

# Living at or Living Beyond the K-Edge? Is it Iodine Forever?

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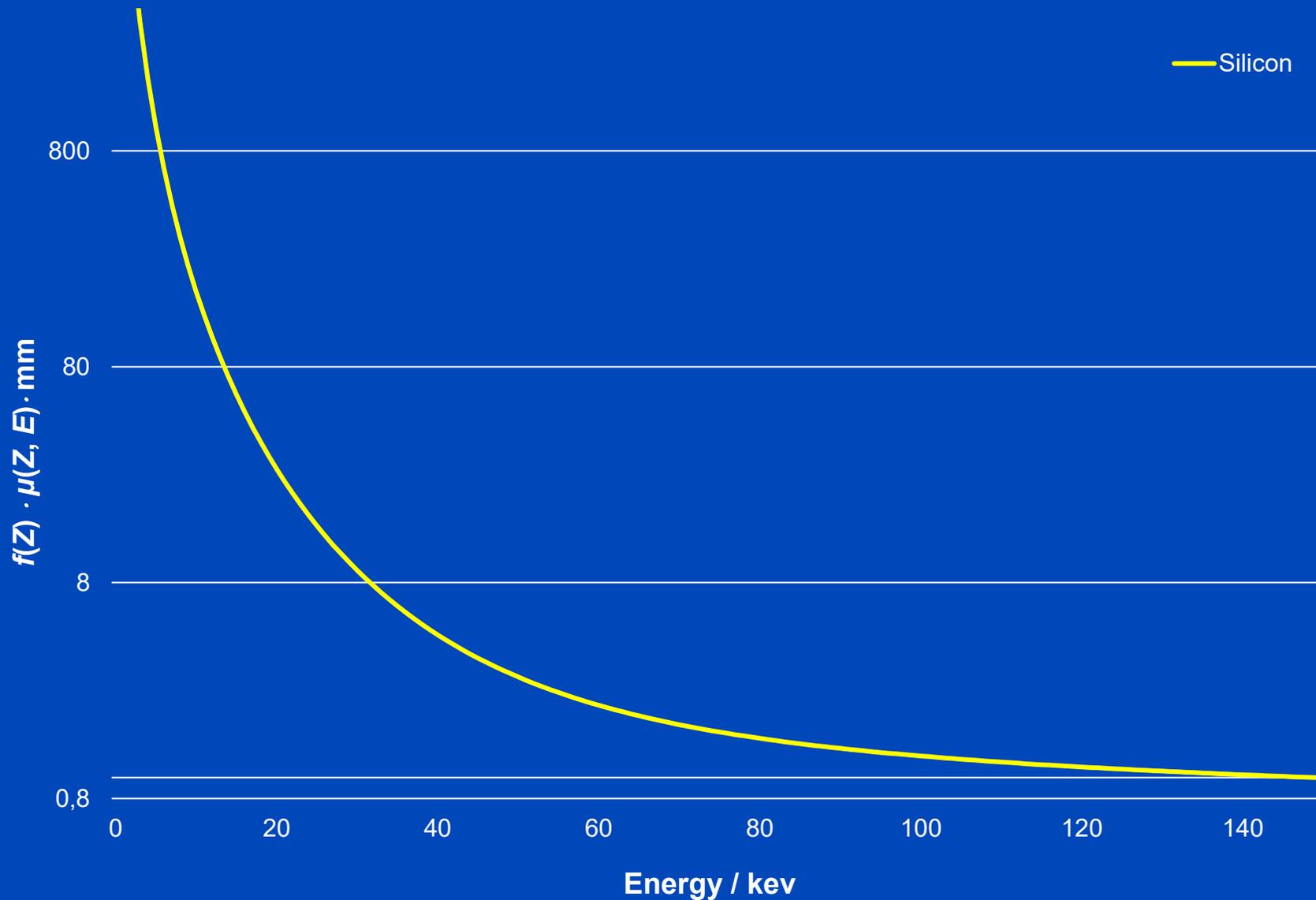
DEUTSCHES  
KREBSFORSCHUNGSZENTRUM  
IN DER HELMHOLTZ-GEMEINSCHAFT

**NEW CONTRAST AGENTS?**

Element	Z	K-edge	HVL	HVL×ρ	Hygros.	Cost (2025)	Machinability	
Silicon	14	1.8 keV	13.213 mm	3.08 g/cm <sup>2</sup>	Low	1.70 \$/kg	Moderate	} Used or proposed as prefilter
Calcium	20	4.0 keV	11.862 mm	2.05 g/cm <sup>2</sup>	High	2.28 \$/kg	Low	
Copper	29	9.0 keV	1.001 mm	0.89 g/cm <sup>2</sup>	Low	6.00 \$/kg	High	
Silver	47	25.5 keV	0.251 mm	0.26 g/cm <sup>2</sup>	Low	521.00 \$/kg	High	
Cadmium	48	26.7 keV	0.293 mm	0.25 g/cm <sup>2</sup>	Low	4.10 \$/kg	Low	
Tin	50	29.2 keV	0.315 mm	0.23 g/cm <sup>2</sup>	Low	18.70 \$/kg	High	} K-edges quite low to discriminate Ca and CA.
Iodine	53	33.2 keV	0.404 mm	0.20 g/cm <sup>2</sup>	Moderate	35.00 \$/kg	Low	
Barium	56	37.4 keV	0.505 mm	0.18 g/cm <sup>2</sup>	High	0.26 \$/kg	Low	
Cerium	58	40.4 keV	0.239 mm	0.16 g/cm <sup>2</sup>	Moderate	4.64 \$/kg	Moderate	
Gadolinium	64	50.2 keV	0.169 mm	0.13 g/cm <sup>2</sup>	Moderate	28.60 \$/kg	Moderate	
Holmium	67	55.6 keV	0.164 mm	0.14 g/cm <sup>2</sup>	Moderate	57.10 \$/kg	Moderate	} K-edges covered by most kV
Ytterbium	70	61.3 keV	0.190 mm	0.13 g/cm <sup>2</sup>	Moderate	17.10 \$/kg	Moderate	
Hafnium	72	65.4 keV	0.098 mm	0.13 g/cm <sup>2</sup>	Low	900.00 \$/kg	Moderate	
Tantalum	73	67.4 keV	0.079 mm	0.13 g/cm <sup>2</sup>	Low	305.00 \$/kg	Low	
Tungsten	74	69.5 keV	0.071 mm	0.14 g/cm <sup>2</sup>	Low	35.30 \$/kg	Low	
Gold	79	80.7 keV	0.076 mm	0.15 g/cm <sup>2</sup>	Low	44800.00 \$/kg	Moderate	
Bismuth	83	90.5 keV	0.170 mm	0.16 g/cm <sup>2</sup>	Low	6.61 \$/kg	Moderate	

HVLs are calculated for the 120 kV Tucker spectrum with intrinsic + 32 cm water prefiltration as seen for a 1.6 mm CdTe sensor above 20 keV.

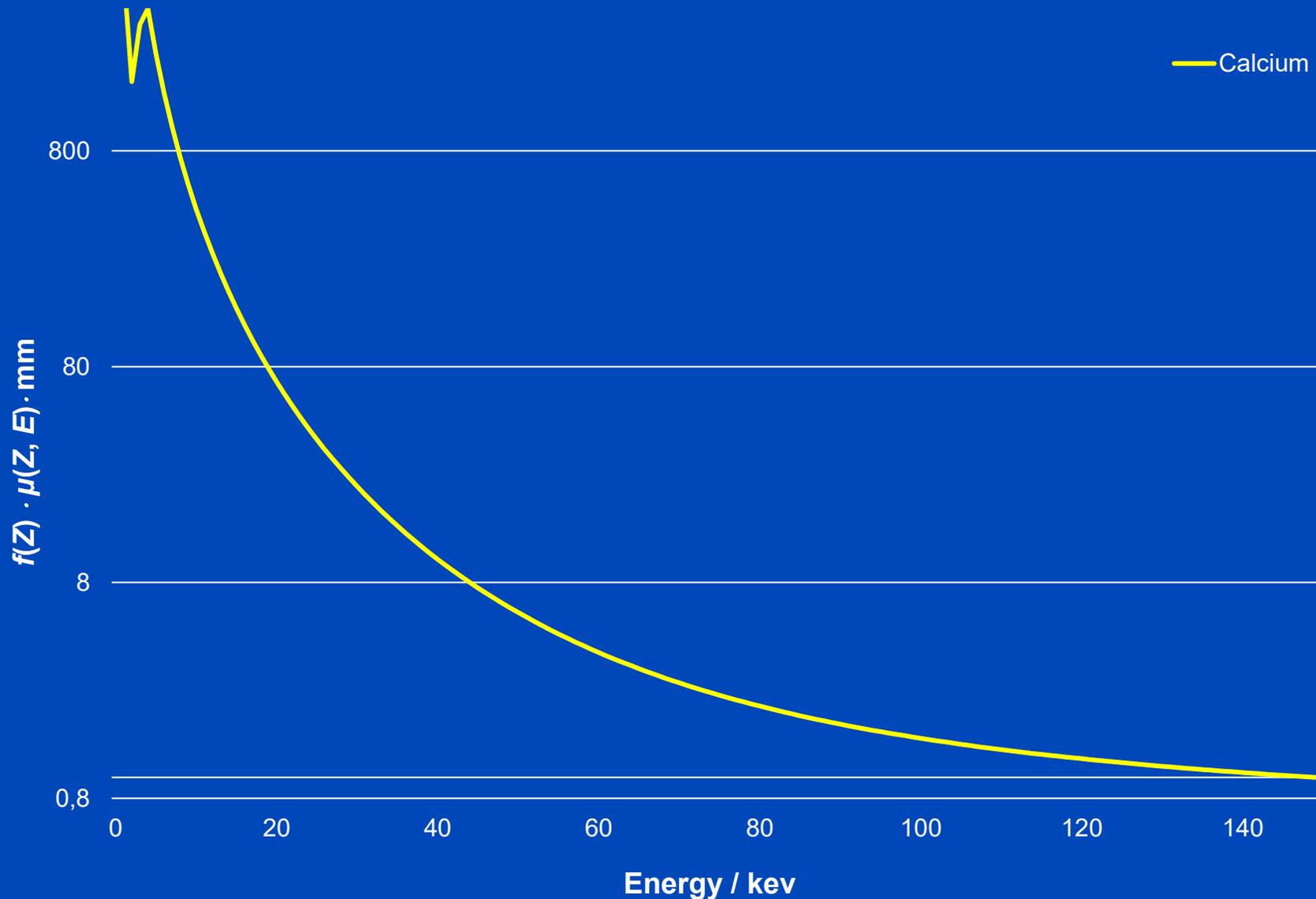
# Attenuation Coefficients



Element	$f(Z)$
Silicon	29.65
Calcium	38.57
Copper	5.03
Silver	1.75
Tin	2.24
Iodine	2.90
Barium	3.65
Cerium	1.73
Gadolinium	1.15
Holmium	0.92
Ytterbium	1.07
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$$f(Z) = \frac{1}{\mu(Z, 150 \text{ keV})}$$

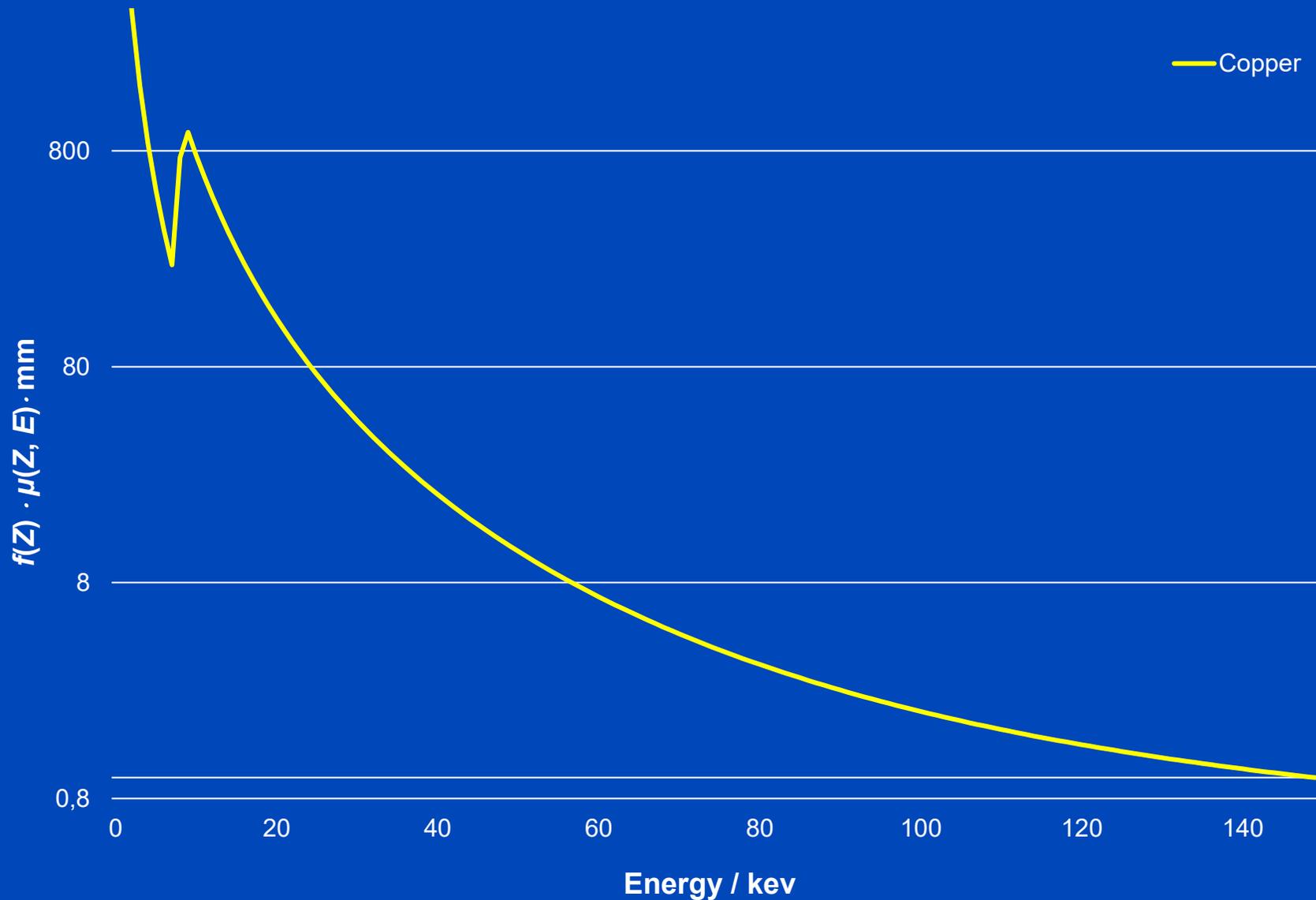
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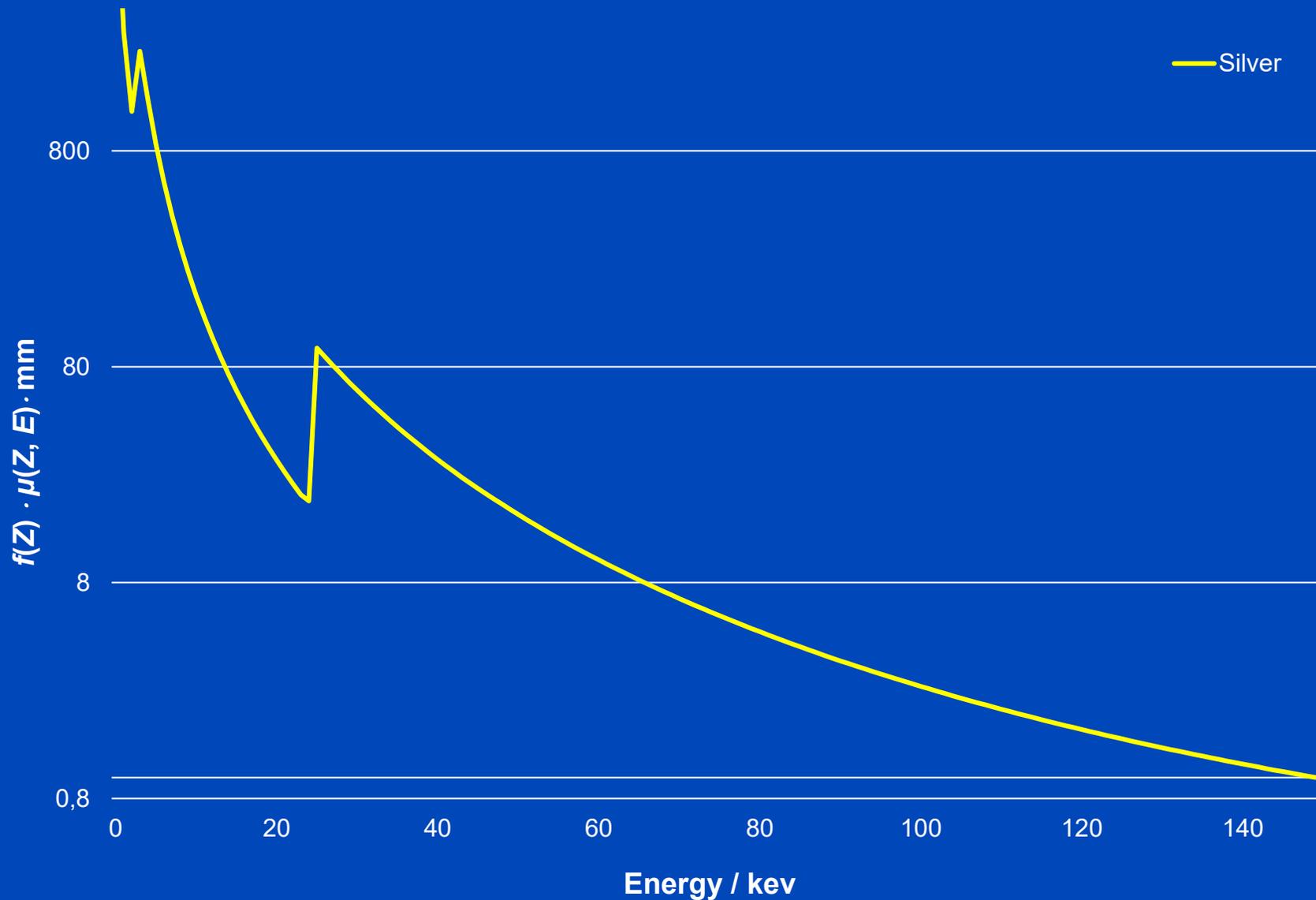
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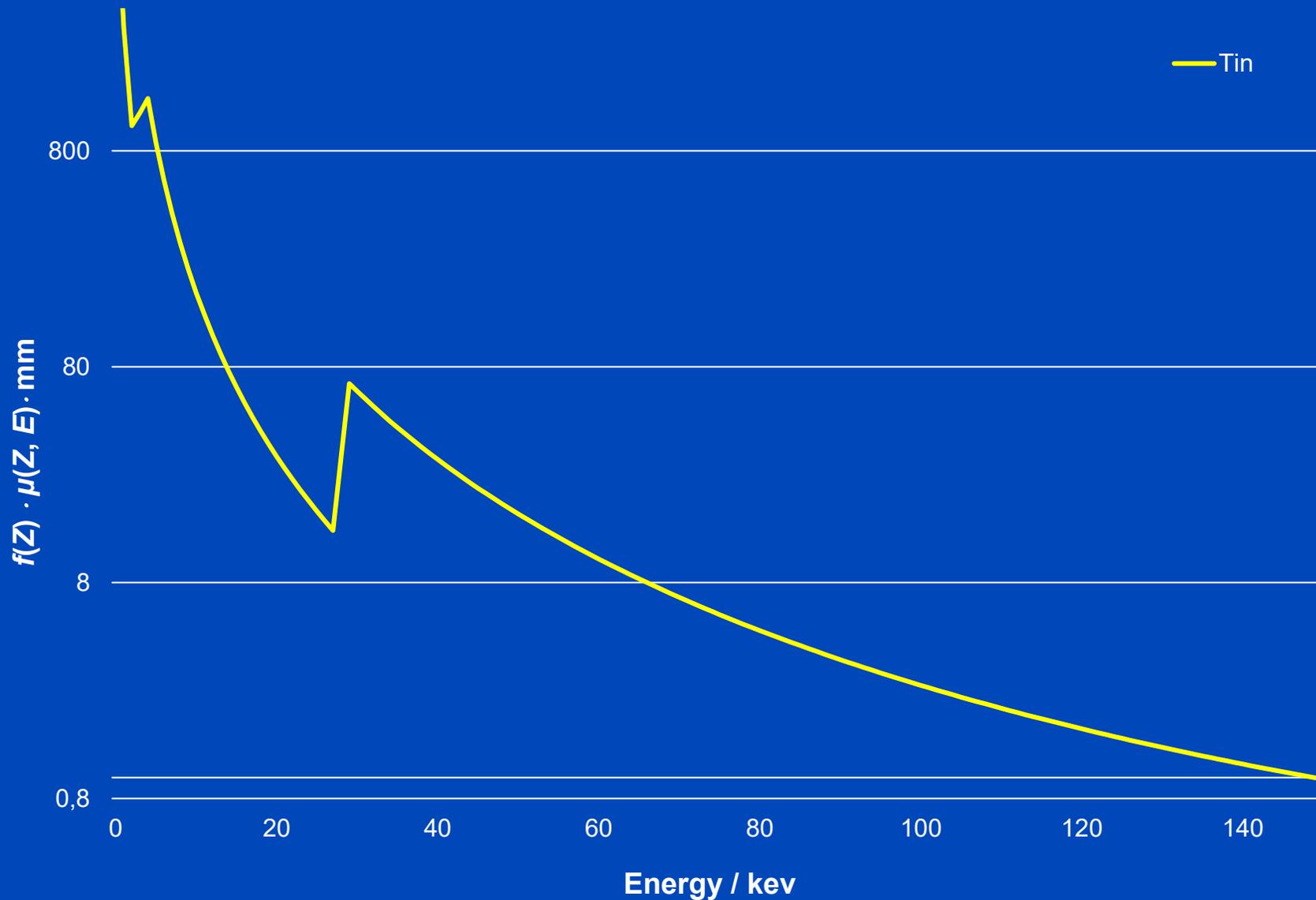
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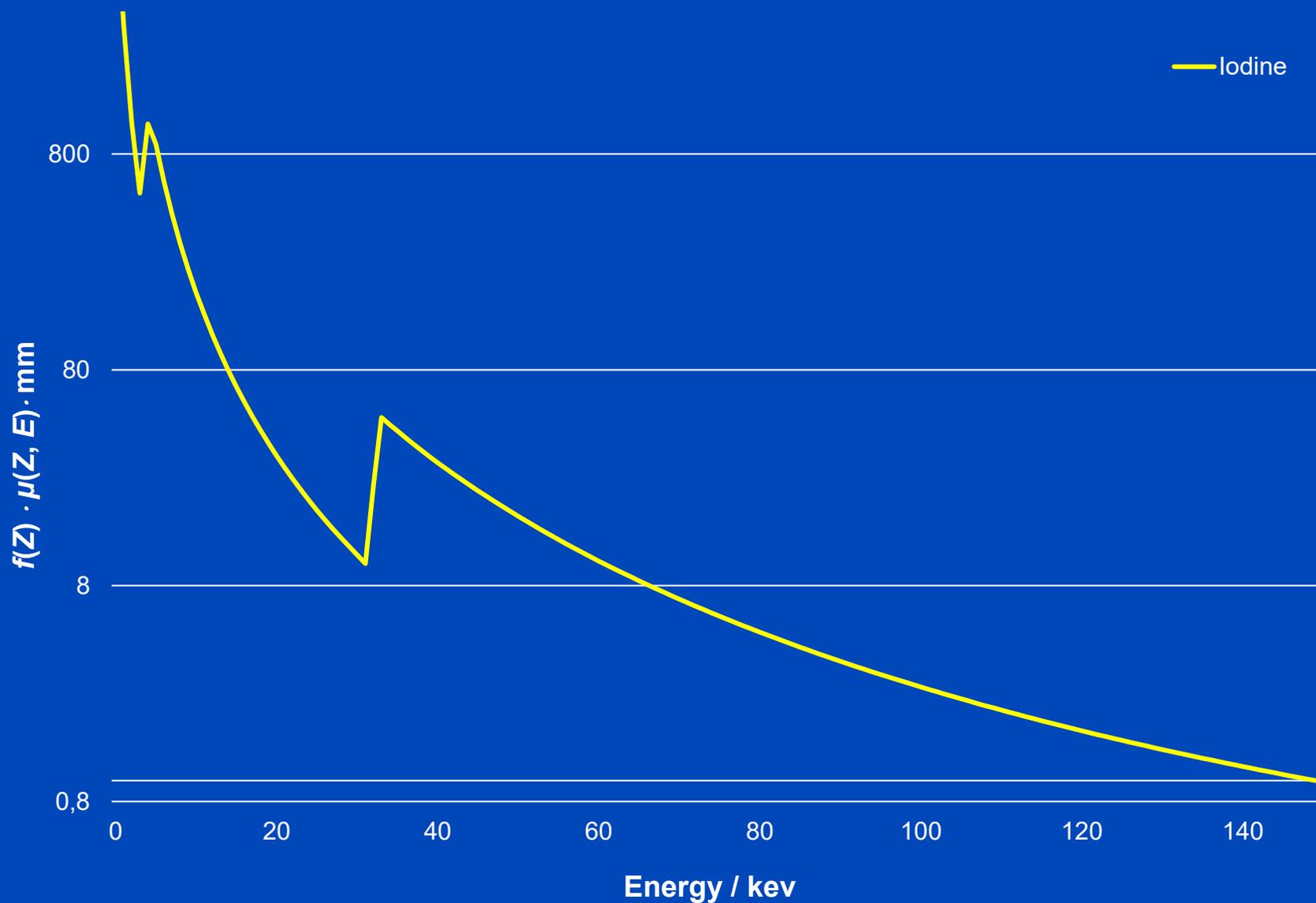
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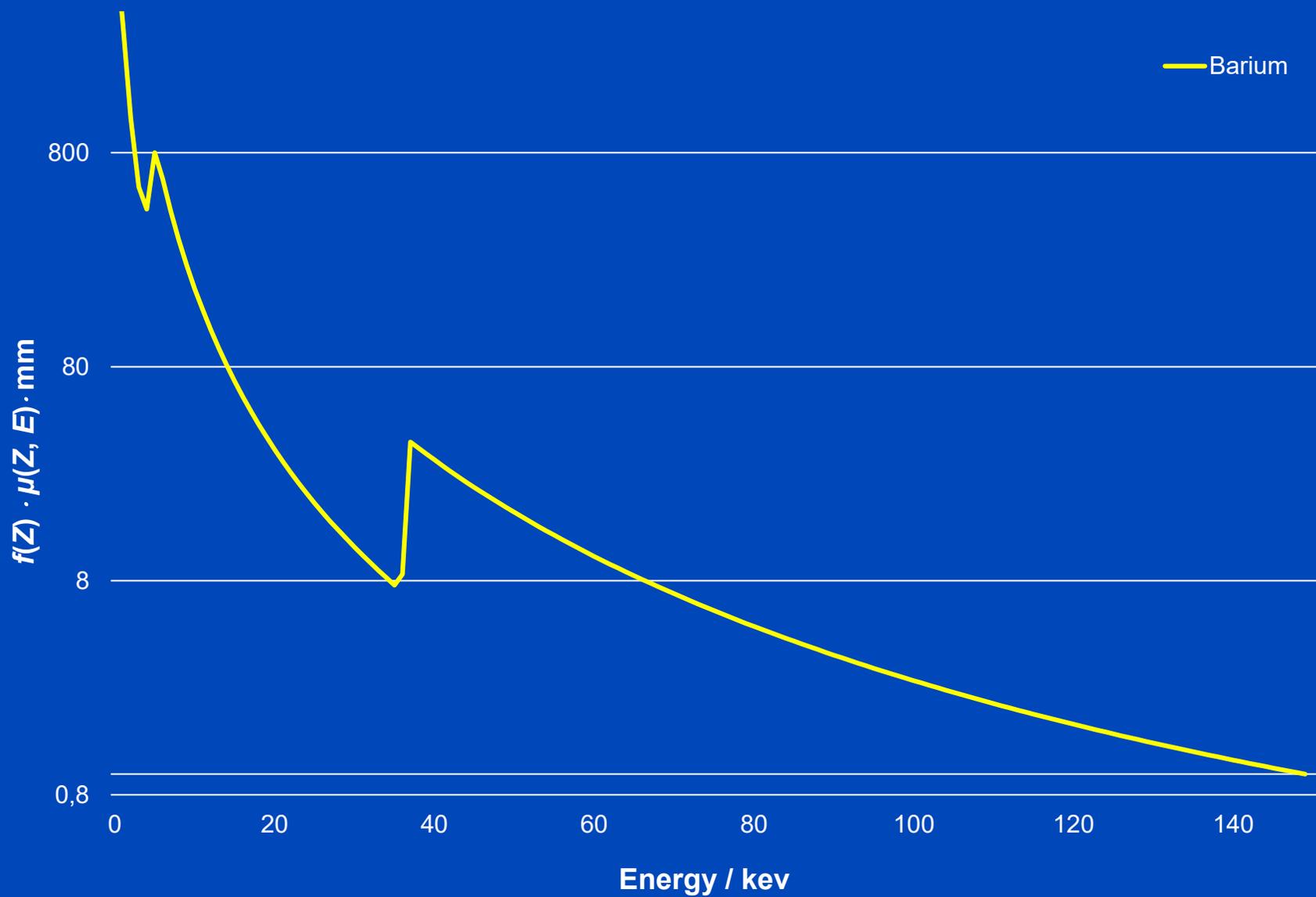
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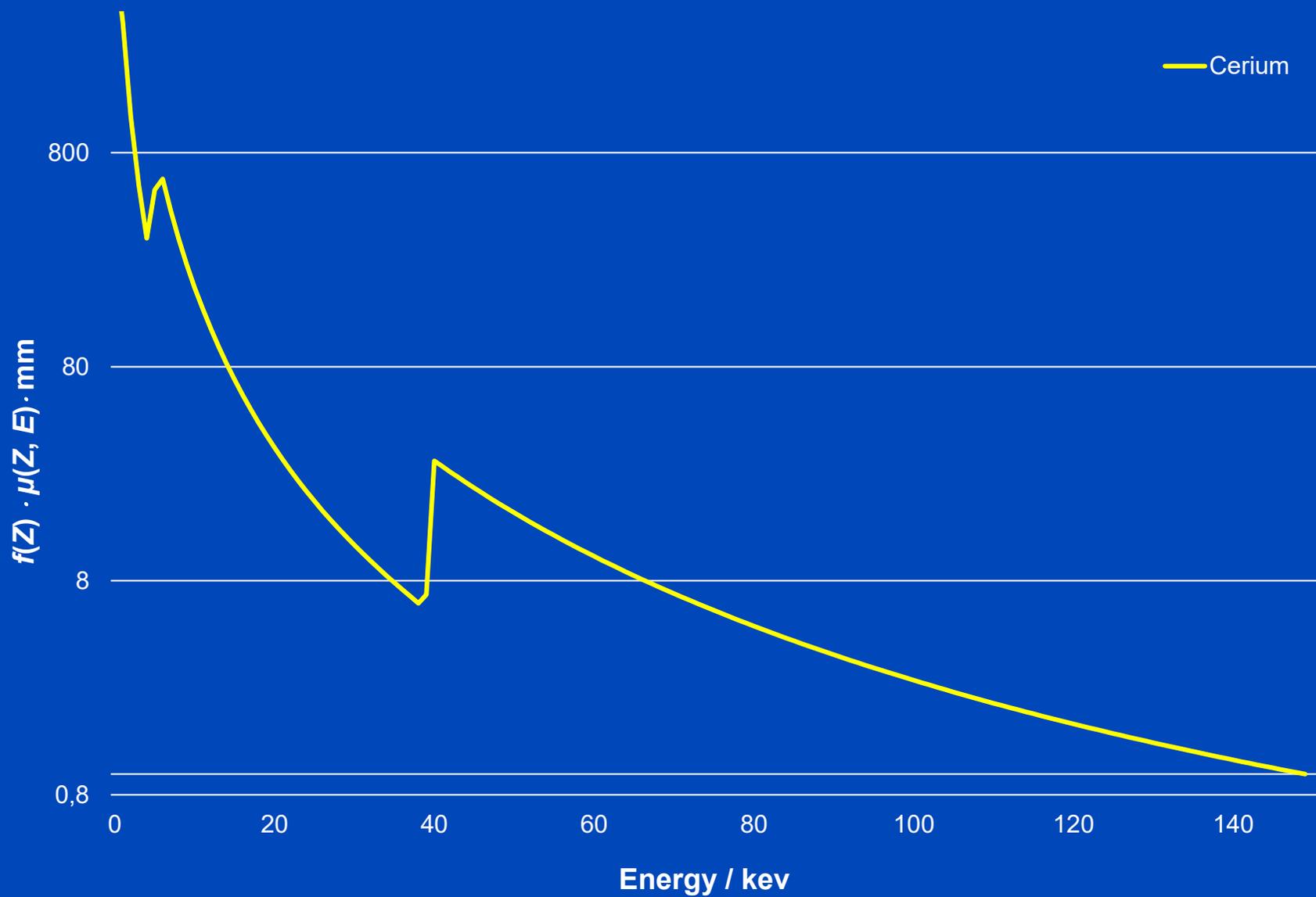
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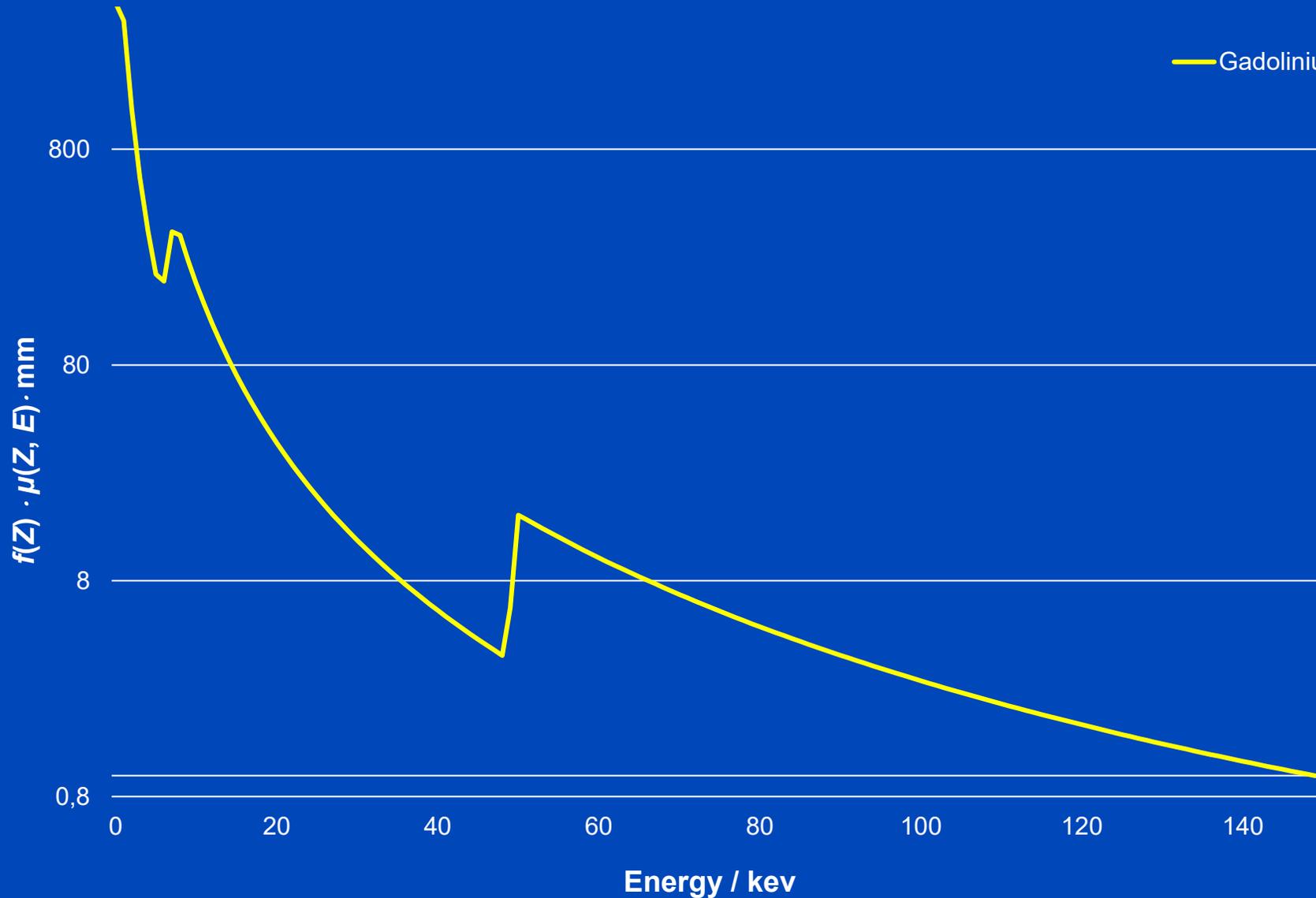


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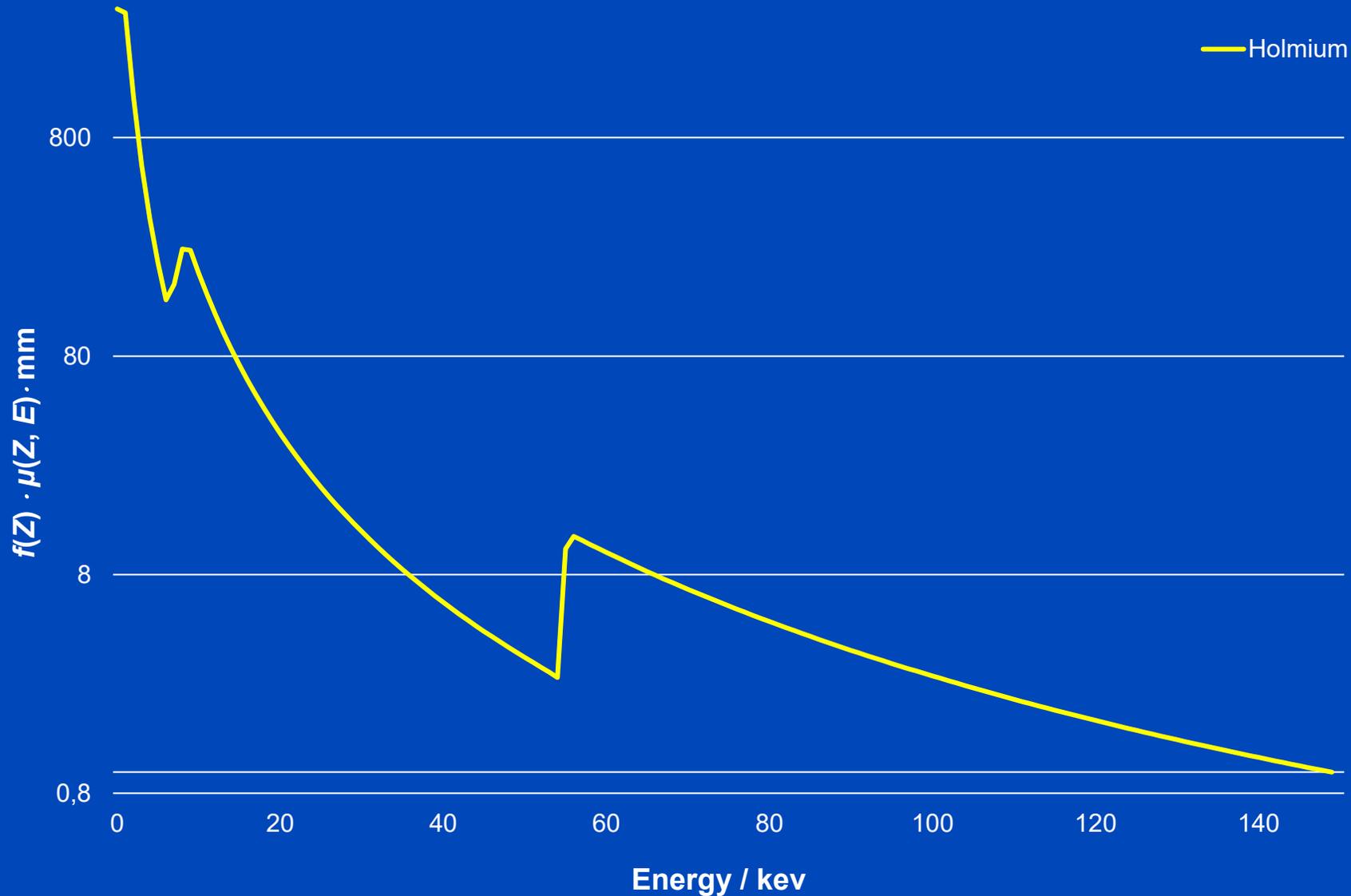
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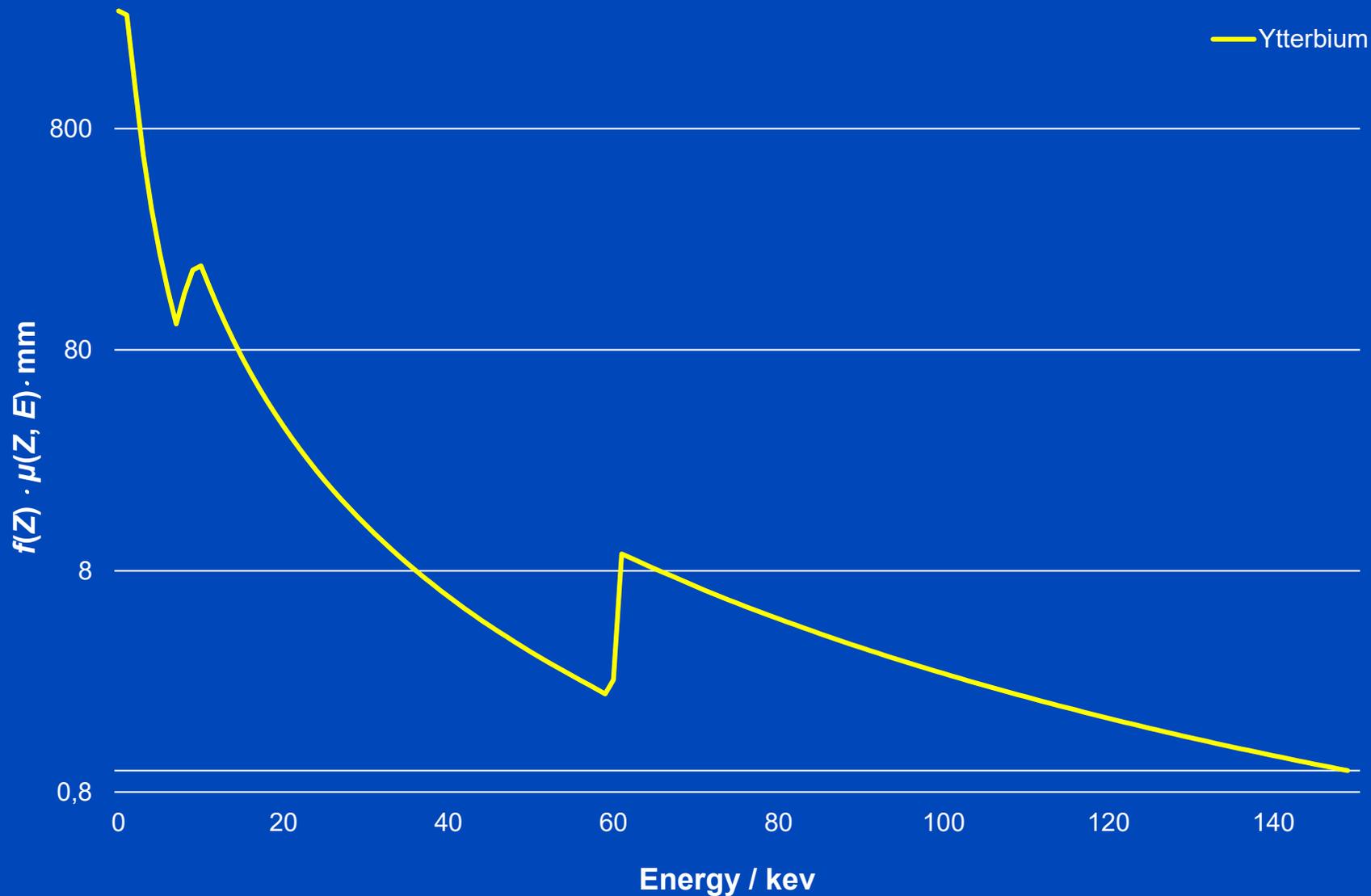
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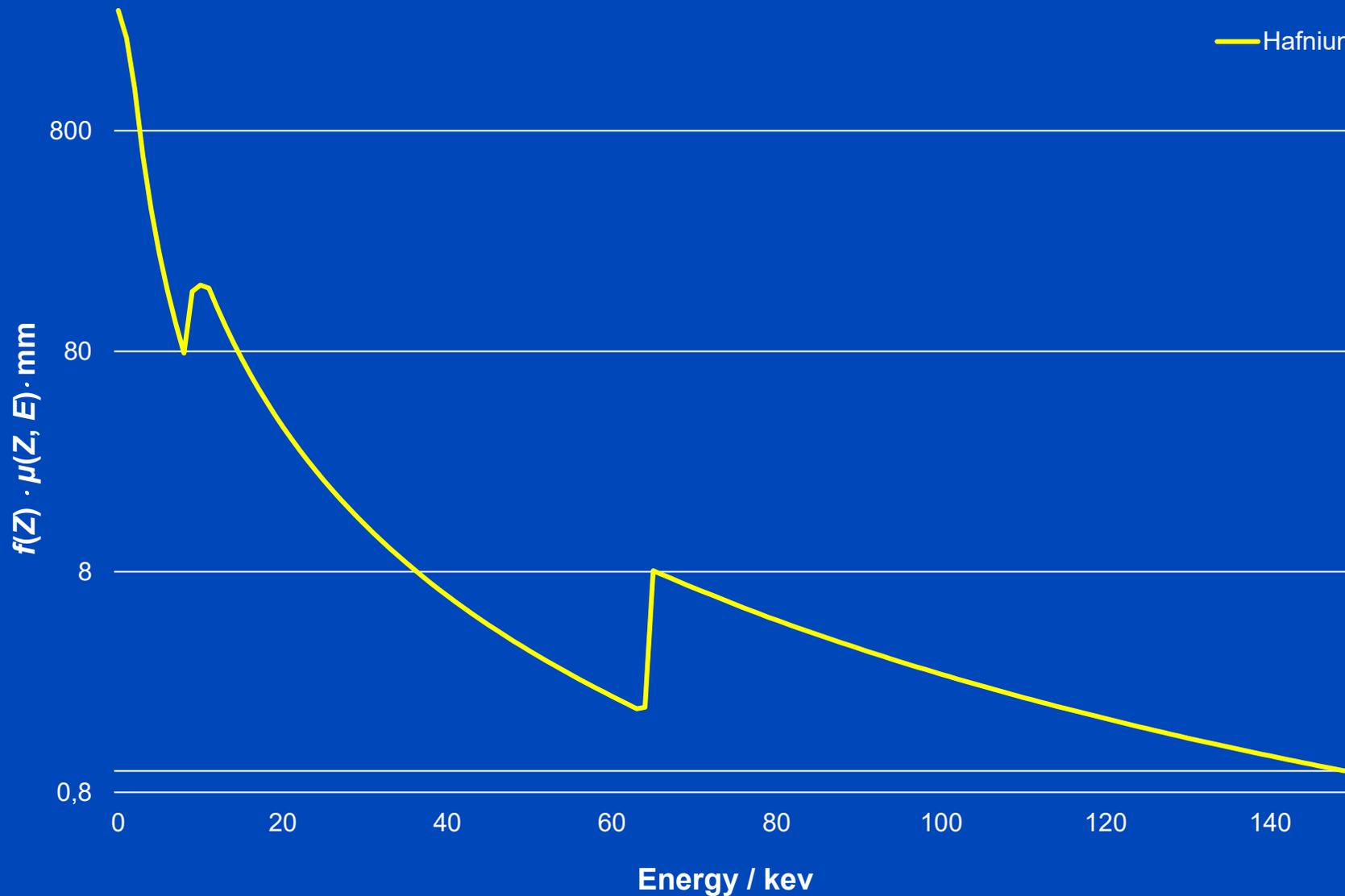


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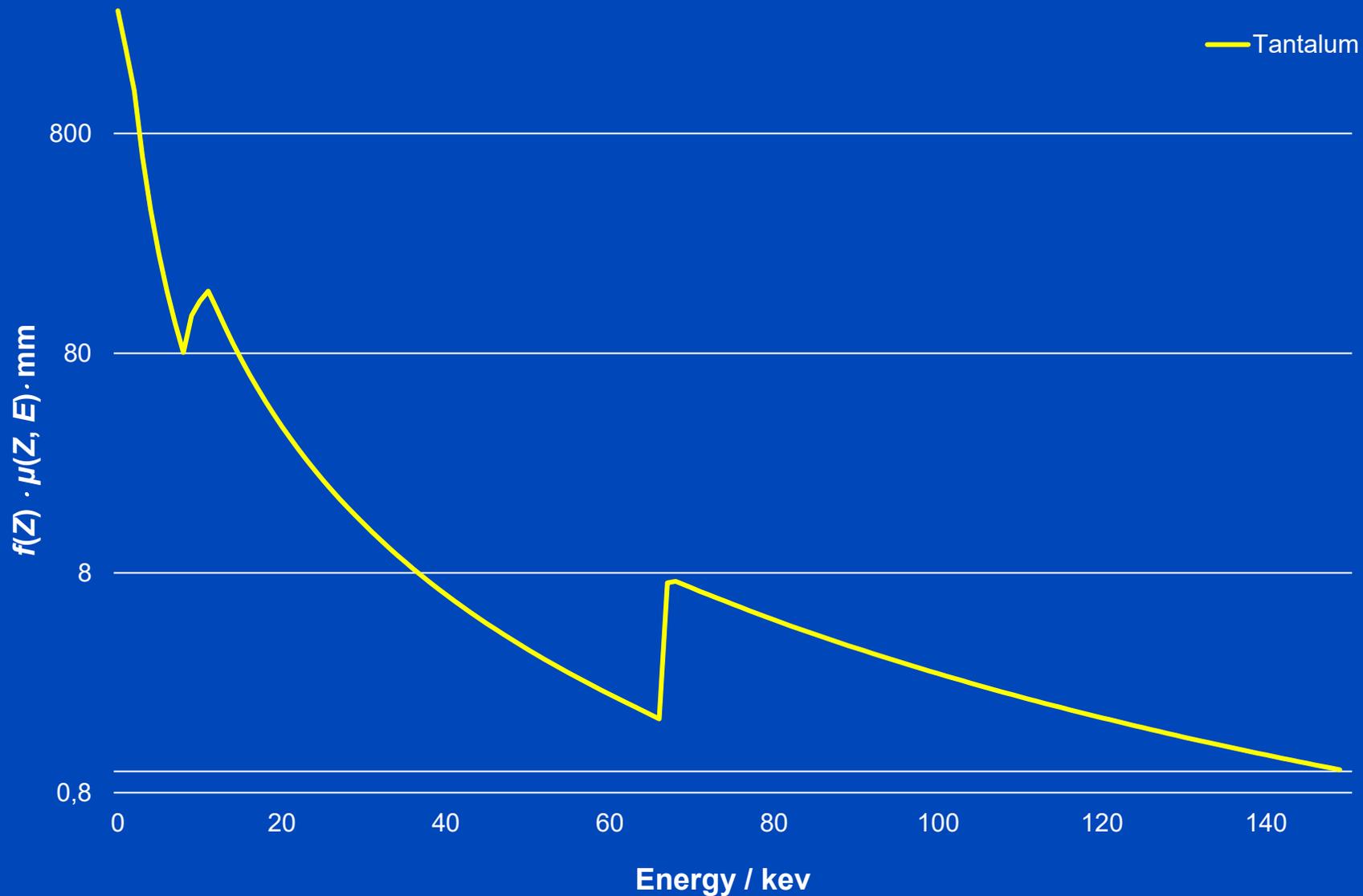
— Hafnium



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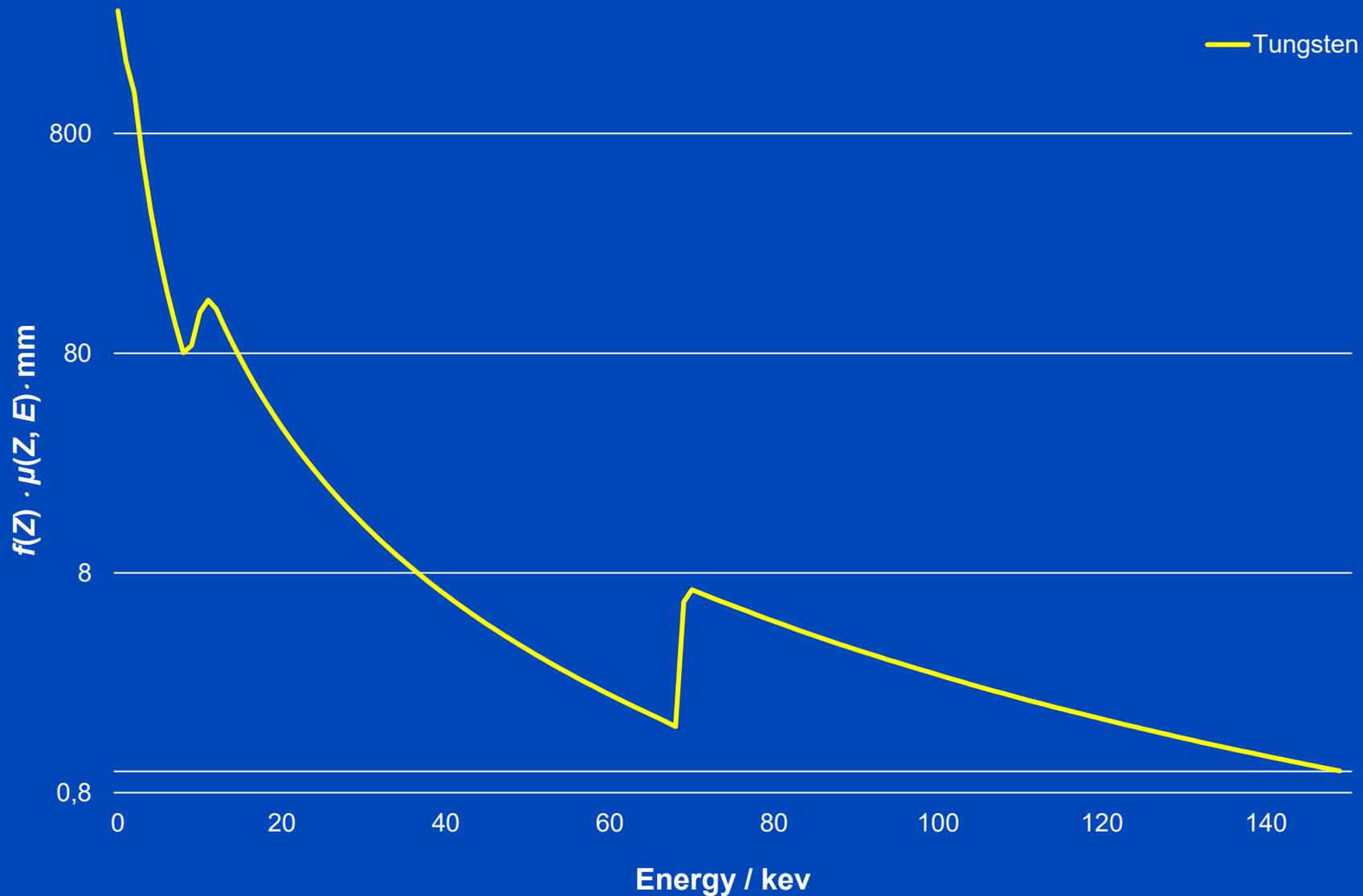
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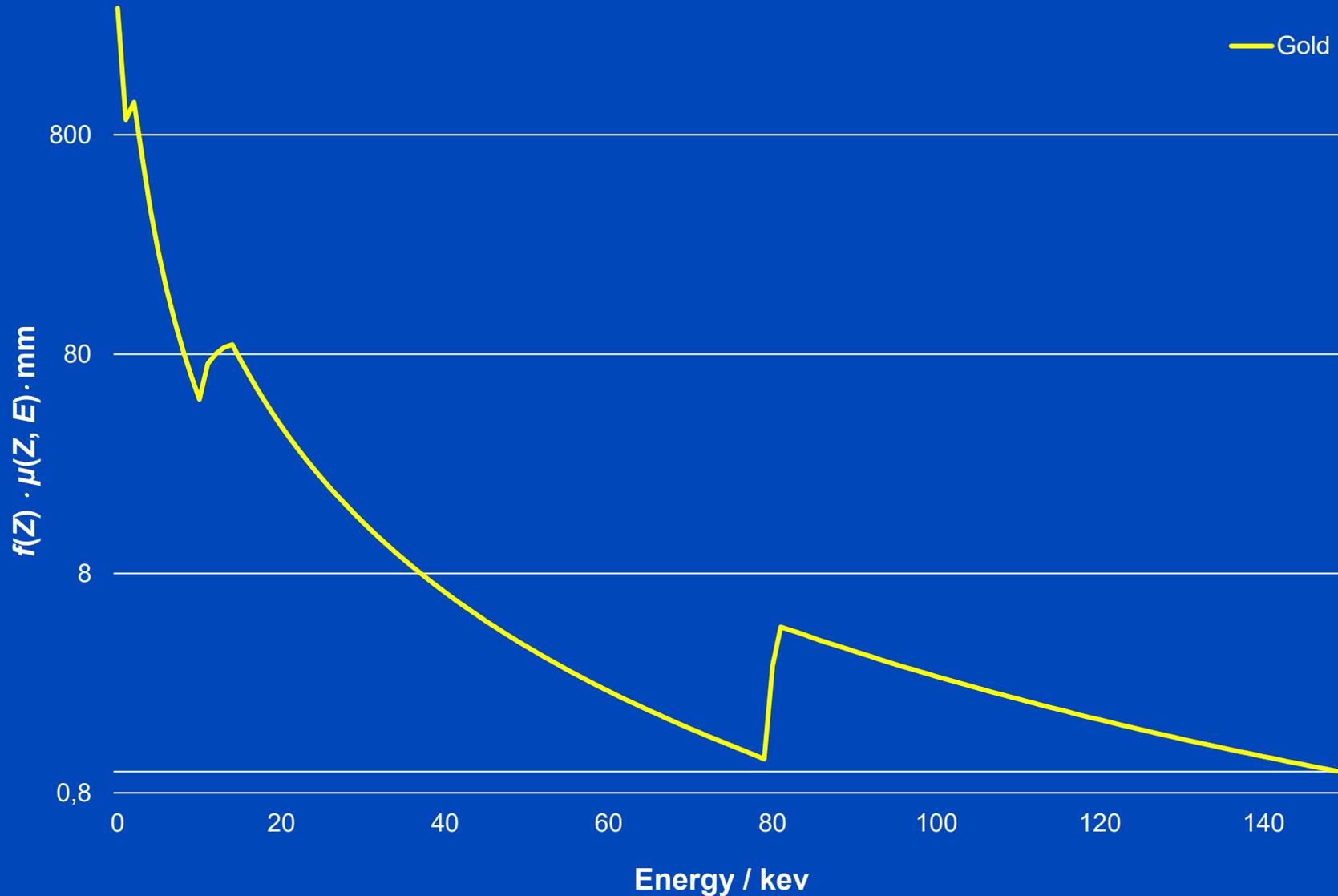
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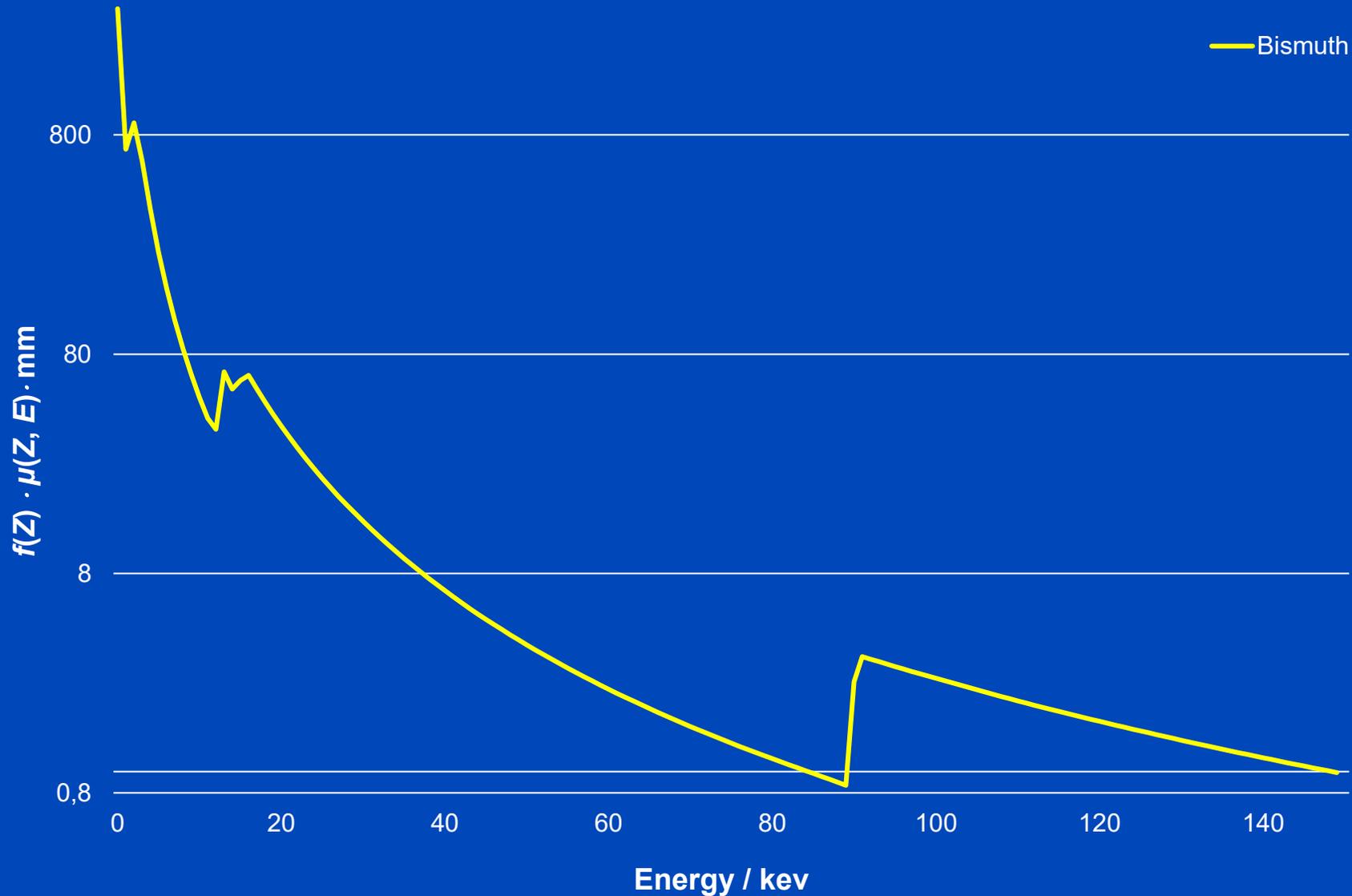
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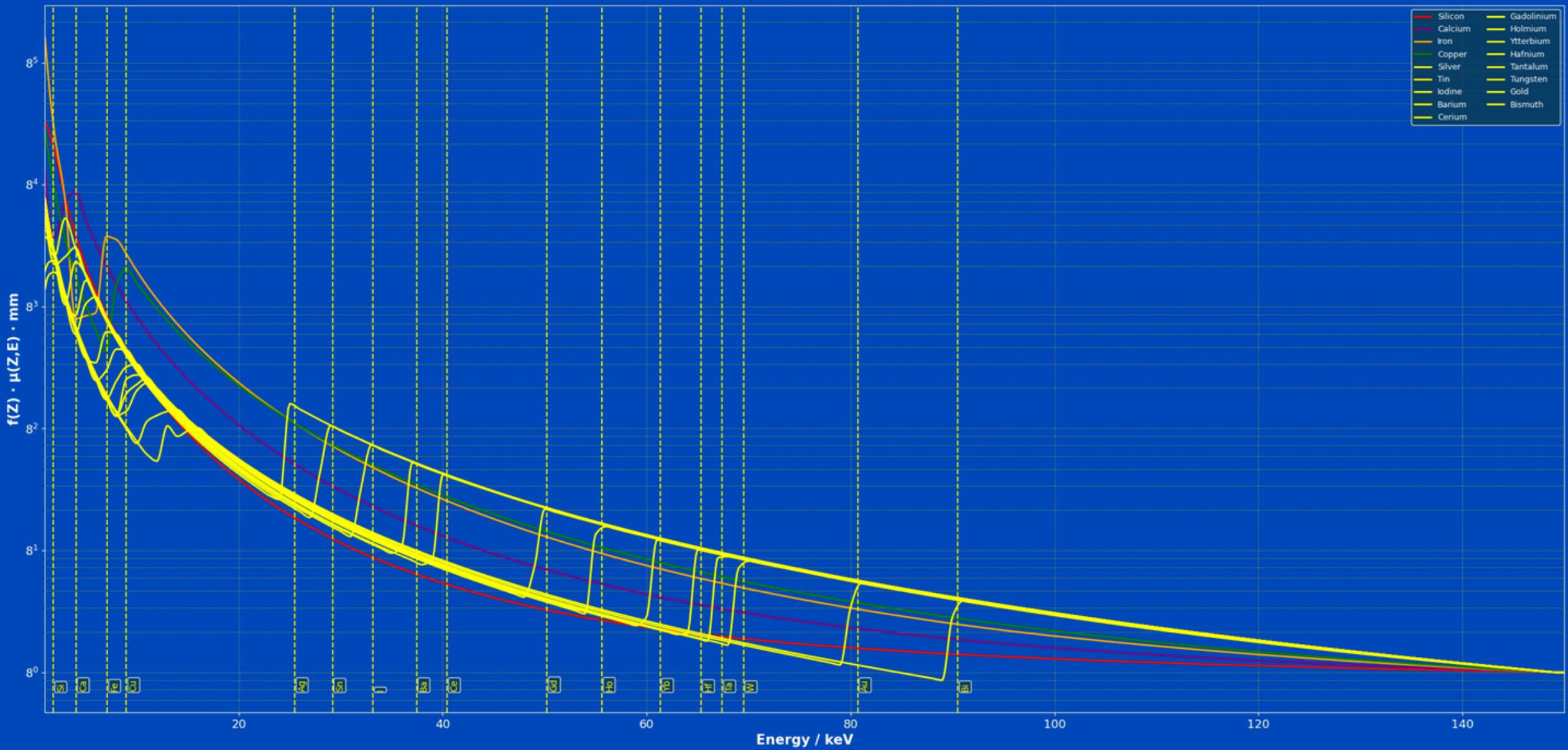
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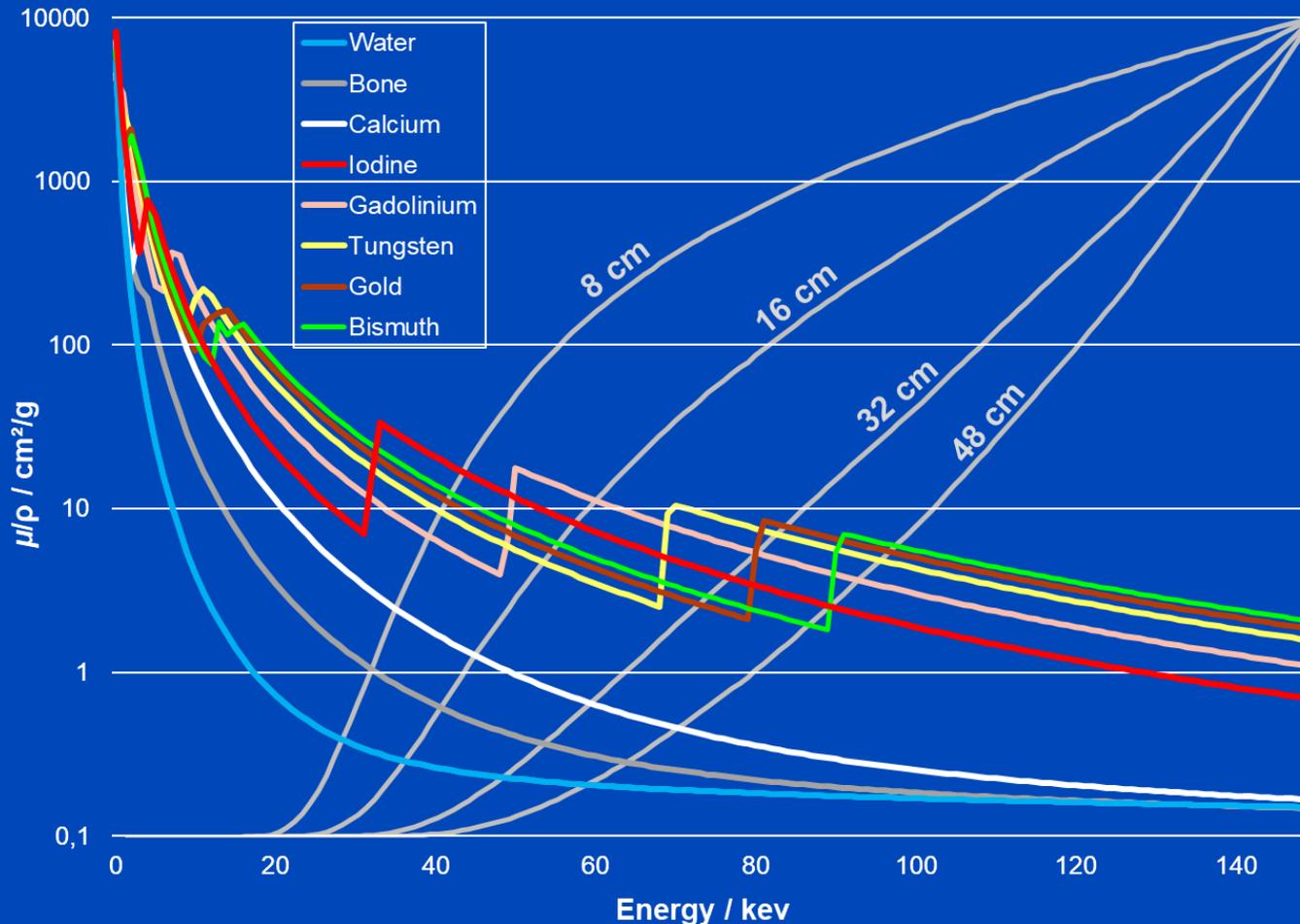
# Attenuation Coefficients - All Elements



# More than Two Materials?

$$\mu(\mathbf{r}, E) = f_1(\mathbf{r})\psi_1(E) + f_2(\mathbf{r})\psi_2(E) + \underbrace{f_3(\mathbf{r})\psi_3(E) + \dots}_{\text{Only, if we inject high Z materials!}}$$

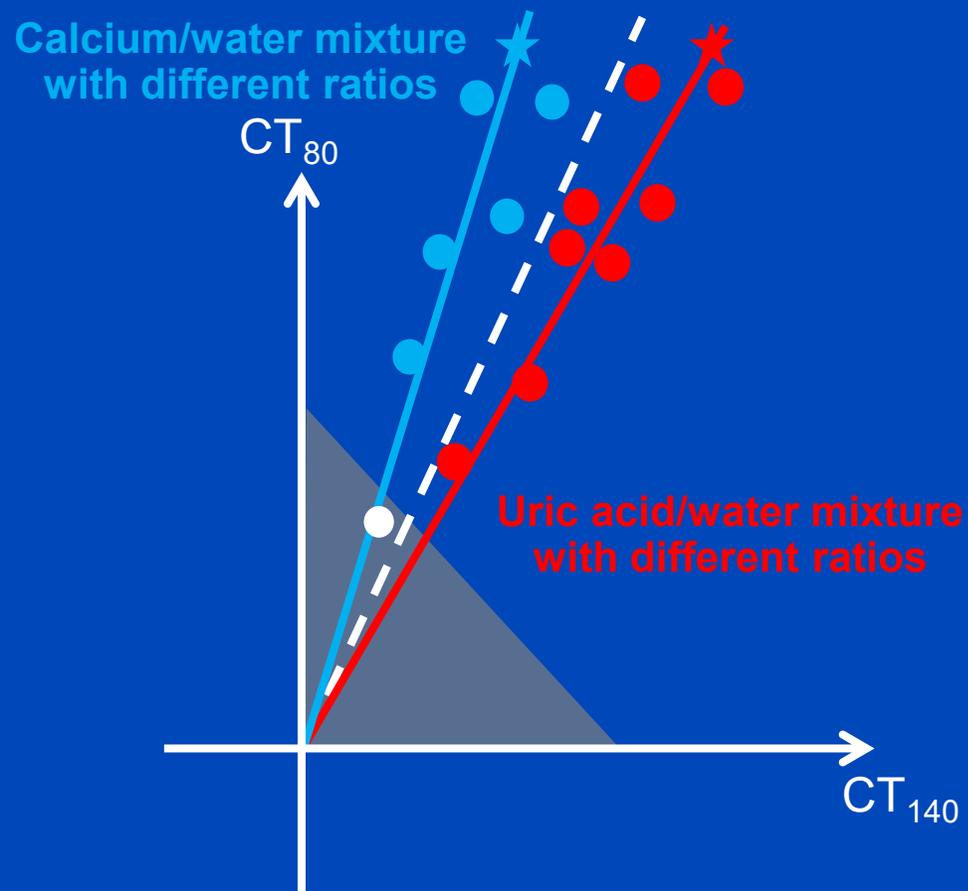
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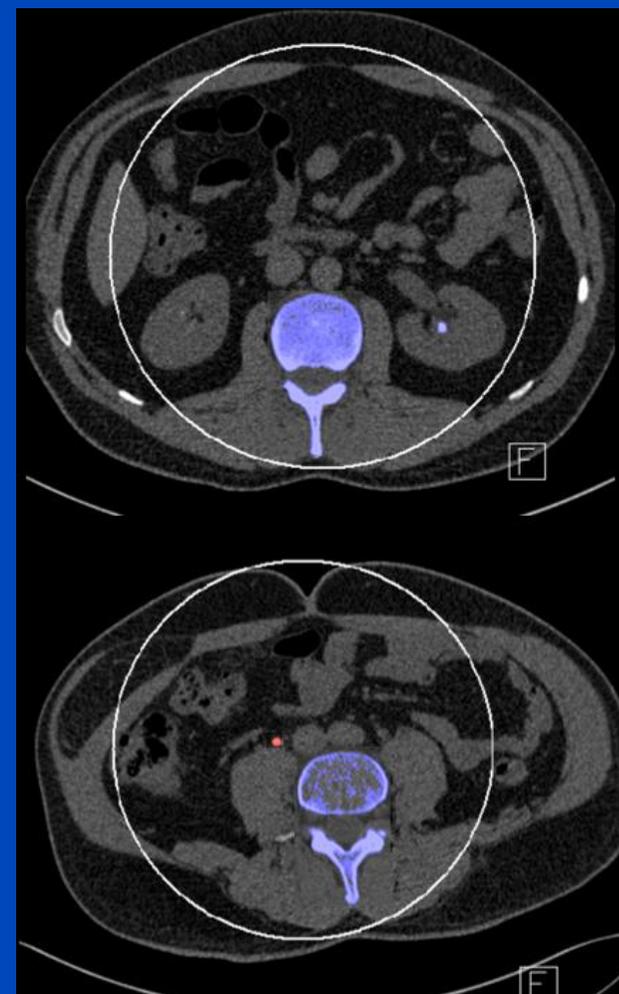
Element	K-edge
O (61%)	< 1 keV
C (23 %)	< 1 keV
H (10%)	< 1 keV
N (2.6%)	< 1 keV
Ca (1.7 %)	4.0 keV
P (1.1%)	2.1 keV
<b>I</b>	<b>33.2 keV</b>
<b>Gd</b>	<b>50.2 keV</b>
<b>W</b>	<b>69.5 keV</b>
<b>Au</b>	<b>80.7 keV</b>
<b>Bi</b>	<b>90.5 keV</b>

Gray curves: 120 kV water transmission on a non-logarithmic ordinate individually normalized to 1 at 140 keV.

# What? Only if we inject high Z materials?



- ★ ★ Pure calcium and pure uric acid
- ● Measured bone and uric acid



Courtesy of Klinikum Großhadern, LMU München and of Siemens Healthineers

# Iodine Contrast Agent

- About 400 million CT examinations are performed worldwide each year.<sup>1, 2</sup>
- More than 40% of all CT examinations are contrast-enhanced scans.<sup>3</sup>
- Low-osmolar contrast media are most widely used in CT and well tolerated.<sup>4</sup>
- Overall rate of acute adverse reactions to nonionic iodinated CM is 1%.<sup>5</sup>
- **Physico-chemical properties**
  - High stability
  - High density & solubility at acceptable low osmolality & viscosity
  - No penetration of cell membranes or blood-brain barrier, high local tolerability, minimal side effects
- **Pharmacokinetics**
  - Rapid distribution and fast elimination via the renal system
  - High stability and no metabolization in vivo
- **Spectral properties**
  - High x-ray attenuation, high atomic number, high content per molecule

<sup>1</sup>Sabiniewicz-Ziajka et al. Redefining radiation metrics: Evaluating actual doses in CT scans. *Biomedicines* 12(3):600 (14 pages), 2024

<sup>2</sup>UNSCEAR. Sources and Effects of Ionizing Radiation. Volume I: Sources: Report to the General Assembly, Scientific Annex A. New York, 2022.

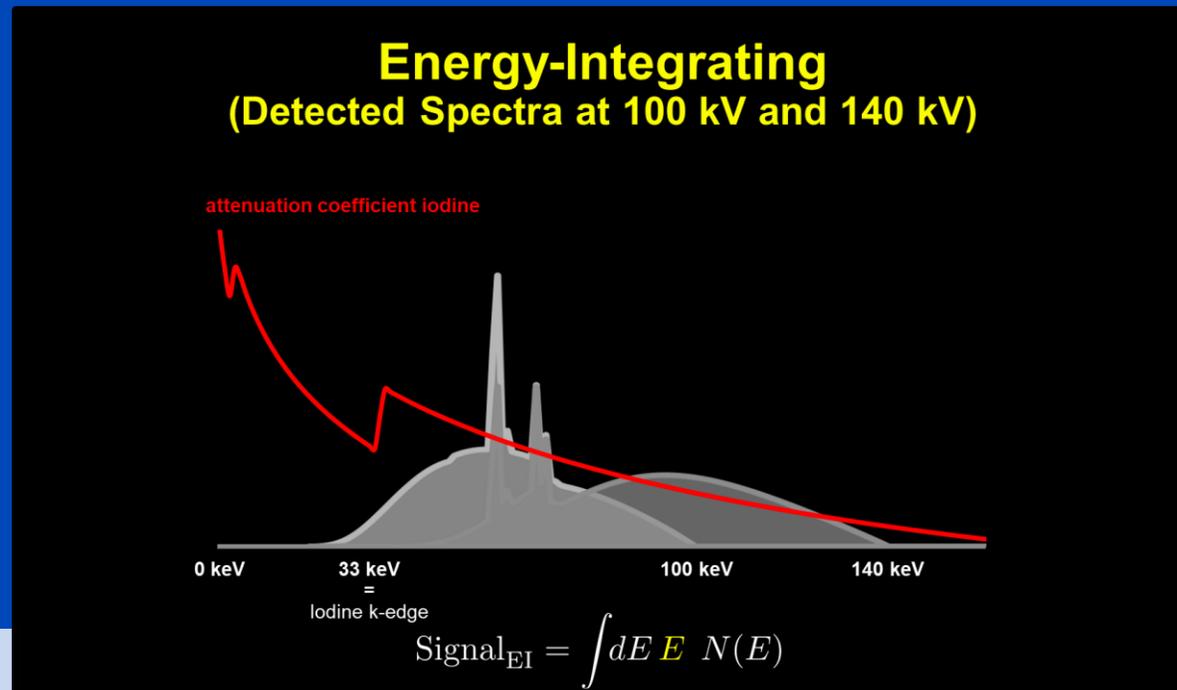
<sup>3</sup>England et al. More sustainable use of iodinated contrast media - Why? *Radiography* 30(1):S74-S80, 2024

<sup>4</sup>C. Becker. Selecting a contrast medium for MDCT investigation. *Eur. Radiol. Suppl.* 16(Suppl 4):D33–D37, 2006

<sup>5</sup>Suh et al. Acute adverse reactions to nonionic iodinated contrast media. A Meta-Analysis. *Invest. Radiol.* 54(9):589-599, 2019

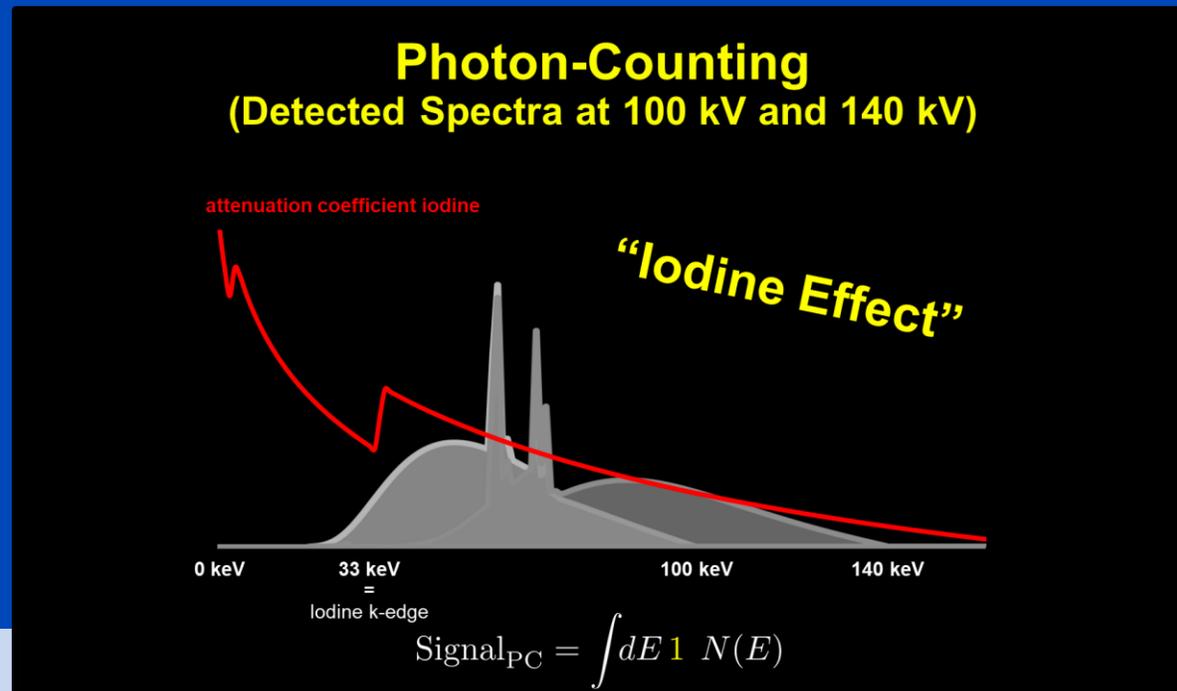
# Iodine in Conventional (Non-Spectral CT)

- Requirement for CA in non-spectral CT: Attenuate as much as possible!
- Iodine used successfully for decades as the CT contrast agent.
- However:
  - Iodine's k-edge is at 33 keV and forces us to scan with low kV, e.g. 70 kV.
  - Iodine contrast decreases at higher kV, and thus for thicker patients.
- Contrast agents (CAs) with higher k-edges may thus have an advantage.



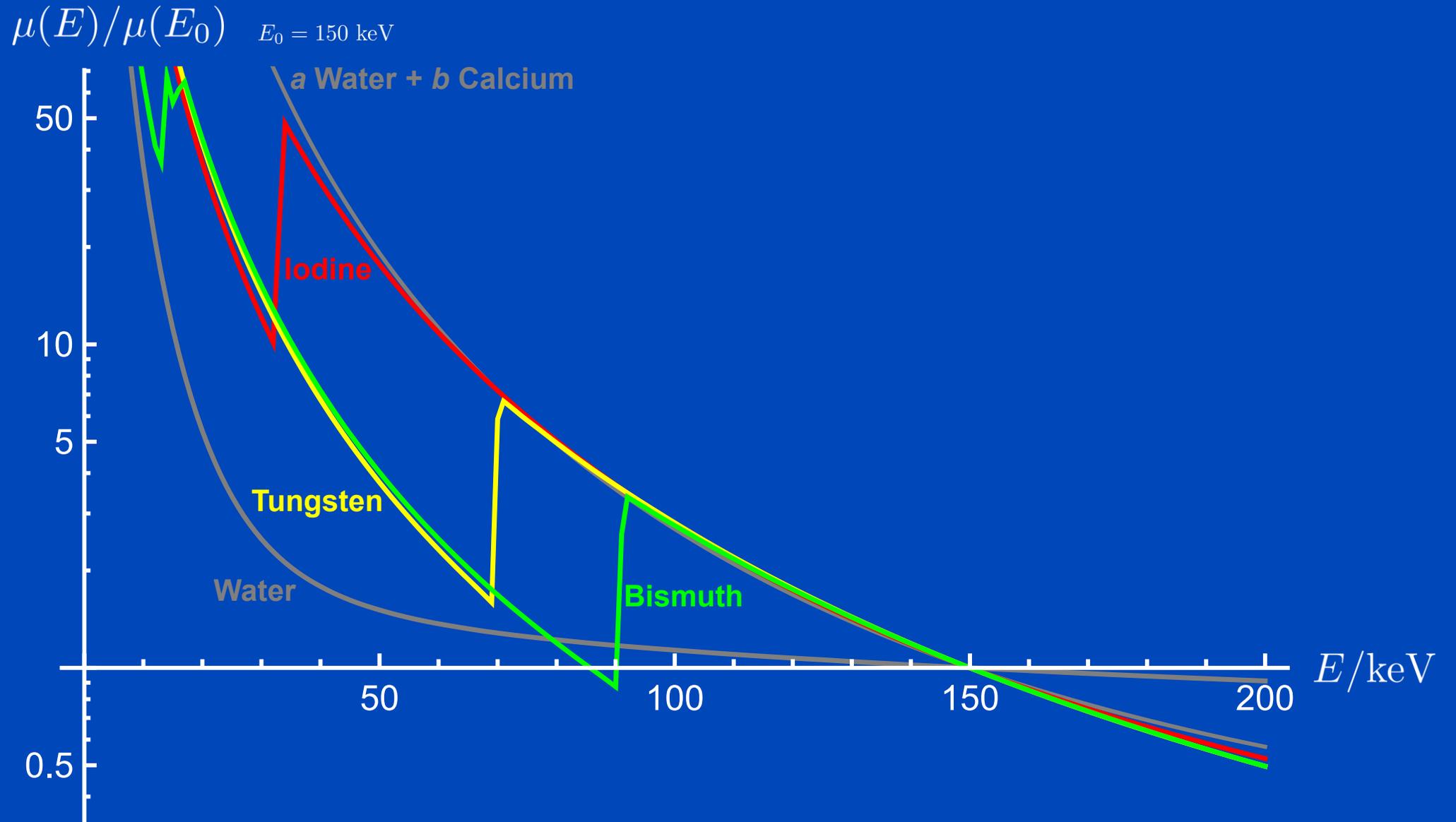
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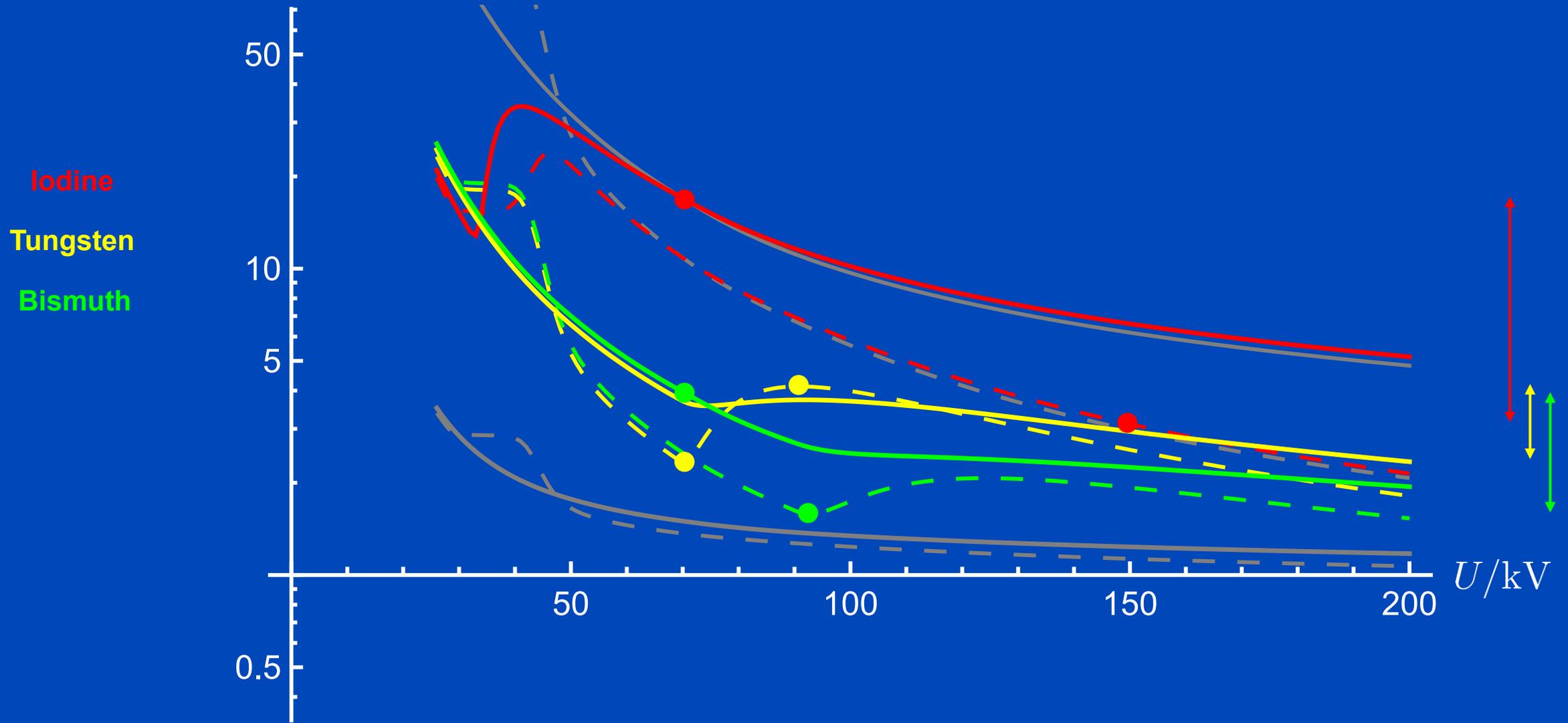


Material	$E_K$	$Z_{\text{eff}}$	$\mu_{\text{eff}}$ at 140 kV
H <sub>2</sub> O	0 keV	7.4	0.019 / mm
Uric acid	0 keV	6.9	0.032 / mm
HA400	0 keV	11.3	0.023 / mm
Si	2 keV	14	0.060 / mm
Ca	4 keV	20	0.074 / mm
Cu	9 keV	29	0.964 / mm
Ag	26 keV	47	3.961 / mm
Cd	27 keV	48	3.381 / mm
Sn	29 keV	50	3.135 / mm
I	33 keV	53	2.427 / mm
Ba	37 keV	56	1.906 / mm
Ce	40 keV	58	3.936 / mm
Gd	50 keV	64	5.169 / mm
Ho	56 keV	67	5.821 / mm
Yb	61 keV	70	3.751 / mm
Hf	65 keV	72	7.180 / mm
Ta	67 keV	73	8.440 / mm
W	70 keV	74	9.423 / mm
Au	81 keV	79	9.399 / mm
Bi	91 keV	83	4.661 / mm

← Gd is used in MRI

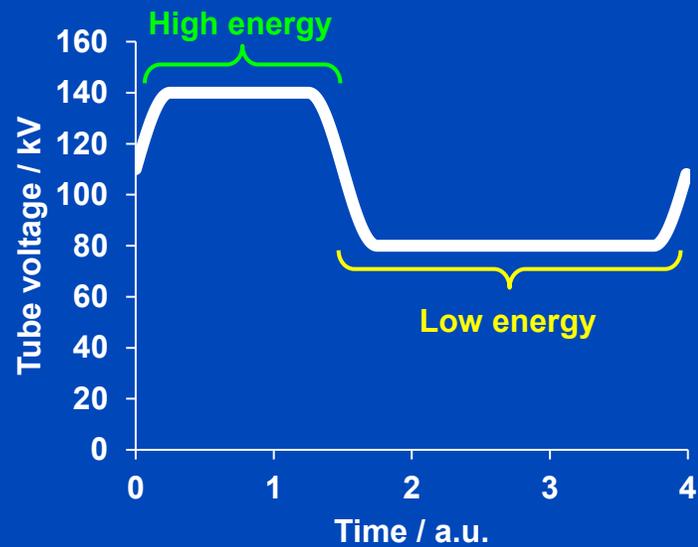


$$\mu_{\text{eff}}(U) / \mu(E_0) \quad E_0 = 150 \text{ keV}$$



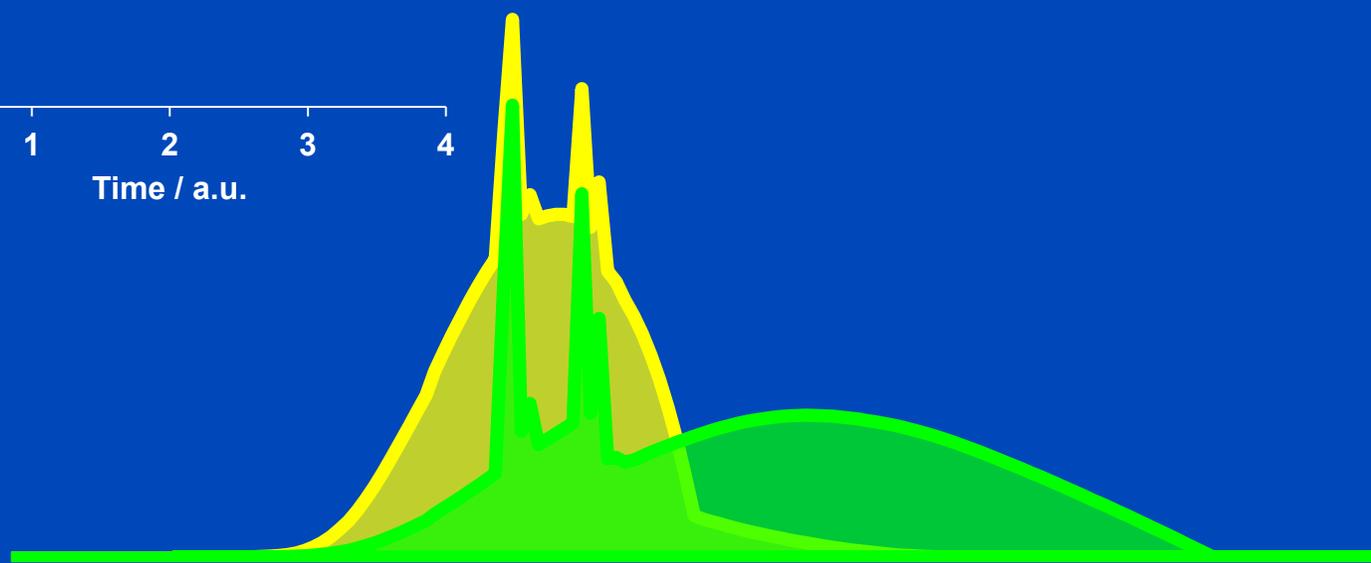
Effective attenuation wrt 16 cm water layer and typical EI detector. Dashed curves are with 0.6 mm tin filter.

# 80 kV / 140 kV Sinrect kV-Switching



Used in

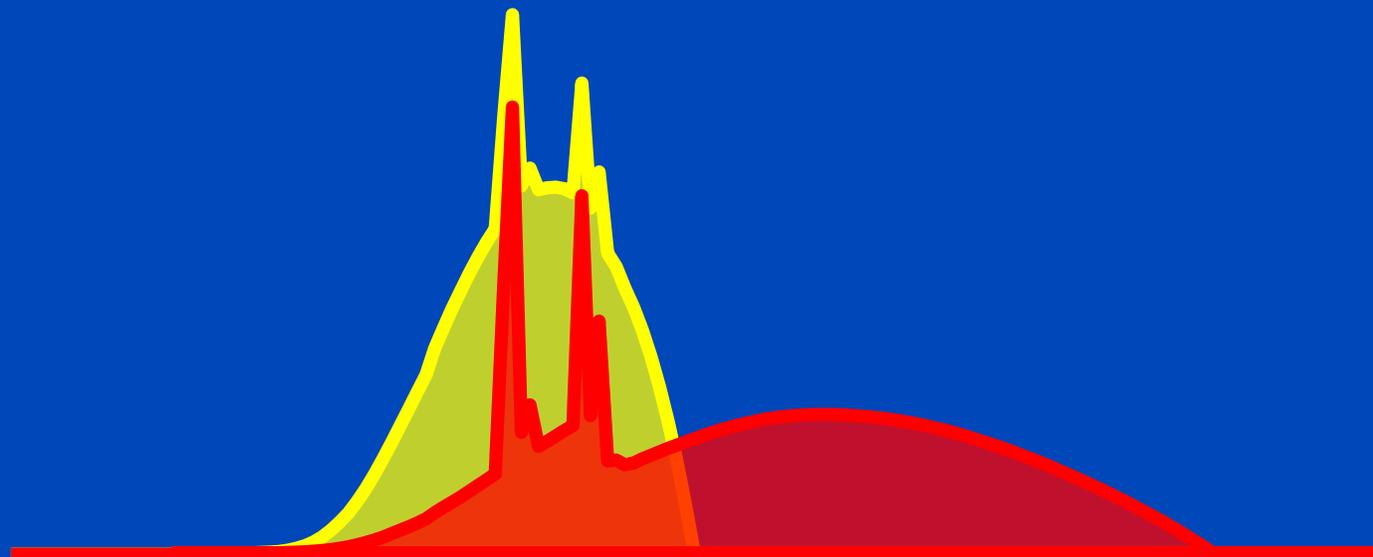
- GE's fast tube voltage switching CT



Spectra as seen after having passed a 32 cm water layer.

80 kV / 140 kV

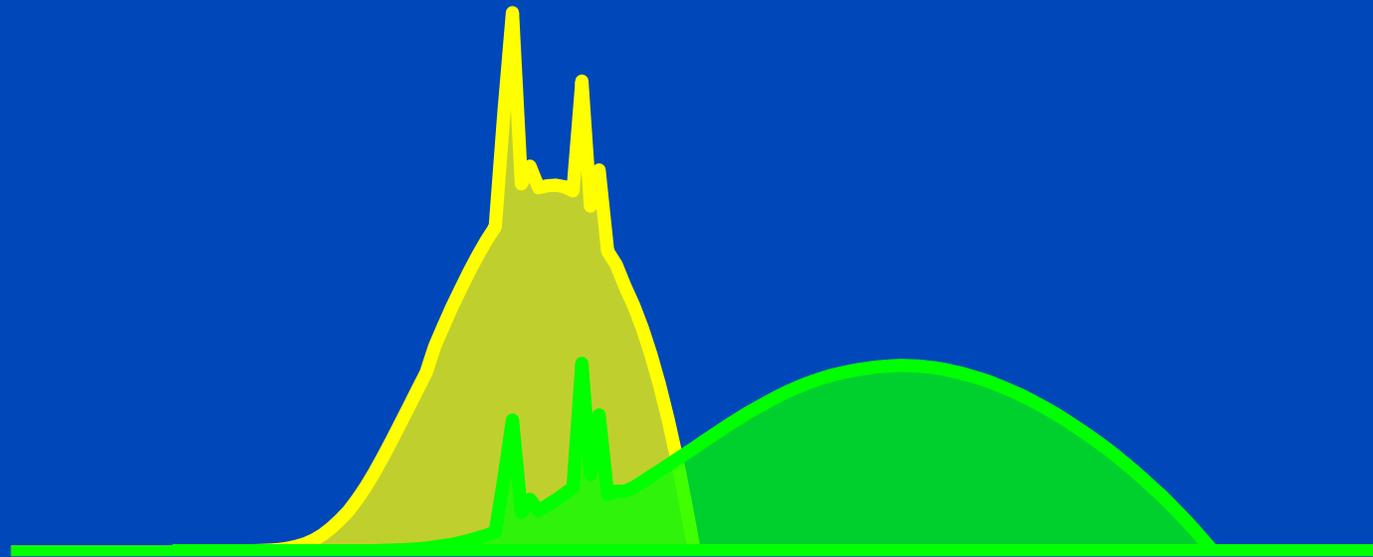
Used in  
• Siemens' 1<sup>st</sup> generation DSCT



Spectra as seen after having passed a 32 cm water layer.

80 kV / 140 kV Sn<sub>0.4</sub> mm

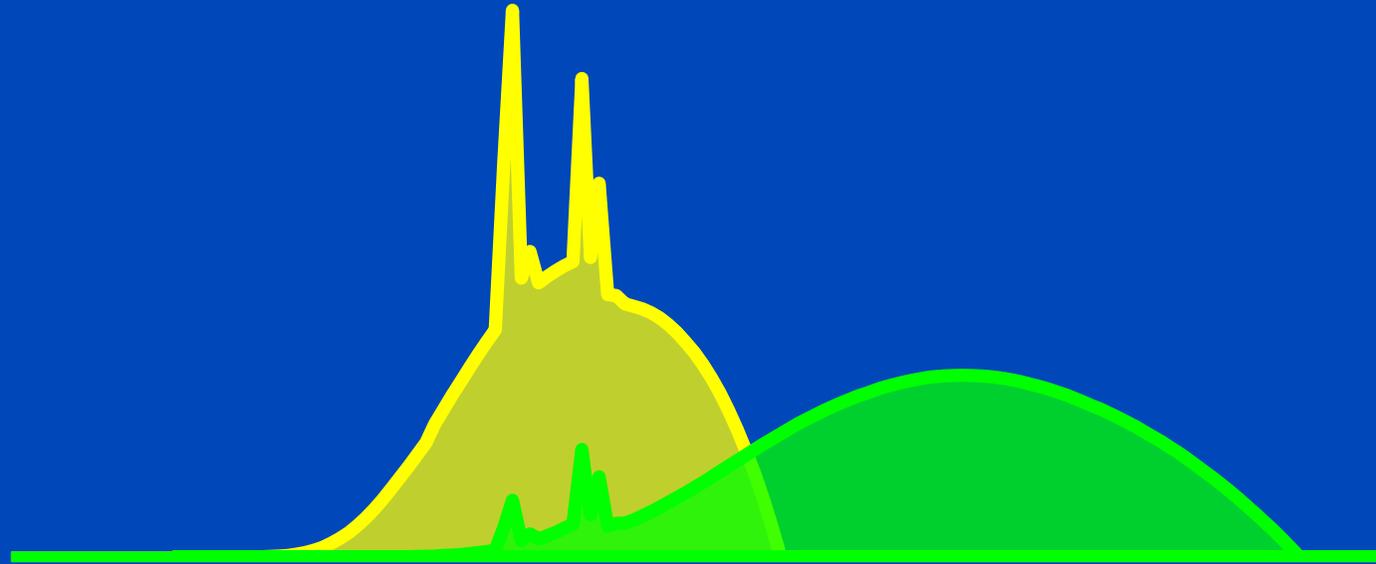
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• Siemens' 2<sup>nd</sup> generation DSCT



Spectra as seen after having passed a 32 cm water layer.

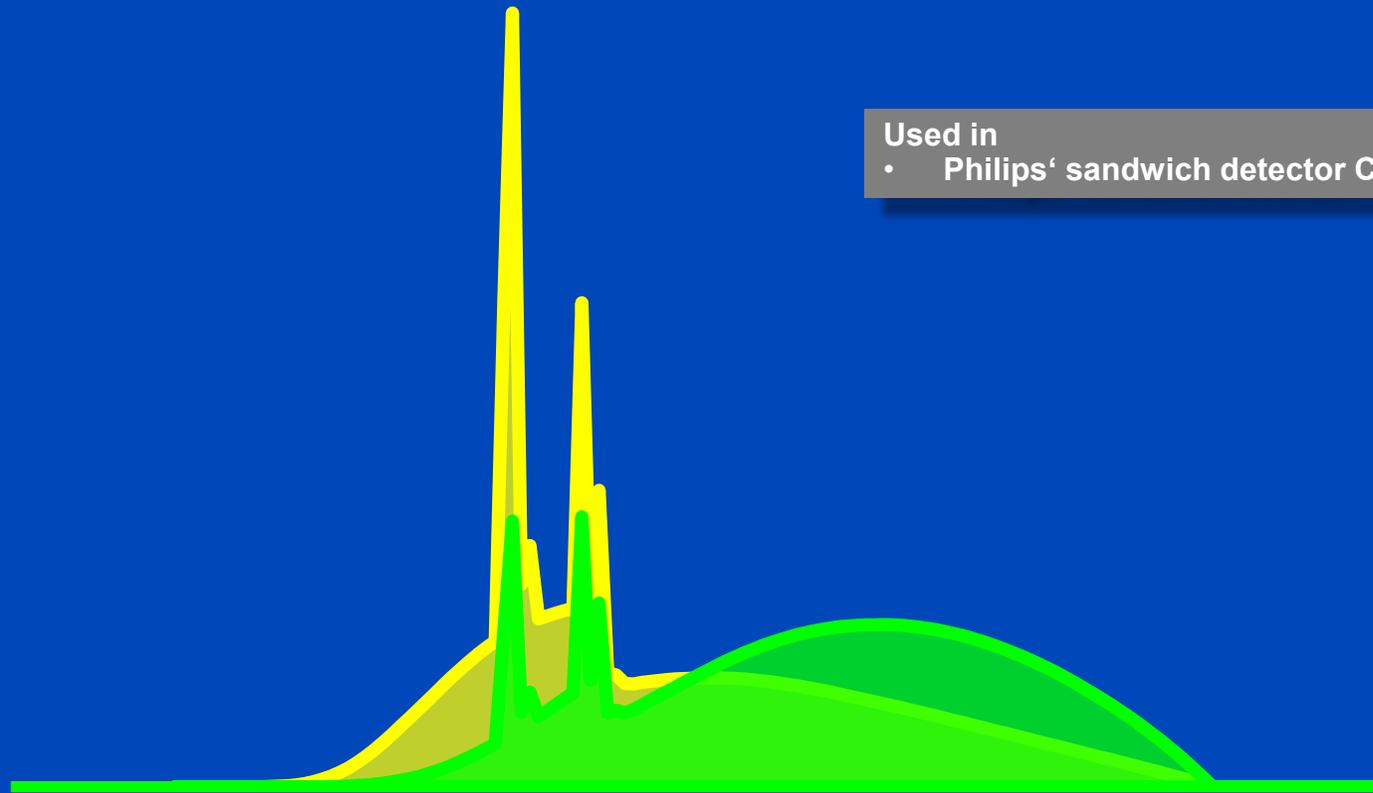
90 kV / 150 kV Sn<sub>0.6</sub> mm

Used in  
• Siemens' 3<sup>rd</sup> generation DSC



Spectra as seen after having passed a 32 cm water layer.

# 140 kV YAG / GOS

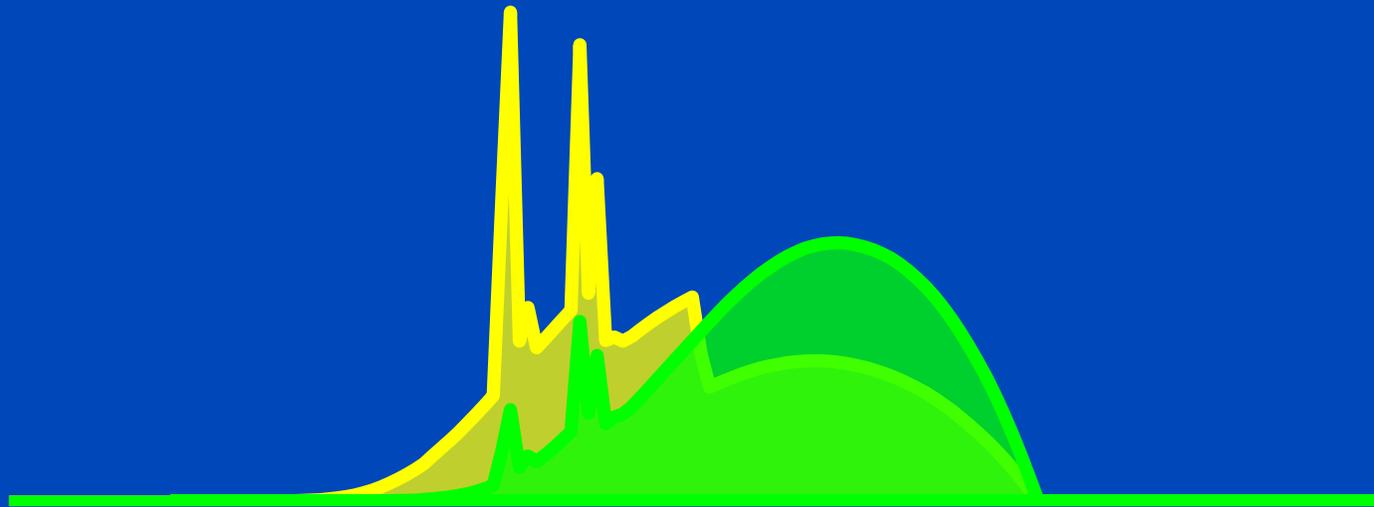


Spectra as seen after having passed a 32 cm water layer.

# Split filter 120 kV (Au+Sn)

Used in

- Siemens' split filter DSCT



Spectra as seen after having passed a 32 cm water layer.

# Why is Subtraction Potentially Better? (in case of no motion)

- $W$  = soft tissue (water) signal,  $X$  = iodine signal
- Assume same noise  $N$ , e.g. 50 HU, in both measurements  $M_1$  and  $M_2$ 
  - $\text{Var } M_1 = \text{Var } M_2 = N^2$  regardless of whether iodine is present or not
- DECT
  - Measurement 1 (high kV):  $M_1 = W + 0.25 X$
  - Measurement 2 (low kV):  $M_2 = W + 0.5 X$
  - Estimated iodine:  $4 (M_2 - M_1)$       Variance =  $16 (\text{Var } M_2 + \text{Var } M_1) = 32 N^2$
  - Estimated soft tissue:  $2 M_1 - M_2$       Variance =  $4 \text{Var } M_1 + \text{Var } M_2 = 5 N^2$
- Subtraction
  - Measurement 1 (native):  $M_1 = W$
  - Measurement 2 (enhanced):  $M_2 = W + 0.5 X$
  - Estimated iodine:  $2 (M_2 - M_1)$       Variance =  $4 (\text{Var } M_2 + \text{Var } M_1) = 8 N^2$
  - Estimated soft tissue:  $M_1$       Variance =  $\text{Var } M_1 = N^2$

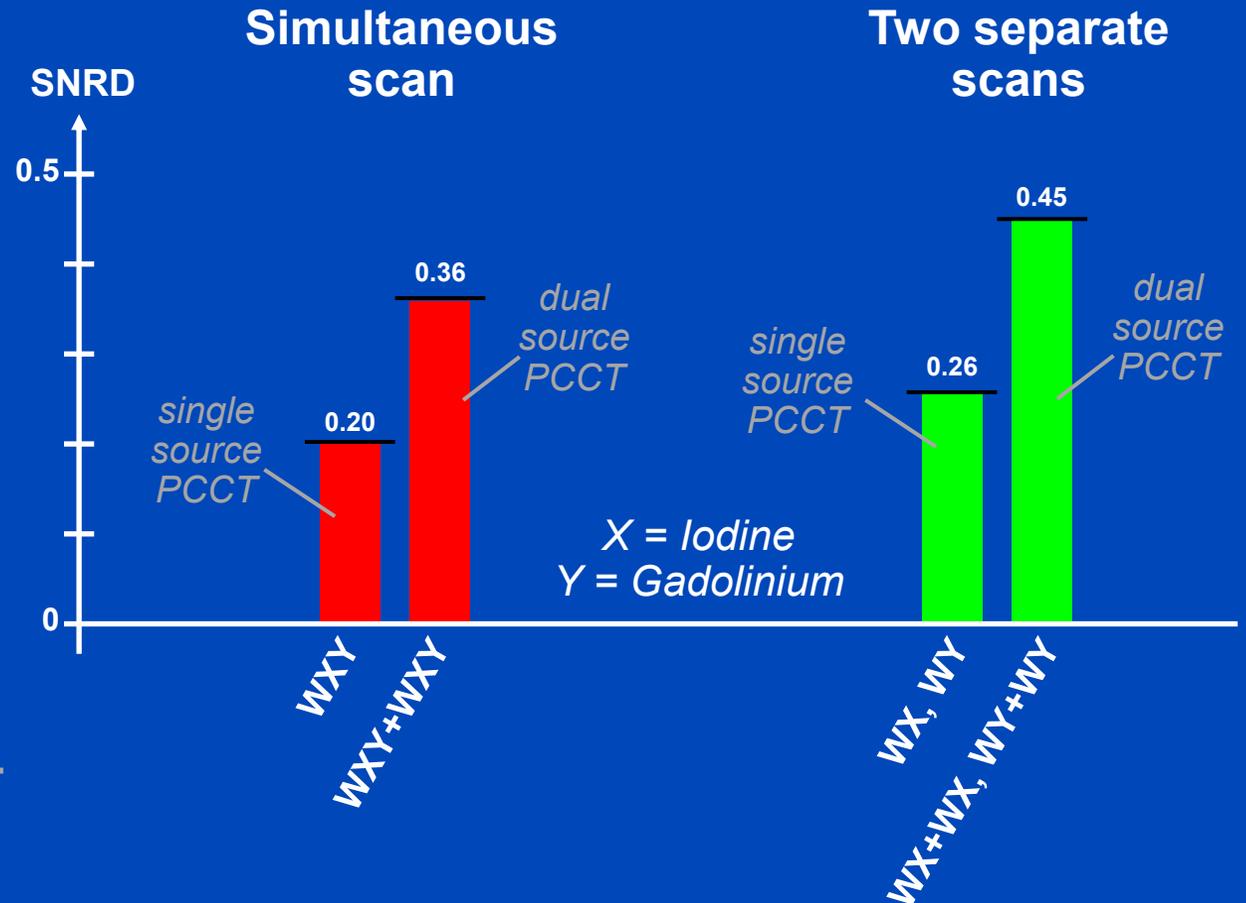
**VNC and iodine noise (standard deviation)  
in DECT is about twice as high as in subtraction imaging.**

# Proposals to Simultaneously use More than One Contrast Agent, X and Y

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18. ... many many more since 2020 ...

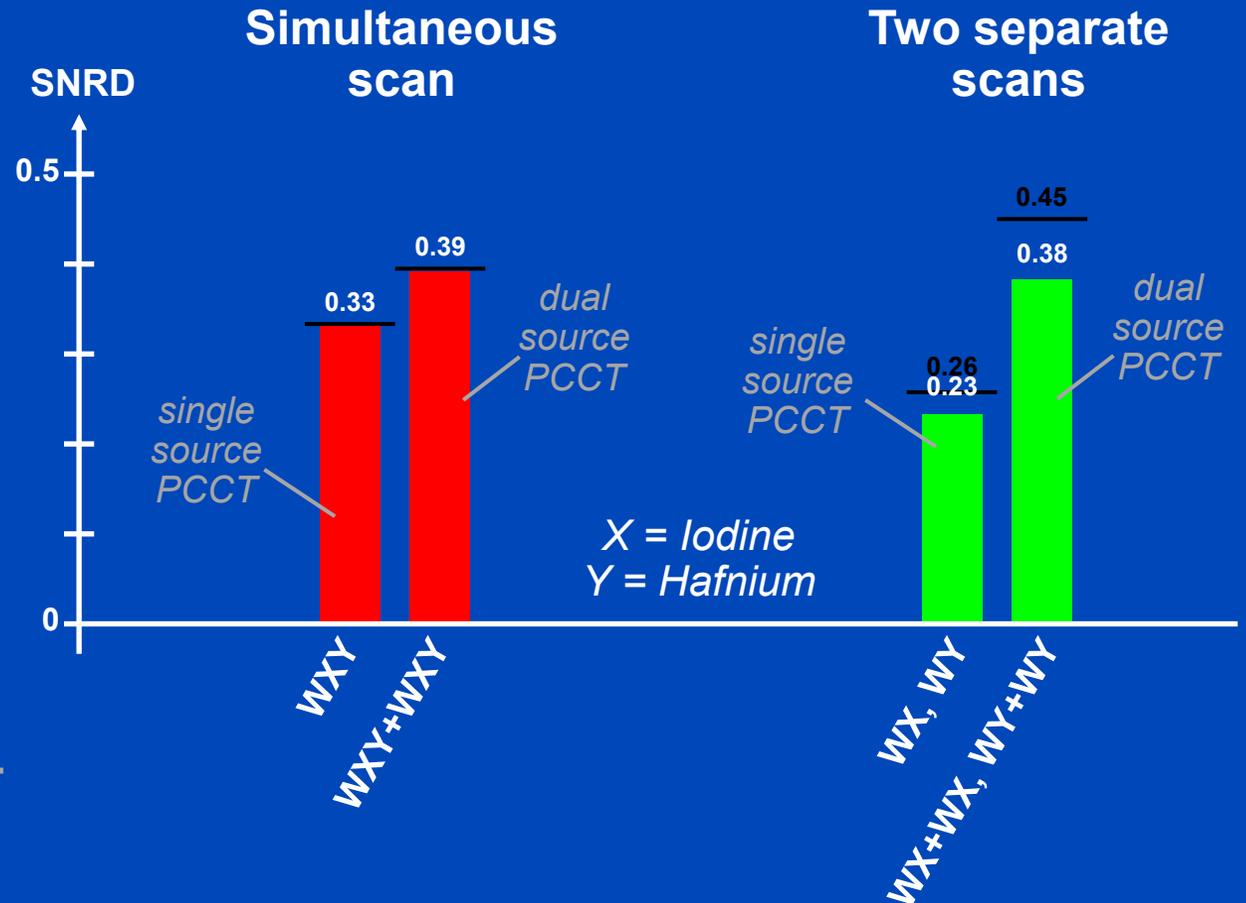
# Two Contrast Agents X and Y in the Same Region

- Must have  $X \neq Y$  if scanned simultaneously.
- Can have  $X = Y$  if scanned separately.
- Separate scans require less dose!
- Good old liver protocols are optimal:
  - $X = Y = \text{iodine}$  (today)
  - Two separate scans
  - Only one CA injection required
  - Unenhanced scan not necessary with PCCT



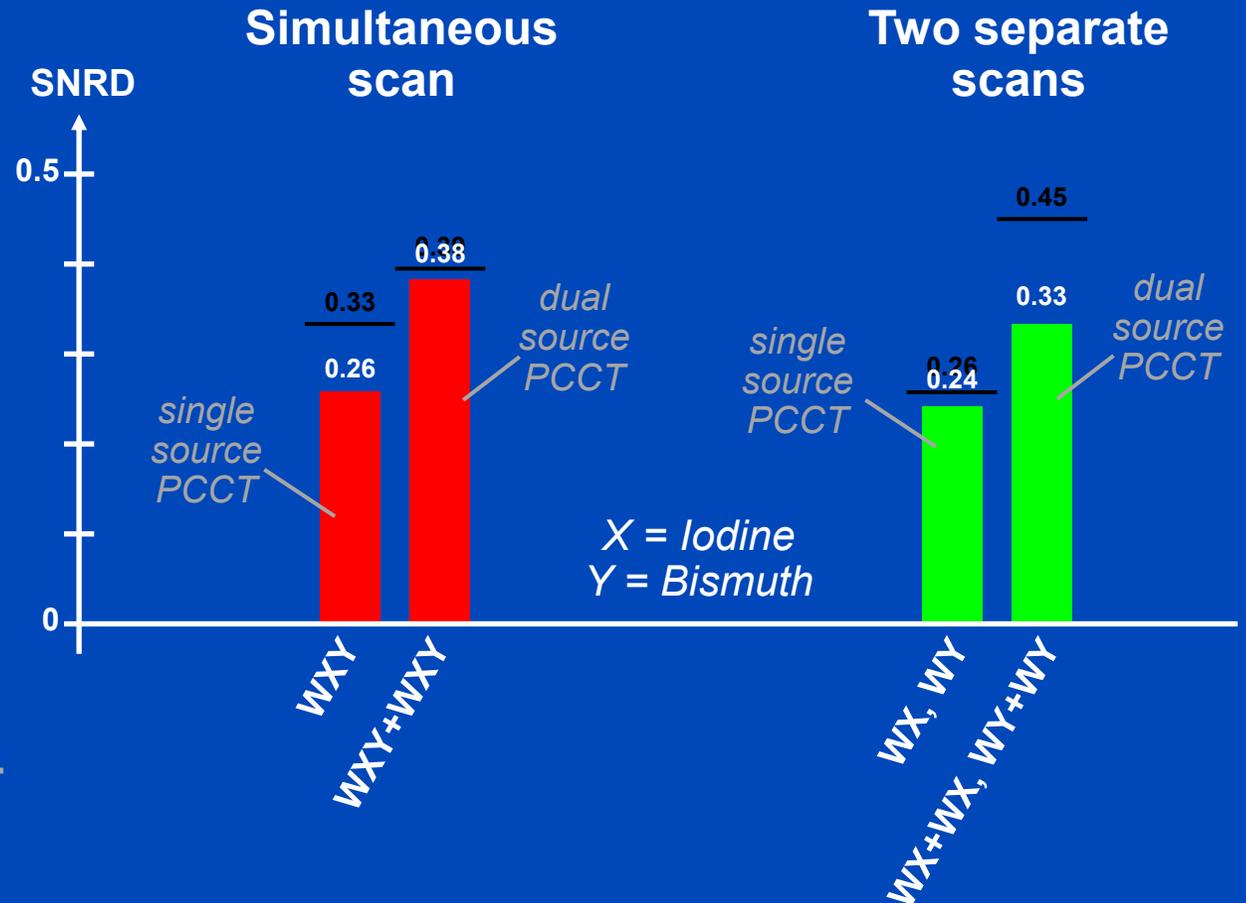
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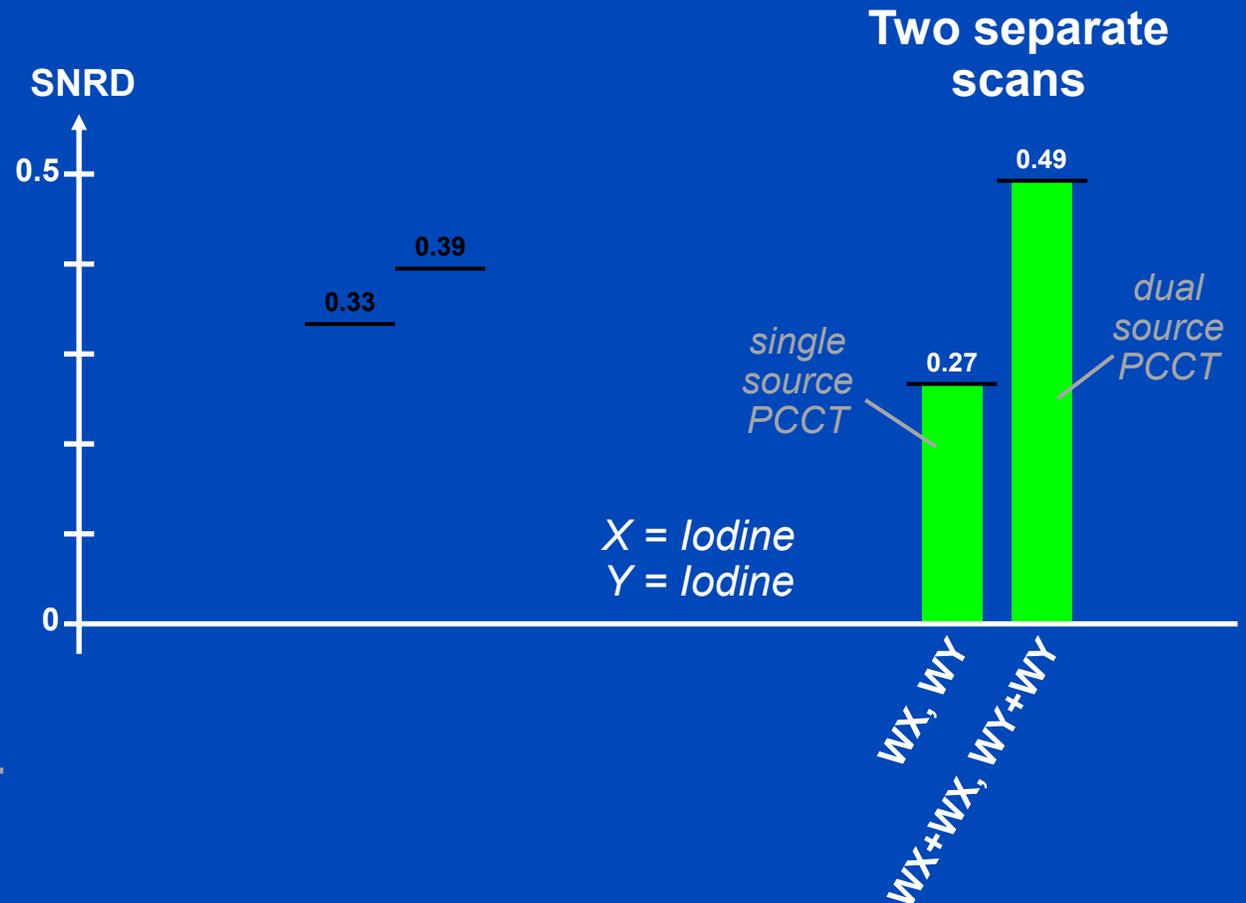
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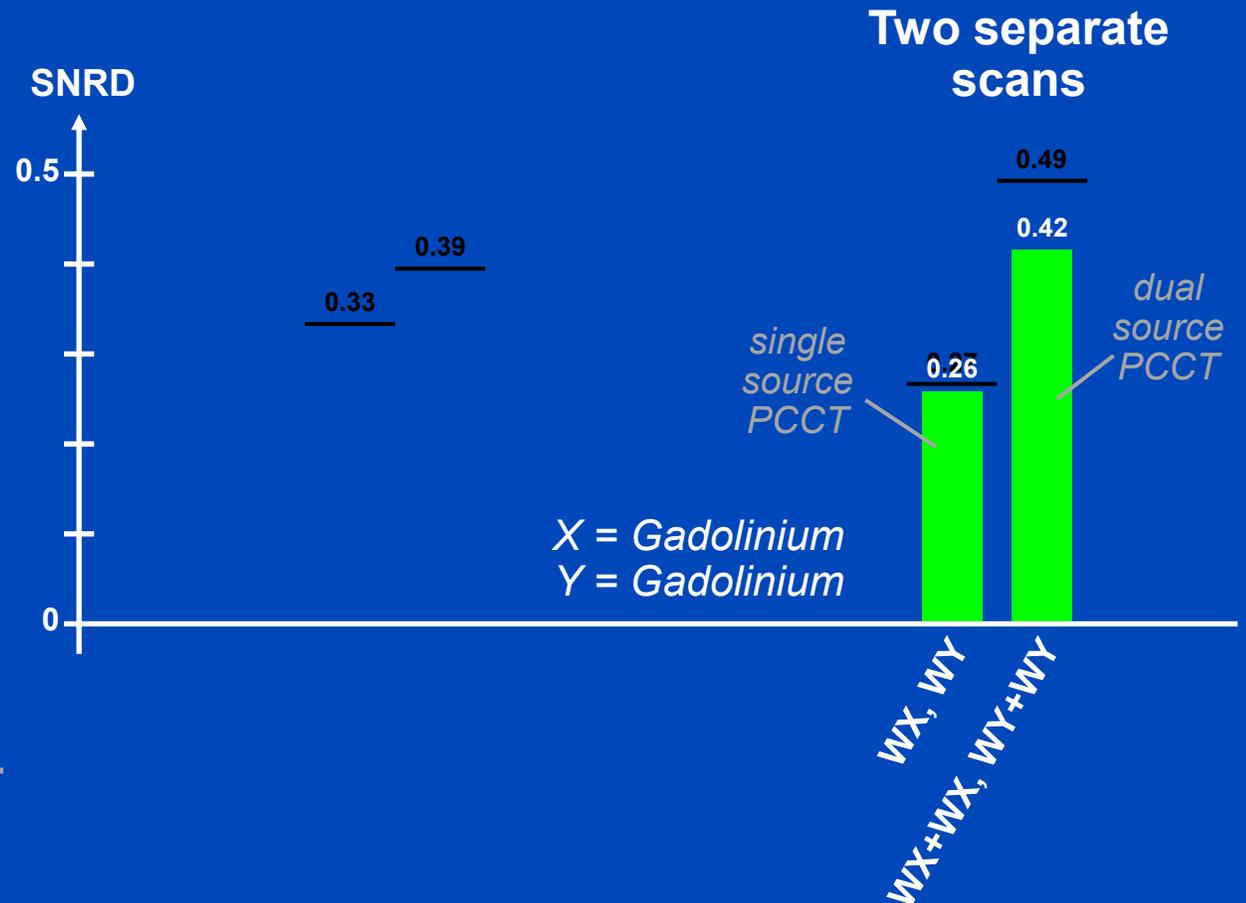
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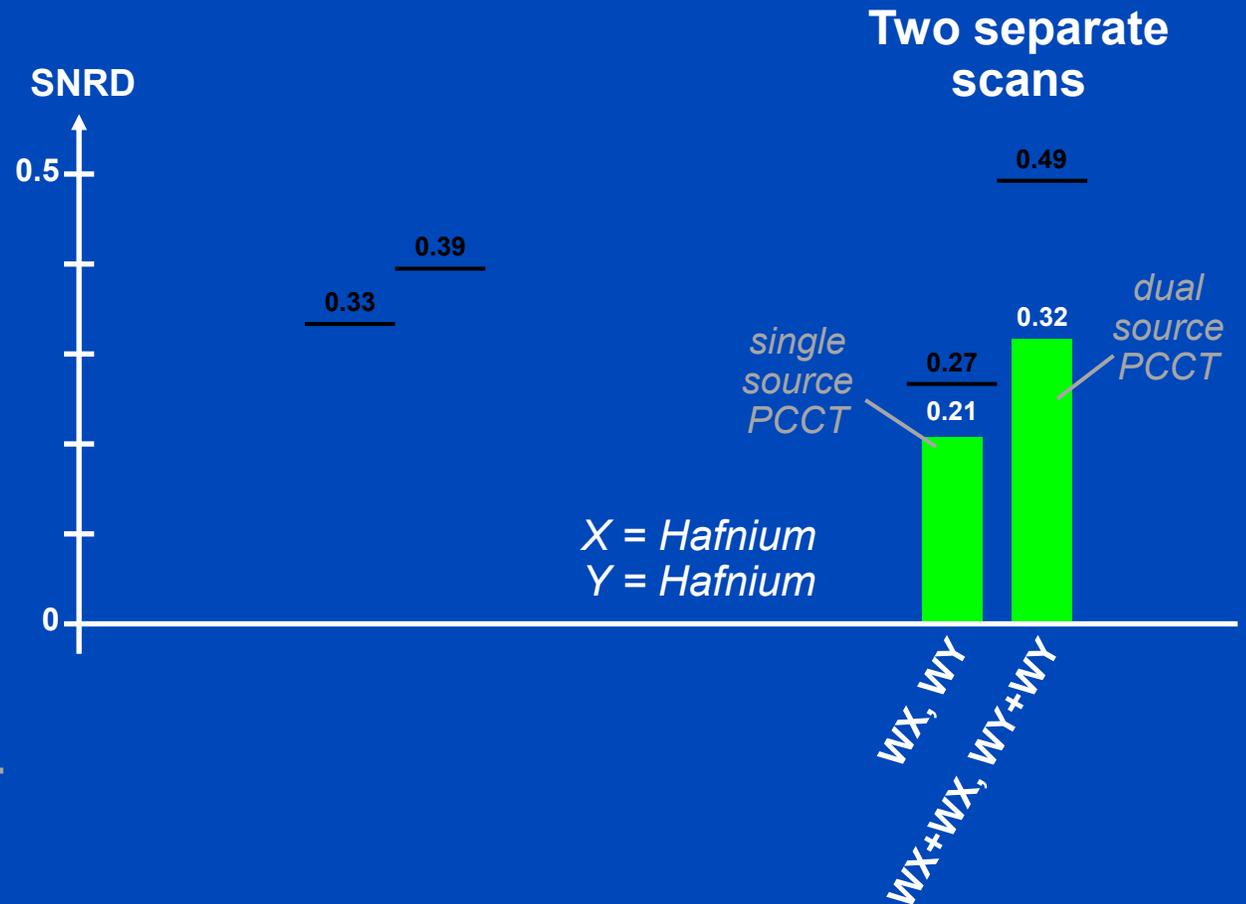
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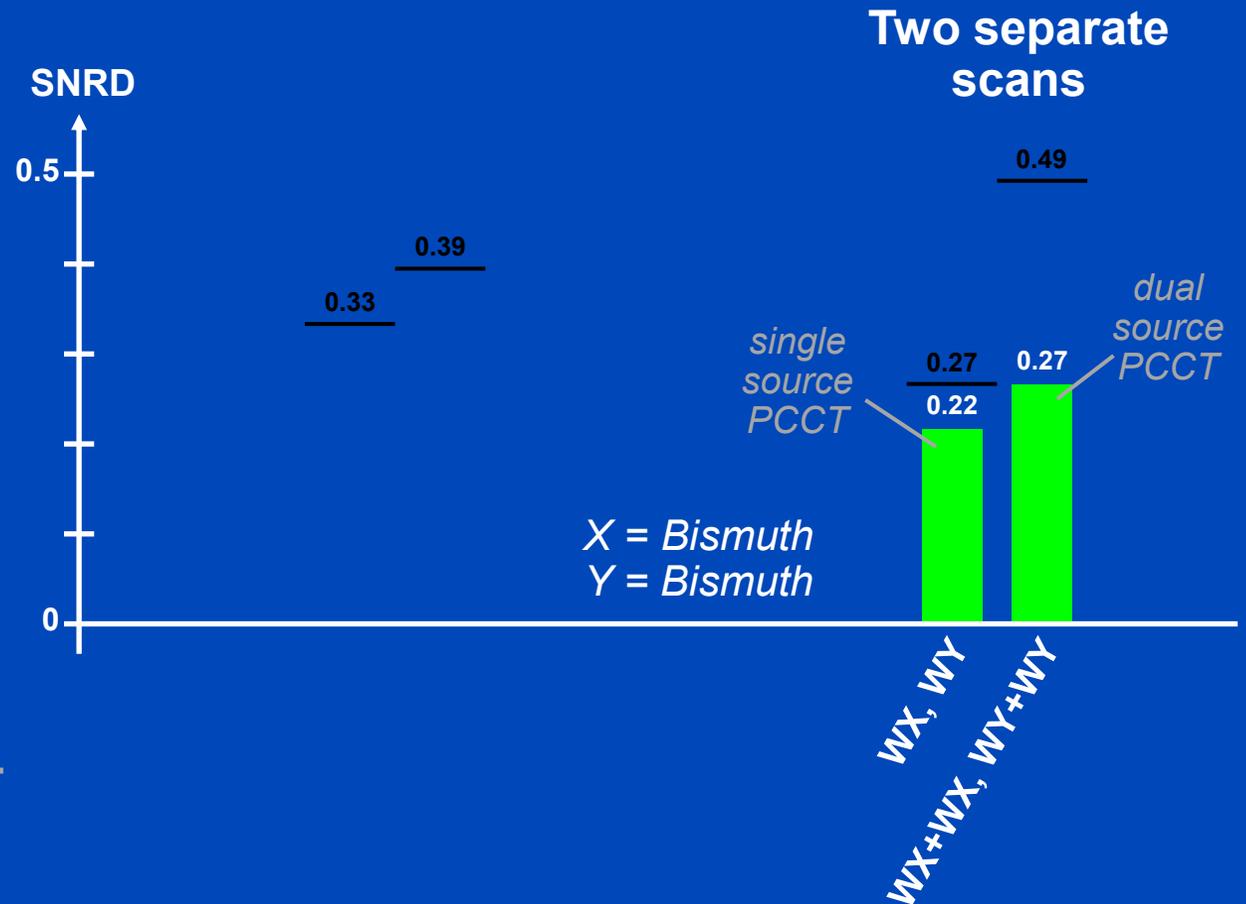
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  - Only one CA injection required
  - Unenhanced scan not necessary with PCCT



# Two Contrast Agents X and Y in Different Regions

- That's trivial, it's different regions
- Any reason for not using  $X=Y$ ?

# Is Iodine Good (or even God)?

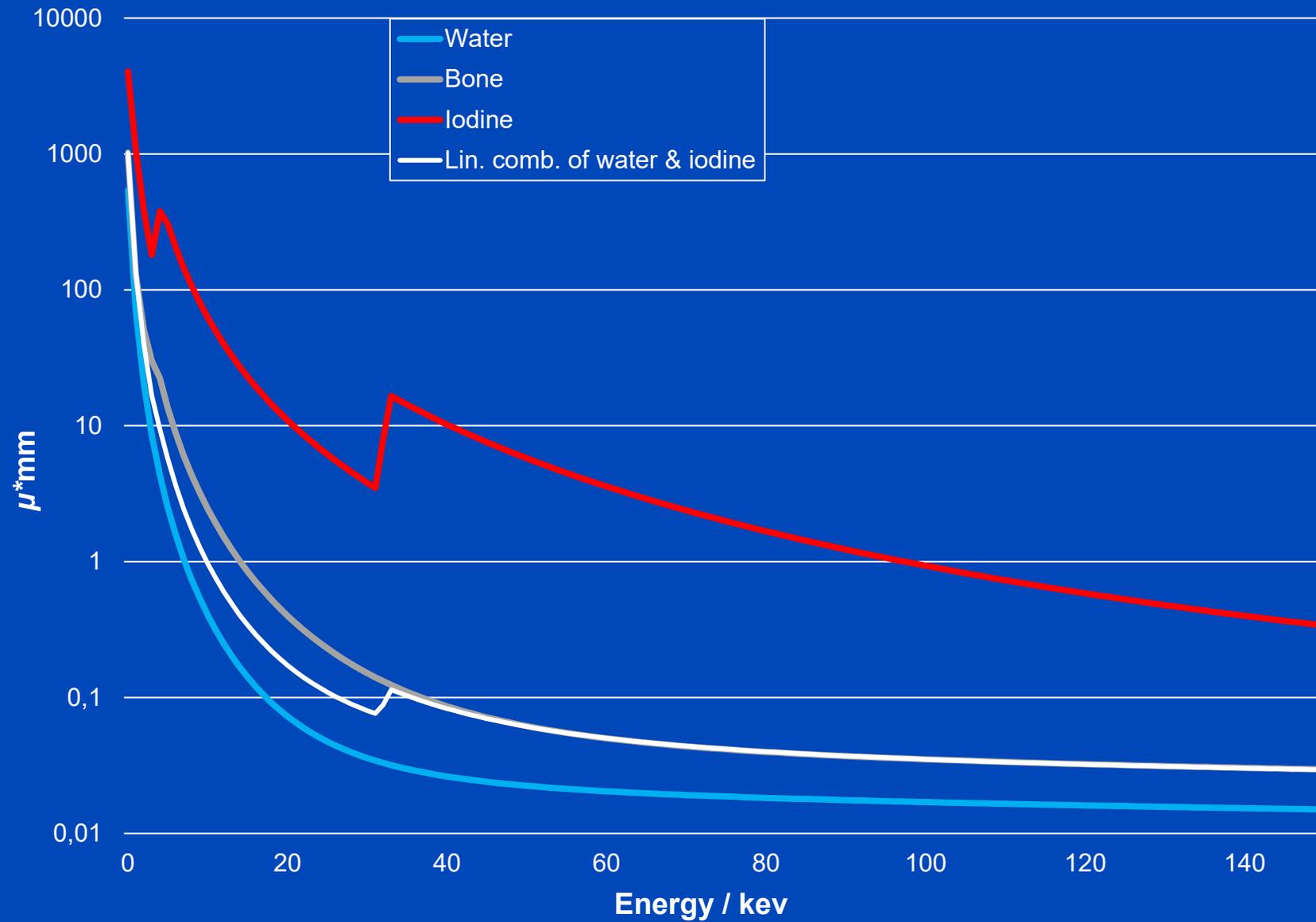
- PCCT simulation with tube voltage, prefilter and energy threshold position optimization and optimized linear reconstruction<sup>1</sup>.
- CAs diluted to have 200 HU in the center of a 32 cm water phantom when scanned at 120 kV spectrum with only intrinsic filtration.
- Patient sizes 20 cm, 30 cm, 40 cm.
- Scan parameters maximizing SNRD of W and X yield:

200 mm, $B = 3$ , real	X=Iodine SNRDs of W, X, tot	X=Gadolinium SNRDs of W, X, tot	X=Hafnium SNRDs of W, X, tot	X=Bismuth SNRDs of W, X, tot
WX	14.7, 3.16, 3.39	12.4, 2.55, 2.74	10.1, 2.30, 2.47	9.91, 2.33, 2.51
WX+WX	21.5, 6.08, 6.45	17.6, 3.89, 4.17	13.2, 2.87, 3.08	17.1, 4.05, 4.35
400 mm, $B = 3$ , real	X=Iodine SNRDs of W, X, tot	X=Gadolinium SNRDs of W, X, tot	X=Hafnium SNRDs of W, X, tot	X=Bismuth SNRDs of W, X, tot
WX	2.28, 0.38, 0.41	2.03, 0.36, 0.39	1.62, 0.29, 0.31	1.63, 0.31, 0.34
WX+WX	3.12, 0.69, 0.74	3.00, 0.60, 0.64	2.02, 0.45, 0.48	1.93, 0.38, 0.40

# Bone as a Linear Combination of Water and Iodine

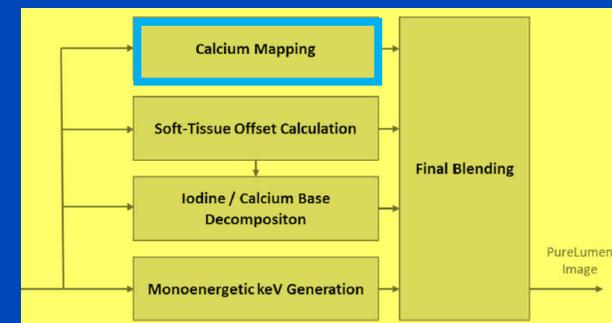
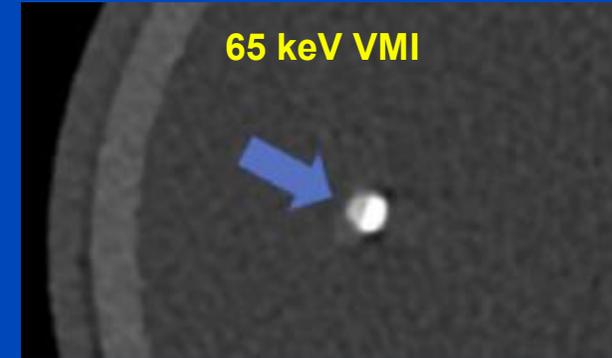
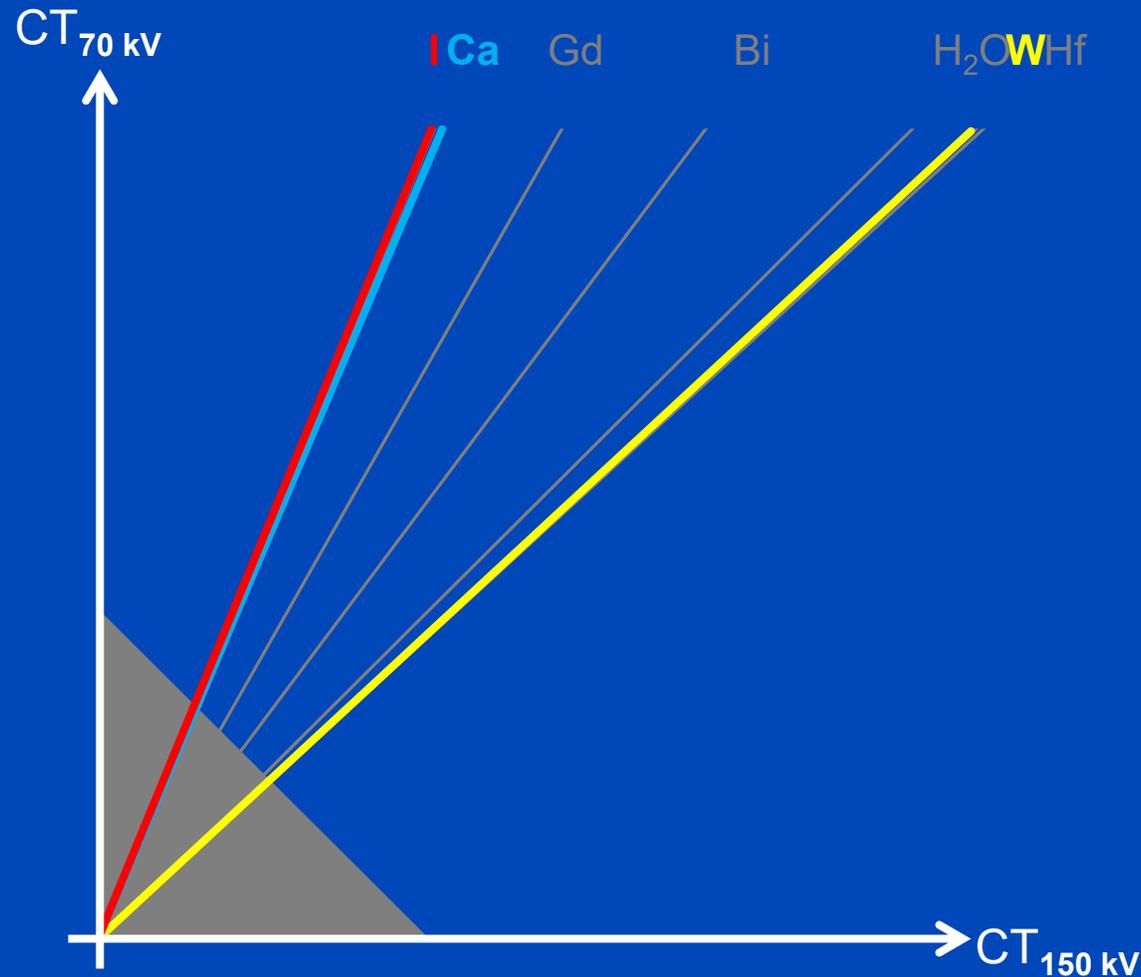
$$C^2 = \min_{a,b} \int_{50 \text{ keV}}^{150 \text{ keV}} dE \left( a \mu_W(E) + b \mu_I(E) - \mu_B(E) \right)^2$$

Material	<i>a</i>	<i>b</i>	<i>C</i>
Bone	1.8860	0.0033	0.0016/mm
Cortical Bone	1.6461	0.0066	0.0031/mm
Spongiosa	1.1924	0.0002	0.0001/mm
Yellow Marrow	0.9334	-0.0003	0.0001/mm
HA50	0.9421	0.0003	0.0001/mm
HA100	0.9840	0.0006	0.0002/mm
HA400	1.3250	0.0028	0.0014/mm



**a = 1.8860**  
**b = 0.0033**  
**C = 0.0016 mm<sup>-1</sup>**

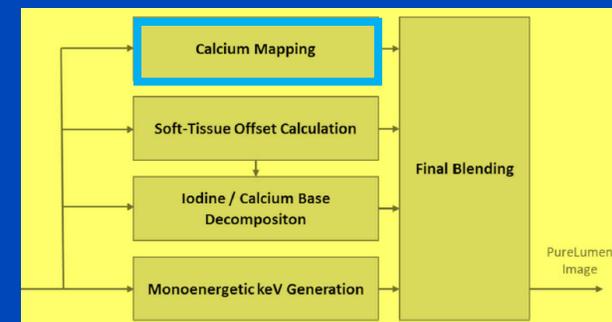
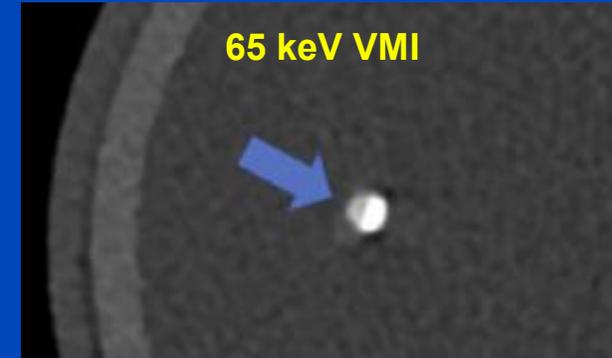
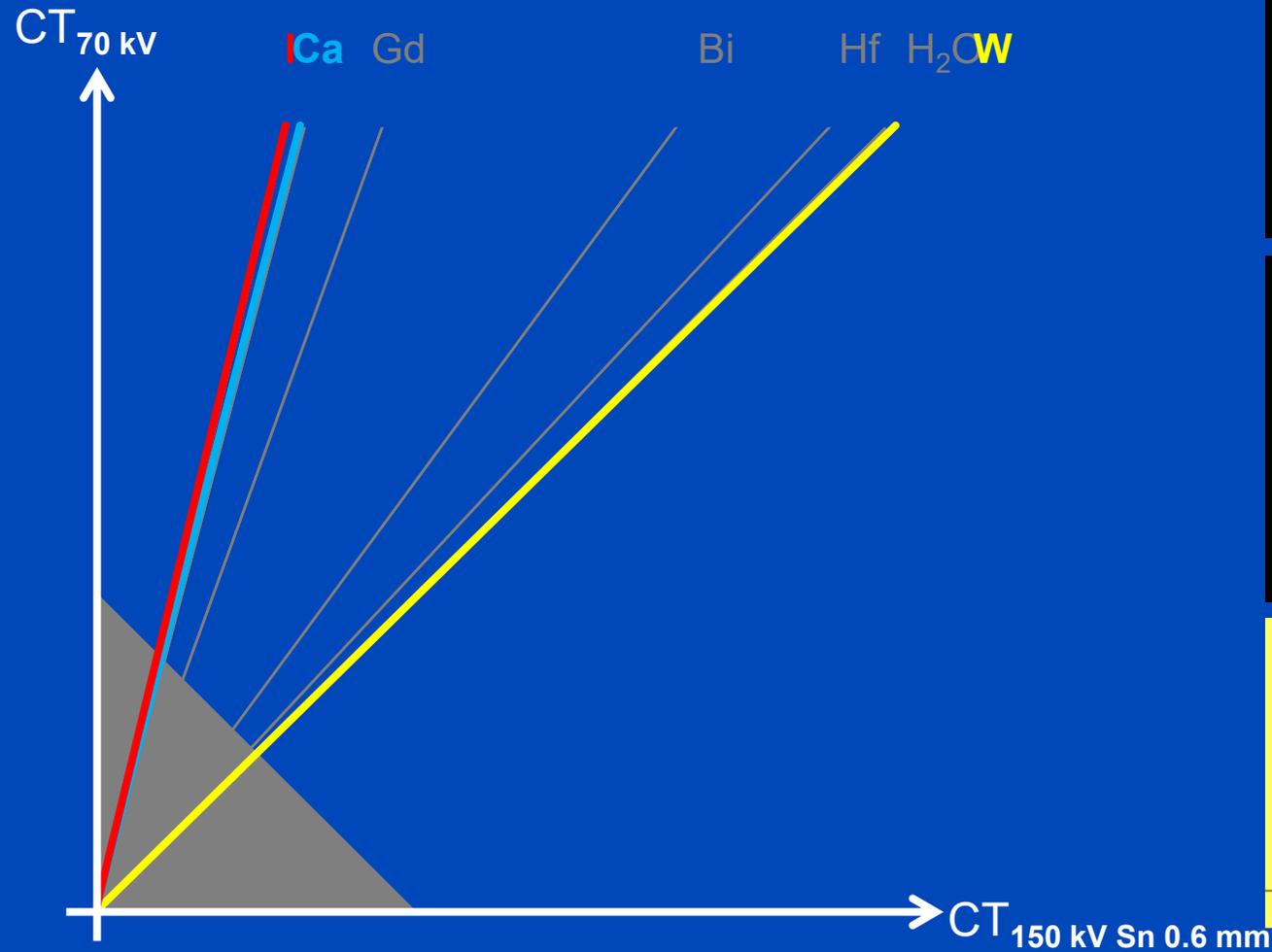
# What if We Want to Discriminate Ca from CA?



Allmendinger et al., Invest Radiol 57(6), 2022

Lines run through points  $(CT_{\text{eff}}(\text{Hi}), CT_{\text{eff}}(\text{Lo}))$  with  $CT_{\text{eff}}$  calculated from  $\mu_{\text{eff}}$  using Tucker spectra that have passed through 32 cm of water. In the energy range of clinical CT and with objects similar to patients we find that  $0.5 \text{ mm Ag} \approx 0.6 \text{ mm Sn} \approx 2.0 \text{ mm Cu}$ .

# What if We Want to Discriminate Ca from CA?

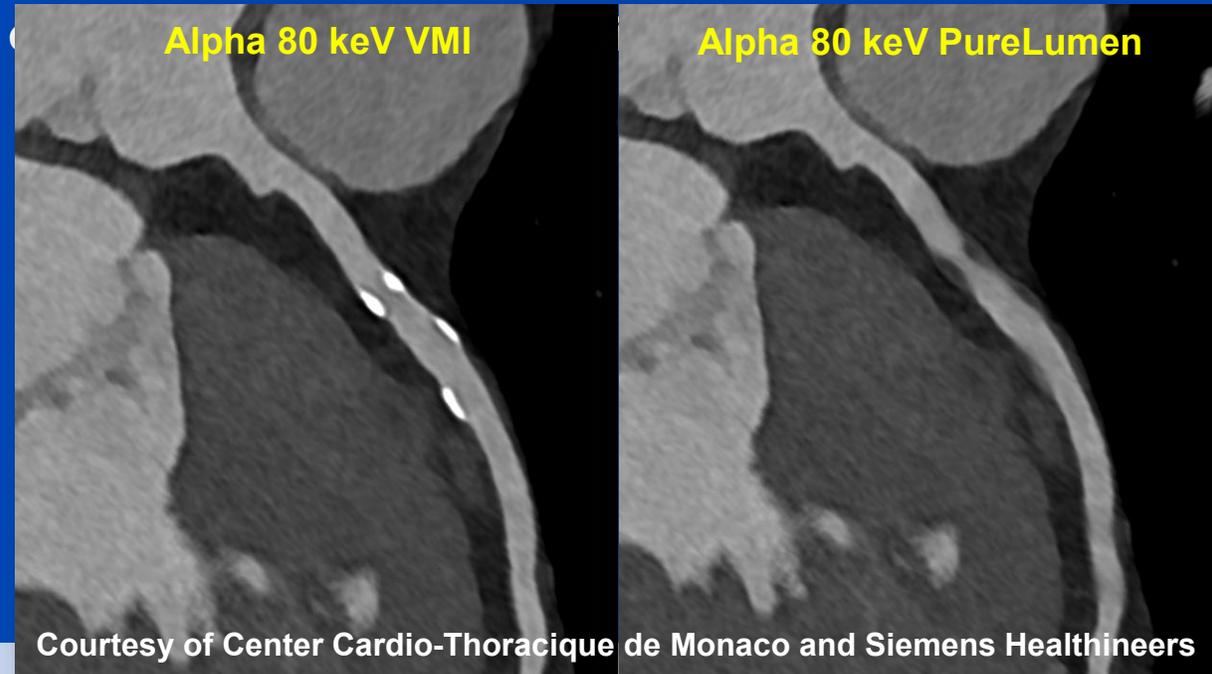


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# Conclusions

- Dual contrast in one scan may not make sense.
- If it does not make sense, then scan separately and save dose.
- Iodine is great!
- Higher Z may help to better discriminate Ca from CA.
  - In particular a tungsten CA ( $Z = 74$ ) seems good to tell Ca from CA.
  - However, tungsten is not easy to discriminate from soft tissue by spectral means.
  - This means, potential tungsten maps may be of limited use.
  - Special application in coronary arteries?
  - Tungsten could be mixed with iodine!
- It is iodine forever!
- Maybe it will have a little sister.



# Thank You!



This presentation will soon be available at [www.dkfz.de/ct](http://www.dkfz.de/ct).

Job opportunities through [marc.kachelriess@dkfz.de](mailto:marc.kachelriess@dkfz.de) or through DKFZ's international PhD or Postdoctoral Fellowship programs.

Parts of the reconstruction software were provided by RayConStruct® GmbH, Nürnberg, Germany.