Production Pathways for Medically Interesting Isotopes

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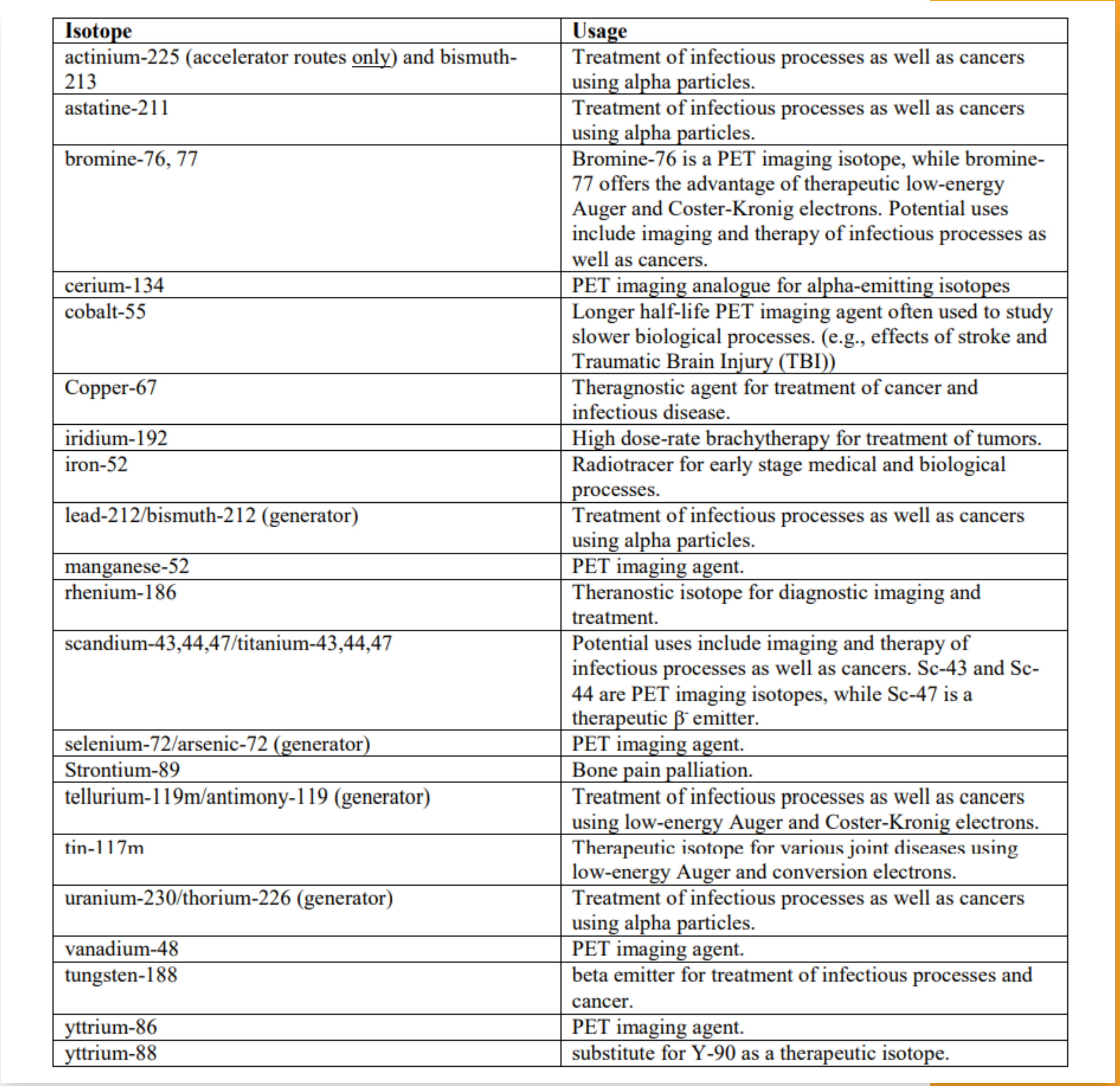
Introduction

- The DOE has published a list of future radioisotopes of medical interest
- All of which have limited production
- The goal is an overview of all possible production pathways by irradiation and cascade production



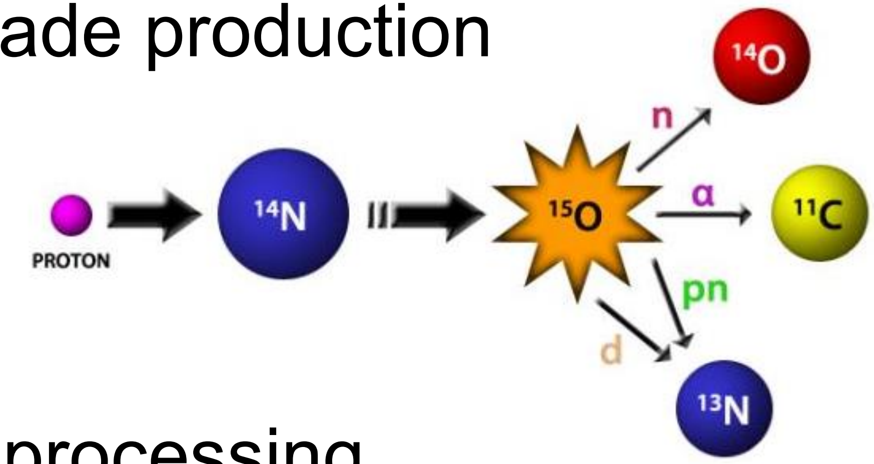
Isotope	Usage
actinium-225 (accelerator routes only) and bismuth-213	Treatment of infectious processes as well as cancers using alpha particles.
astatine-211	Treatment of infectious processes as well as cancers using alpha particles.
bromine-76, 77	Bromine-76 is a PET imaging isotope, while bromine-77 offers the advantage of therapeutic low-energy Auger and Coster-Kronig electrons. Potential uses include imaging and therapy of infectious processes as well as cancers.
cerium-134	PET imaging analogue for alpha-emitting isotopes
cobalt-55	Longer half-life PET imaging agent often used to study slower biological processes. (e.g., effects of stroke and Traumatic Brain Injury (TBI))
Copper-67	Theragnostic agent for treatment of cancer and infectious disease.
iridium-192	High dose-rate brachytherapy for treatment of tumors.
iron-52	Radiotracer for early stage medical and biological processes.
lead-212/bismuth-212 (generator)	Treatment of infectious processes as well as cancers using alpha particles.
manganese-52	PET imaging agent.
rhenium-186	Theranostic isotope for diagnostic imaging and treatment.
scandium-43,44,47/titanium-43,44,47	Potential uses include imaging and therapy of infectious processes as well as cancers. Sc-43 and Sc-44 are PET imaging isotopes, while Sc-47 is a therapeutic β^- emitter.
selenium-72/arsenic-72 (generator)	PET imaging agent.
Strontium-89	Bone pain palliation.
tellurium-119m/antimony-119 (generator)	Treatment of infectious processes as well as cancers using low-energy Auger and Coster-Kronig electrons.
tin-117m	Therapeutic isotope for various joint diseases using low-energy Auger and conversion electrons.
uranium-230/thorium-226 (generator)	Treatment of infectious processes as well as cancers using alpha particles.
vanadium-48	PET imaging agent.
tungsten-188	beta emitter for treatment of infectious processes and cancer.
yttrium-86	PET imaging agent.
yttrium-88	substitute for Y-90 as a therapeutic isotope.

Department of Energy Office of Science Isotope R&D and Production. (2021). Advancing Novel Medical Isotopes for Clinical Trials FOA. DE-FOA-0002532

The SNIPP Computer Program

- Search for New Isotope Production Pathways
  - Irradiation production

- Cascade production



- Post-processing

The SNIPP Computer Program

Irradiation production section

Input: particle, target material, production method, start and end isotopes

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Gets cross sections corresponding to the energy entered from TENDL[1] library and half-lives for each daughter produced from NDW[2]

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1. A.J. Koning, D. Rochman, J. Sublet. (2019) https://tendl.web.psi.ch/tendl_2019/tendl2019.html
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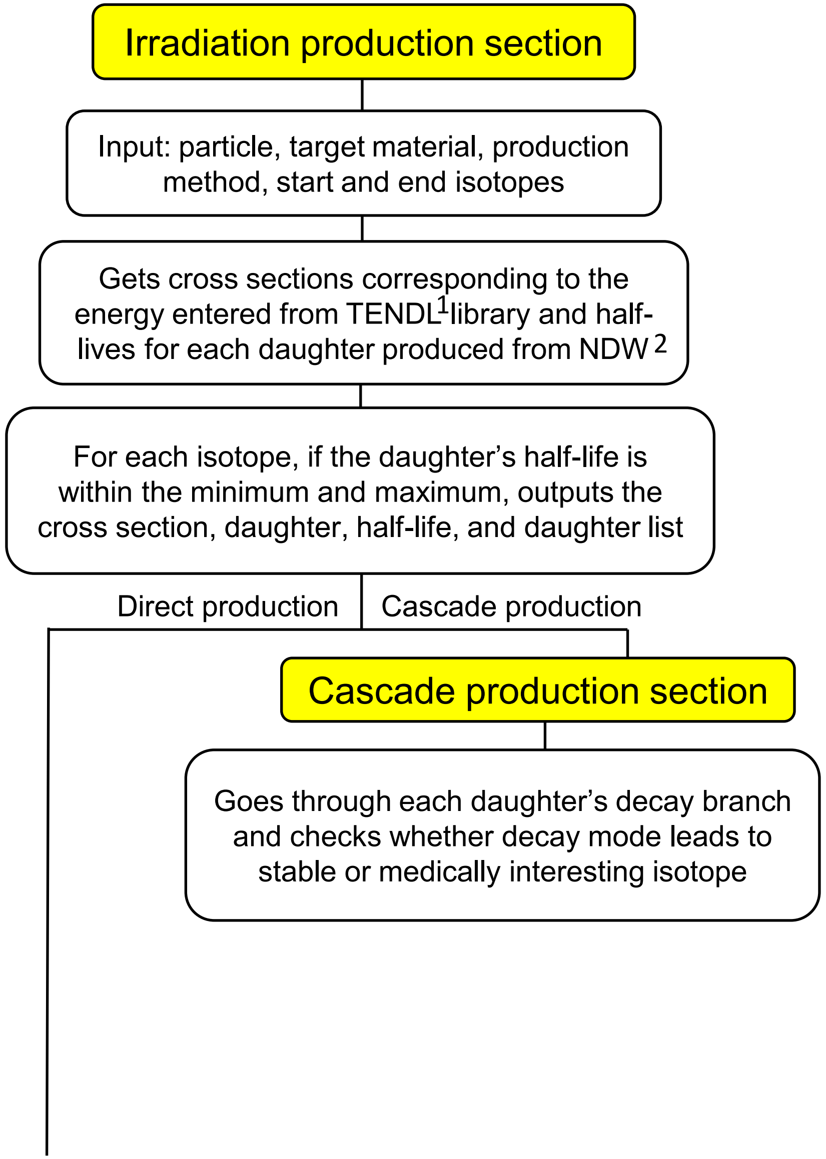

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Direct production

Cascade production

Cascade production section

Goes through each daughter's decay branch and checks whether decay mode leads to stable or medically interesting isotope

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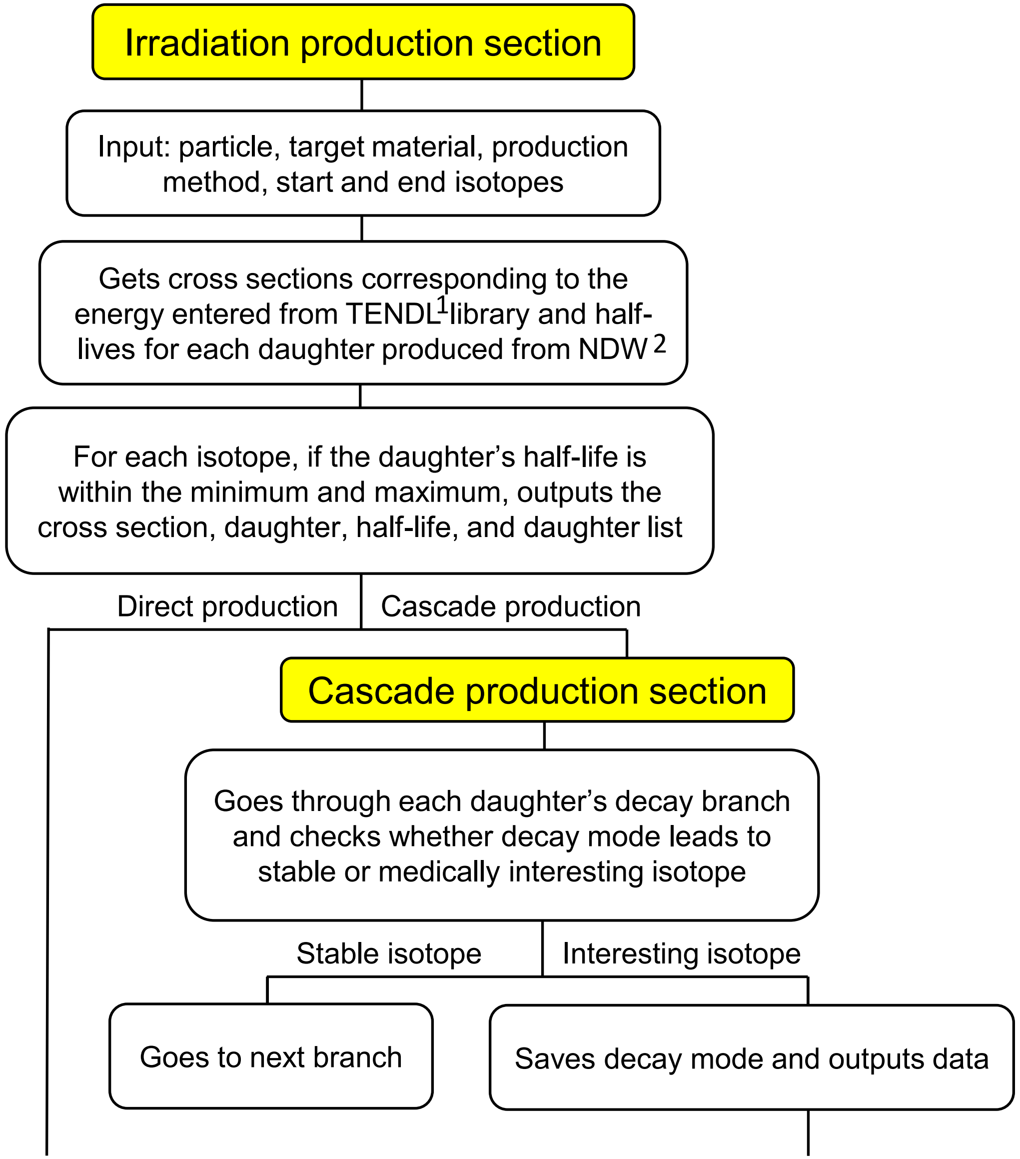

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Goes through each daughter's decay branch and checks whether decay mode leads to stable or medically interesting isotope

Stable isotope

Interesting isotope

Goes to next branch

Saves decay mode and outputs data

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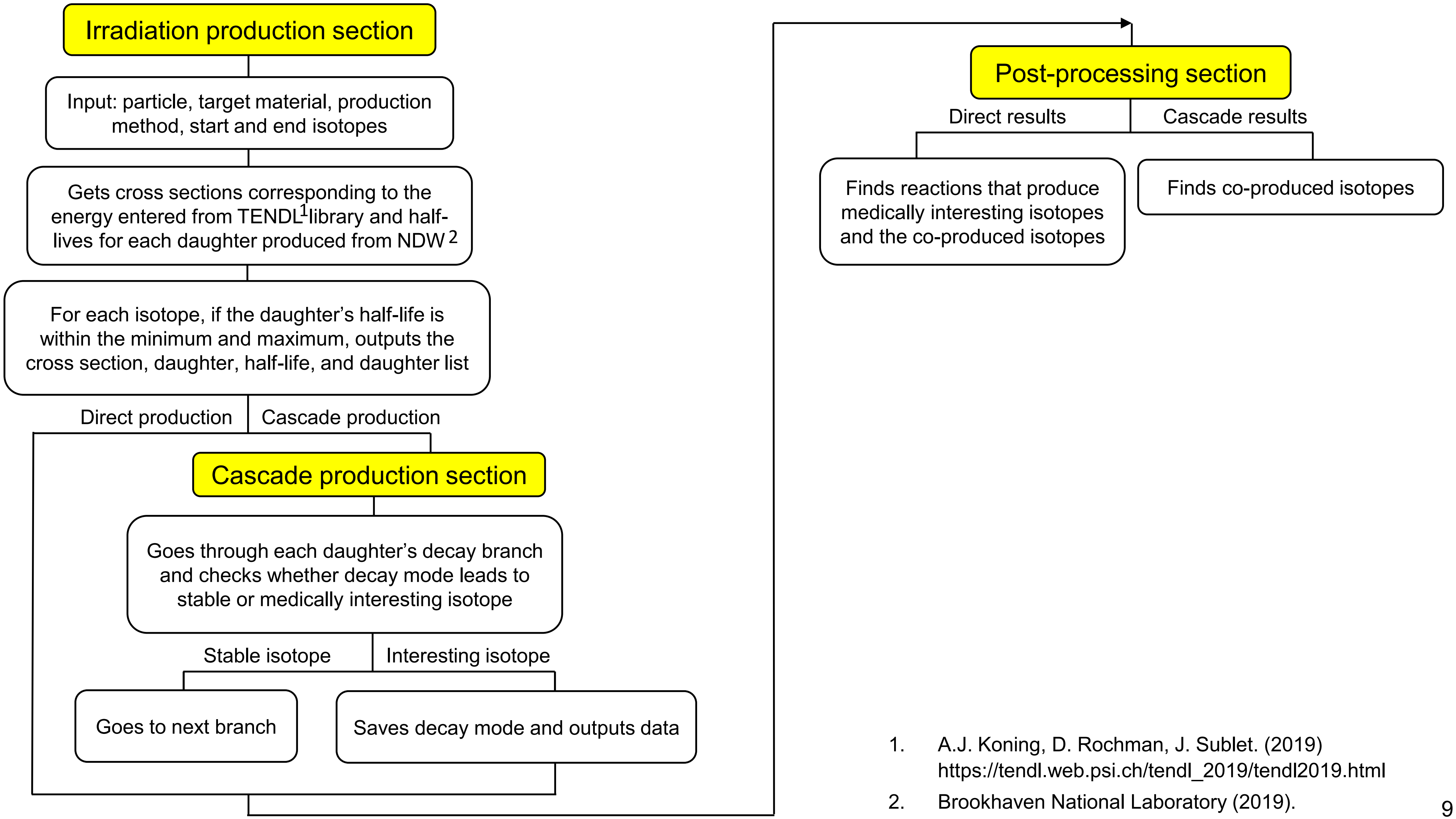

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Post-processing section

Direct results

Cascade results

Finds reactions that produce medically interesting isotopes and the co-produced isotopes

Finds co-produced isotopes

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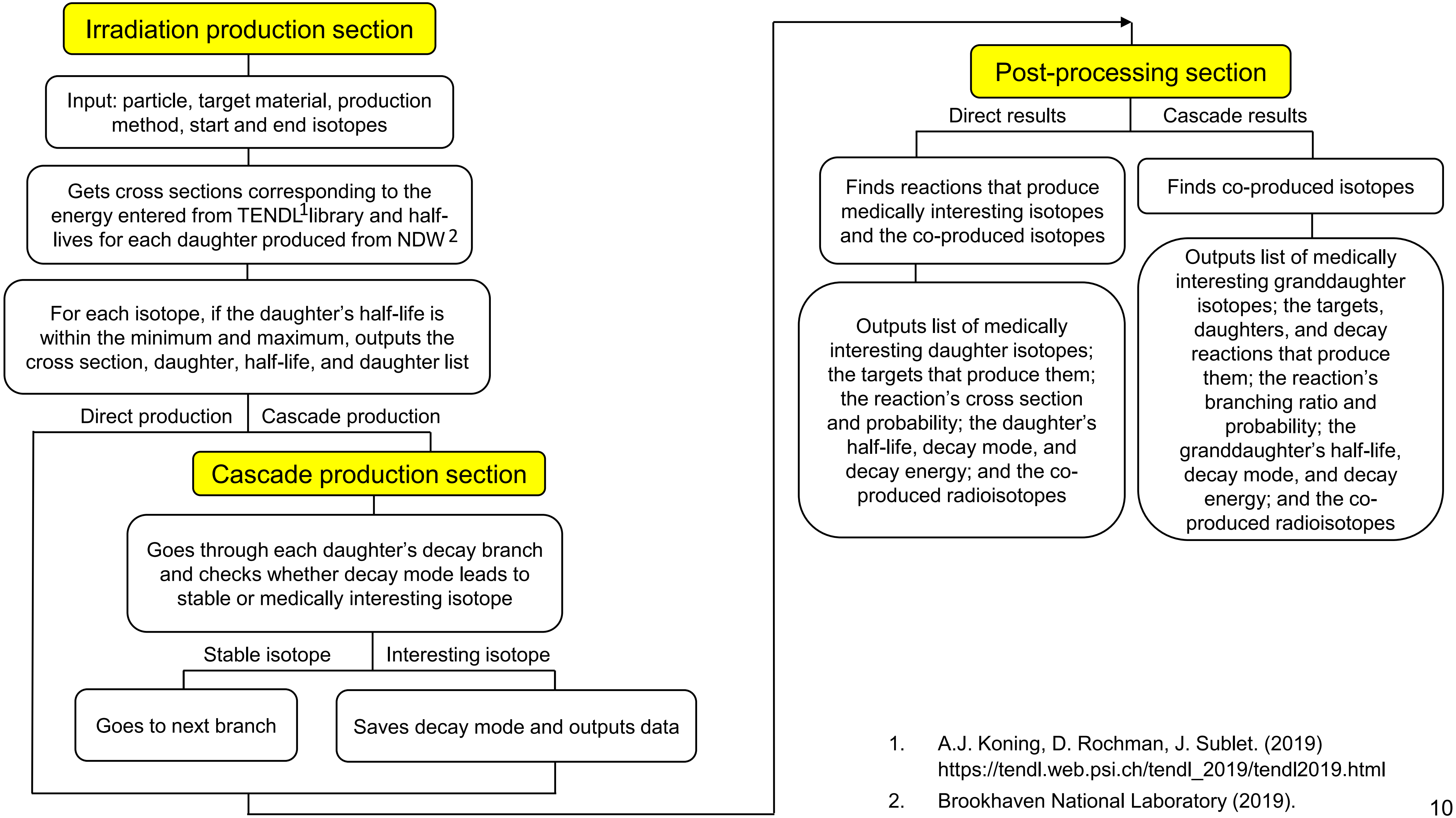

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Saves decay mode and outputs data

Post-processing section

Direct results

Finds reactions that produce medically interesting isotopes and the co-produced isotopes

Outputs list of medically interesting daughter isotopes; the targets that produce them; the reaction's cross section and probability; the daughter's half-life, decay mode, and decay energy; and the co-produced radioisotopes

Cascade results

Finds co-produced isotopes

Outputs list of medically interesting granddaughter isotopes; the targets, daughters, and decay reactions that produce them; the reaction's branching ratio and probability; the granddaughter's half-life, decay mode, and decay energy; and the co-produced radioisotopes

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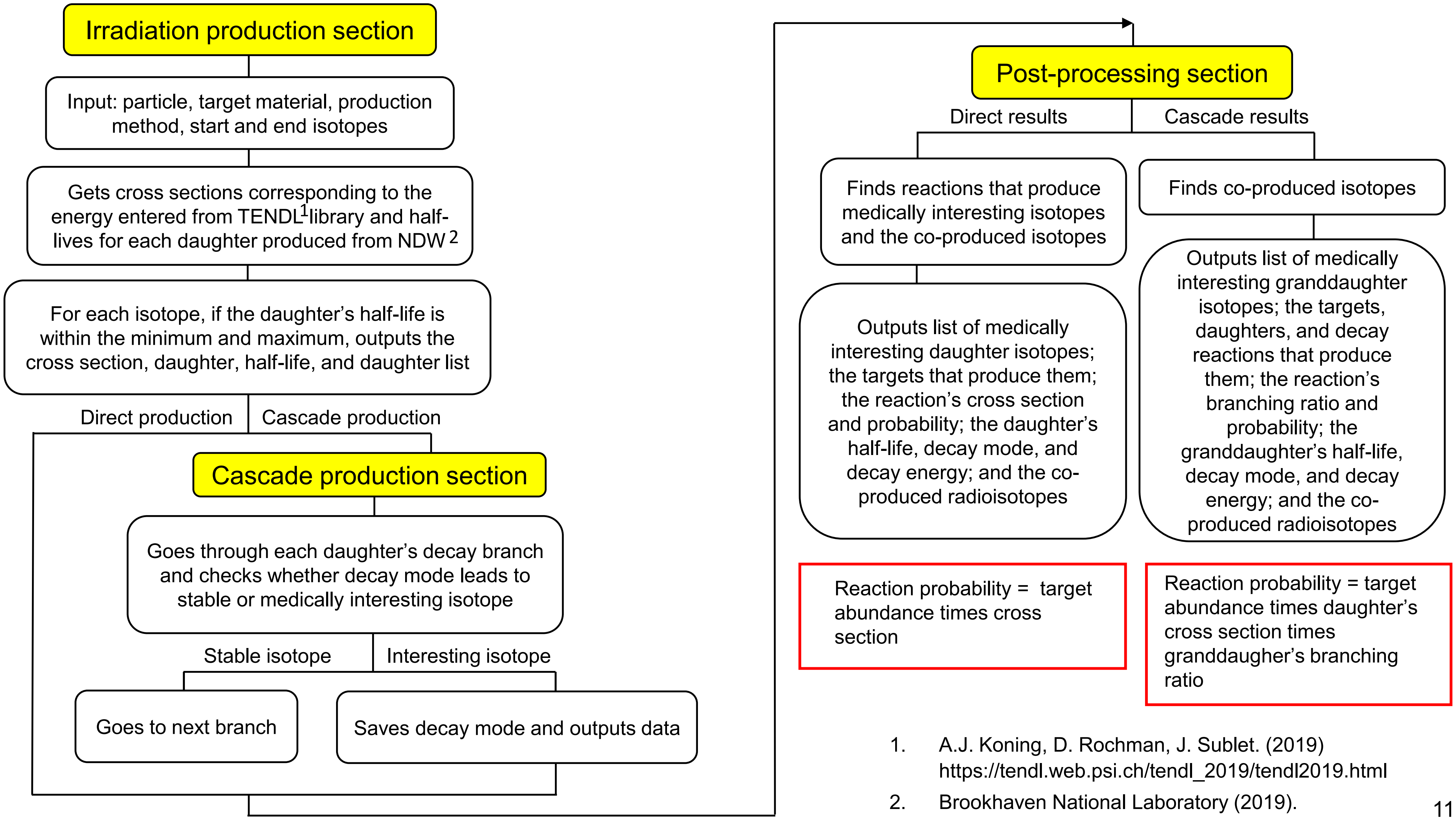

Irradiation production section

Input: particle, target material, production method, start and end isotopes

Gets cross sections corresponding to the energy entered from TENDL[1] library and half-lives for each daughter produced from NDW[2]

For each isotope, if the daughter's half-life is within the minimum and maximum, outputs the cross section, daughter, half-life, and daughter list

Direct production

Cascade production

Cascade production section

Goes through each daughter's decay branch and checks whether decay mode leads to stable or medically interesting isotope

Stable isotope

Interesting isotope

Goes to next branch

Saves decay mode and outputs data

Post-processing section

Direct results

Cascade results

Finds reactions that produce medically interesting isotopes and the co-produced isotopes

Outputs list of medically interesting daughter isotopes; the targets that produce them; the reaction's cross section and probability; the daughter's half-life, decay mode, and decay energy; and the co-produced radioisotopes

Reaction probability = target abundance times cross section

Finds co-produced isotopes

Outputs list of medically interesting granddaughter isotopes; the targets, daughters, and decay reactions that produce them; the reaction's branching ratio and probability; the granddaughter's half-life, decay mode, and decay energy; and the co-produced radioisotopes

Reaction probability = target abundance times daughter's cross section times granddaugher's branching ratio

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Input parameters – Irradiation and decay production

- Gammas: produced by bremsstrahlung radiation from 40 MeV electrons
  - Gamma energy: 20 MeV
  - Half-life for irradiation production: 1 – 20 days
  - Half-life for cascade production: 0 – 1000 days

- Low energy protons: produced by hospital cyclotrons at 15-25 MeV
  - Proton energy: 20 MeV
  - Half-life for irradiation production: 1 hour – 20 days
  - Half-life for cascade production: 0 – 1000 days

- Reactions were designated “not viable" for target isotopes with low proportion or difficult prior separation, low cross-sections, or medically dangerous co-produced radioisotopes
- Examples with large cross sections and small co-production of undesirable isotopes were selected

Results for 20 MeV Gamma Pathway for ^{47}Sc

	Irradiation Production								
	Target	% of Isotope in Target	Reaction	Cross section (barns)	Daughter	Half-life (days)	Decay mode	Energy (MeV)	Reaction probability (barns)
	^{51}V	99.8%	^{51}V (γ,α) ^{47}Sc	0.6	^{47}Sc	3.3	β-	0.6	0.6
	^{48}Ti	73.7%	^{48}Ti (γ,p) ^{47}Sc	13.3	^{47}Sc	3.3	β-	0.6	9.8
Co-Produced	^{49}Ti	5.4%	^{49}Ti (γ,p) ^{48}Sc	4.6	^{48}Sc	1.8	β-	4.0	0.2

- Titanium reaction co-produces ^{48}Sc, which could be significantly reduced by using an isotopically purified target

Results for 20 MeV Gamma Pathway for ^{67}Cu

	Irradiation Production								
	Target	% of Isotope in Target	Reaction	Cross section (barns)	Daughter	Half-life (days)	Decay mode	Energy (MeV)	Reaction probability (barns)
	^{68}Zn	18.4%	^{68}Zn (γ,p) ^{67}Cu	2.0	^{67}Cu	2.6	β-	0.6	0.4
	^{71}Ga	39.9%	^{71}Ga (γ,α) ^{67}Cu	0.7	^{67}Cu	2.6	β-	0.6	0.3
Co-Produced	^{69}Ga	60.1%	^{69}Ga (γ,2n) ^{67}Ga	20.1	^{67}Ga	3.3	ϵ	1.0	12.1

- Gallium reaction co-produces ^{67}Ga, which could be significantly reduced by using an isotopically purified target

Results for 20 MeV Proton Pathway for ^{52}Mn

	Irradiation Production								
	Target	% of Isotope in Target	Reaction	Cross section (barns)	Daughter	Half-life (days)	Decay mode	Energy (MeV)	Reaction probability (barns)
	^{52}Cr	83.8%	^{52}Cr (p,n) ^{52}Mn	68.8	^{52}Mn	5.6	EC	3.7	57.7
	^{53}Cr	9.5%	^{53}Cr (p,2n) ^{52}Mn	305.0	^{52}Mn	5.6	EC	3.7	29.0
Co-Produced	^{52}Cr	None							
	^{53}Cr	None							

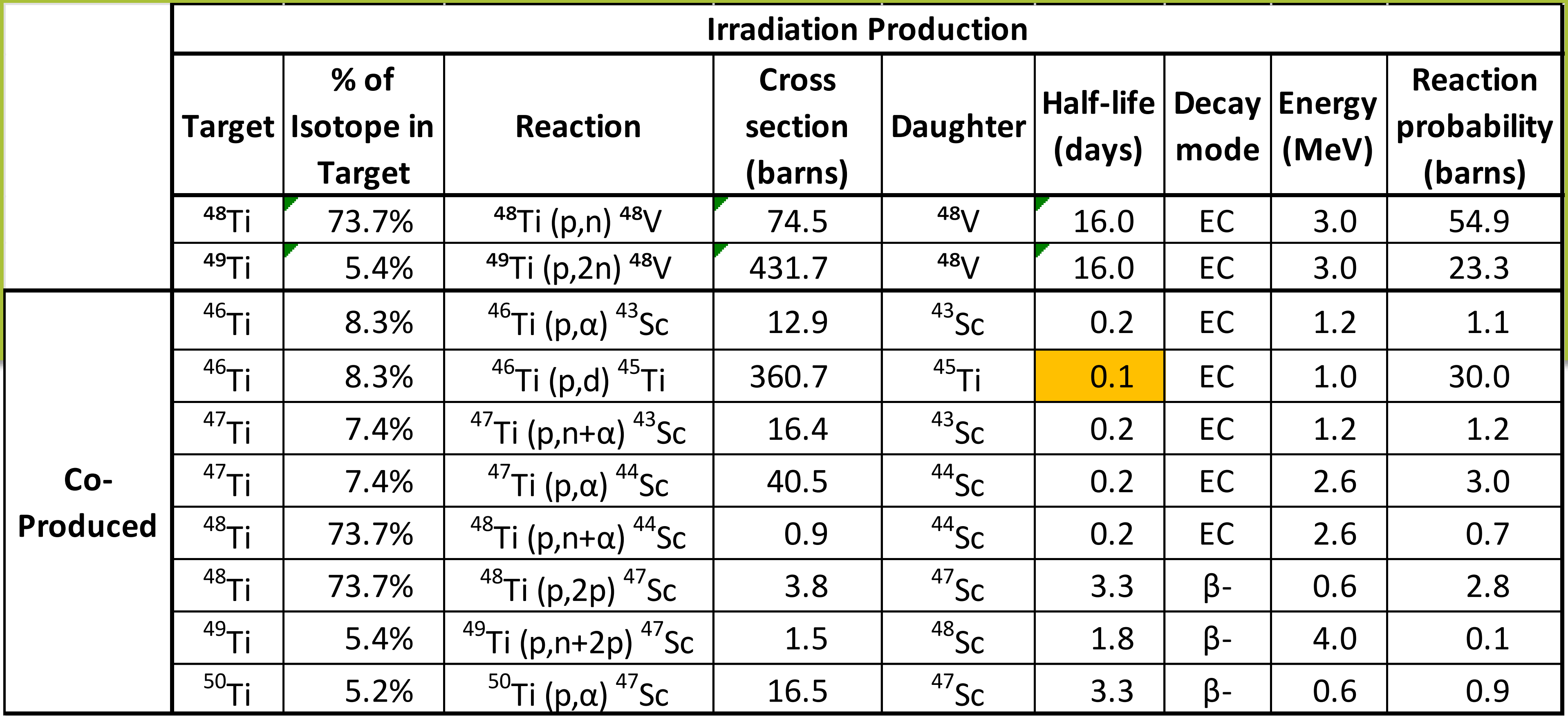
- No other isotopes are co-produced when irradiating naturally occurring chromium
- Total reaction probability of 86.7 barn

Results for 20 MeV Proton Pathway for ^{55}Co

	Irradiation Production								
	Target	% of Isotope in Target	Reaction	Cross section (barns)	Daughter	Half-life (days)	Decay mode	Energy (MeV)	Reaction probability (barns)
	^{56}Fe	91.8%	^{56}Fe (p,2n) ^{55}Co	60.5	^{55}Co	0.7	EC	2.4	55.5
Co-Produced	^{54}Fe	5.8%	^{54}Fe (p,γ) ^{55}Co	0.5	^{55}Co	0.7	EC	2.4	0.03
	^{56}Fe	91.6%	^{56}Fe (p,n+α) ^{52}Mn	0.5	^{52}Mn	5.6	EC	3.7	0.5
	^{57}Fe	2.1%	^{57}Fe (p,2p) ^{56}Mn	4.8	^{56}Mn	0.1	β-	3.7	0.1

- Reaction probabilities are small and chemical separation of the desired radioisotope and the unwanted co-produced radioisotopes would be possible

Results for 20 MeV Proton Pathway for ^{48}V



	Irradiation Production								
	Target	% of Isotope in Target	Reaction	Cross section (barns)	Daughter	Half-life (days)	Decay mode	Energy (MeV)	Reaction probability (barns)
	^{48}Ti	73.7%	^{48}Ti (p,n) ^{48}V	74.5	^{48}V	16.0	EC	3.0	54.9
	^{49}Ti	5.4%	^{49}Ti (p,2n) ^{48}V	431.7	^{48}V	16.0	EC	3.0	23.3
Co-Produced	^{46}Ti	8.3%	^{46}Ti (p,α) ^{43}Sc	12.9	^{43}Sc	0.2	EC	1.2	1.1
	^{46}Ti	8.3%	^{46}Ti (p,d) ^{45}Ti	360.7	^{45}Ti	0.1	EC	1.0	30.0
	^{47}Ti	7.4%	^{47}Ti (p,n+α) ^{43}Sc	16.4	^{43}Sc	0.2	EC	1.2	1.2
	^{47}Ti	7.4%	^{47}Ti (p,α) ^{44}Sc	40.5	^{44}Sc	0.2	EC	2.6	3.0
	^{48}Ti	73.7%	^{48}Ti (p,n+α) ^{44}Sc	0.9	^{44}Sc	0.2	EC	2.6	0.7
	^{48}Ti	73.7%	^{48}Ti (p,2p) ^{47}Sc	3.8	^{47}Sc	3.3	β-	0.6	2.8
	^{49}Ti	5.4%	^{49}Ti (p,n+2p) ^{47}Sc	1.5	^{48}Sc	1.8	β-	4.0	0.1
	^{50}Ti	5.2%	^{50}Ti (p,α) ^{47}Sc	16.5	^{47}Sc	3.3	β-	0.6	0.9

- All co-production reactions have small reaction probabilities, except for ^{45}Ti
- The lifetime of ^{45}Ti is 3 hours, so it will have decayed to negligeable values after a day

Results for cascade reactions:

- The decay reactions returned 21 proton reactions and 7 gamma reactions which produced interesting isotopes
- Most contained a large number of co-produced isotopes, and/or produced isotopes that could not be chemically separated from the original target or the co-produced isotopes

- No acceptable decay reaction pathways were found for isotopes listed in the DOE IP list of medically interesting isotopes

- Irradiation production pathways for medically interesting isotopes not on the DOE IP list were also found. One example is the production of ^{18}F from ^{18}O by proton irradiation, a pathway which is already widely used in hospital cyclotrons

Conclusions:

- SNIPP has already been shown to be efficient in finding new possibilities for producing radioisotopes
- It is now capable of searching for pathways to produce radioisotopes with desired properties, e.g., alpha emitters with a half-life greater than 3 days.
- This provides an opportunity to look at a wide set of radioisotopes, including those of industrial interest
- However, identifying a pathway with SNIPP is a necessary, but not sufficient requirement for exploitation

Gracias

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