaction Pathway to production of ^{47}Sc	Energy Threshold	Comments
^{46}Ti	Not possible		Disregard
^{47}Ti	Not possible		Disregard
^{48}Ti	48Ti (γ, p)	11.44 MeV	Primary reaction studied at all energies
^{49}Ti	49Ti (γ, np)	17.36 MeV	Secondary reaction studied included above 17 MeV
^{50}Ti	50Ti (γ, np)	22.04 MeV	Secondary reaction ignored due to highly suppressed cross section as compared to the primary reaction

An example: Focus on ^{47}Sc

Target	Nat. Abun. (%)	Rxn	Product	Half-life	Strongest γ (KeV) (% Intensity)
^{48}Ti	73.72	**γ,n**	**^{47}Ti**	**STABLE**	
		γ,p	^{47}Sc	3.3492 d	159.4 (68.3)
		γ,2n	**^{46}Ti**	**STABLE**	
		γ,pn	^{46}Sc	83.79 d	1120 (99.9)
		γ,α	**^{44}Ca**	**STABLE**	

^{47}Sc: Shortest half life of 3.3492days produced from the reaction γ,p

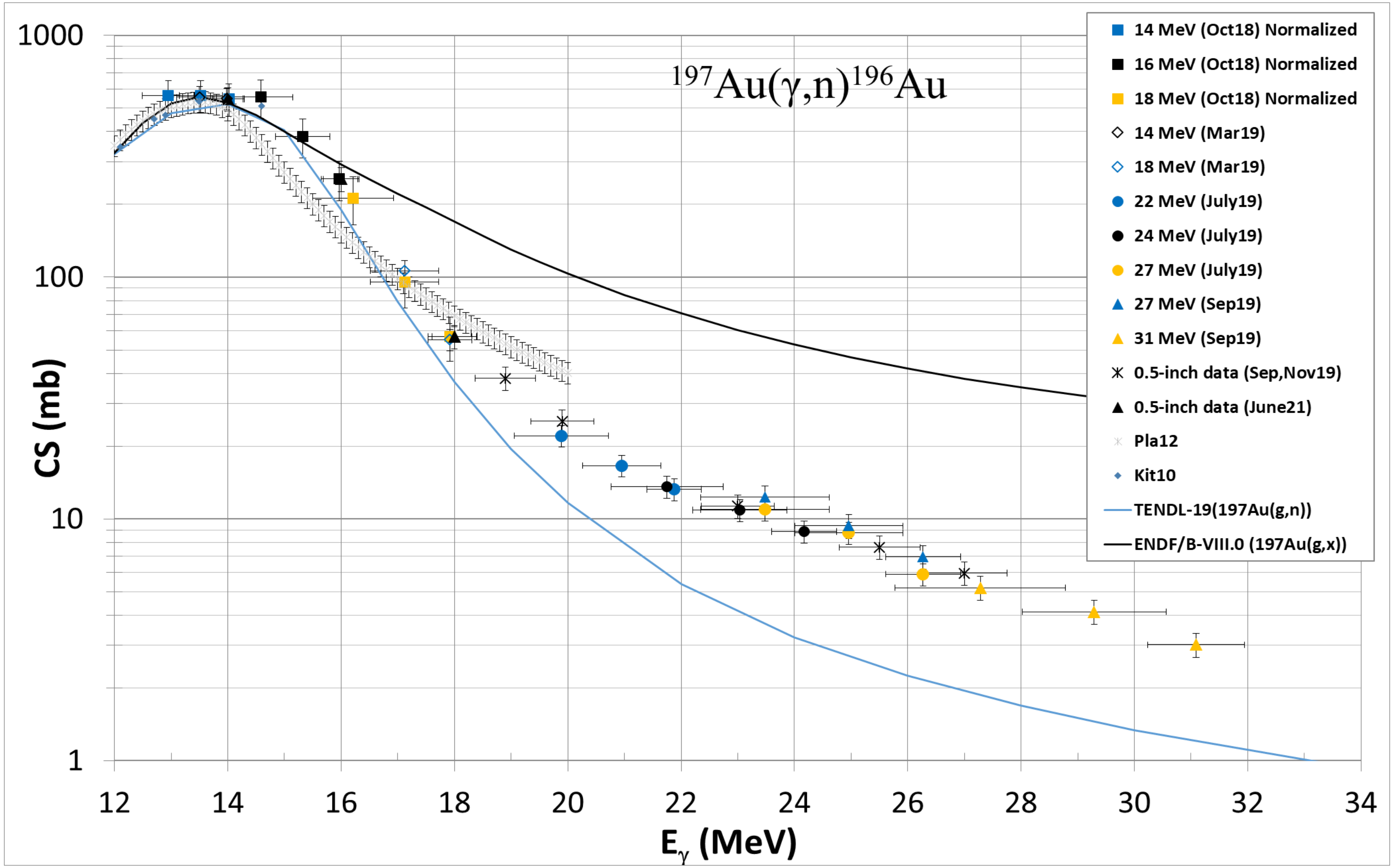
^{47}Sc: Theragnostic agents in nuclear medicine (both purposes: diagnosis as well as treatment)

Benchmarking: The GOLD Standard

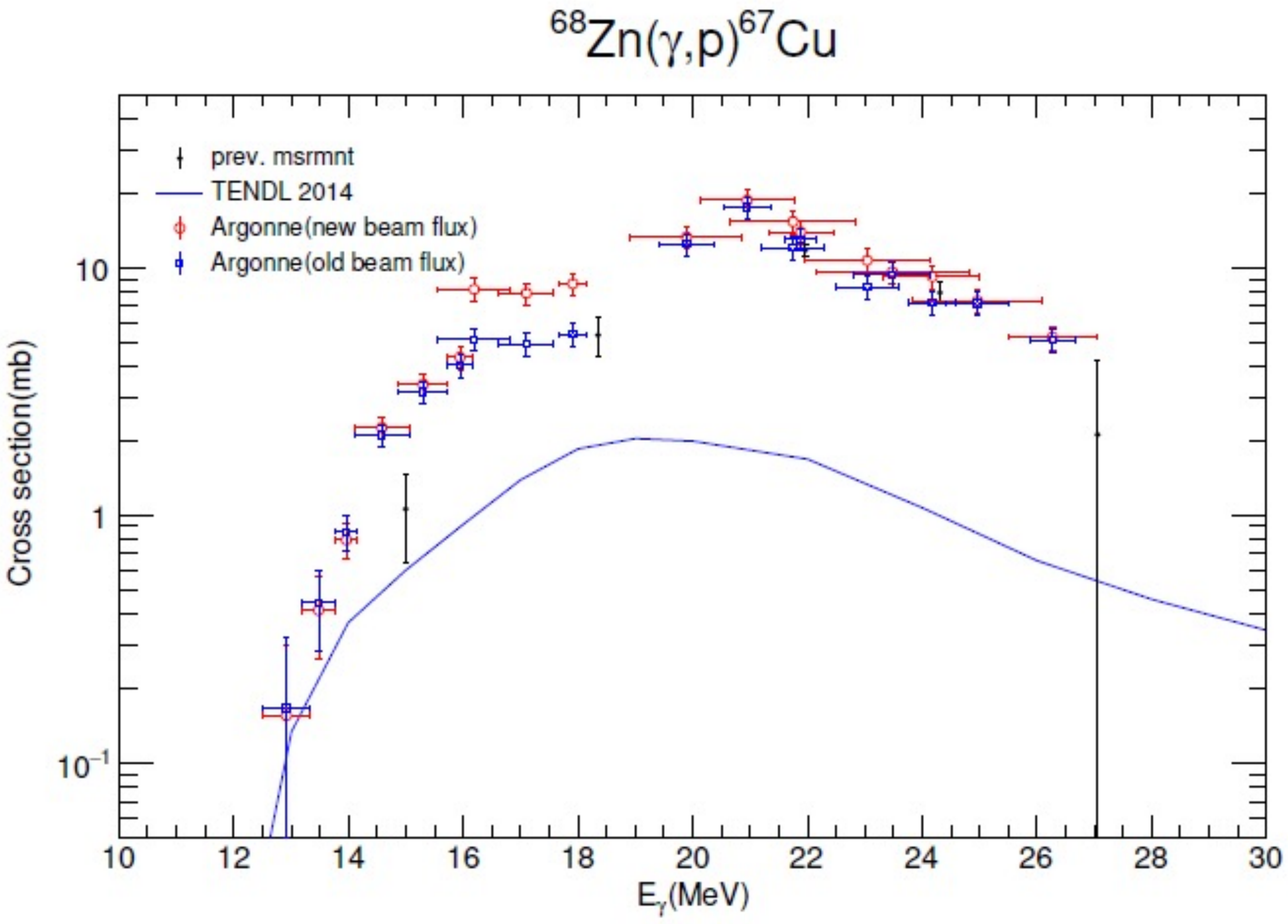
Target	Nat. Abun. (%)	Rxn	Product	Half-life	Strongest γ (KeV) (% Intensity)
^{197}Au	100	γ,n	^{196}Au	6.17 d	355.73 (87) 333.03 (22.9)
		γ,p	**^{196}Pt**	**STABLE**	
		γ,2n	^{195}Au	186.01. d	98.85(11.21)
		γ,pn	^{195}Pt	4.01 d	98.9(11.7)
		γ,α	^{193}Ir	10.53 d	80.22(0.00467)

^{196}Au: Used as calibration and has a half life of 6.17days and is produced from the reaction γ,n

Benchmarking: The GOLD Standard

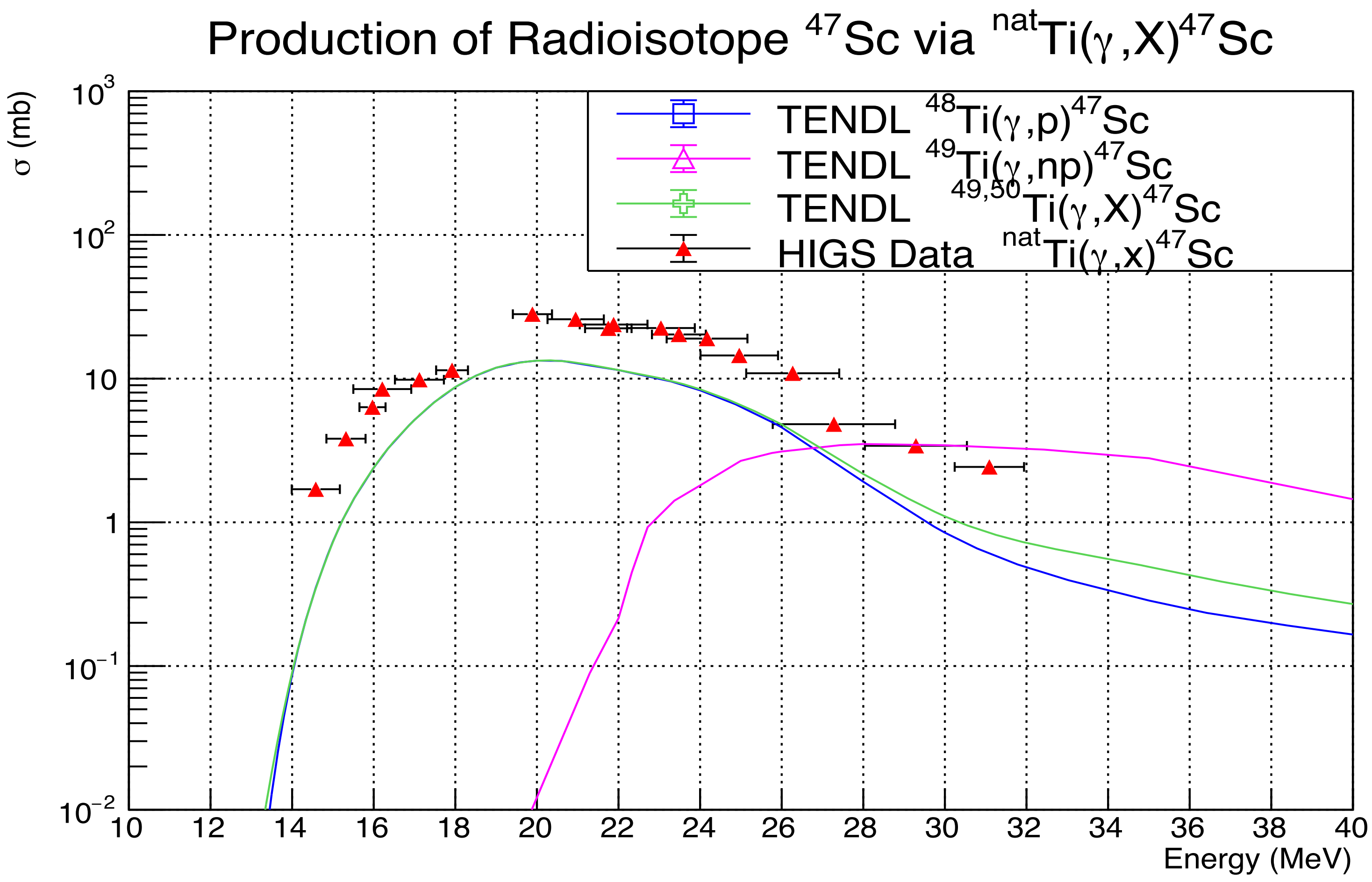


An example: Production of ^{67}Cu from $^{68}Zn(\gamma,p)$ reaction



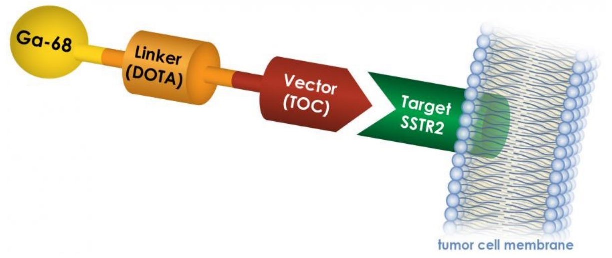
Copper-67 ($t_{1/2}$ = 2.58 days) decays by β^- (E_β—max: 562 keV) and γ-rays (93 keV and 185 keV) rendering it with potential for both radionuclide therapy and single-photon emission computed tomography (SPECT) imaging.

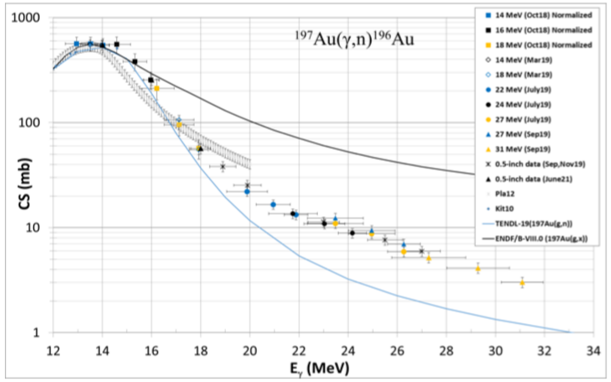
An example: Production of ^{47}Sc from $^{nat}Ti(\gamma,X)$ reaction

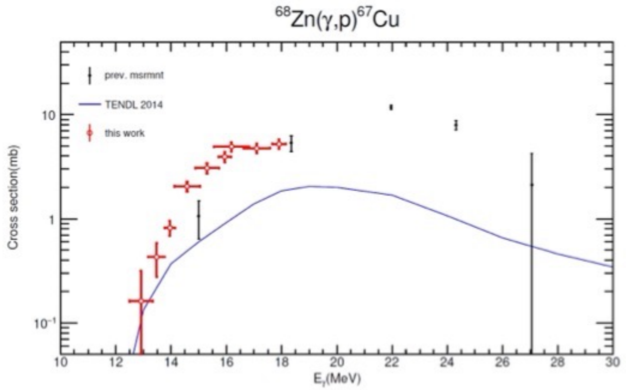


Summary

- Radioisotopes are used for medical therapeutics and diagnostics, e.g., cancer treatment, PET imaging and SPEC imaging
- Radioisotopes are produced using a variety of accelerated charged particle beams, accelerator produced neutron beams, and neutrons in nuclear reactors. Photonuclear reactions provide an option for high specific radioactivity production, i.e., specific activity per unit mass, for isotopes needed in medicine.
- Designing systems for radioisotope production requires realistic simulations of complex systems. The GEANT-4 is the standard transport code using in this application. The reliability of the simulations depends on having libraries of accurate photonuclear reaction data at photon energies across the GDR region where most of the photoabsorption strength exist. Databases used in the simulations include TENDL, JENDL, ENDF, JEFF, CENDL. The data and evaluations in these databases must be validated with experiment. Examples of (γ, n) and (γ, p) and (γ, pn) reactions were presented in this talk.
- Cross-section measurements were recently performed at HIGS on reaction pathways to the production of ^{47}Sc [^{48}Ti(γ, p) + ^{49}Ti(γ, pn) + ^{50}Ti(γ, t)], ^{67}Cu [^{68}Zn(γ, p)], and ^{195m}Pt [^{196}Pt(γ, n)].
- More cross-section measurements that produce radioisotopes important for medical treatment and diagnostics, e.g., ^{177}Lu [^{178}Hf(γ, p), ^{179}Hf(γ, pn), ^{180}Hf(γ, t), ^{181}Ta(γ, α)].







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