

*XV CPAN DAYS*

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# A Monte Carlo Study of Different LET Definitions using PENH

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**Daniel Puerta**  
Marta Anguiano  
Wilfredo González  
Antonio M. Lallena



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# Protontherapy

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- ❖ Growth of proton therapy.
- ❖ Biological effect may not only be given by physical dose.
- ❖ (Unrestricted) **linear energy transfer (LET)** = Electronic Stopping Power =  $\frac{dE}{dz}$
- ❖ Only defined for a determined particle with specific energy.

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# LET Averages

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- ❖ Average of LET needed for many particles.
- ❖ In our previous studies, we used the intuitive formulas:

$$\bar{L}_t(z) = \frac{\int \phi_E(z) S(E) dE}{\int \phi_E(z) dE} \quad \bar{L}_d(z) = \frac{\int \phi_E(z) S^2(E) dE}{\int \phi_E(z) S(E) dE}$$

- ❖ Analytical formulas available (Wilkins et al., 2003).

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# Monte Carlo Simulations

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- ❖ Monte Carlo simulations are the gold standard in radiation transport.
- ❖ Different options to implement LET averages. -> No consensus (Kalholm, 2021)
- ❖ Source of uncertainty for treatment's biological effect.

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# Implementations Considered

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$$\bar{L}_t(z) = \frac{\sum_{E_i} \phi_{E_i}(z) S(E_i) \Delta E}{\sum_{E_i} \phi_{E_i}(z) \Delta E}$$

❖  $\phi_{E_i}$  : proton energy spectrum.

❖  $S(E_i)$  : electronic stopping power.

❖ Implicit assumption:

$$\bar{L}_d(z) = \frac{\sum_{E_i} \phi_{E_i}(z) S^2(E_i) \Delta E}{\sum_{E_i} \phi_{E_i}(z) S(E_i) \Delta E}$$

$$D(E_i) = \phi_{E_i} \cdot S(E_i)$$

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# Implementations Considered

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- ❖ Previous formulas have issues.
- ❖ Here (Granville et al., 2015):

$$\bar{L}_t = \frac{\sum_i^N dx_i S_i(E)}{\sum_i^N dx_i}$$

$$\bar{L}_d = \frac{\sum_i^N e_i S_i(E)}{\sum_i^N e_i}$$

- ❖ We will test them and compare with TOPAS and FLUKA.

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# Benchmarking

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❖ Self consistency tests.

1. Nuclear reactions suppressed.

2. Full calculations.

❖ Comparison with previous Monte Carlo studies.

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# Simulation Details

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MC Codes Comparison

TOPAS, FLUKA

Type of beam

Pencil beam

Energies

75, 160, 250 MeV

Geometry

1 cm x 1cm x (7, 30.1, 50) cm

Voxelization

1 cm x 1 cm x (0.07, 0.2, 0.2) cm

Cutoffs protons

0.025 MeV

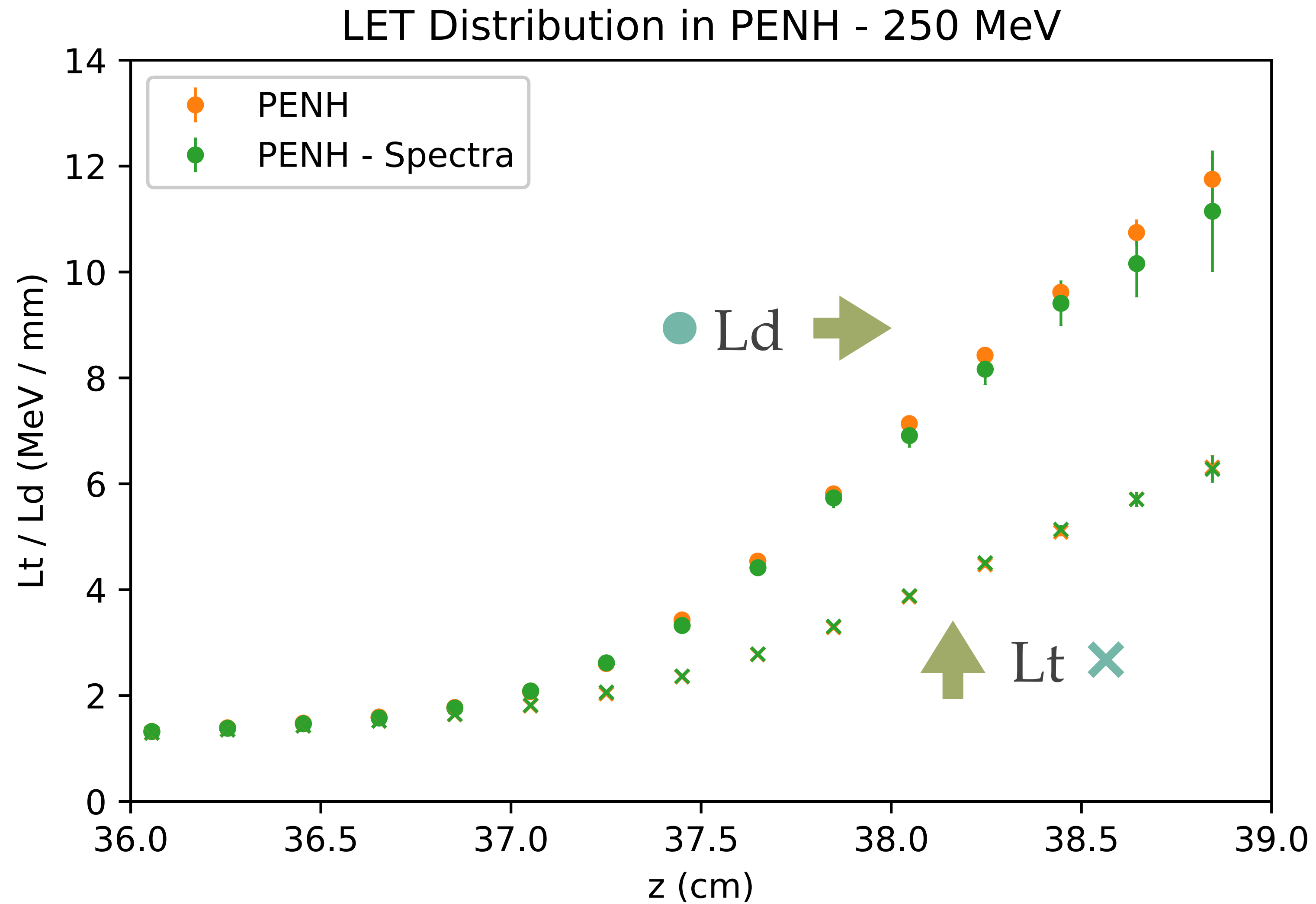
Quantity

Unrestricted LET in water. Only protons contribute.



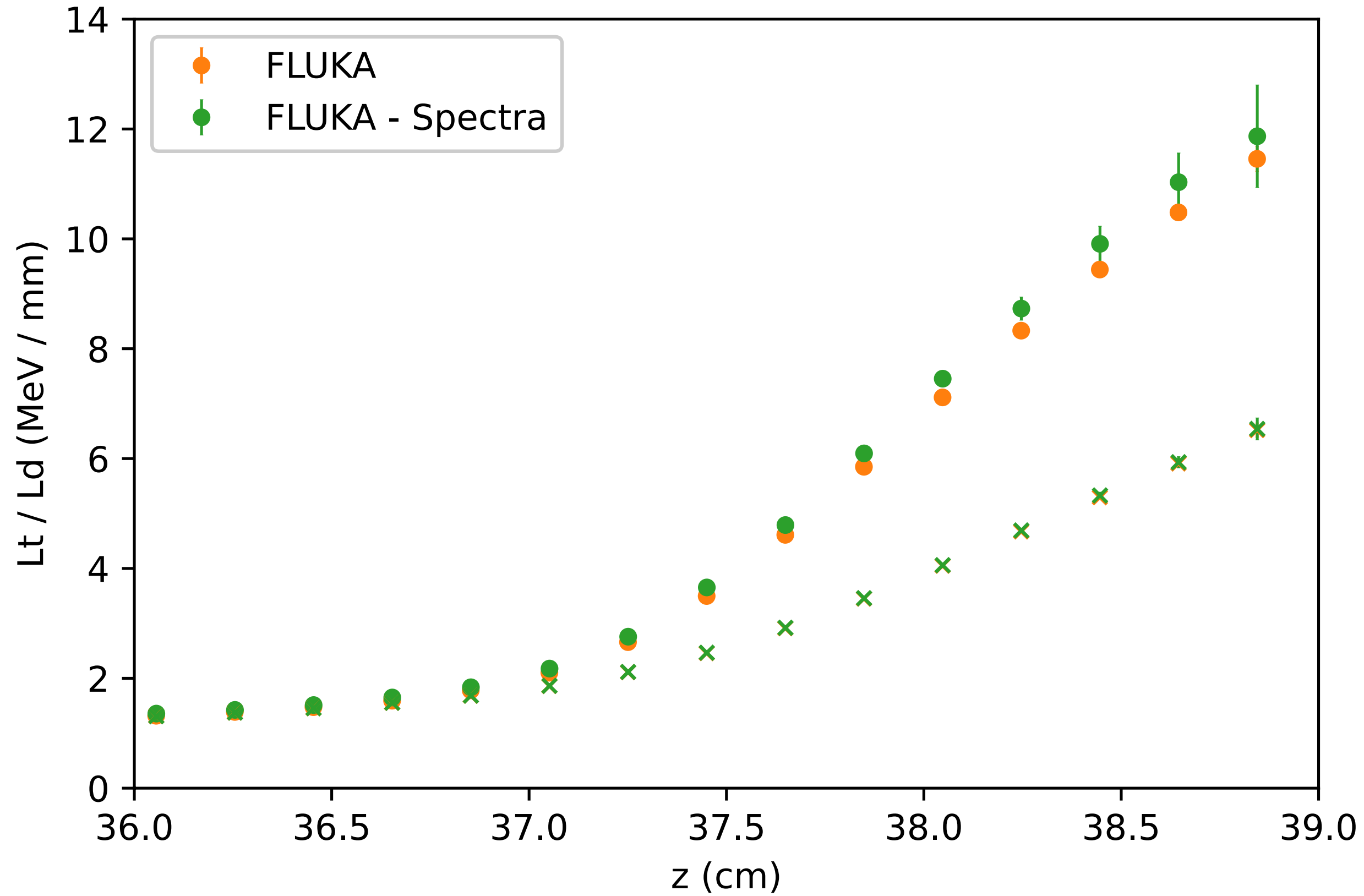
# Nuclear Reactions Suppressed

# Example

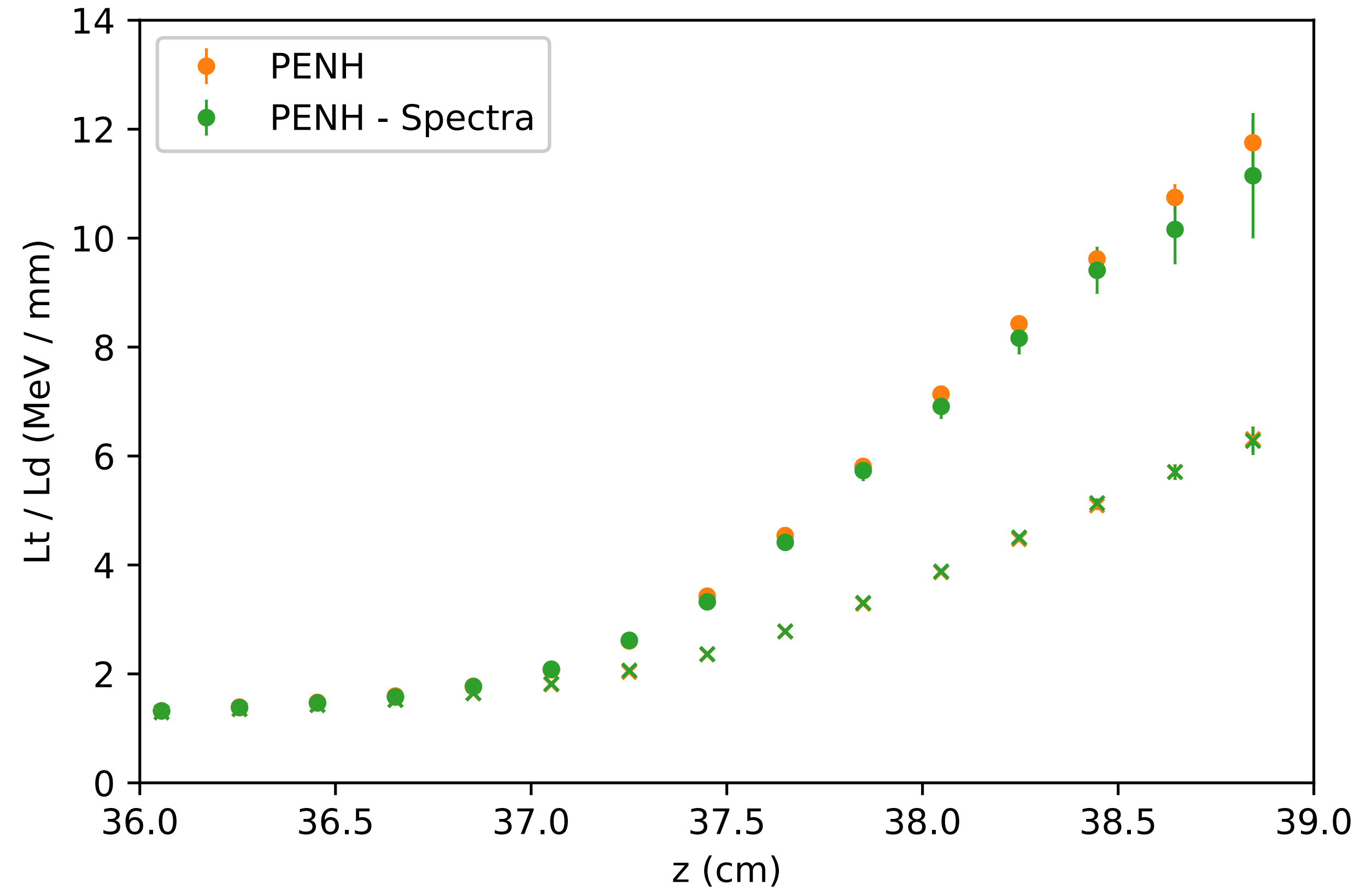


# 250 MeV

LET Distribution in FLUKA - 250 MeV

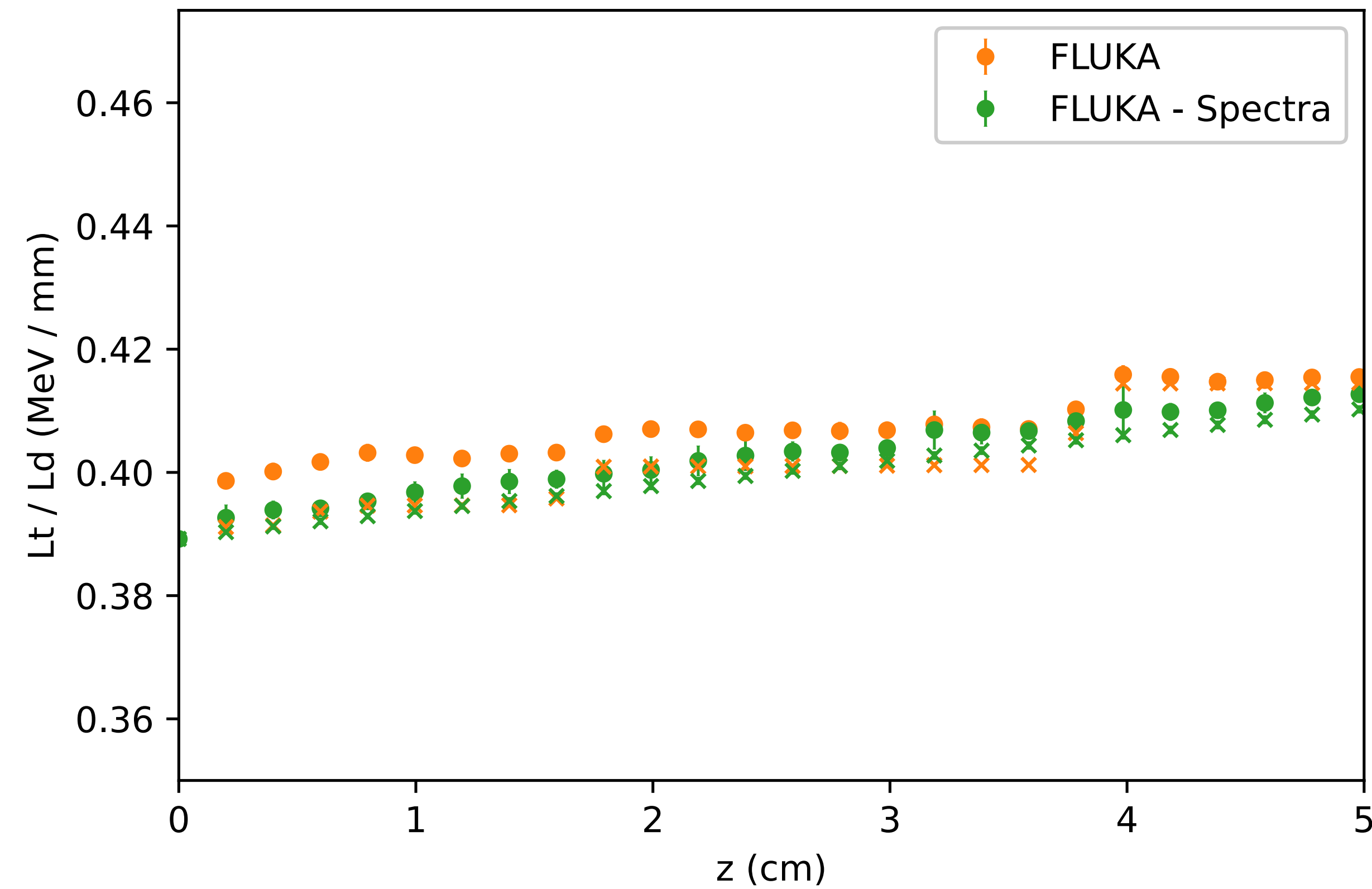


LET Distribution in PENH - 250 MeV

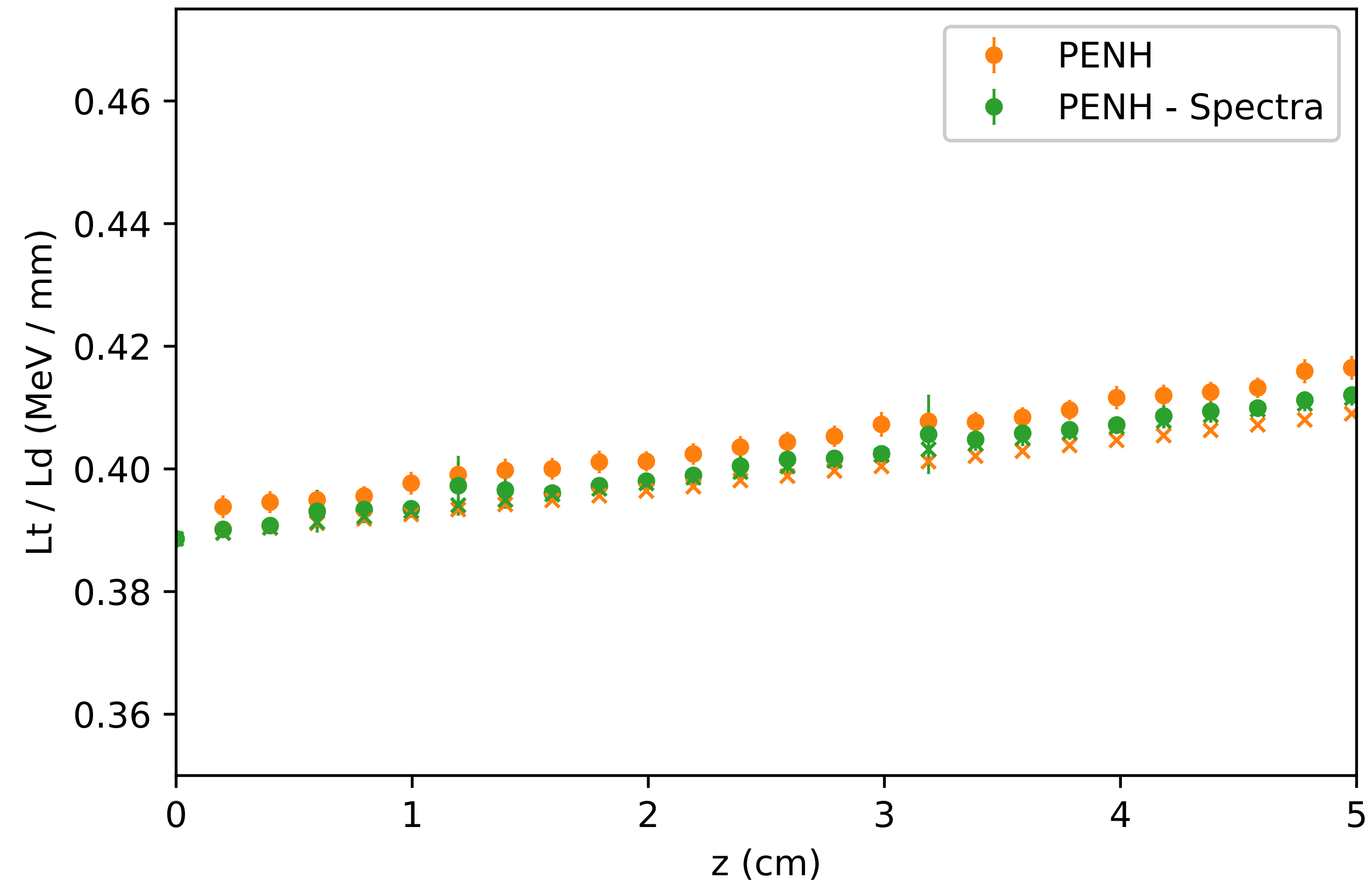


# 250 MeV

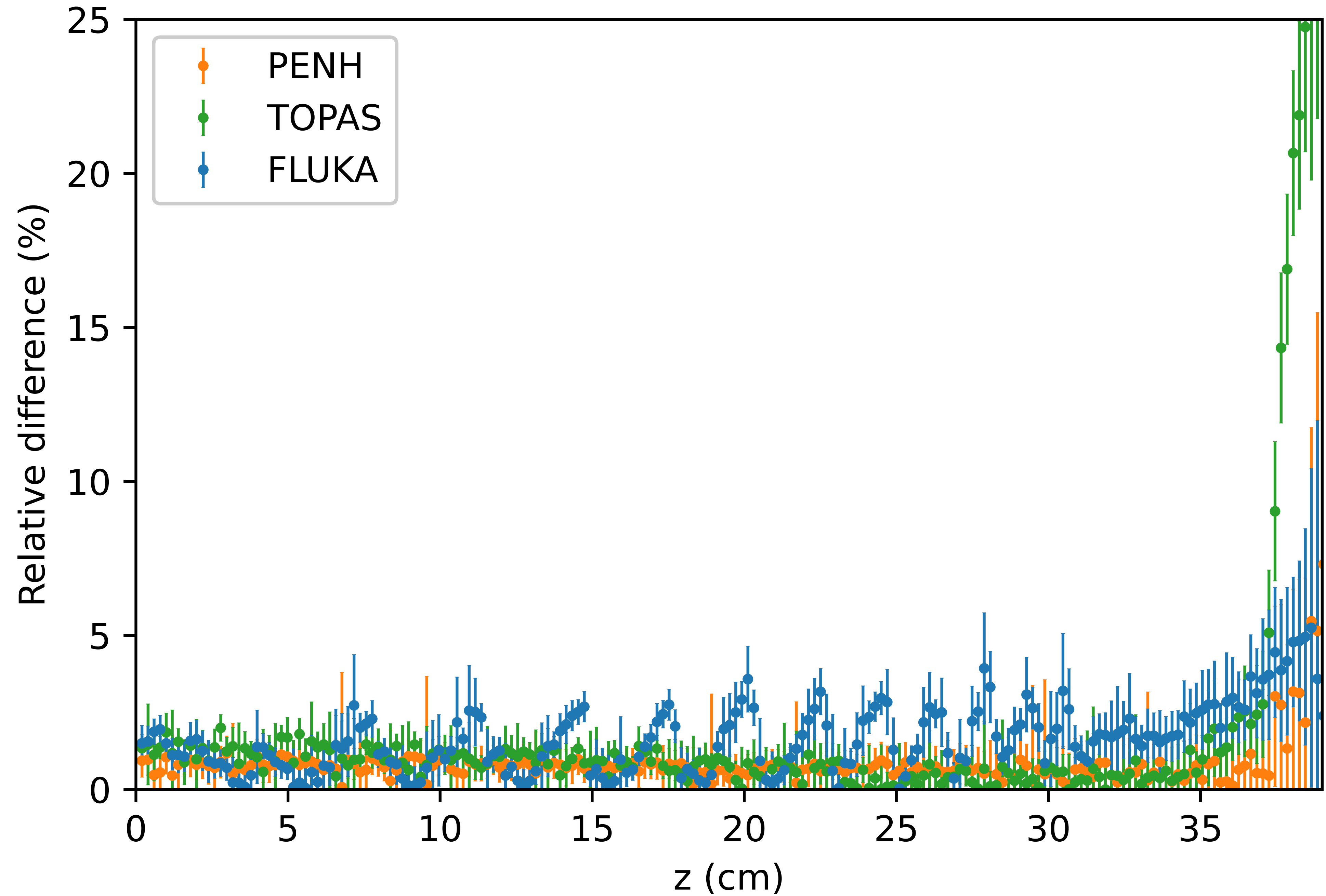
LET Distribution in FLUKA - 250 MeV



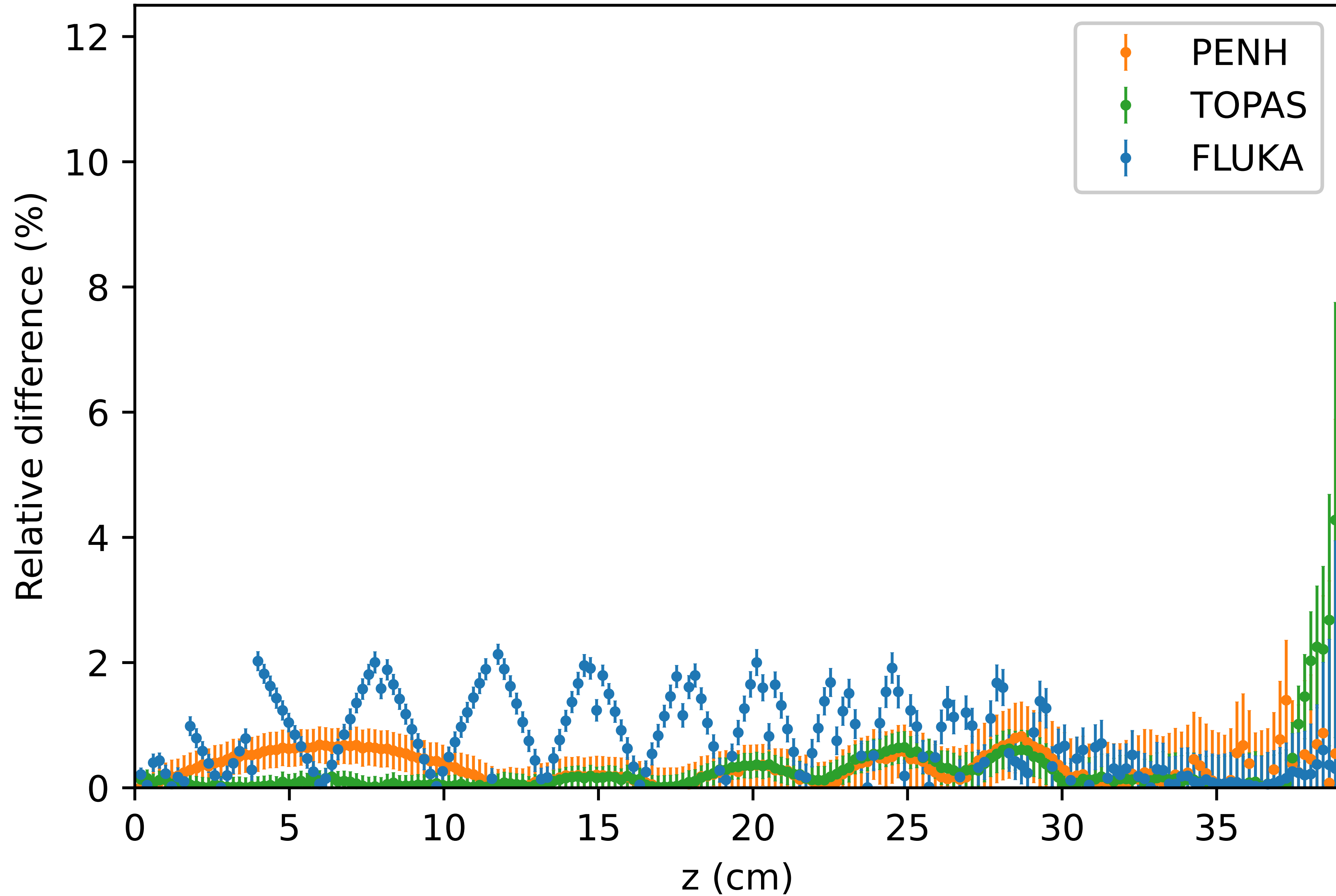
LET Distribution in PENH - 250 MeV



Differences in Ld - 250 MeV - No NR

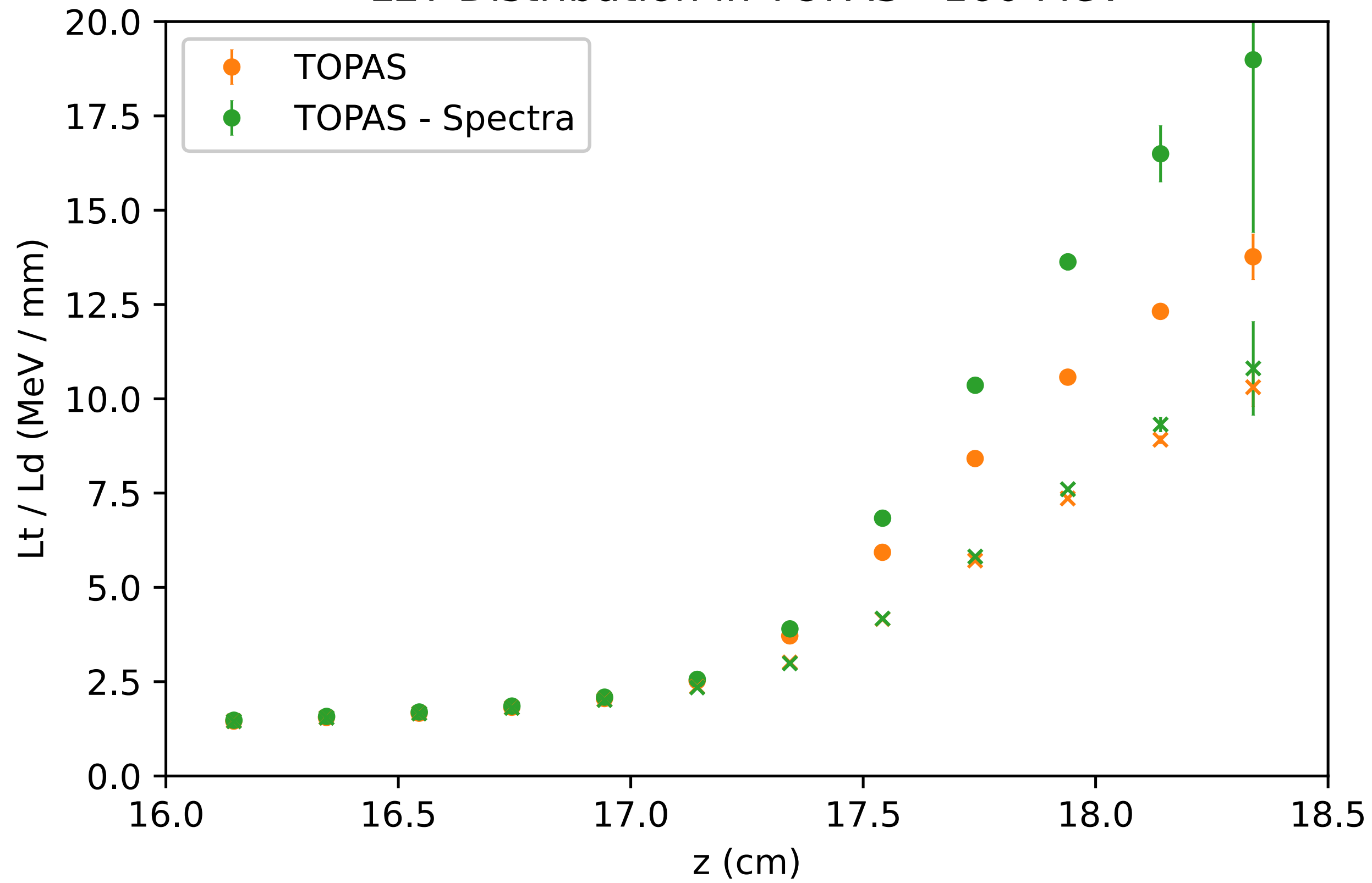


# Differences in Lt - 250 MeV - No NR

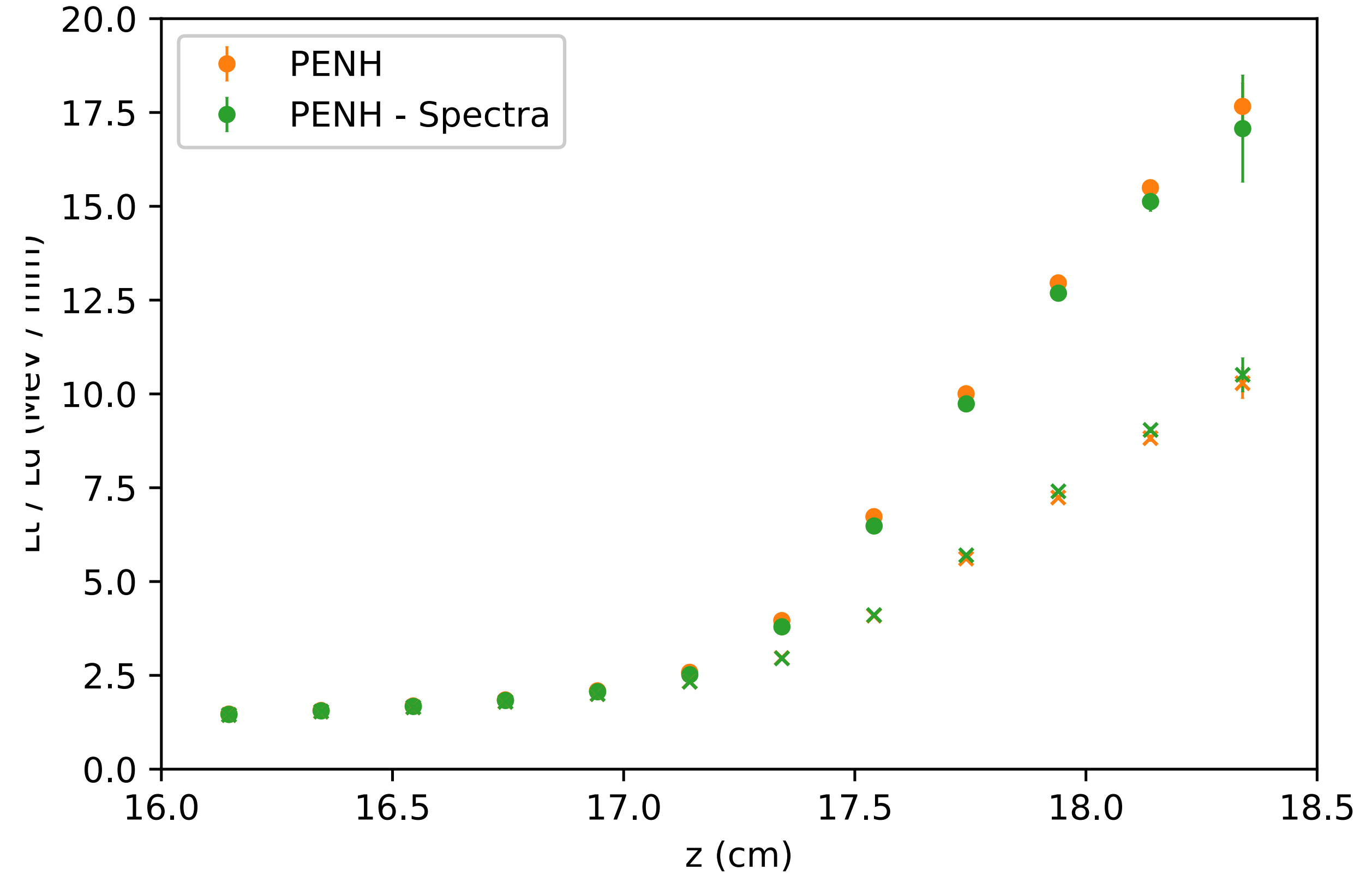


# 160 MeV

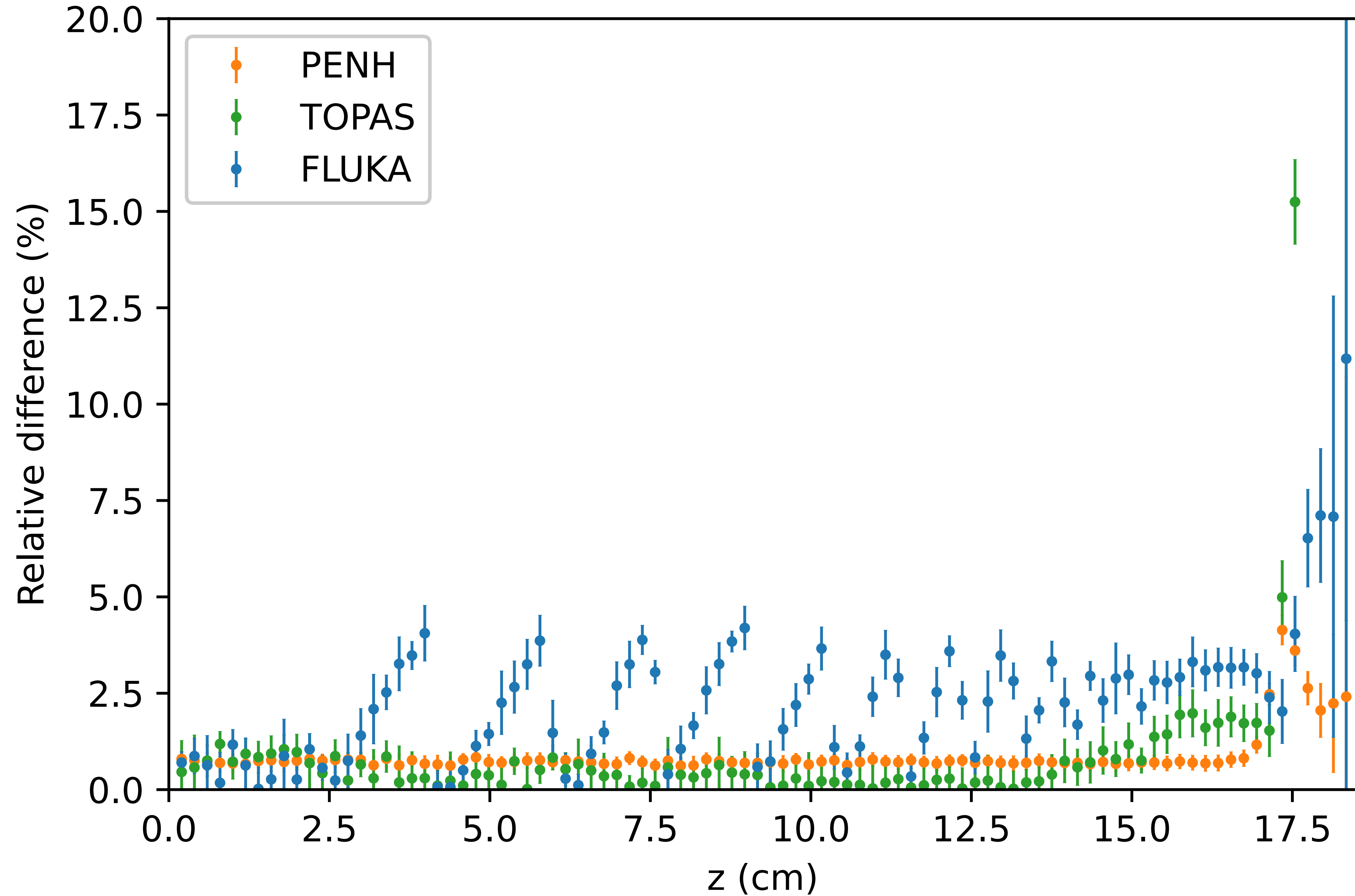
LET Distribution in TOPAS - 160 MeV



LET Distribution in PENH - 160 MeV

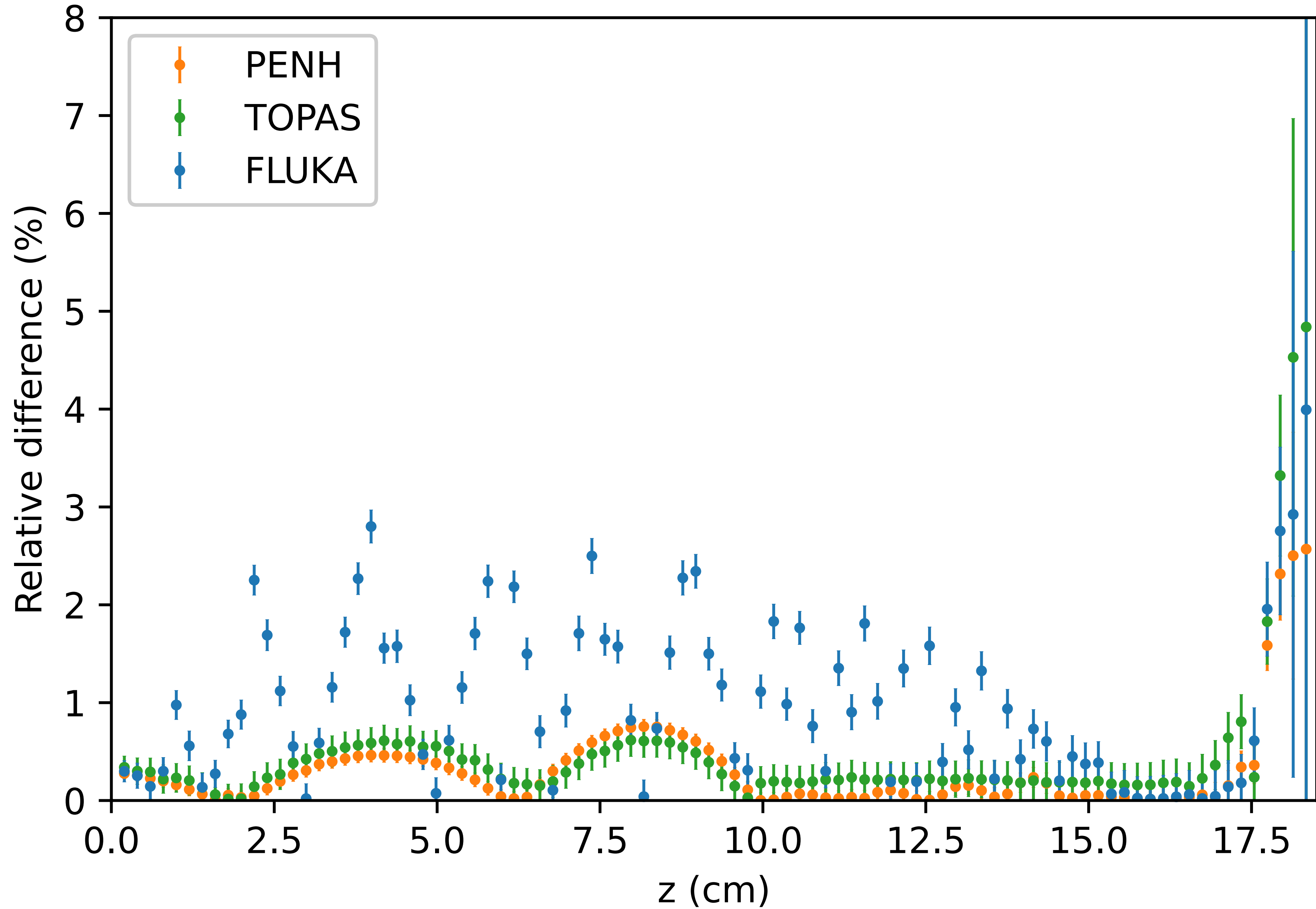


Differences in Ld - 160 MeV - No NR



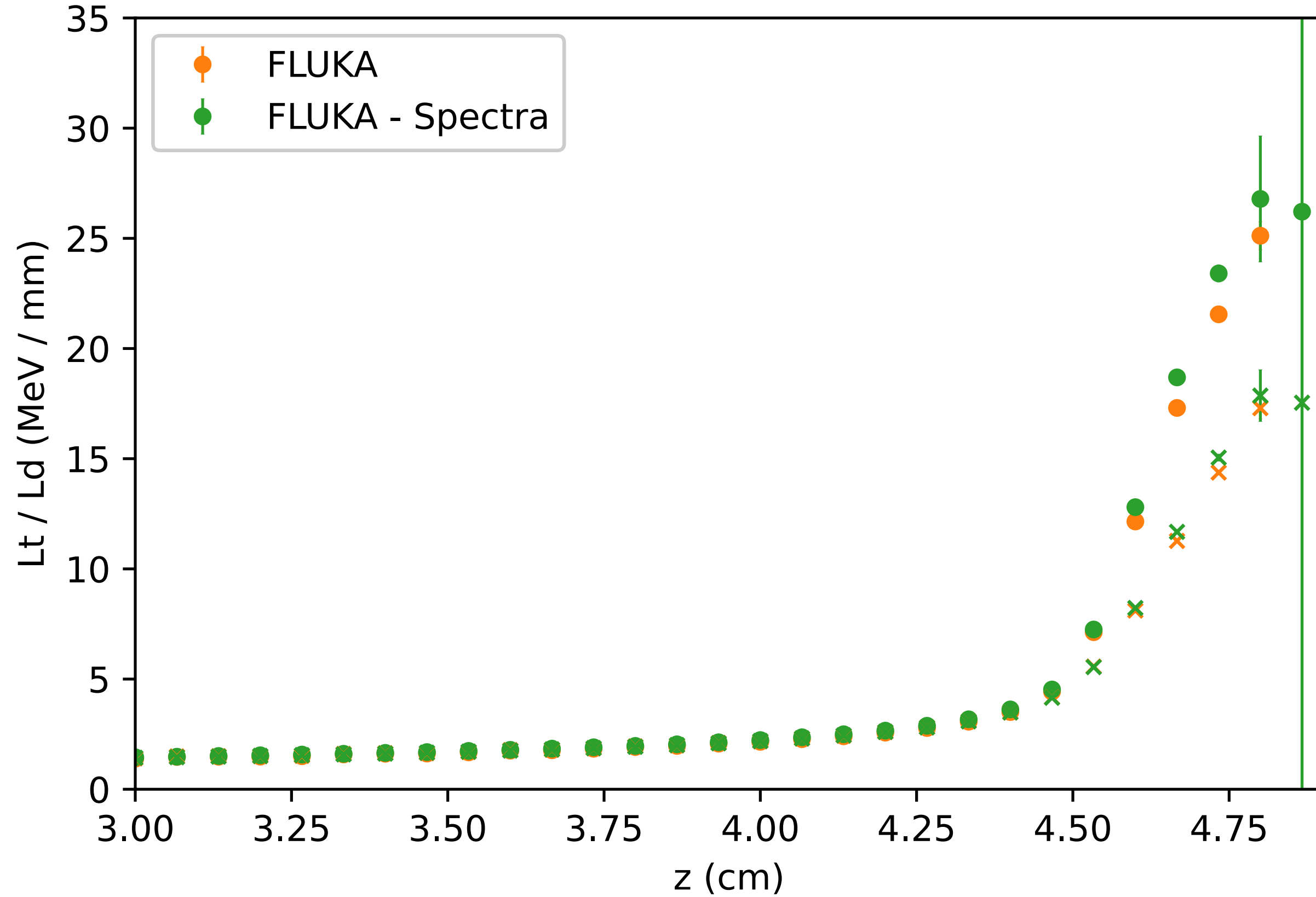


Differences in Lt - 160 MeV - No NR

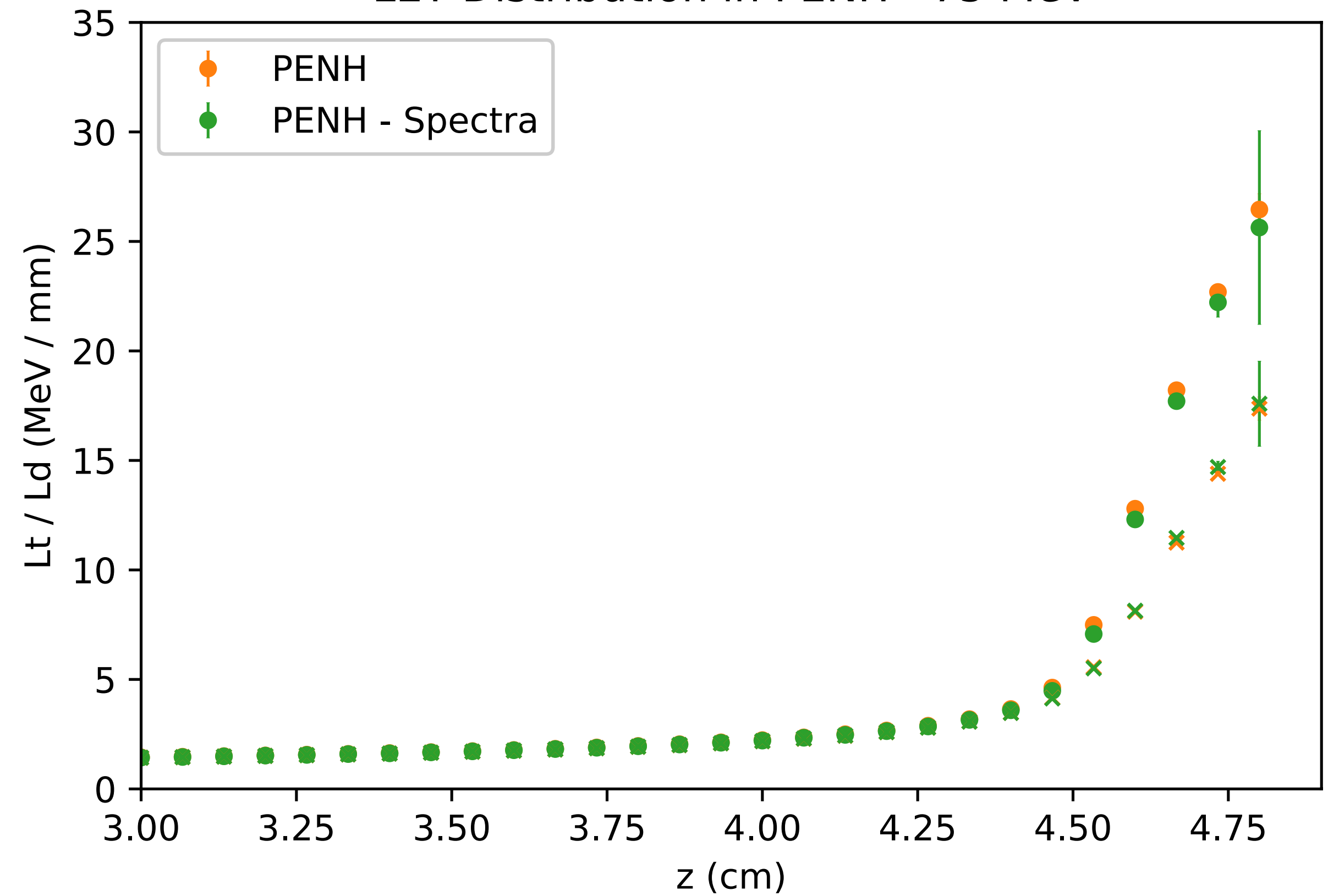


# 75 MeV

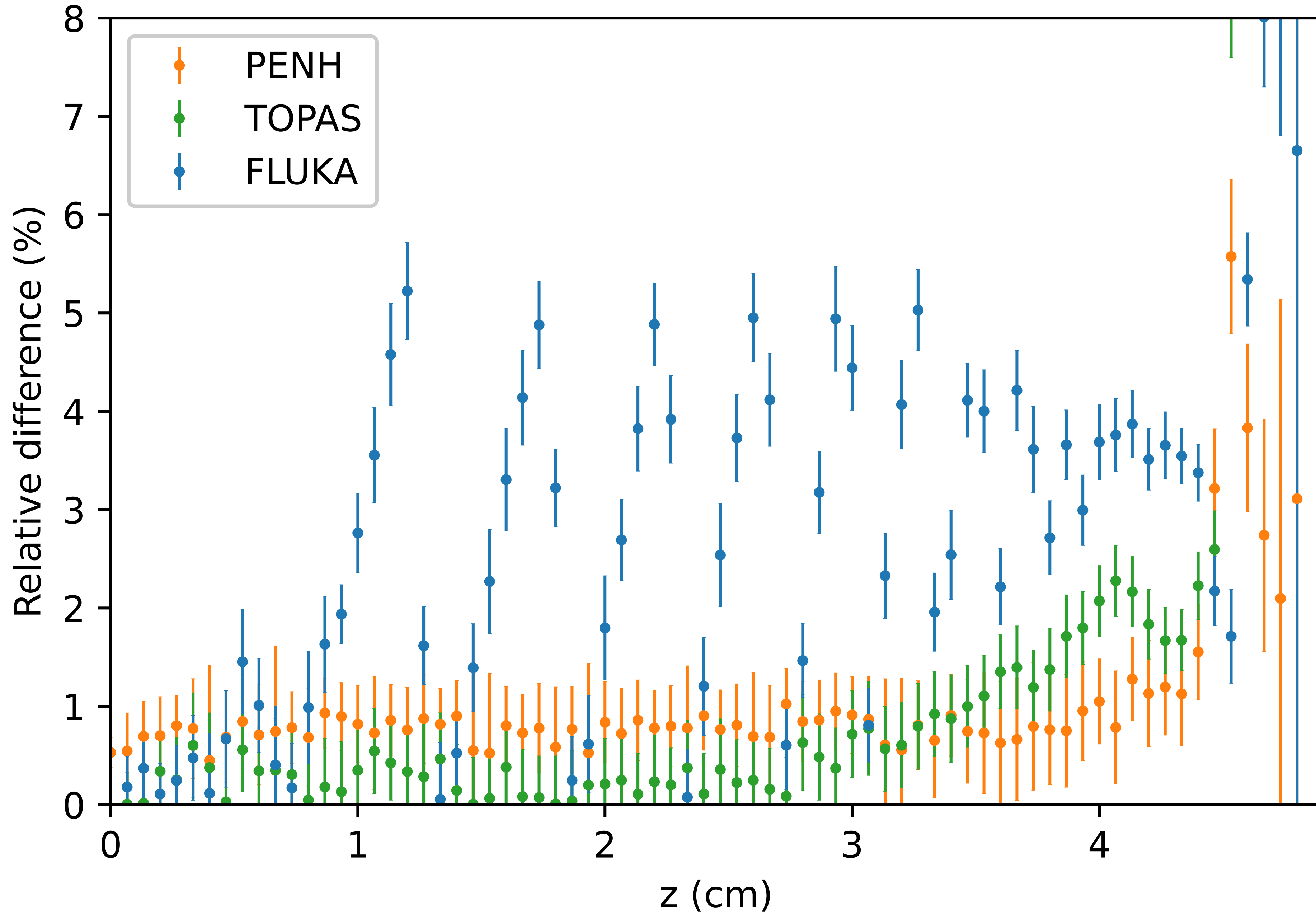
LET Distribution in FLUKA - 75 MeV



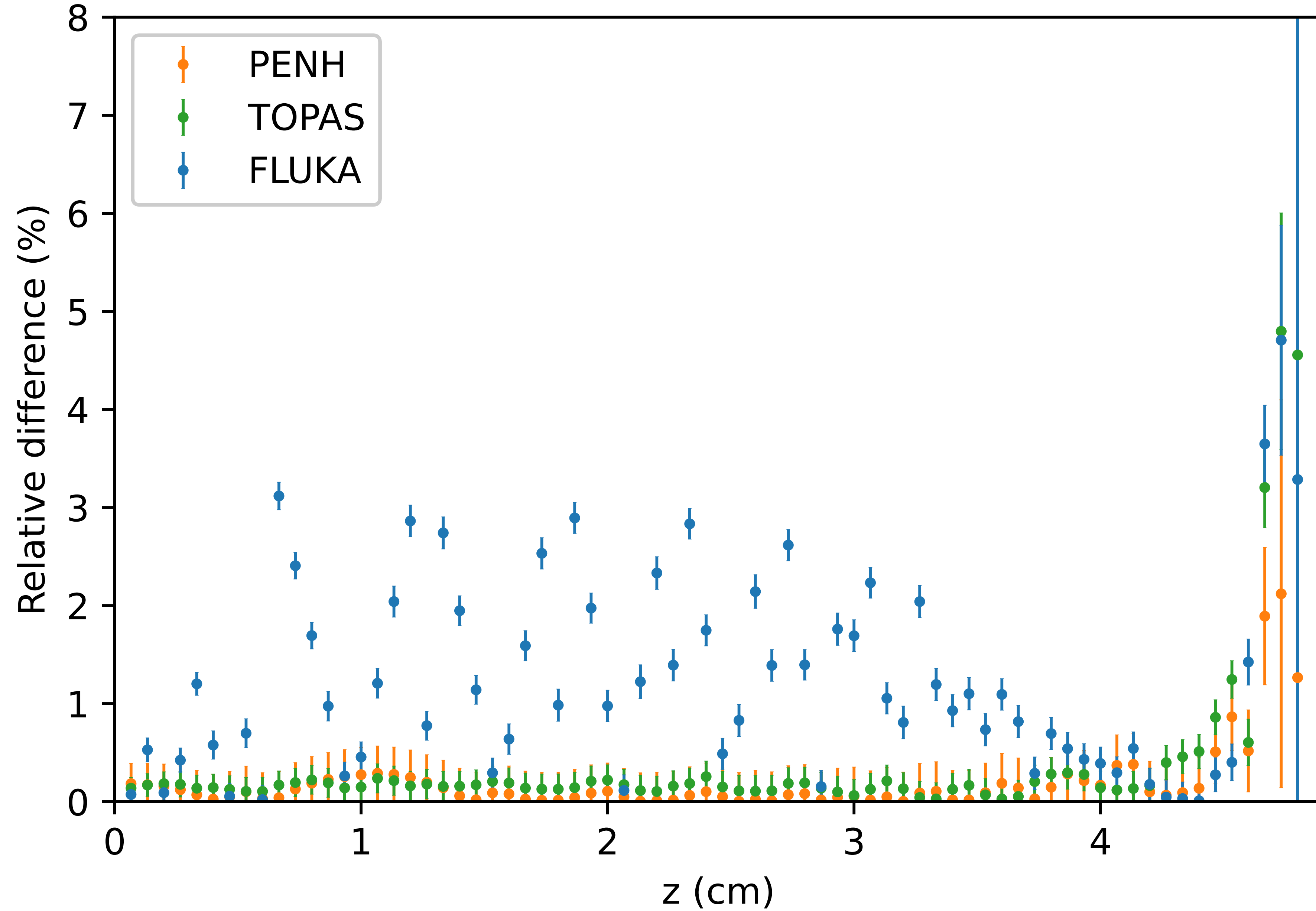
LET Distribution in PENH - 75 MeV



Differences in Ld - 75 MeV - No NR



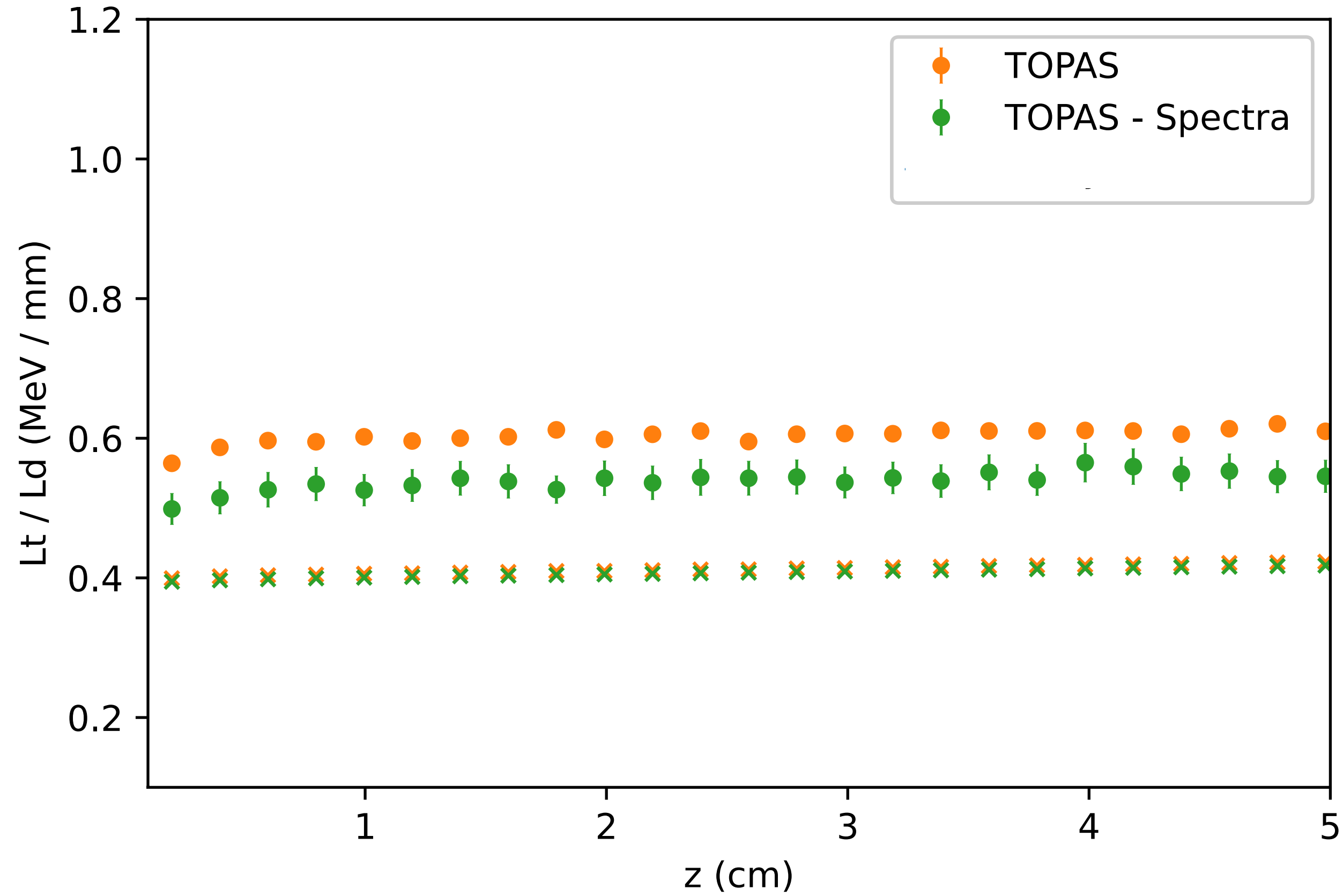
# Differences in Lt - 75 MeV - No NR



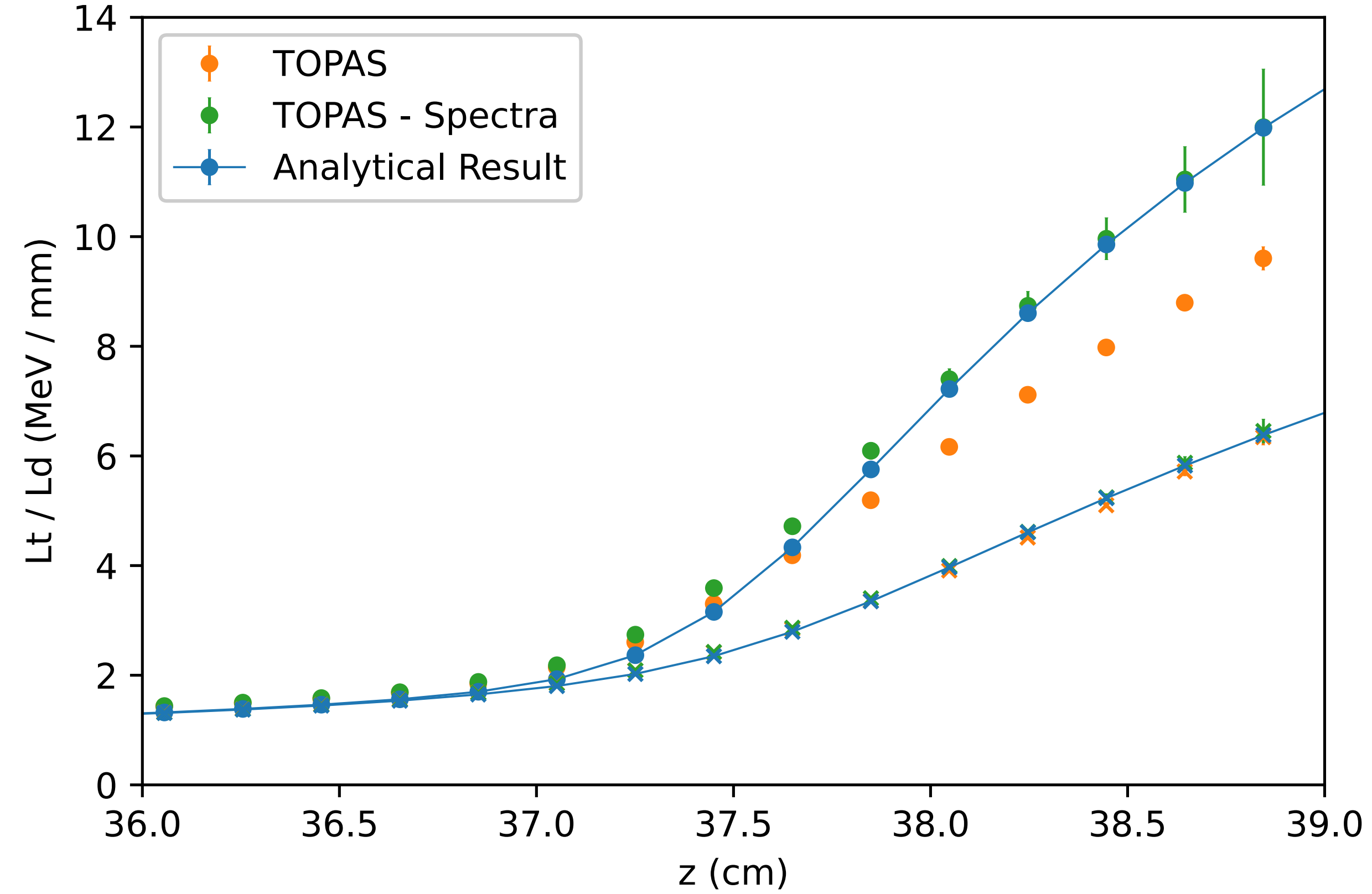
# Full Calculations

# 250 MeV

LET Distribution in TOPAS - 250 MeV

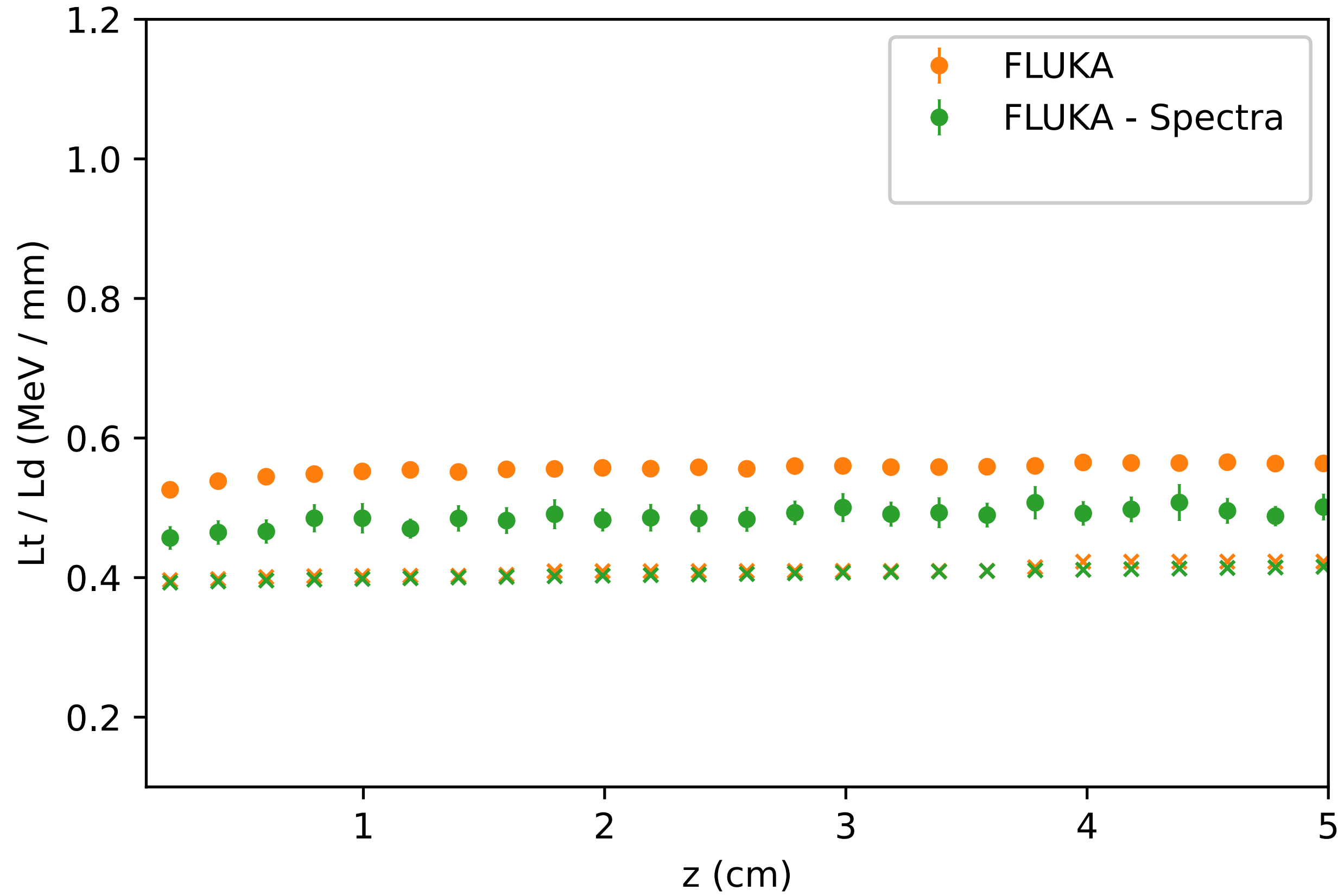


LET Distribution in TOPAS - 250 MeV

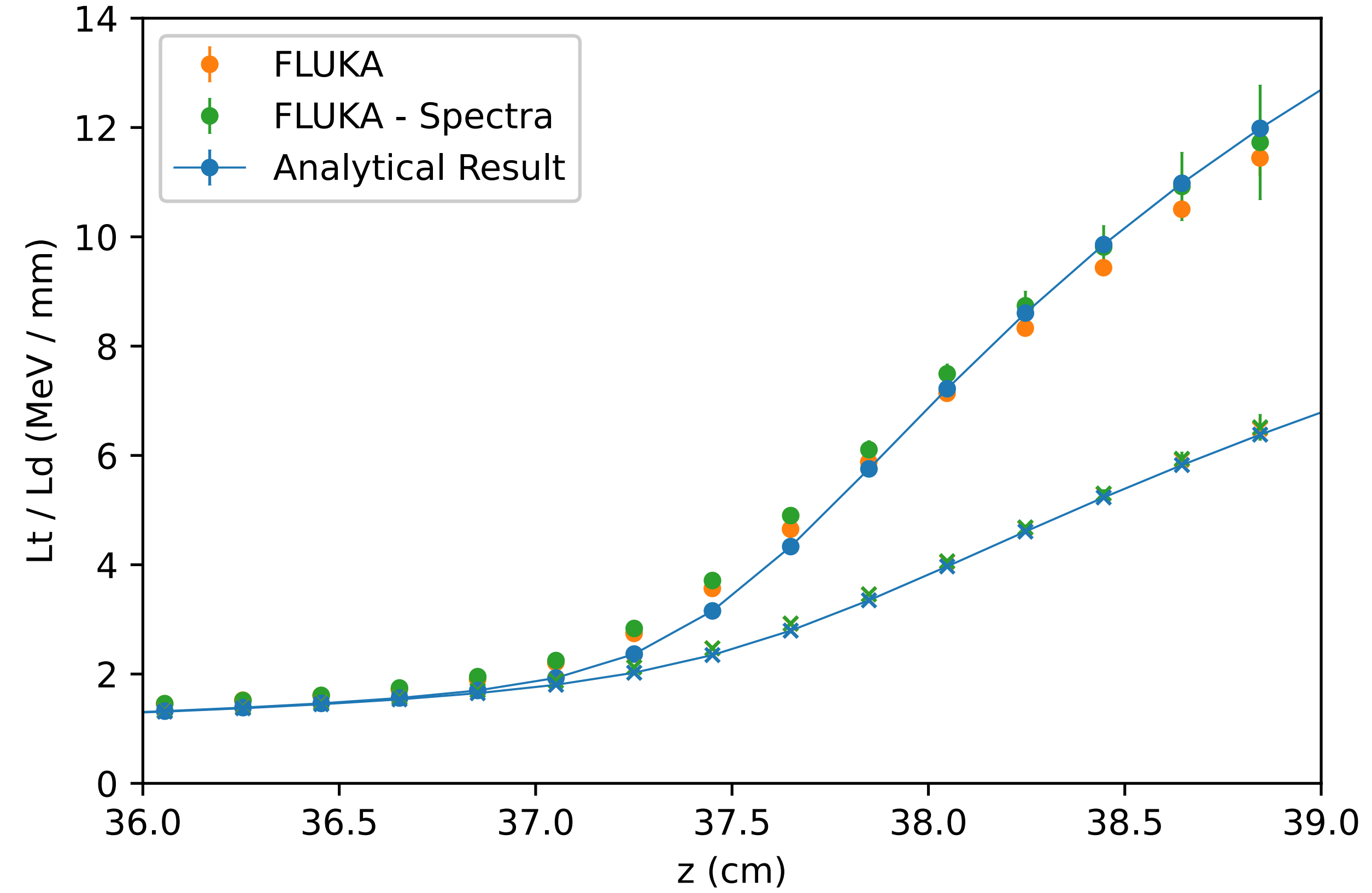


# 250 MeV

LET Distribution in FLUKA - 250 MeV

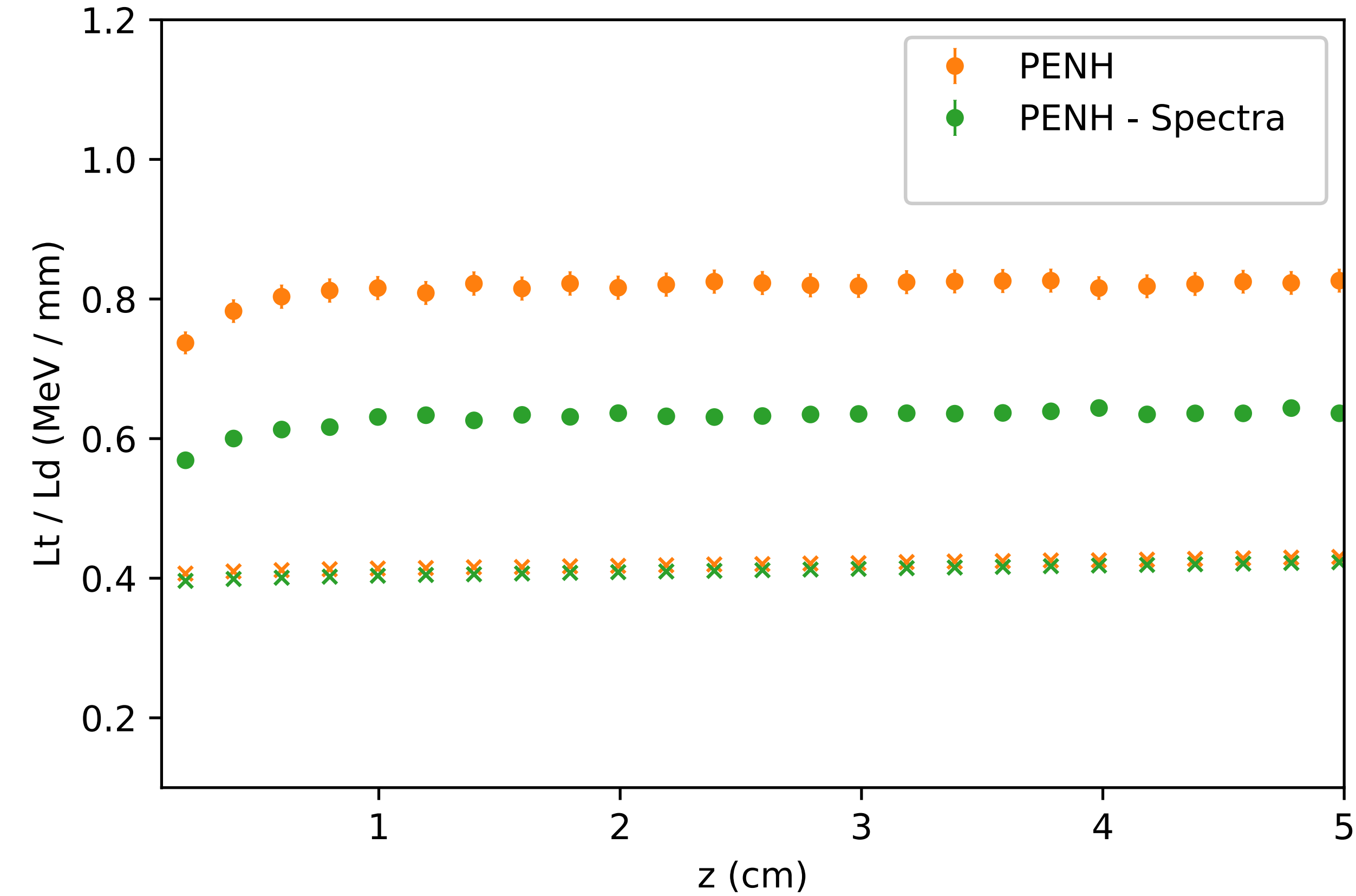


LET Distribution in FLUKA - 250 MeV

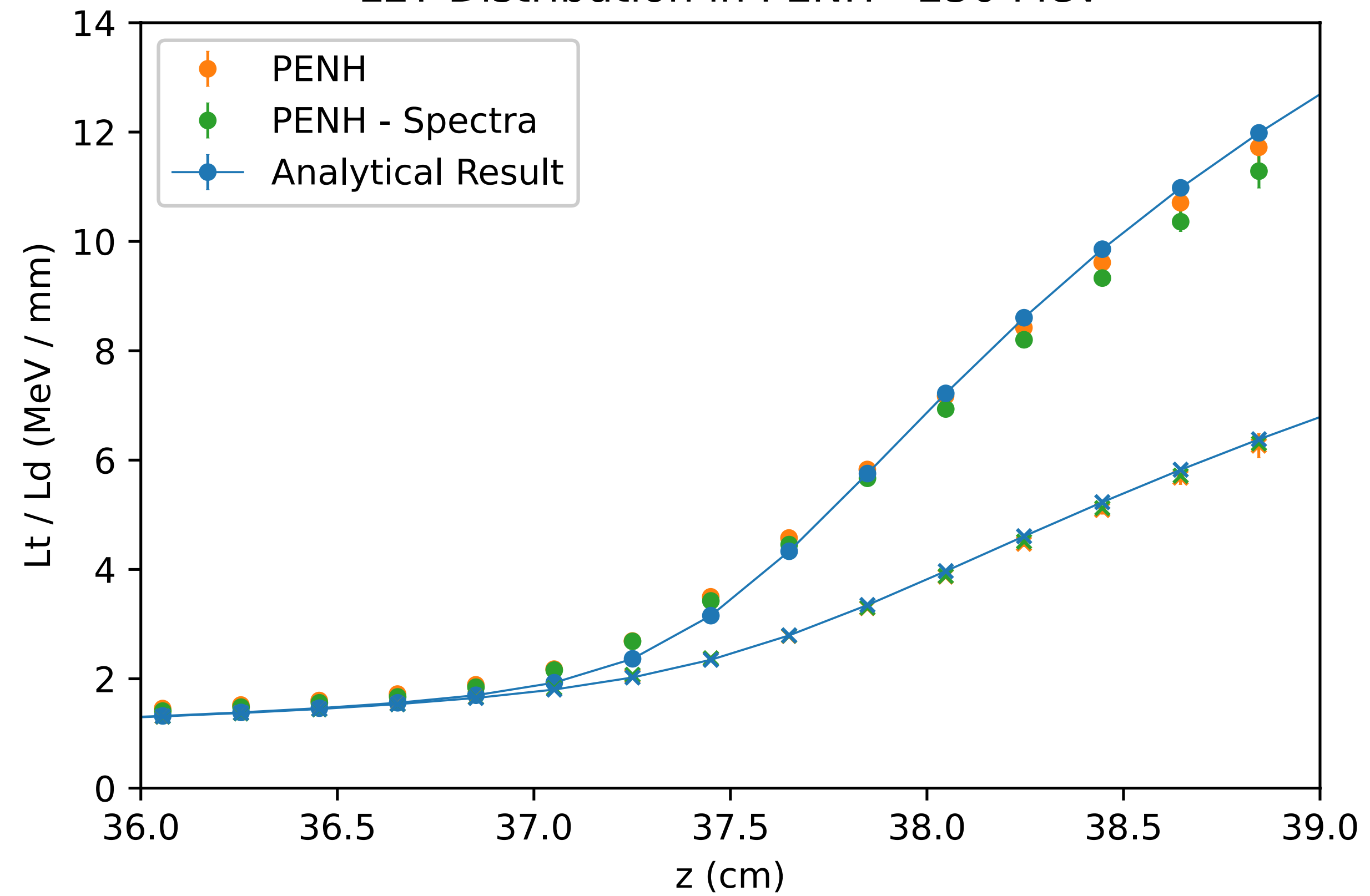


# 250 MeV

LET Distribution in PENH - 250 MeV

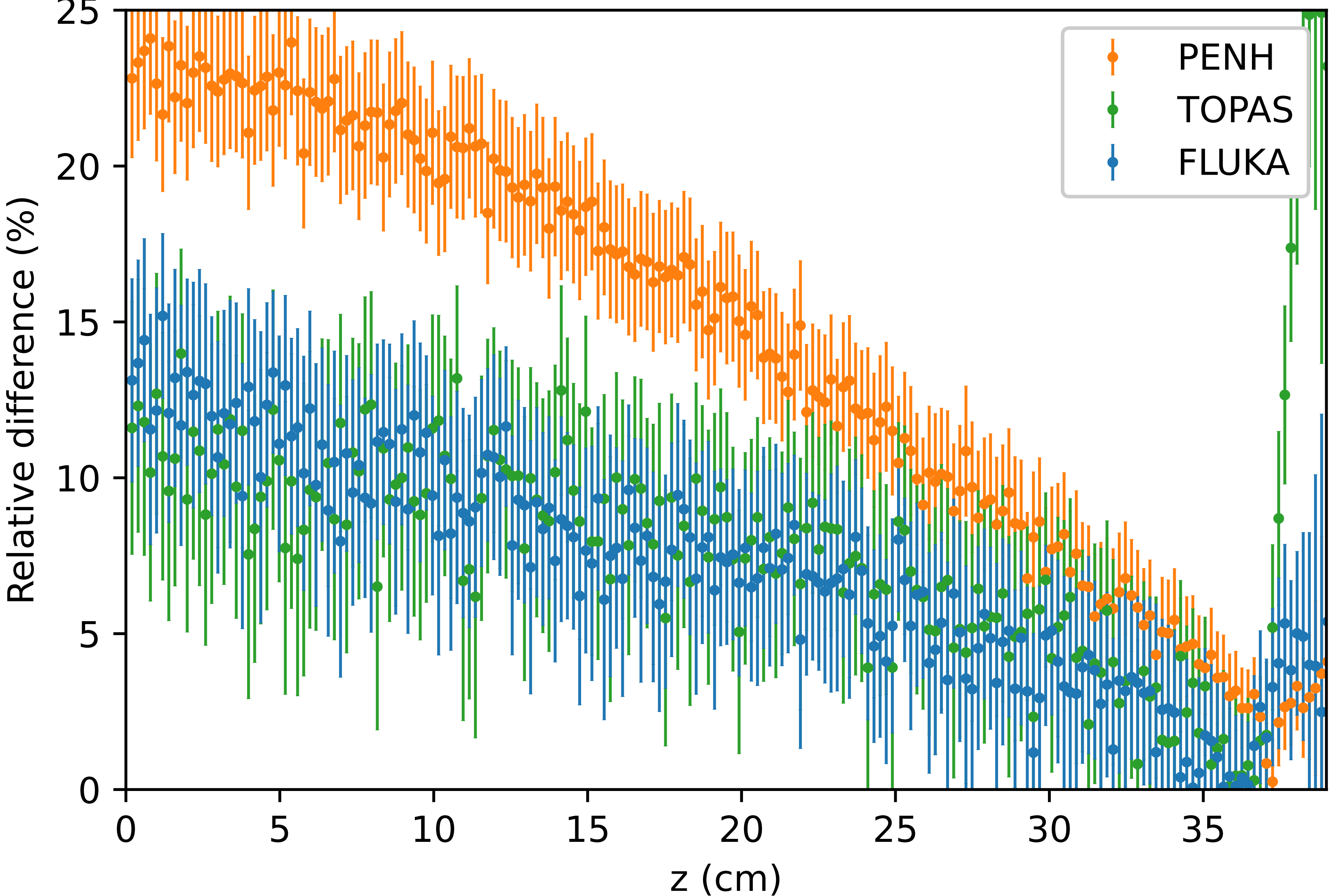


LET Distribution in PENH - 250 MeV

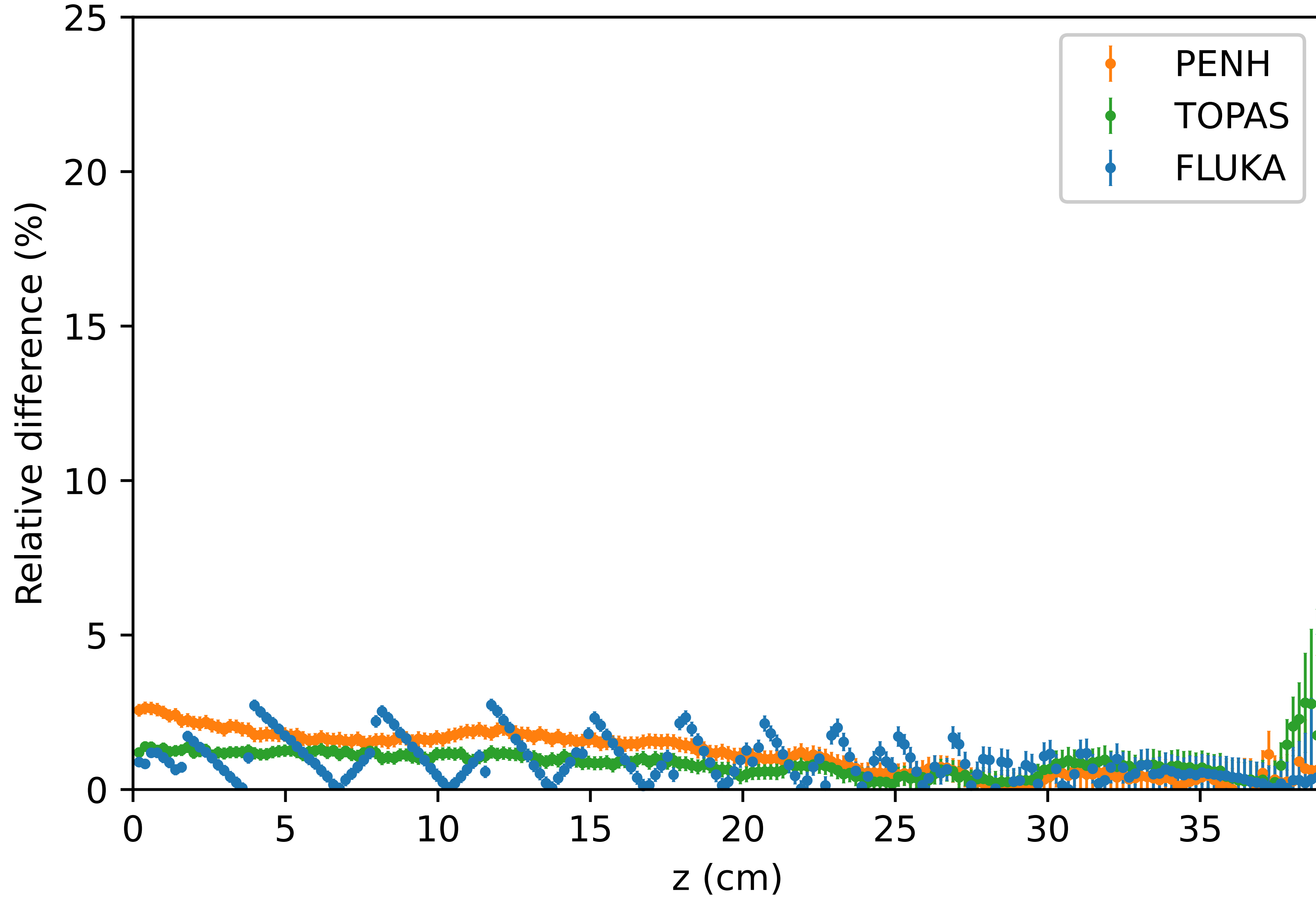




# Differences in Ld - 250 MeV



Differences in Lt - 250 MeV



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# Upshot

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Difference between implementations is lower for **Lt**.

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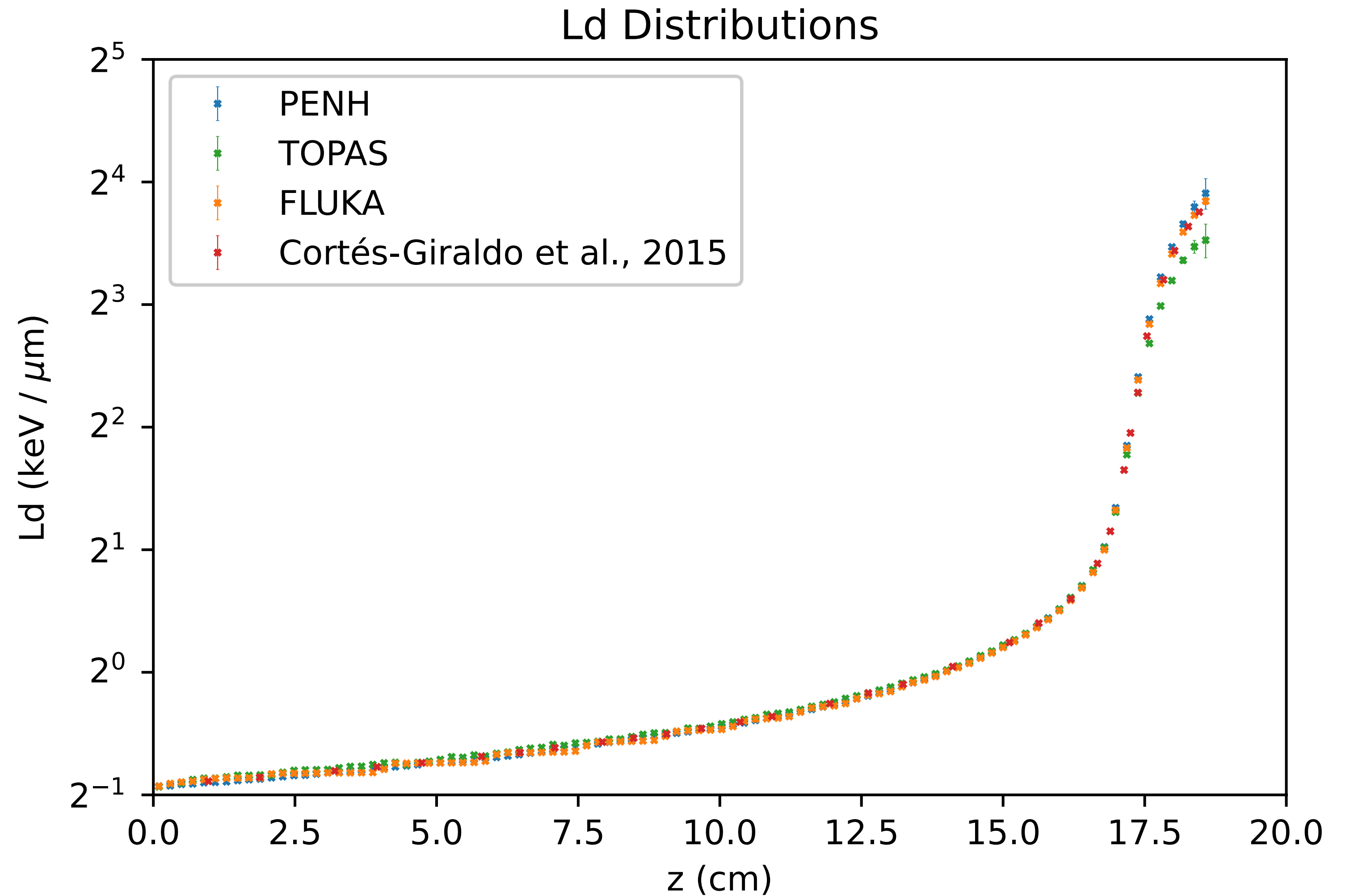
# Replication of Previous Studies

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- ❖ Granville et al., 2015.
- ❖ **Cortés-Giraldo et al., 2015.**
- ❖ Grassberger et al., 2011.
- ❖ Wilkens et al., 2003.

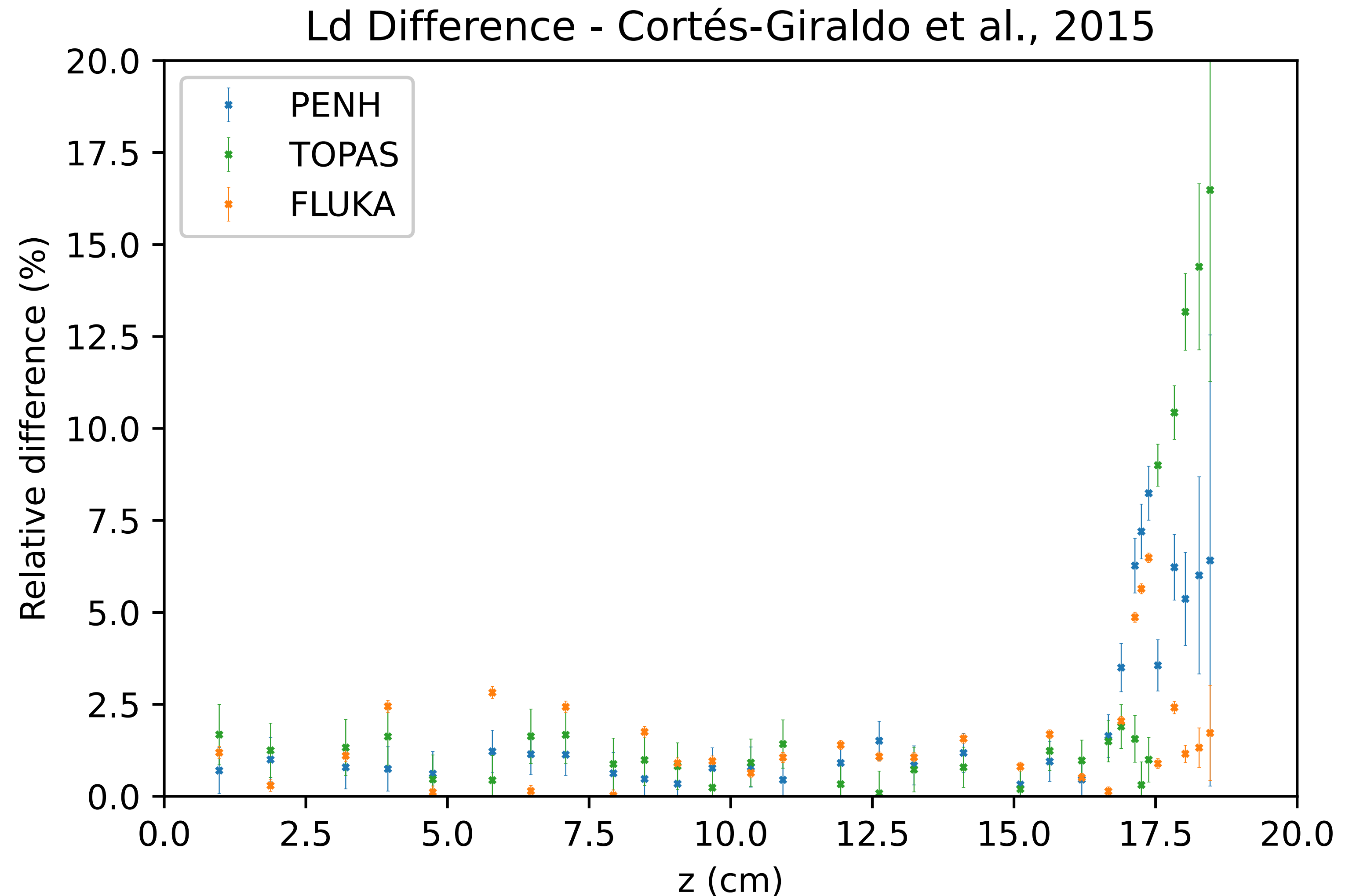
# Cortés-Giraldo et al., 2015 - Figure 5 (bottom)

- ❖ Gaussian beam in energy and spatial distribution.  
( $\bar{E} = 160$  MeV;  $\sigma_E = 1.04$  MeV)
- ❖ Only electronic contribution to dose considered.



# Cortés-Giraldo et al., 2015 - Figure 5 (bottom)

- ❖ Gaussian beam in energy and spatial distribution.
- ❖ Only electronic contribution to dose considered.



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# Summary

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- ❖ Implemented a new format of LET calculation in PENH.
- ❖ Lt results are more stable.
- ❖ All codes' implementations reproduce previous studies' behaviour.

# Extra Slides



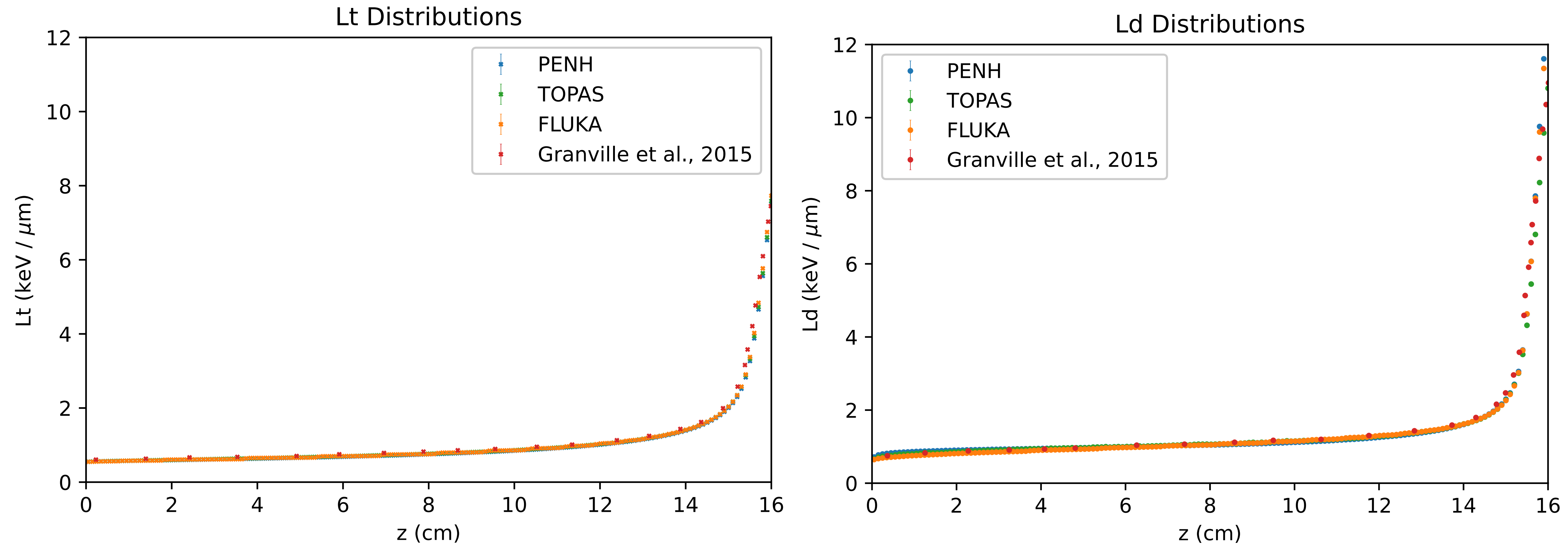
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# References

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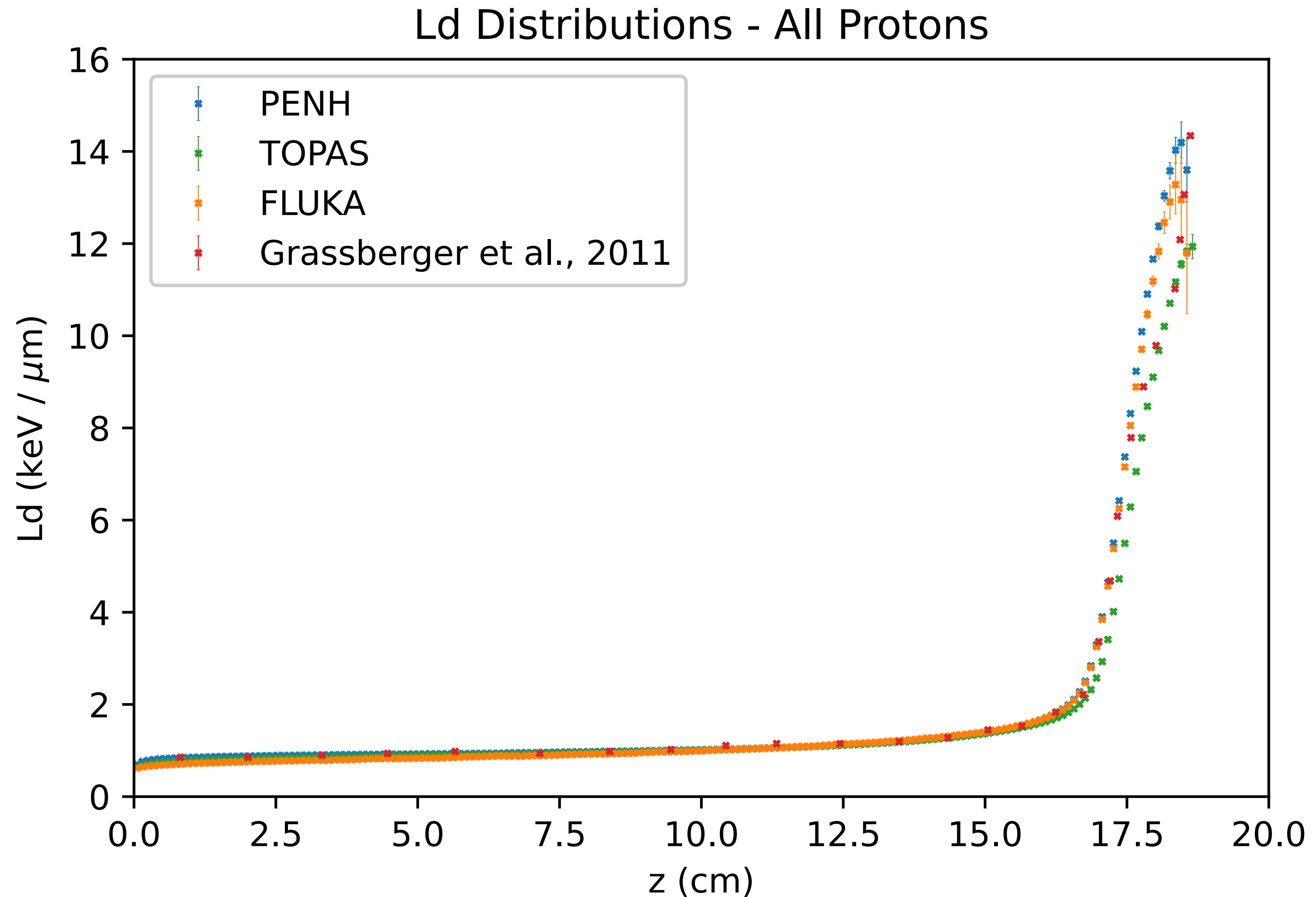
- ❖ [1] Paganetti, "Relative biological effectiveness (RBE) values for proton beam therapy. Variations as a function of biological endpoint, dose, and linear energy transfer". *Phys Med Biol.* 2014 Nov 21;59(22):R419-72.
- ❖ [2] Kalholm, F., Grzanka, L., Traneus, E., & Bassler, N. "A systematic review on the usage of averaged LET in radiation biology for particle therapy". In *Radiotherapy and Oncology* (Vol. 161, pp. 211–221). Elsevier BV, (2021).
- ❖ [3] Wilkens and Oelfke, "Analytical linear energy transfer calculations for proton therapy". *Med Phys.* 2003 May;30(5):806-15.
- ❖ [4] D. A. Granville and G. O. Sawakuchi, "Comparison of linear energy transfer scoring techniques in Monte Carlo simulations of proton beams" 2015 *Phys. Med. Biol.* 60 N283.
- ❖ [5] M. A. Cortés-Giraldo and A. Carabe, "A critical study of different Monte Carlo scoring methods of dose average linear-energy-transfer maps calculated in voxelized geometries irradiated with clinical proton beams" 2015 *Phys. Med. Biol.* 60 2645
- ❖ [6] F. Salvat, J.M. Fernández-Varea and J. Sempau, "Penelope 2018: a code system for Monte Carlo simulation of electron and photon transport", Nuclear Energy Agency, Barcelona 2018; F. Salvat and J. M. Quesada, *Nucl. Ins. Meth. Phys. Res. B* 475 (2020) 49.
- ❖ [7] G. Batistone, "The FLUKA code", *Annals of Nuclear Energy* 82 (2015) 10.
- ❖ [8] J. Perl et al, "TOPAS: an innovative proton Monte Carlo platform for research and clinical applications", *Med. Phys.* 39 (2012) 6818.
- ❖ [9] Guan, F., et al.. (2015). "Analysis of the track- and dose-averaged LET and LET spectra in proton therapy using the geant4 Monte Carlo code". In *Medical Physics* (Vol. 42, Issue 11, pp. 6234–6247).

# Granville et al., 2015 - Figure 2 a)



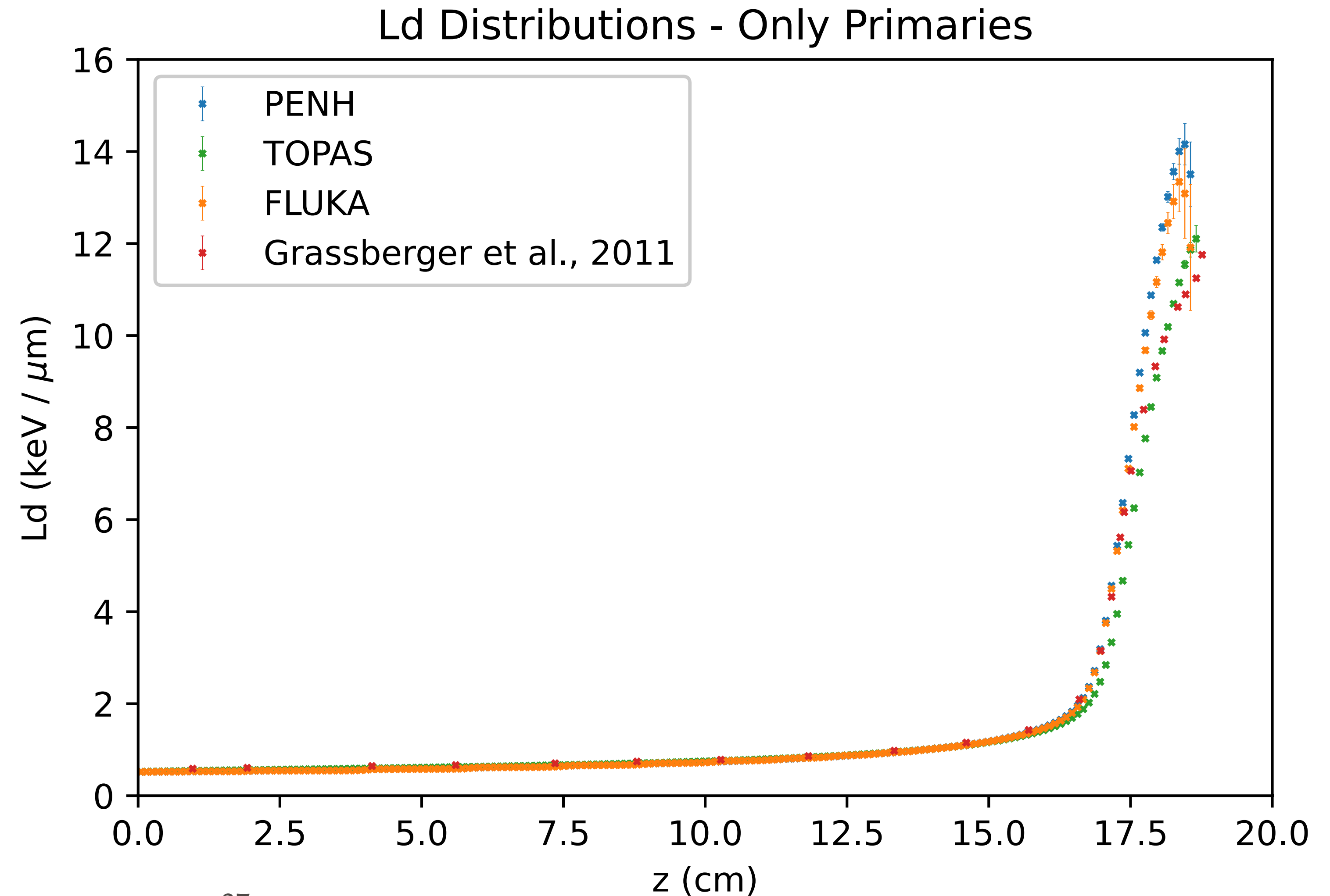
# Grassberger et al., 2011 - Figure 2 (All Protons)

- ❖ Gaussian beam in energy, spatial distribution and direction.
- ❖ Differences observed at the peak.



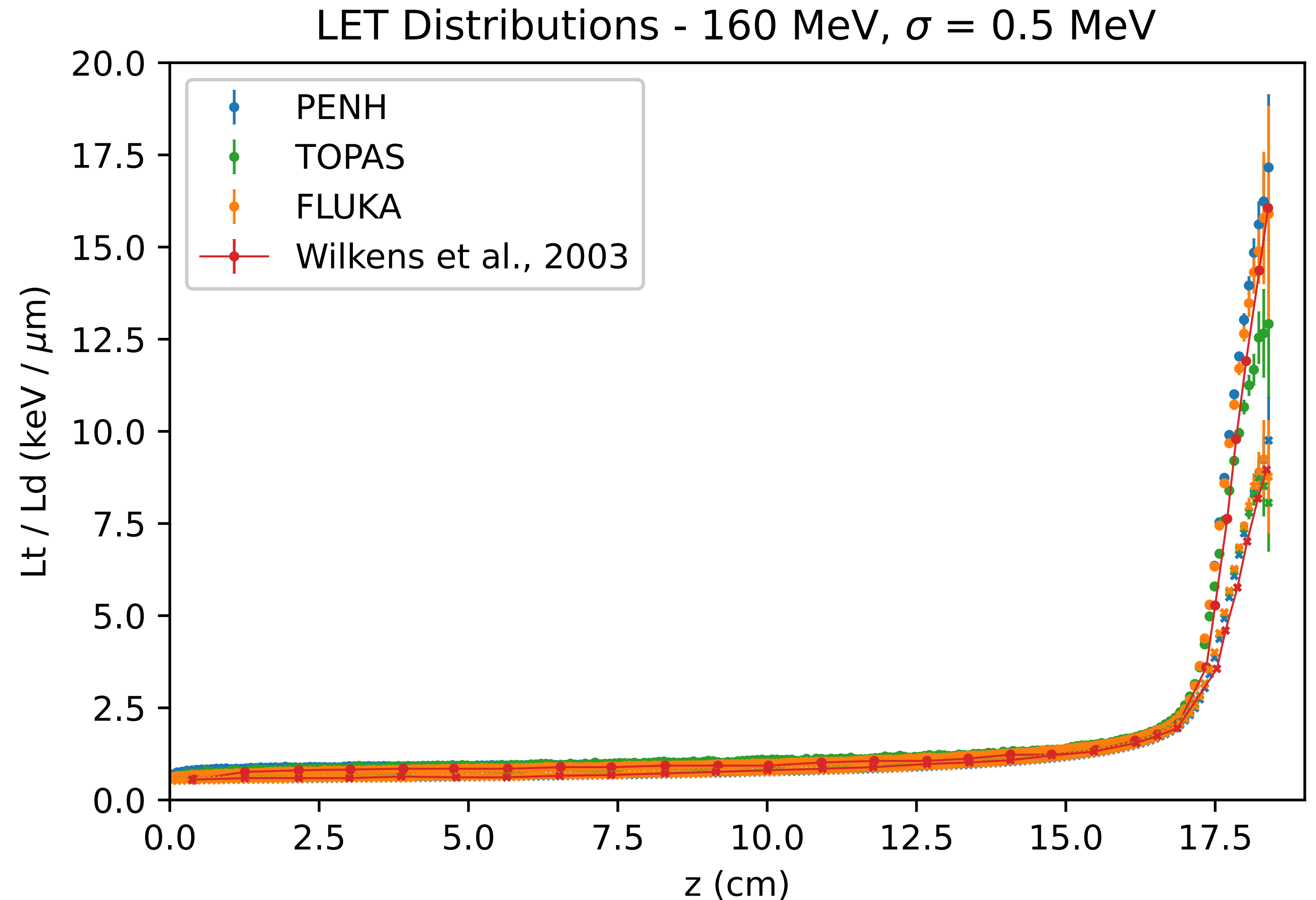
# Grassberger et al., 2011 - Figure 2 (Primaries Only)

- ❖ Differences observed at the peak.



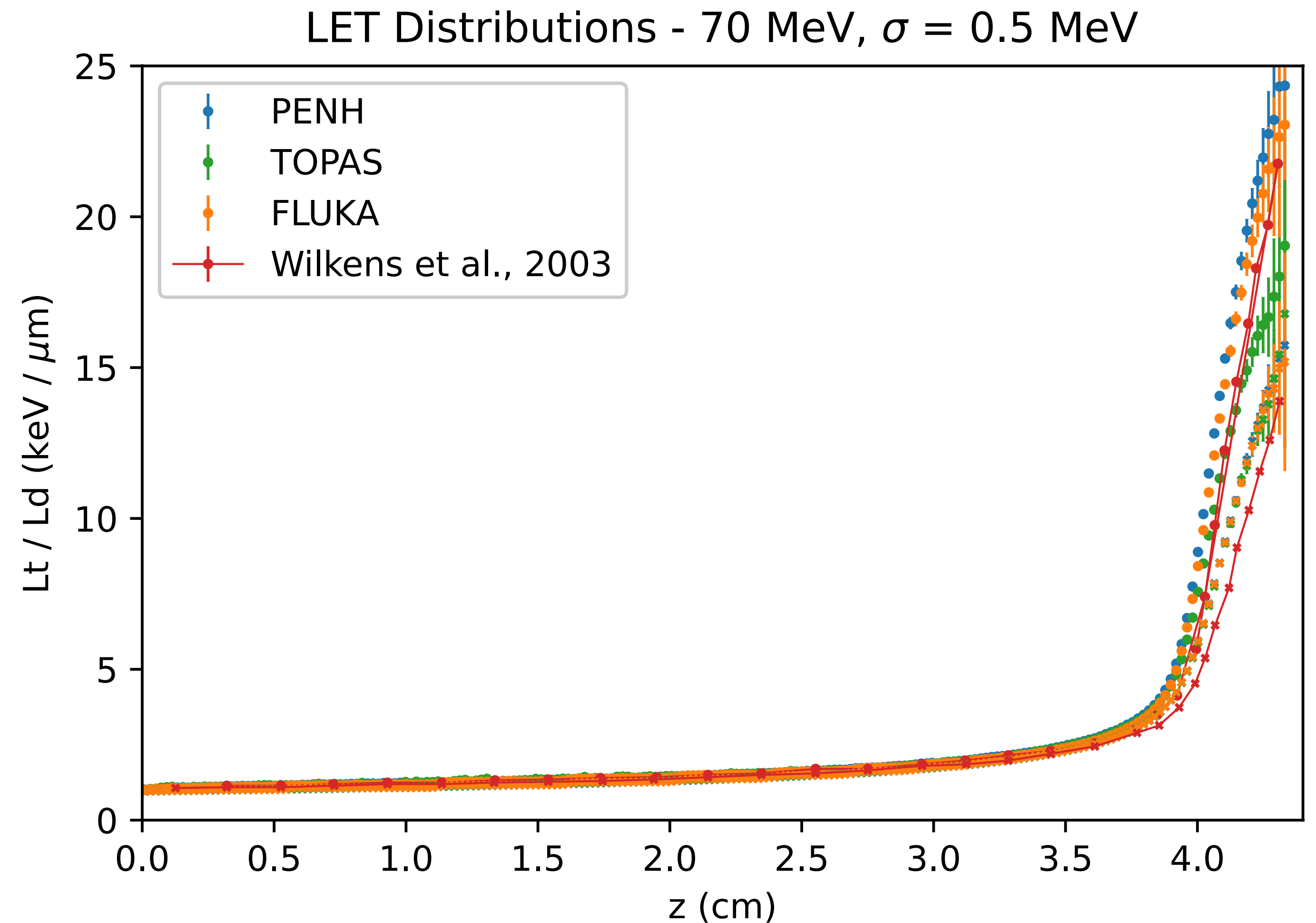
# Wilkins et al., 2003 - Figure 2

- ❖ Wide beam, gaussian energy.
- ❖ Shift of data needed.



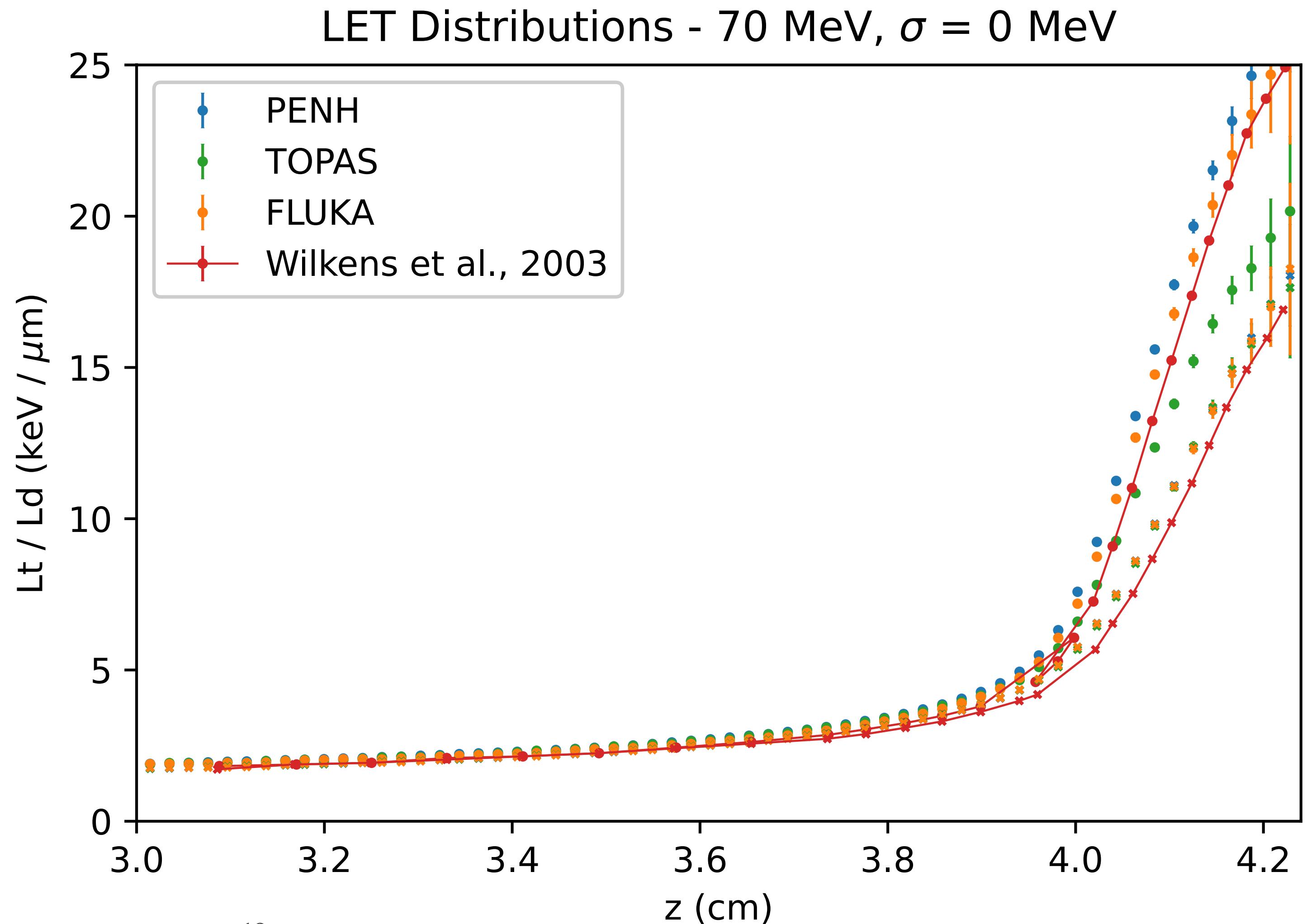
# Wilkins et al., 2003 - Figure 4

- ❖ Wide beam, gaussian energy.
- ❖ Shift of data needed.



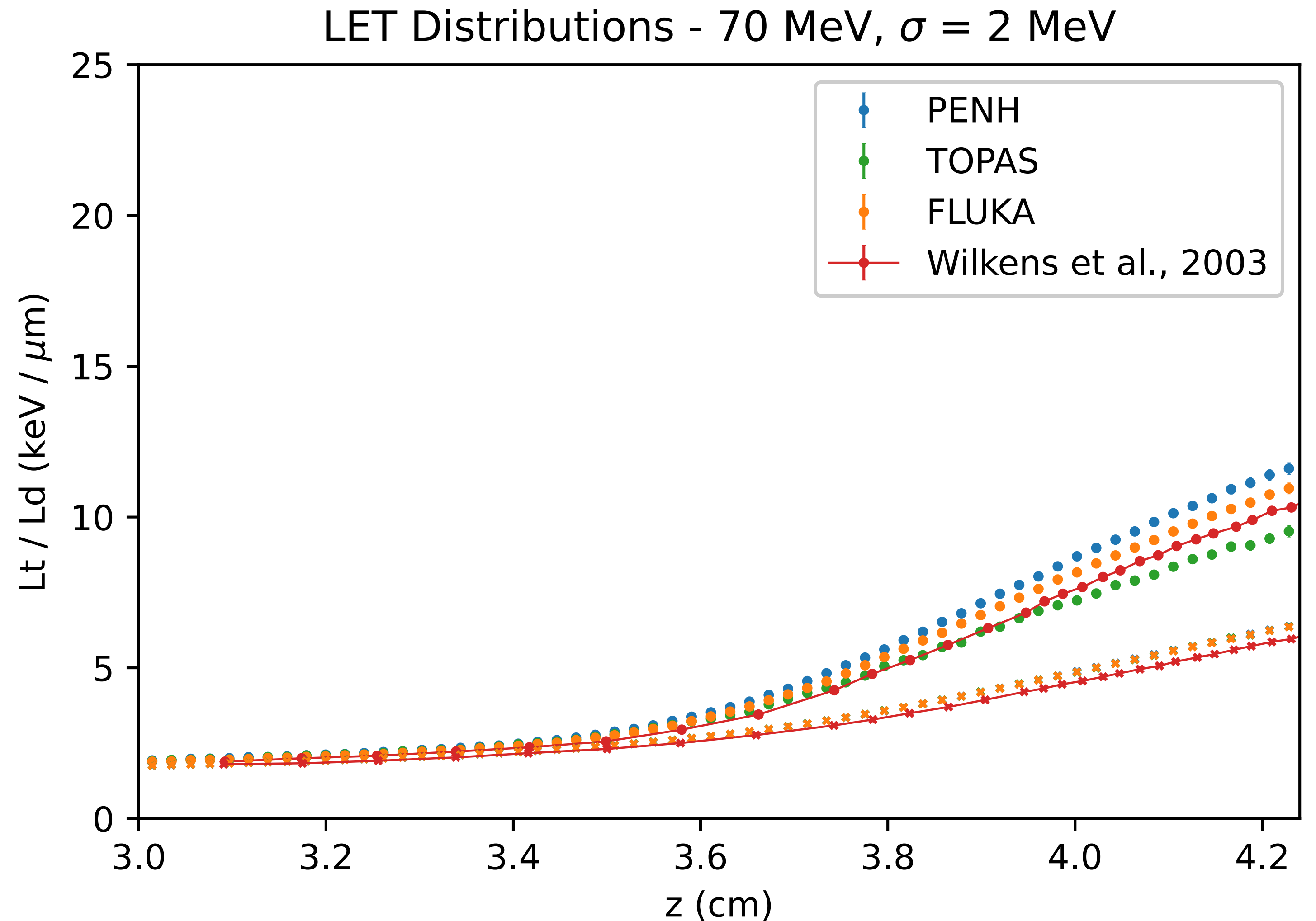
# Wilkins et al., 2003 - Figure 5

- ❖ Wide beam, gaussian energy.
- ❖ Shift of data needed.



# Wilkins et al., 2003 - Figure 5

- ❖ Wide beam, gaussian energy.
- ❖ Shift of data needed.





# Simulation PENH Parameters

Absorption energy for  
electrons and positrons

1e9 eV (Previous studies; Guan et al., 2015)

Absorption energy for  
photons

1e4 eV

WCC, WCR

1e5 eV

C1, C2, C1H, C2H

0.05

Absorption energy for  
neutrons

1e4 eV

C1N, C2N

0

FNABS

0.8

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# Analytical Formula

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$$\diamond LET_d = \frac{\int_0^\infty \phi_r(z) S^2(r) dr}{\int_0^\infty \phi_r(z) S(r) dr}$$

$$\diamond \phi_r(z) = \frac{\Phi_0}{\sqrt{2\pi}\sigma} e^{-(r-(R_0-z))^2/2\sigma^2}$$

$$\diamond S_R(r) = \frac{1}{R\alpha^{1/p}} [(r+R)^{1/p} - r^{1/p}]$$

# Analytical Formula

$$\diamond \text{LET}_d(z) = \frac{\langle S^2(z) \rangle}{\langle S(z) \rangle}$$

$$\diamond \langle S(z) \rangle = \frac{\Phi_0}{\sqrt{2\pi\sigma R\alpha}} \left[ \sigma^{1+1/p} \Gamma\left(1 + \frac{1}{p}\right) \tilde{D}_{1+1/p}(\epsilon, \zeta) - R \left(\frac{1}{2}R\right)^{1/p} e^{-(\epsilon+\zeta)^2/8} \right]$$

$$\diamond \langle S^2(z) \rangle = \frac{\Phi_0}{\sqrt{2\pi\sigma R\alpha^{2/p} p(2-p)}} \left[ \sigma^{2/p} \Gamma\left(\frac{2}{p}\right) \tilde{D}_{2/p}(\epsilon, \zeta) - 2 \left(\frac{1}{2}R\right)^{2/p} e^{-(\epsilon+\zeta)^2/8} \right]$$

$$\diamond \tilde{D}_v(\epsilon, \zeta) = e^{-\epsilon^2/4} D_{-v}(\epsilon) - e^{-\zeta^2/4} D_{-v}(\zeta)$$

$$\diamond \zeta = (z - R_0)/\sigma \quad \epsilon = (z - R_0 - R)/\sigma \quad \rightarrow \text{Problem for "small" } z \text{ because } D_v \text{ gives huge values.}$$

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# LET Averages

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- ❖ Two most common averages definitions (ICRU, 1970):

$$\bar{L}_t = \int L t(L) dL$$

$$\bar{L}_d = \int L d(L) dL$$

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# Ingredients

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$$\bar{L}_t(z) = \frac{\sum_{E_i} \phi_{E_i}(z) S(E_i) \Delta E}{\sum_{E_i} \phi_{E_i}(z) \Delta E}$$

❖  $\phi_{E_i}$  : proton energy spectrum.

❖  $S(E_i)$  : electronic stopping power.

❖ Implicit assumption:

$$\bar{L}_d(z) = \frac{\sum_{E_i} \phi_{E_i}(z) S^2(E_i) \Delta E}{\sum_{E_i} \phi_{E_i}(z) S(E_i) \Delta E}$$

$$D = \phi_{E_i} \cdot S(E_i)$$

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# Ingredients

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$$\bar{L}_t = \frac{\sum_i^N dx_i S_i(E)}{\sum_i^N dx_i}$$

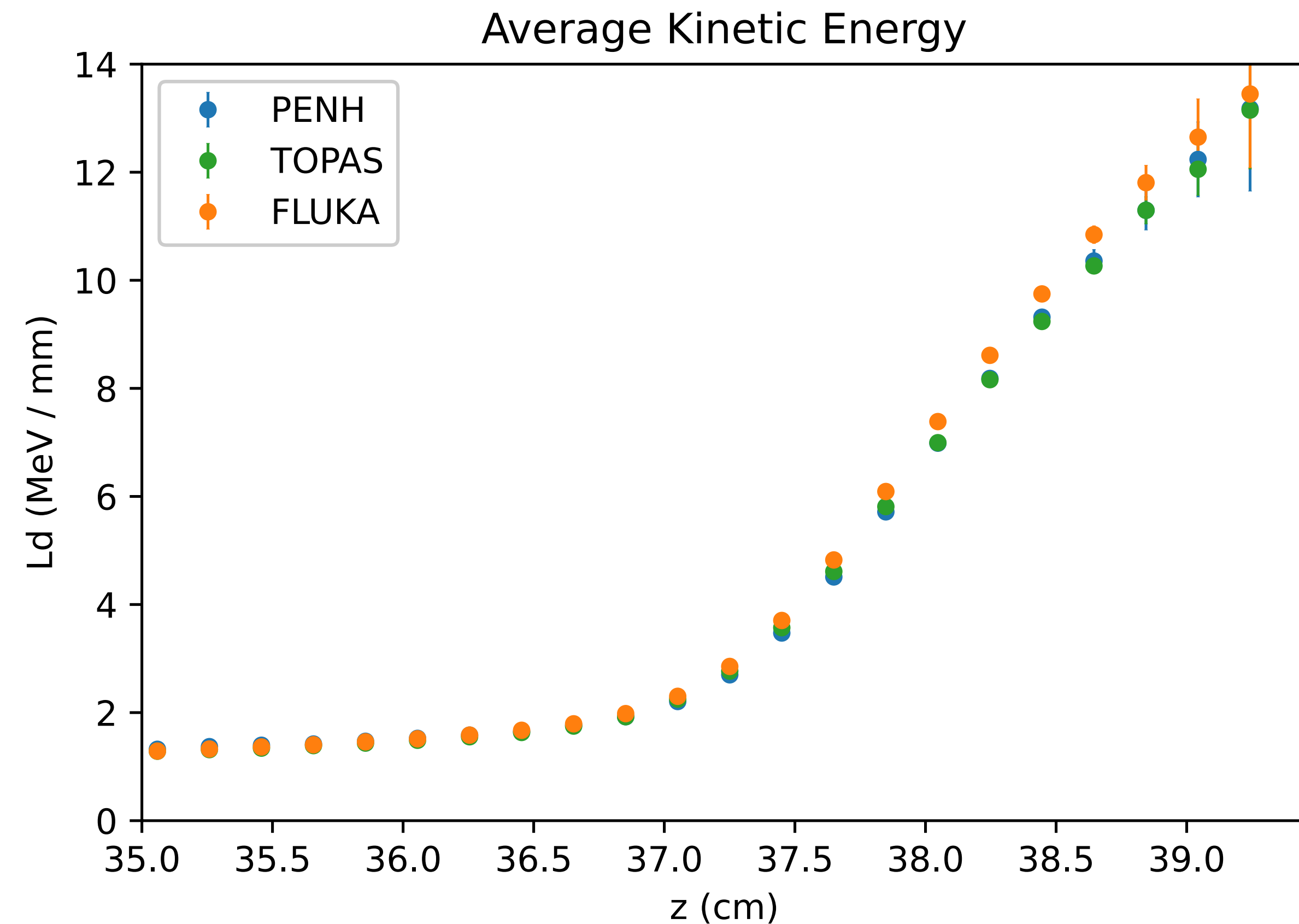
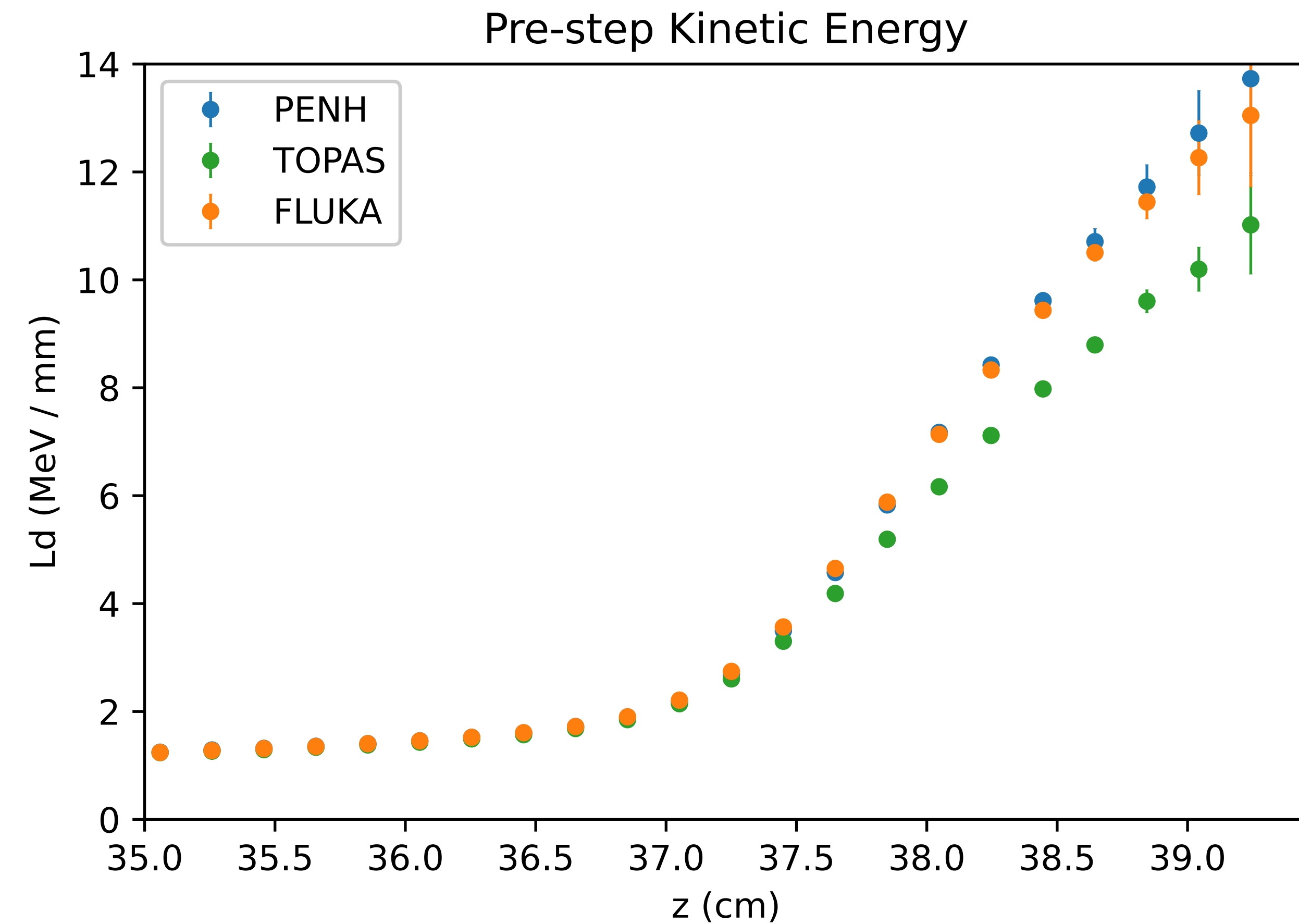
❖  $dx_i$  : length of simulation step.

❖  $e_i$  : energy deposited in step.

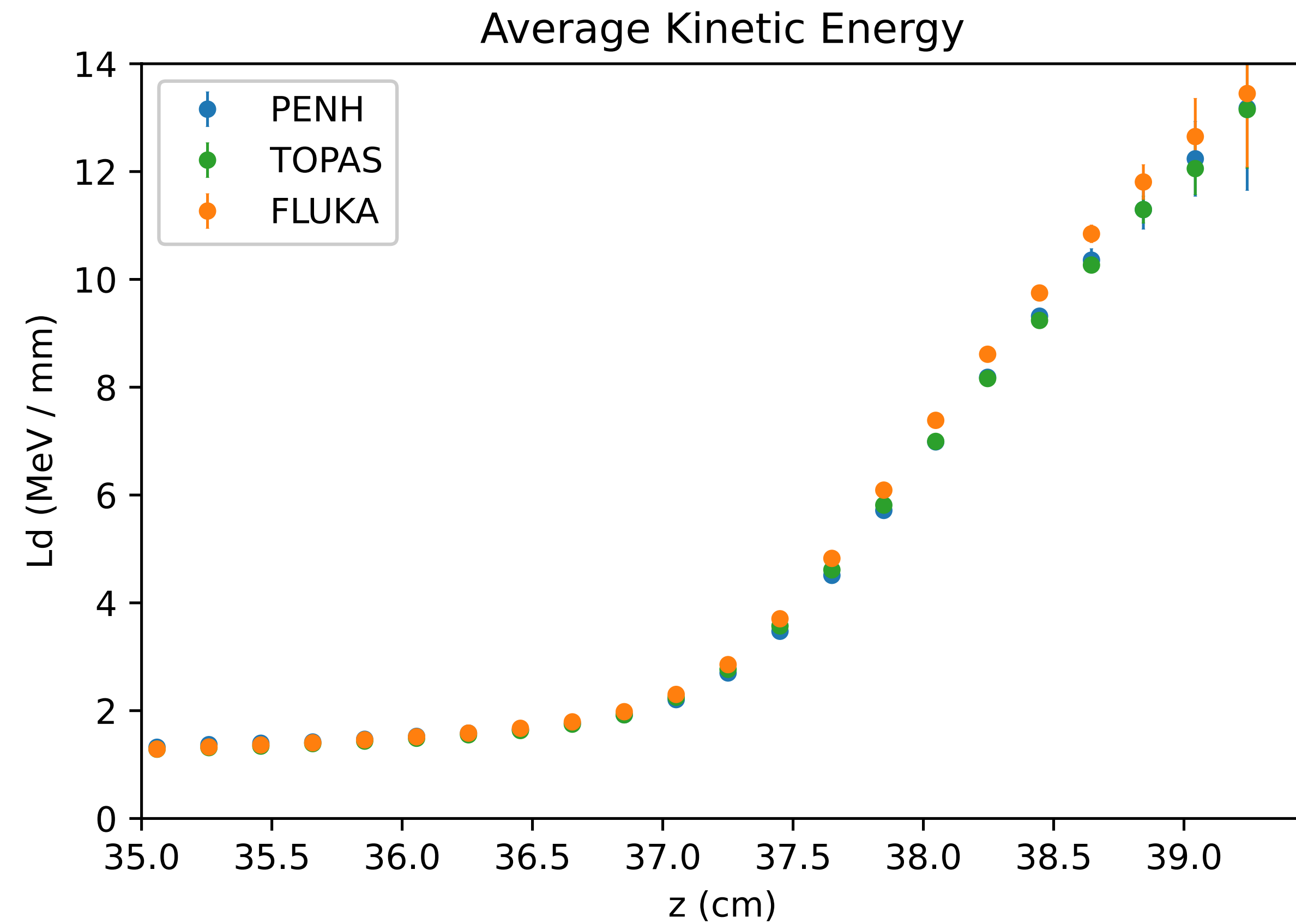
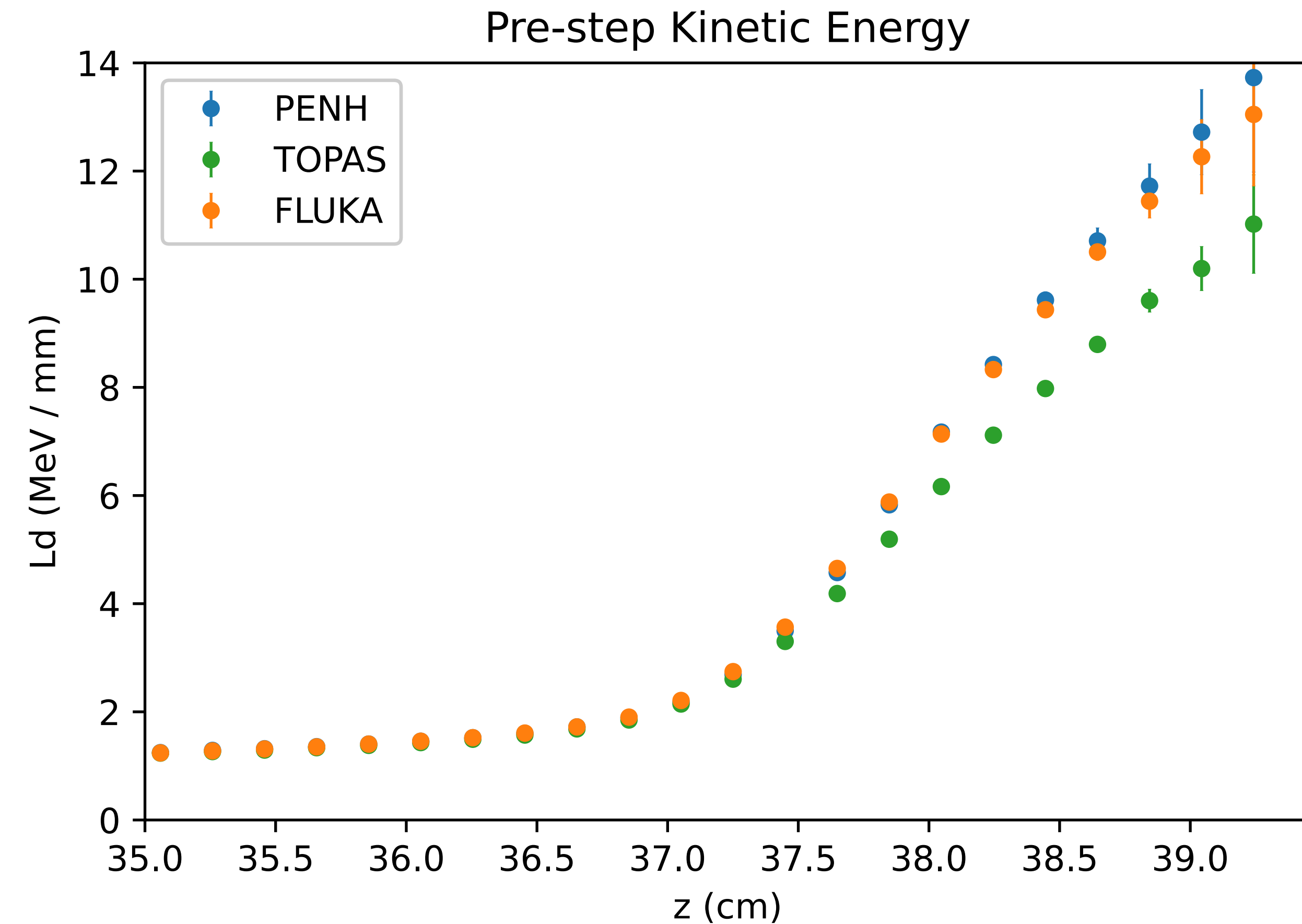
❖  $S_i(E)$  : stopping power of particle depositing energy.

$$\bar{L}_d = \frac{\sum_i^N e_i S_i(E)}{\sum_i^N e_i}$$

# Correcting TOPAS? (Cortés-Giraldo et al., 2015)



# Correcting TOPAS? (Cortés-Giraldo et al., 2015)



❖ Using a different stopping power  $S_i(E)$  seems to give more stable results.



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# Definition of Dose (ICRU 85)

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❖ Absorbed dose:  $D = \frac{d\bar{\epsilon}}{dm}$

❖  $\epsilon = \epsilon_{in} - \epsilon_{out} + Q$

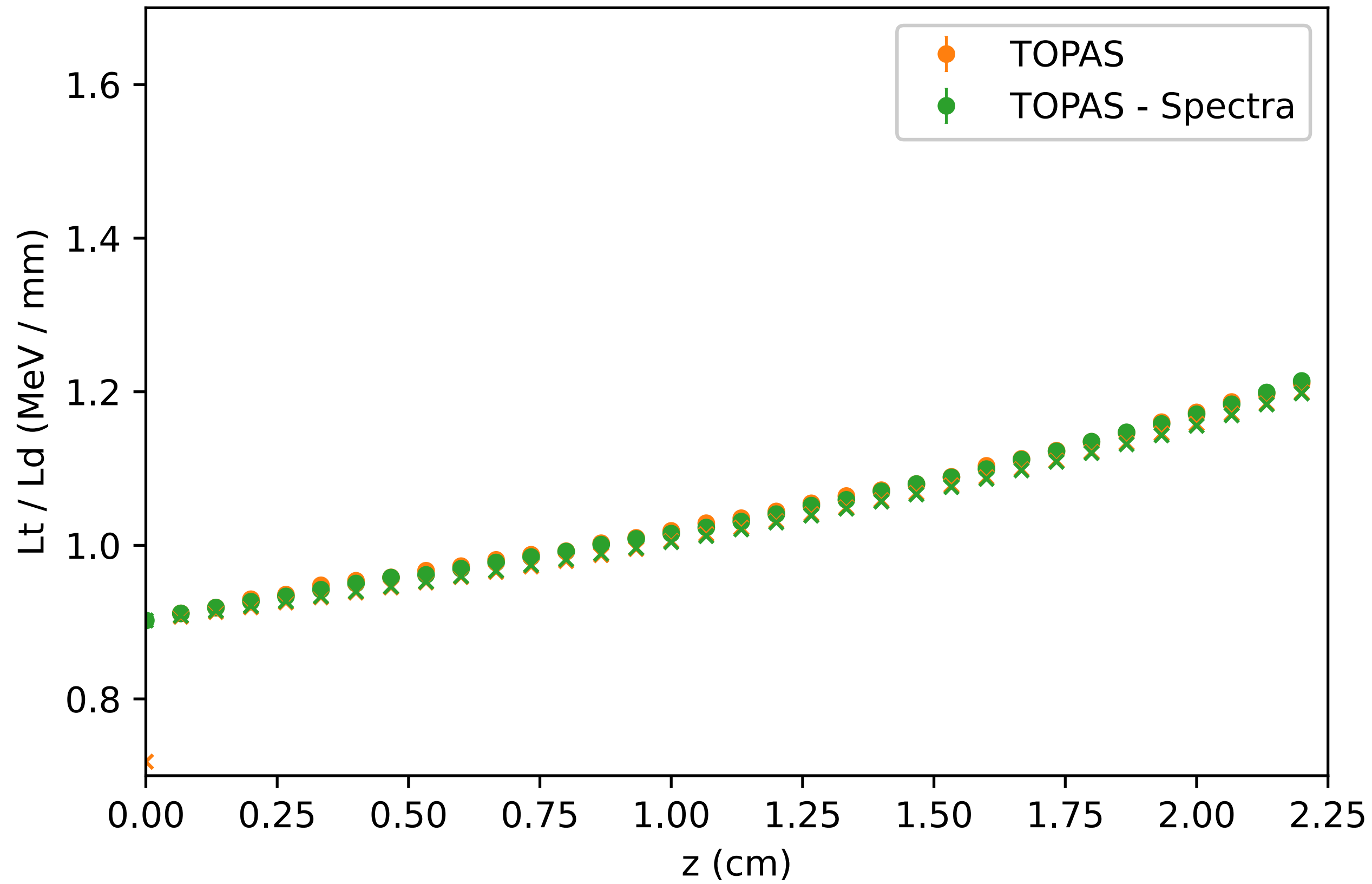
❖ Grussell, 2014: “A desirable property of the absorbed dose is that it should depend only on the set of initial ionizing particles released during the irradiation, and the geometry.”

# Consistency Results

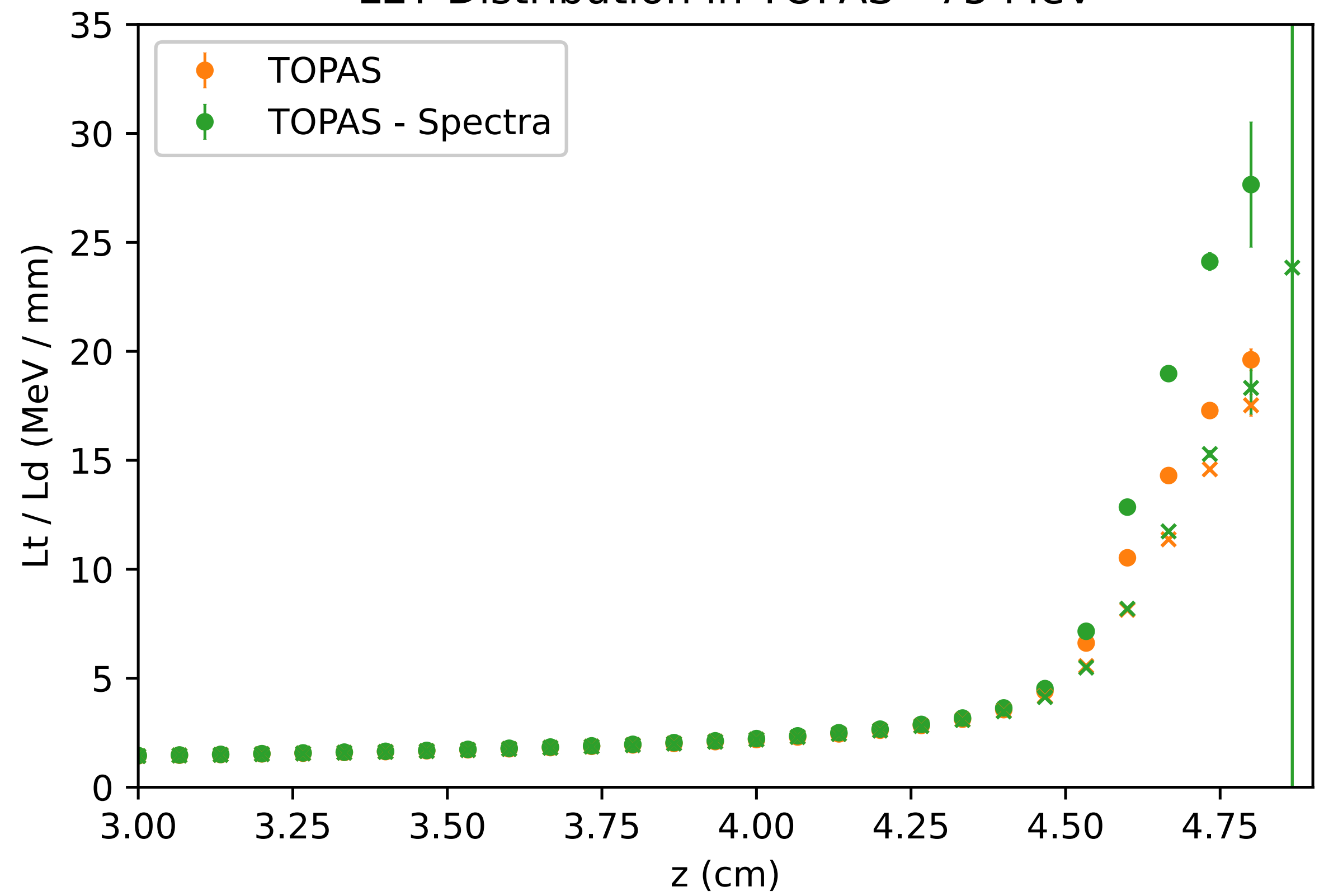
No Nuclear Reactions

# 75 MeV

LET Distribution in TOPAS - 75 MeV

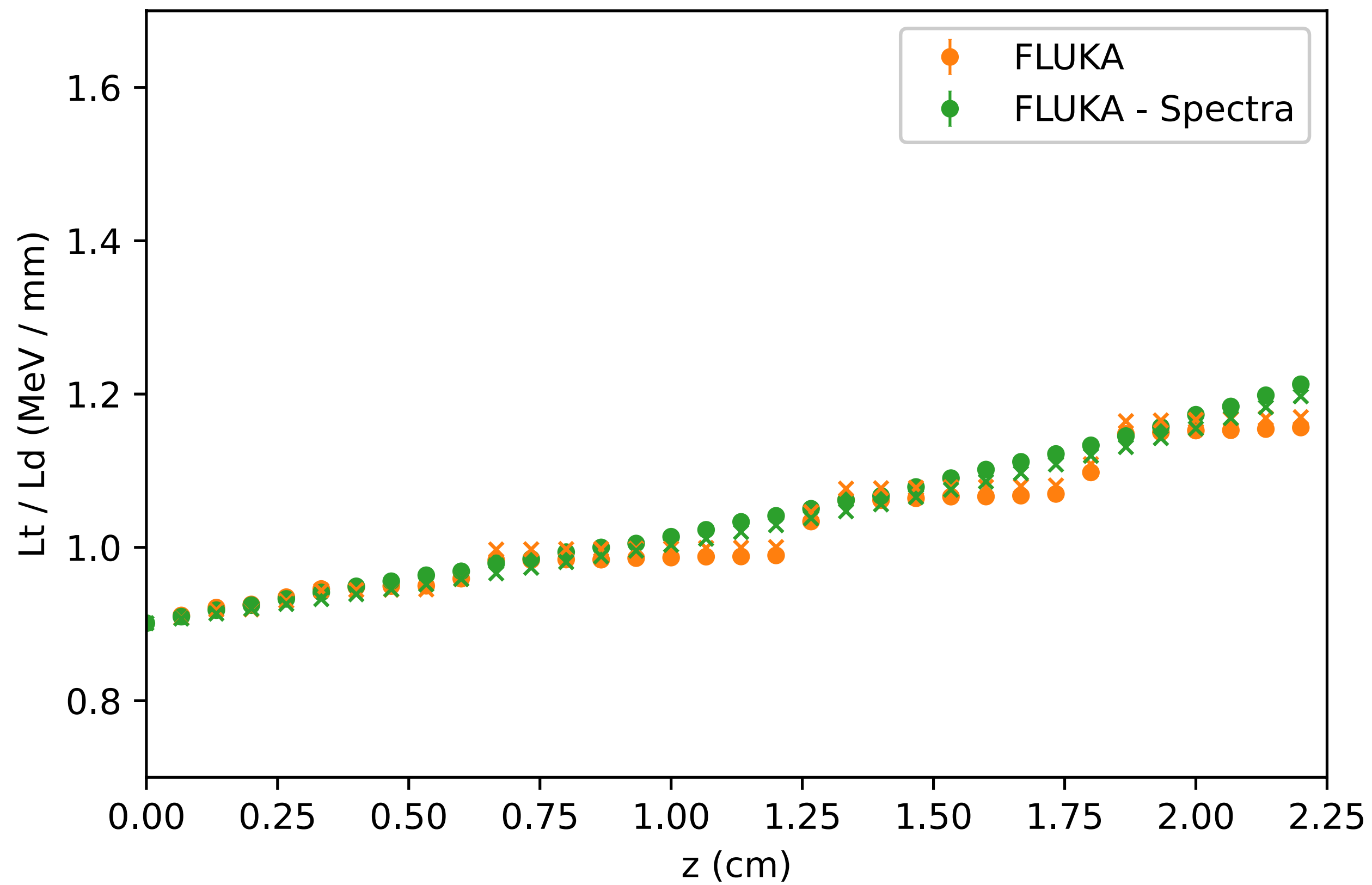


LET Distribution in TOPAS - 75 MeV

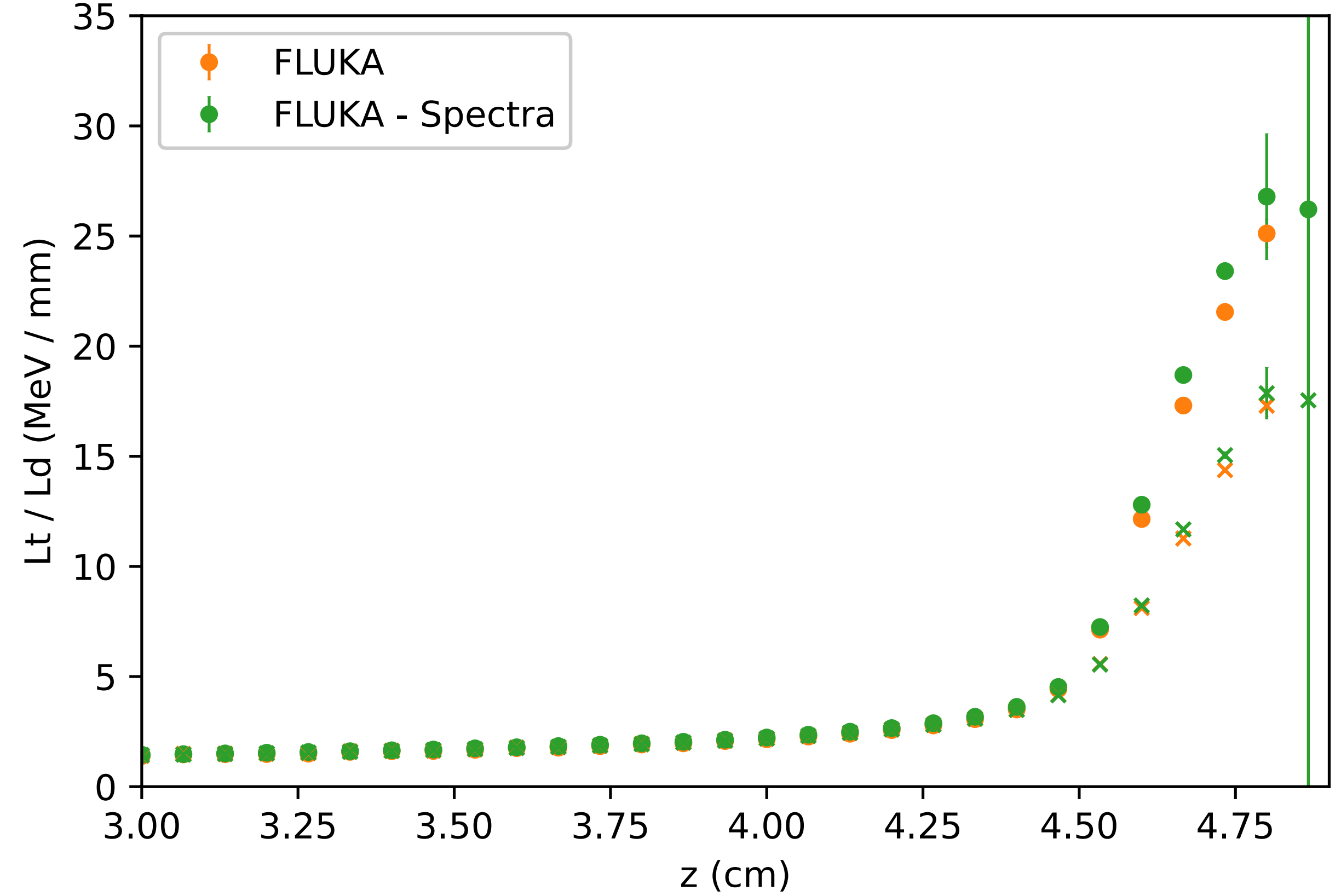


# 75 MeV

LET Distribution in FLUKA - 75 MeV

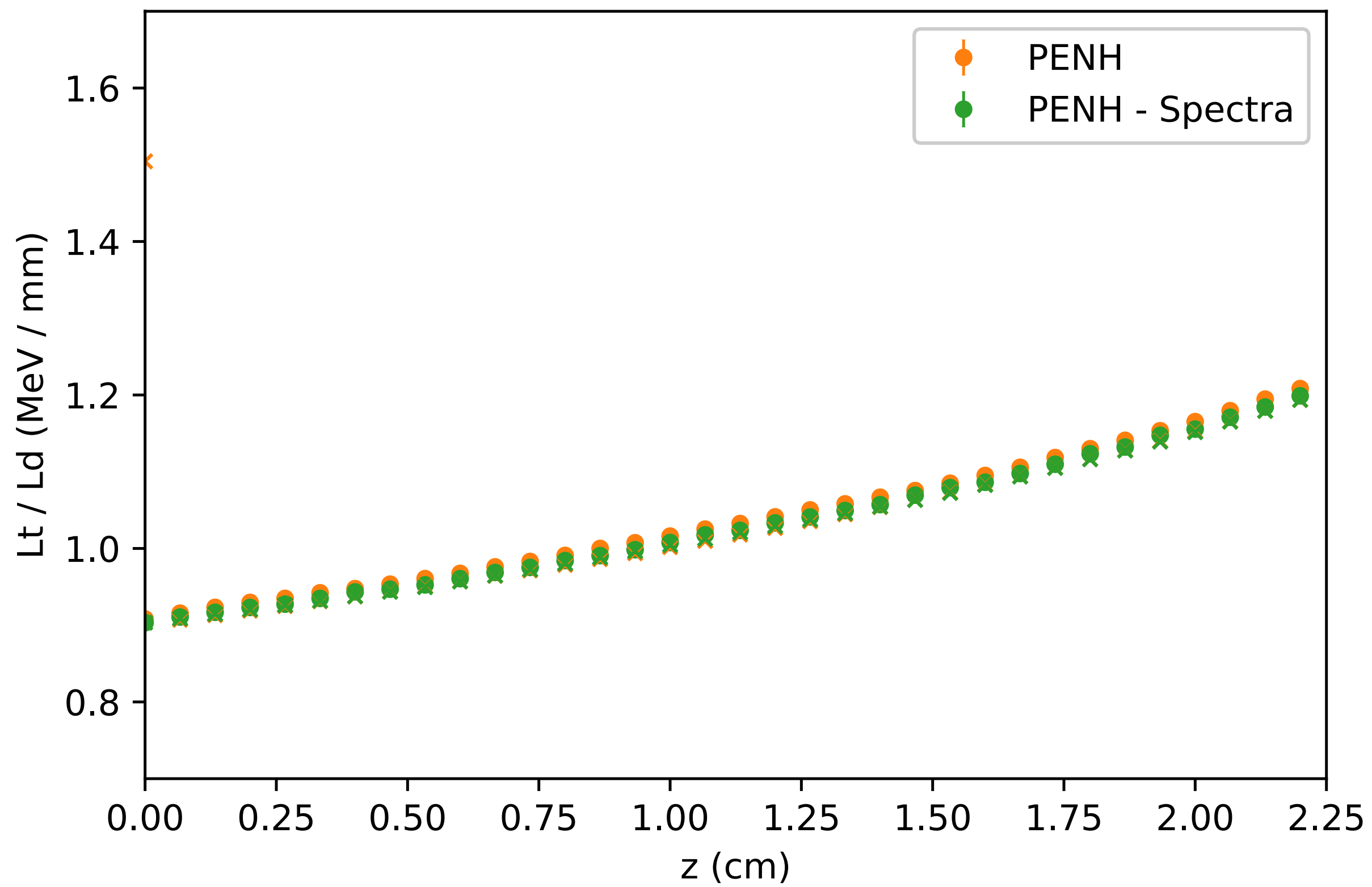


LET Distribution in FLUKA - 75 MeV

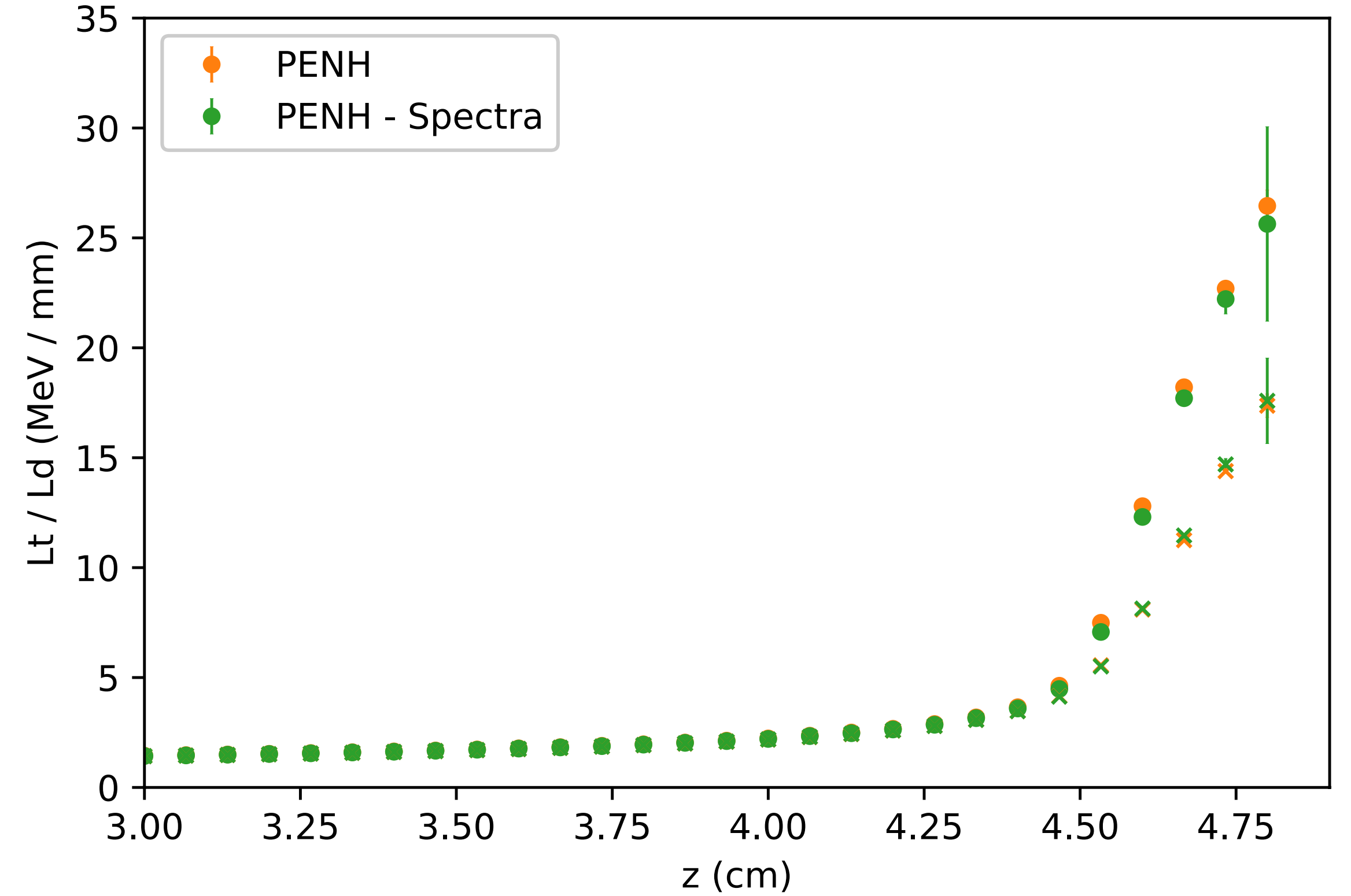


# 75 MeV

LET Distribution in PENH - 75 MeV

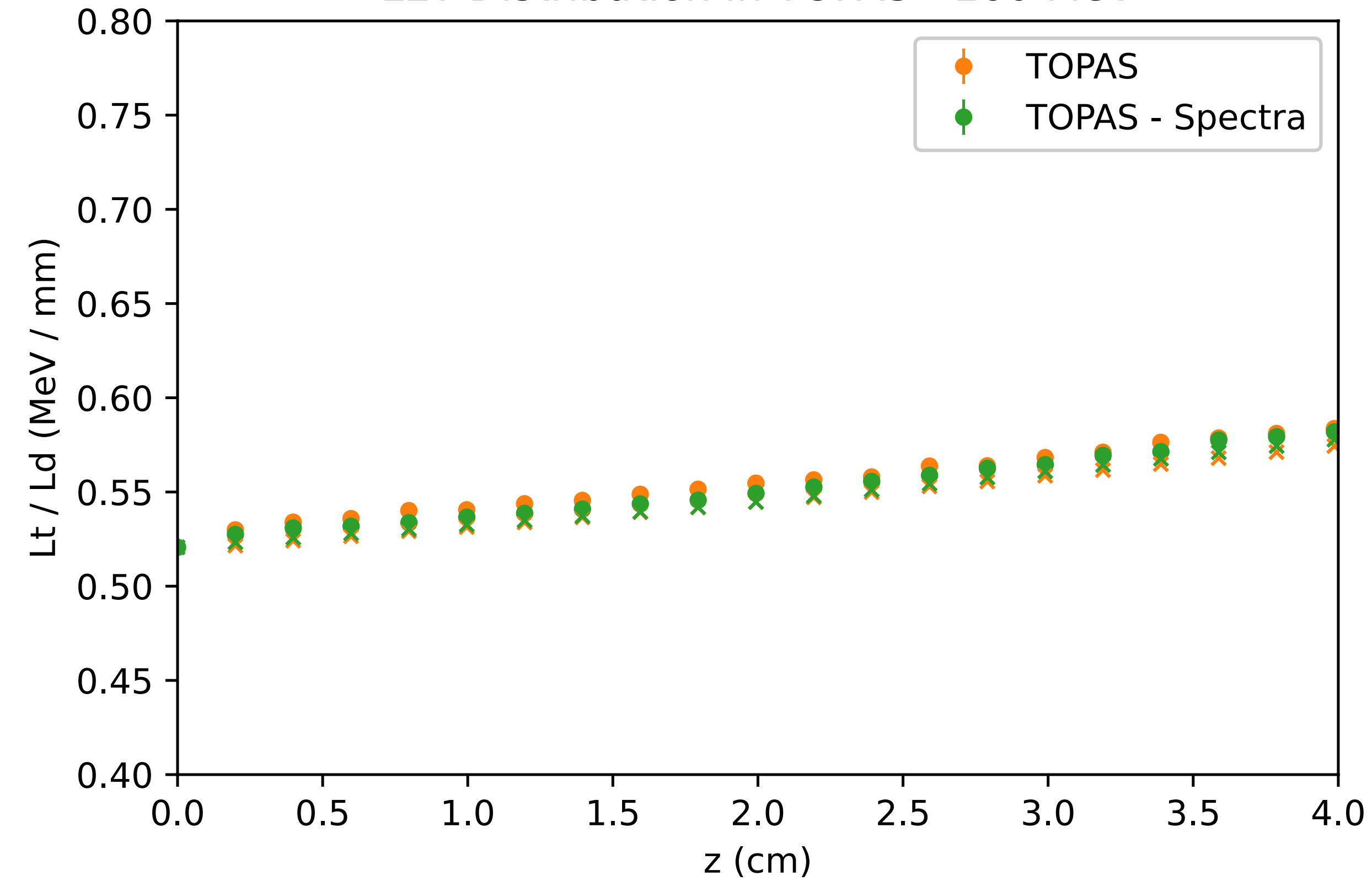


LET Distribution in PENH - 75 MeV

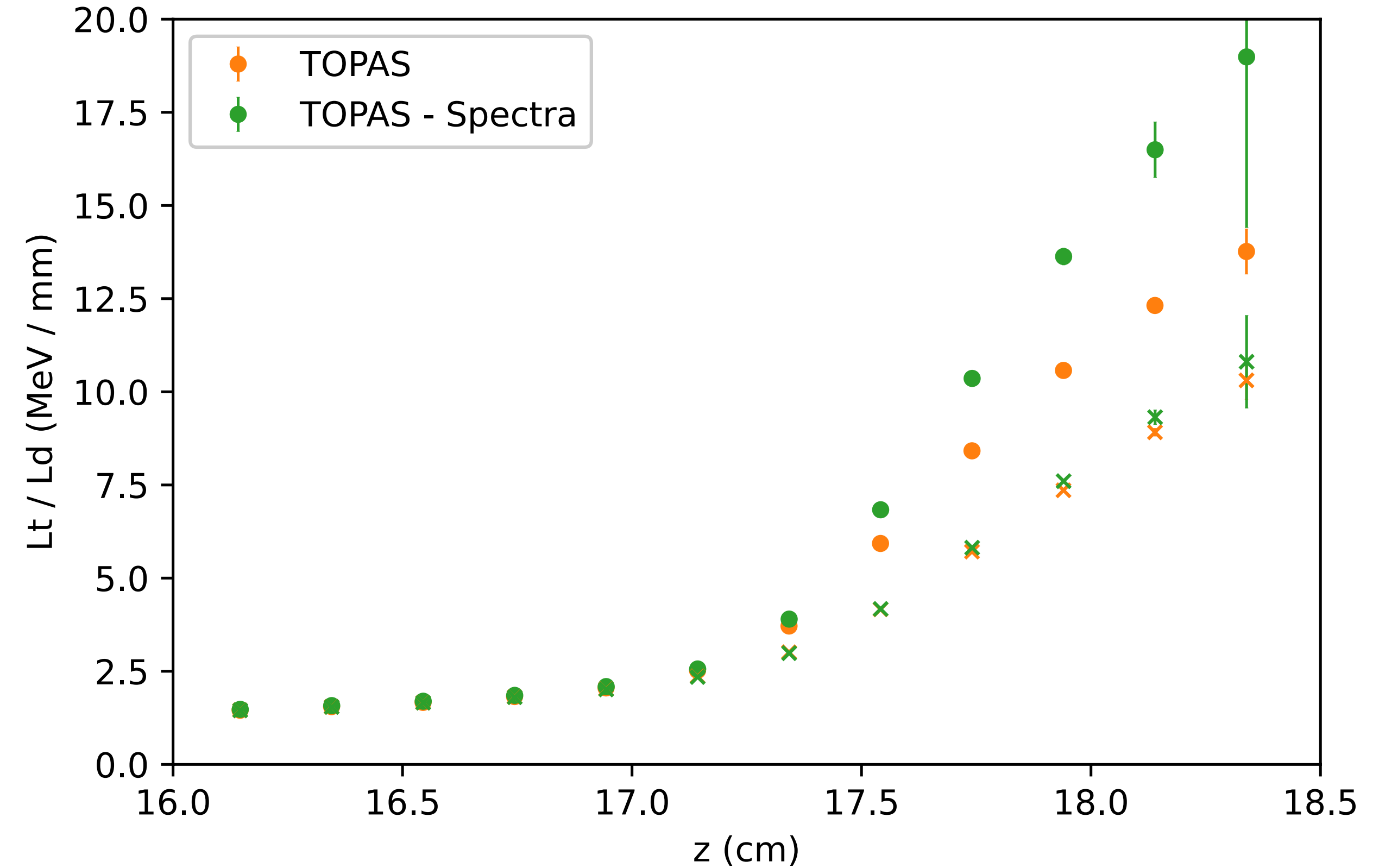


# 160 MeV

LET Distribution in TOPAS - 160 MeV

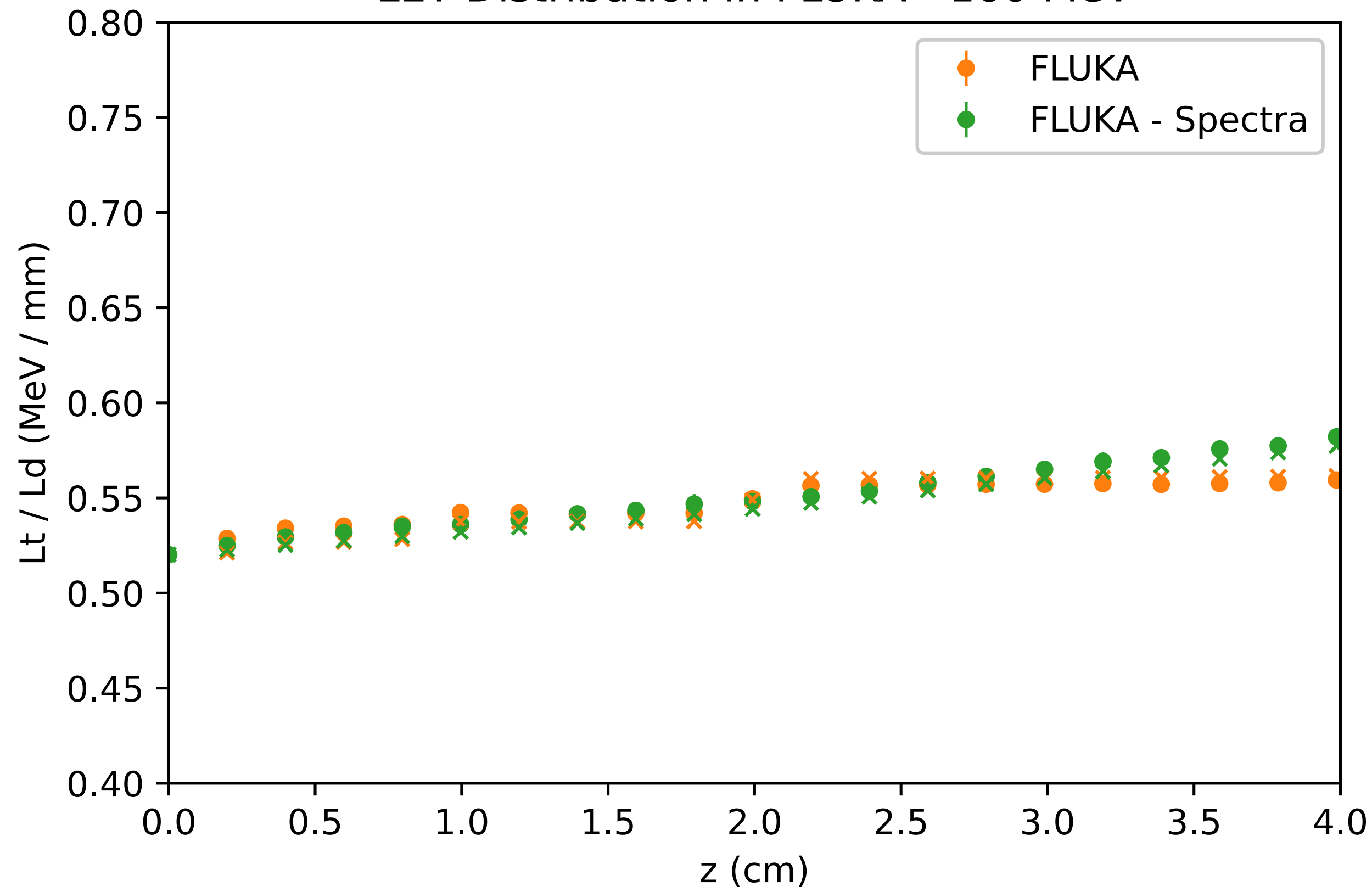


LET Distribution in TOPAS - 160 MeV

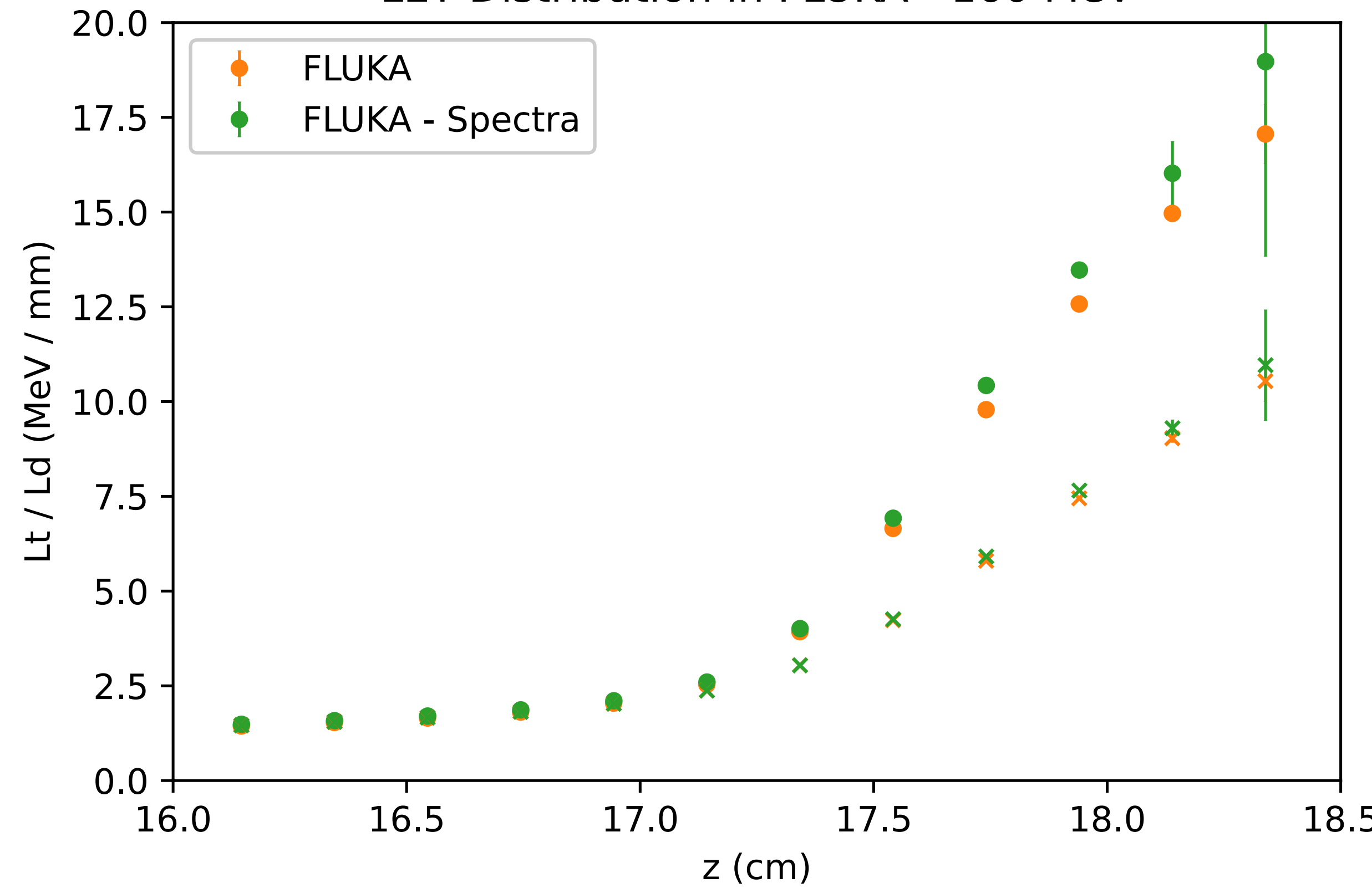


# 160 MeV

LET Distribution in FLUKA - 160 MeV



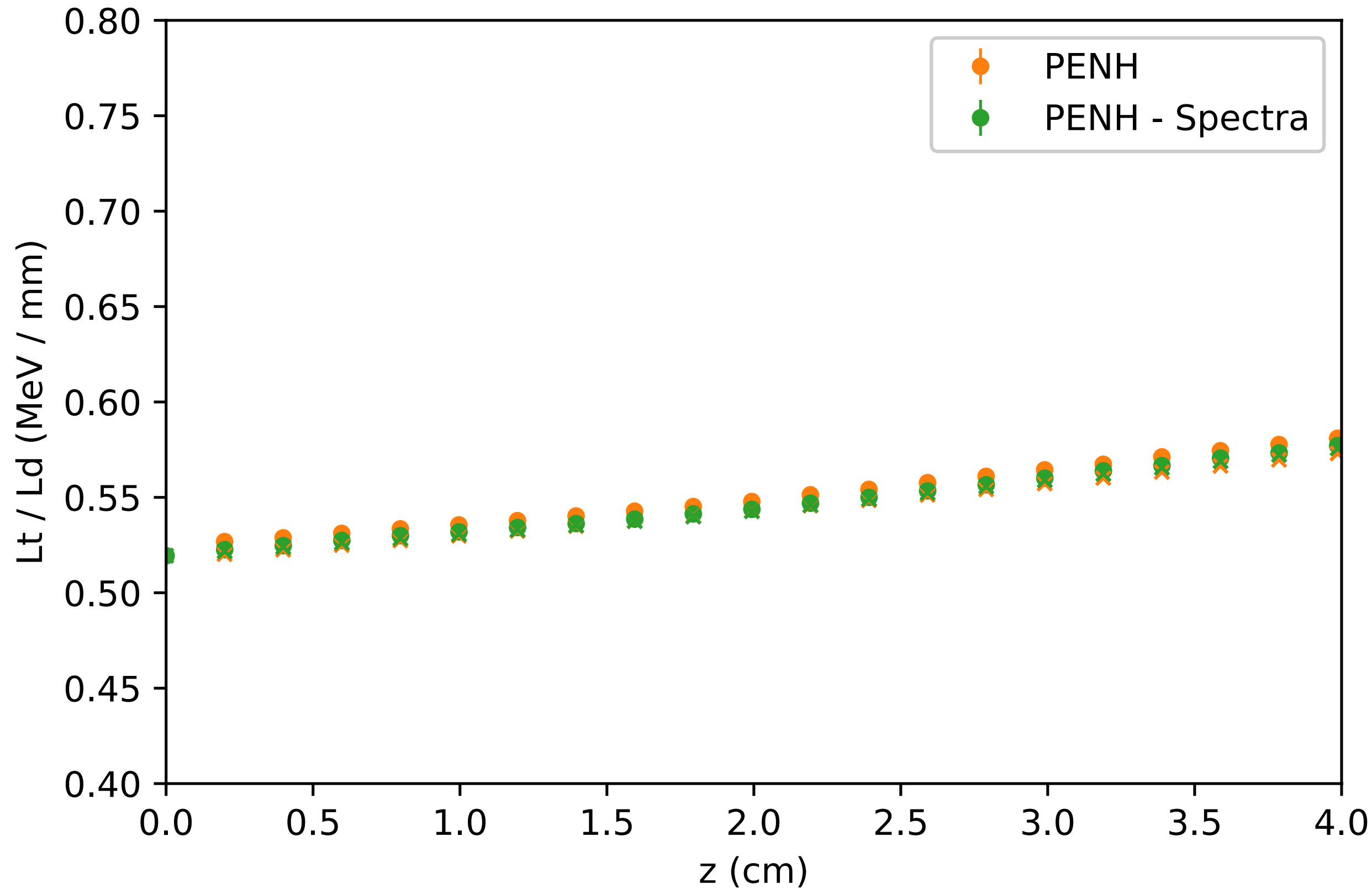
LET Distribution in FLUKA - 160 MeV



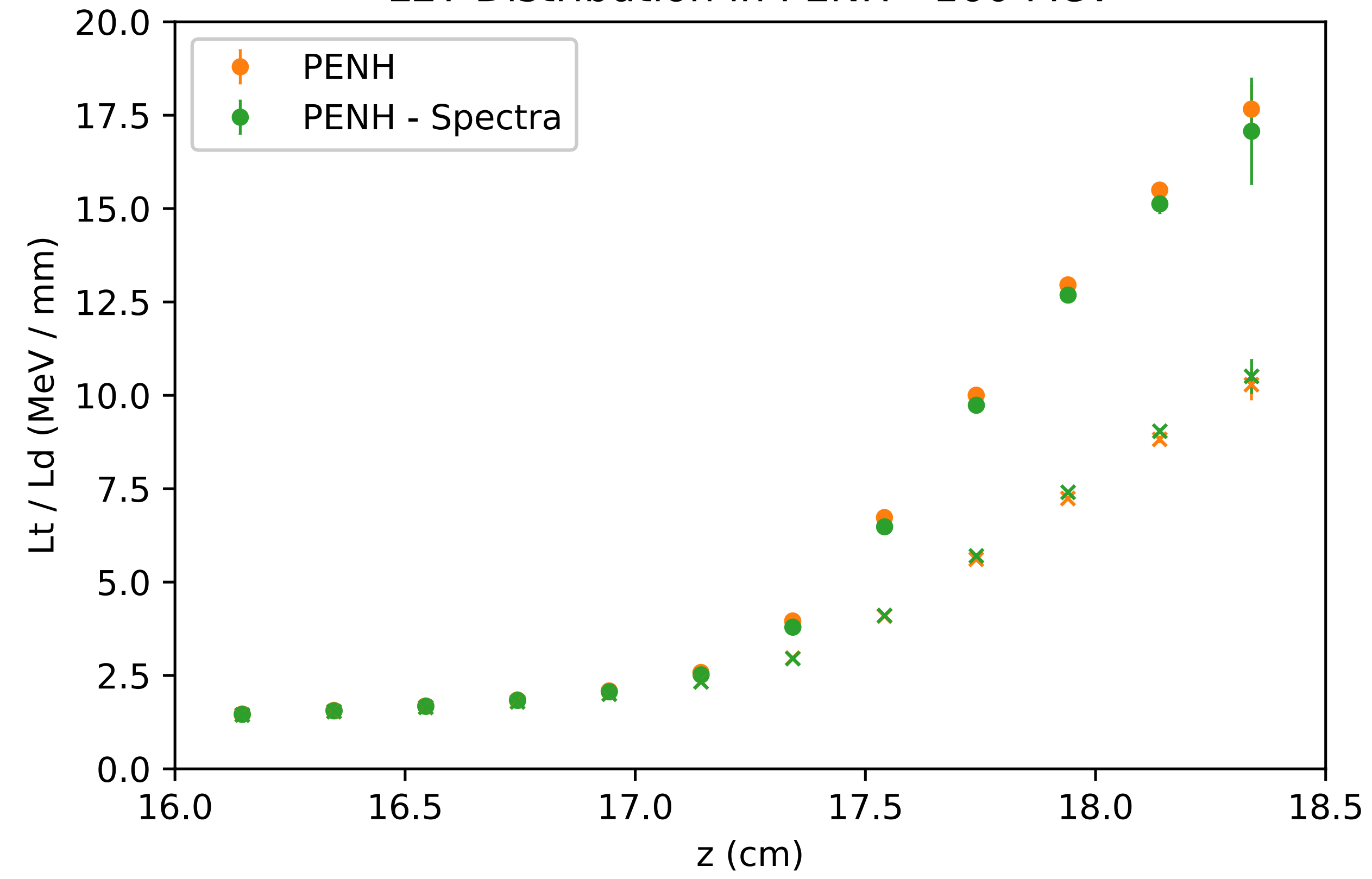


# 160 MeV

LET Distribution in PENH - 160 MeV

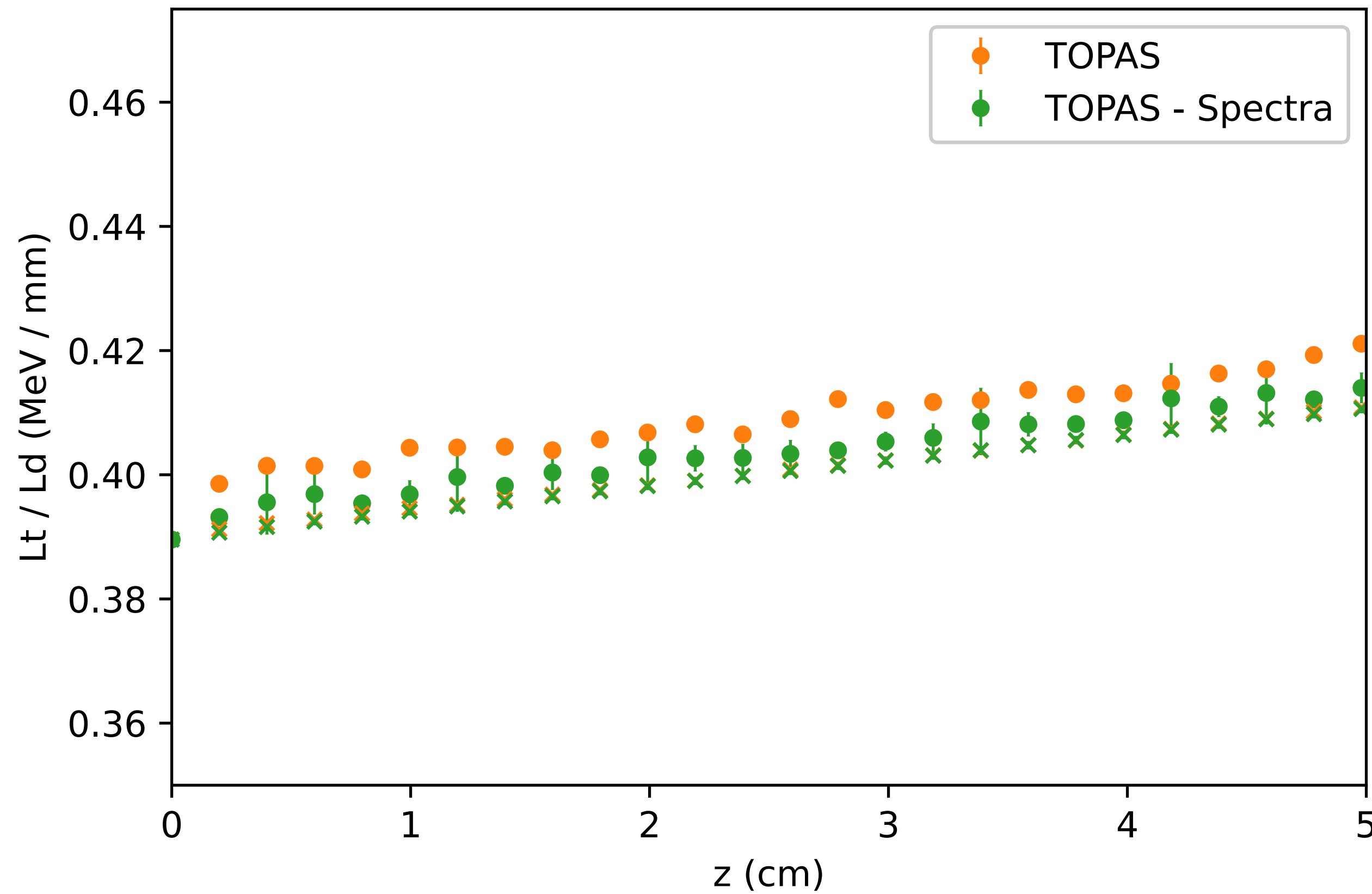


LET Distribution in PENH - 160 MeV

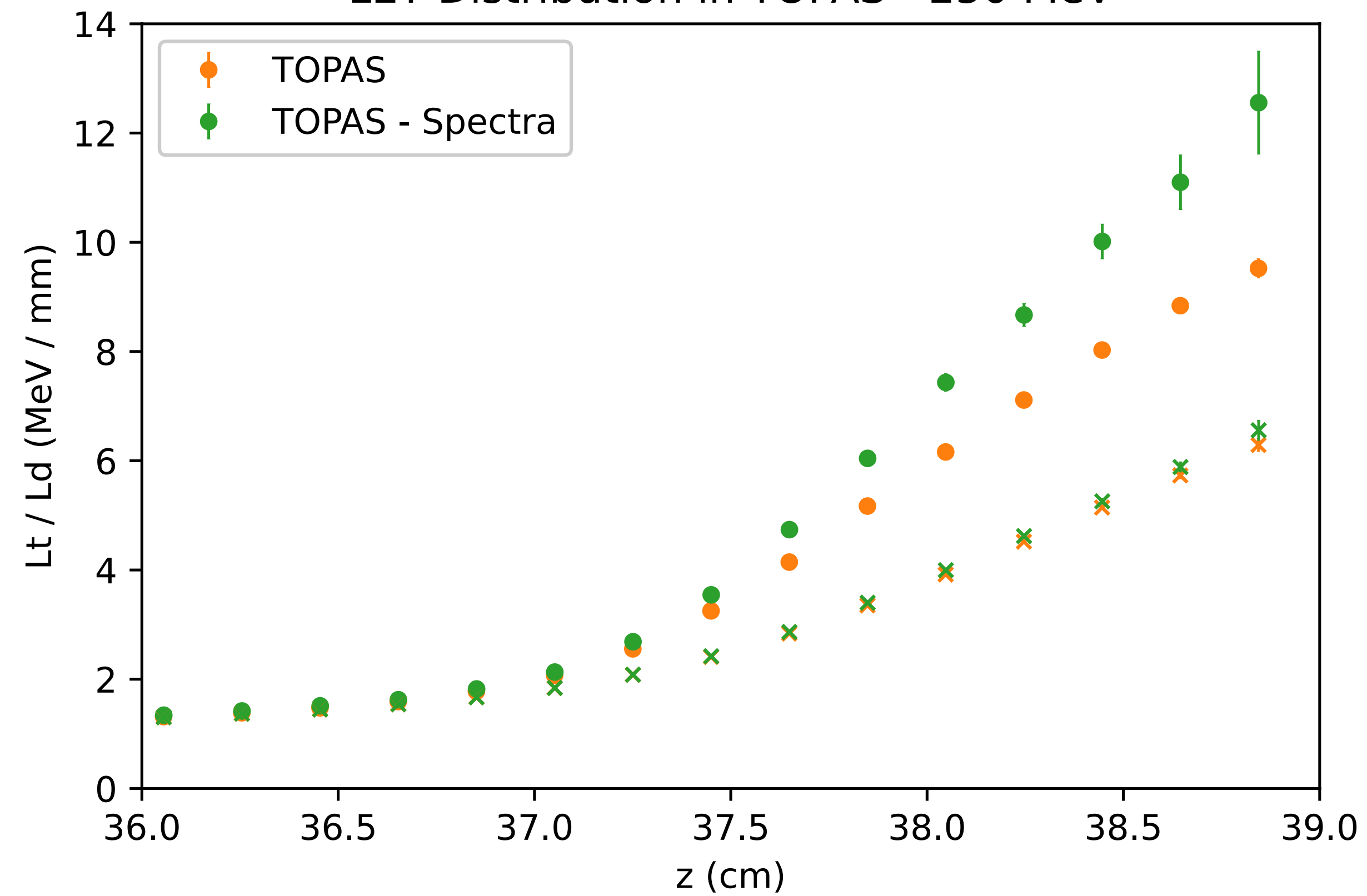


# 250 MeV

LET Distribution in TOPAS - 250 MeV

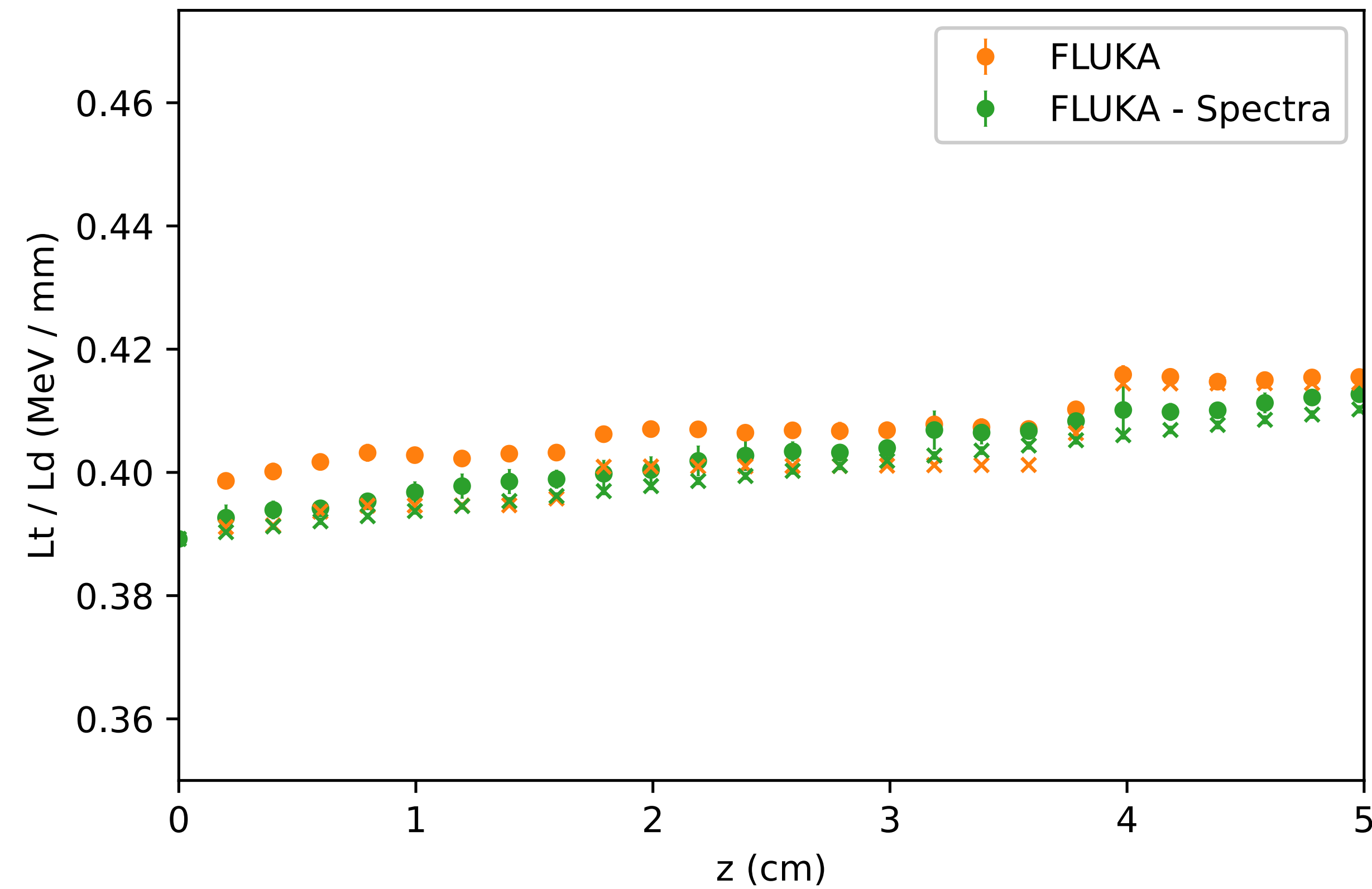


LET Distribution in TOPAS - 250 MeV

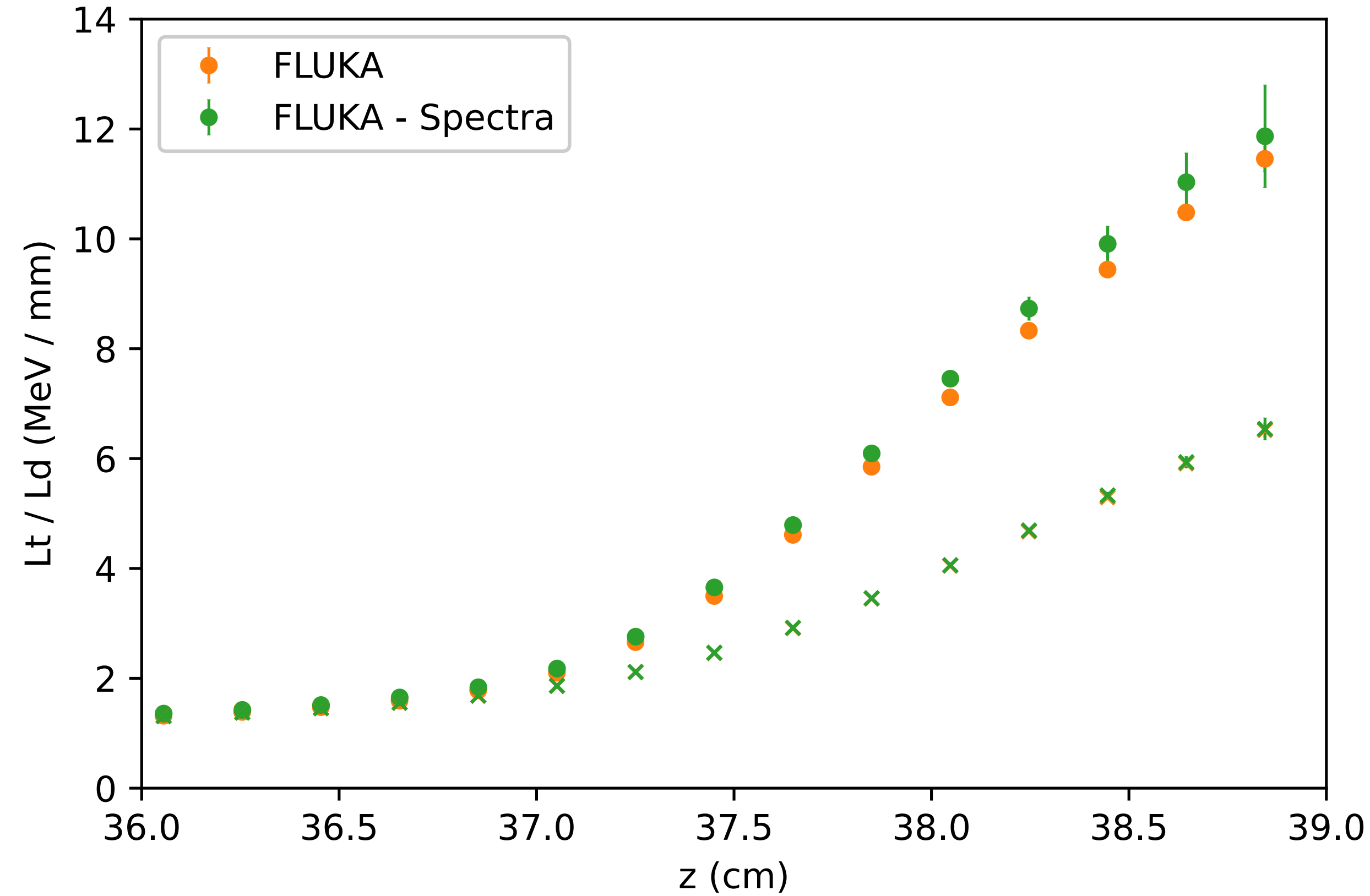


# 250 MeV

LET Distribution in FLUKA - 250 MeV

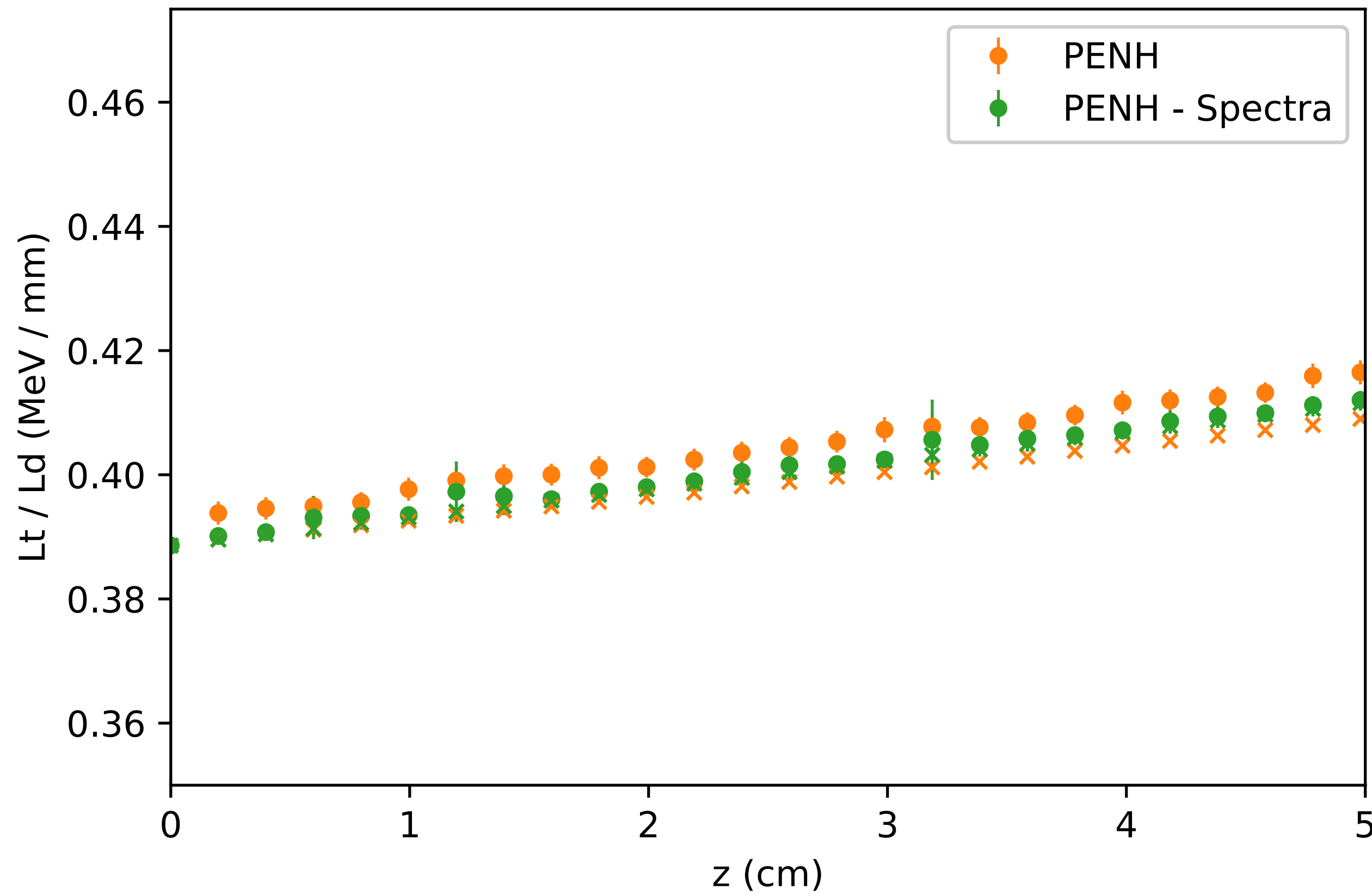


LET Distribution in FLUKA - 250 MeV

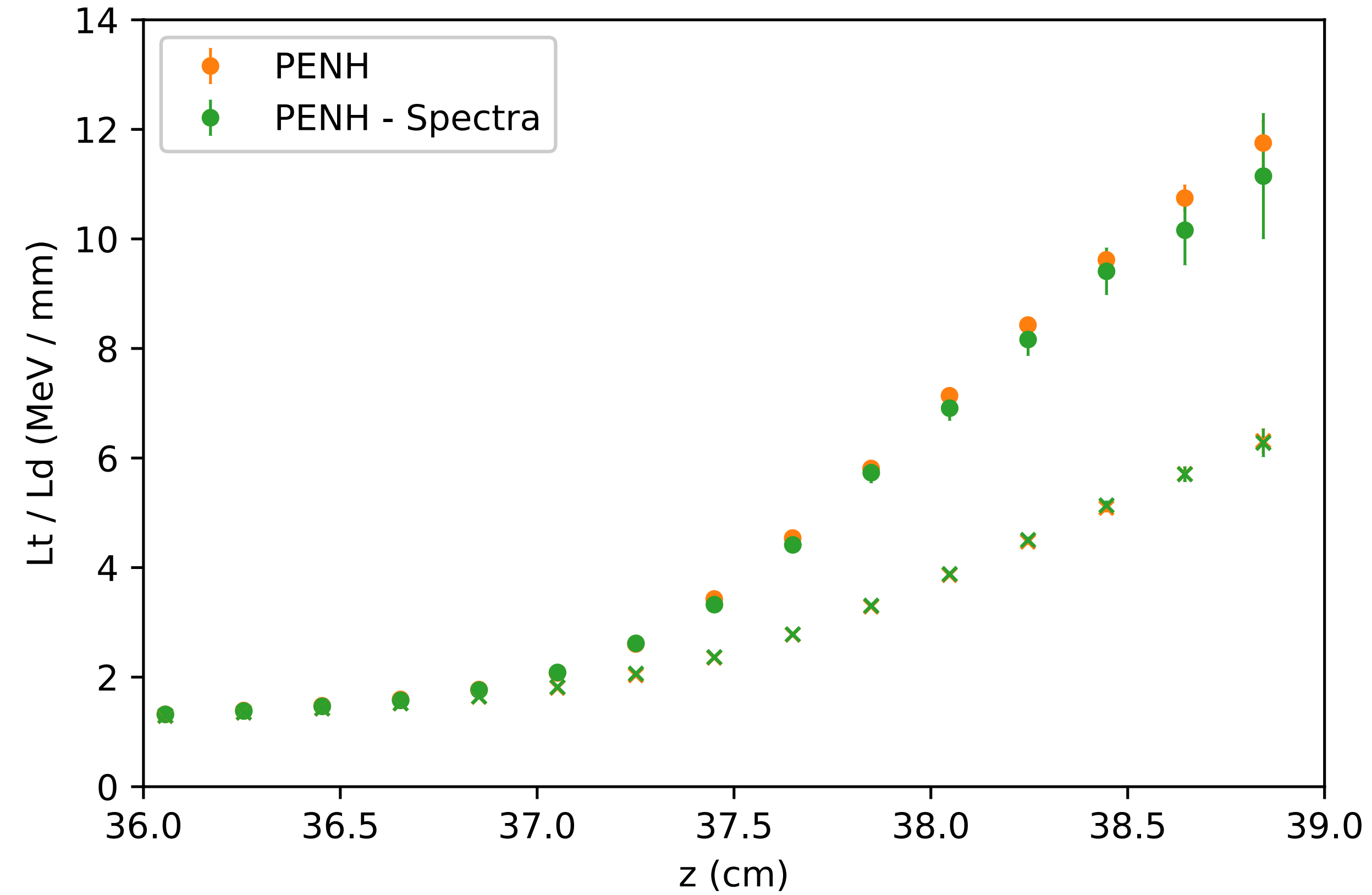


# 250 MeV

LET Distribution in PENH - 250 MeV



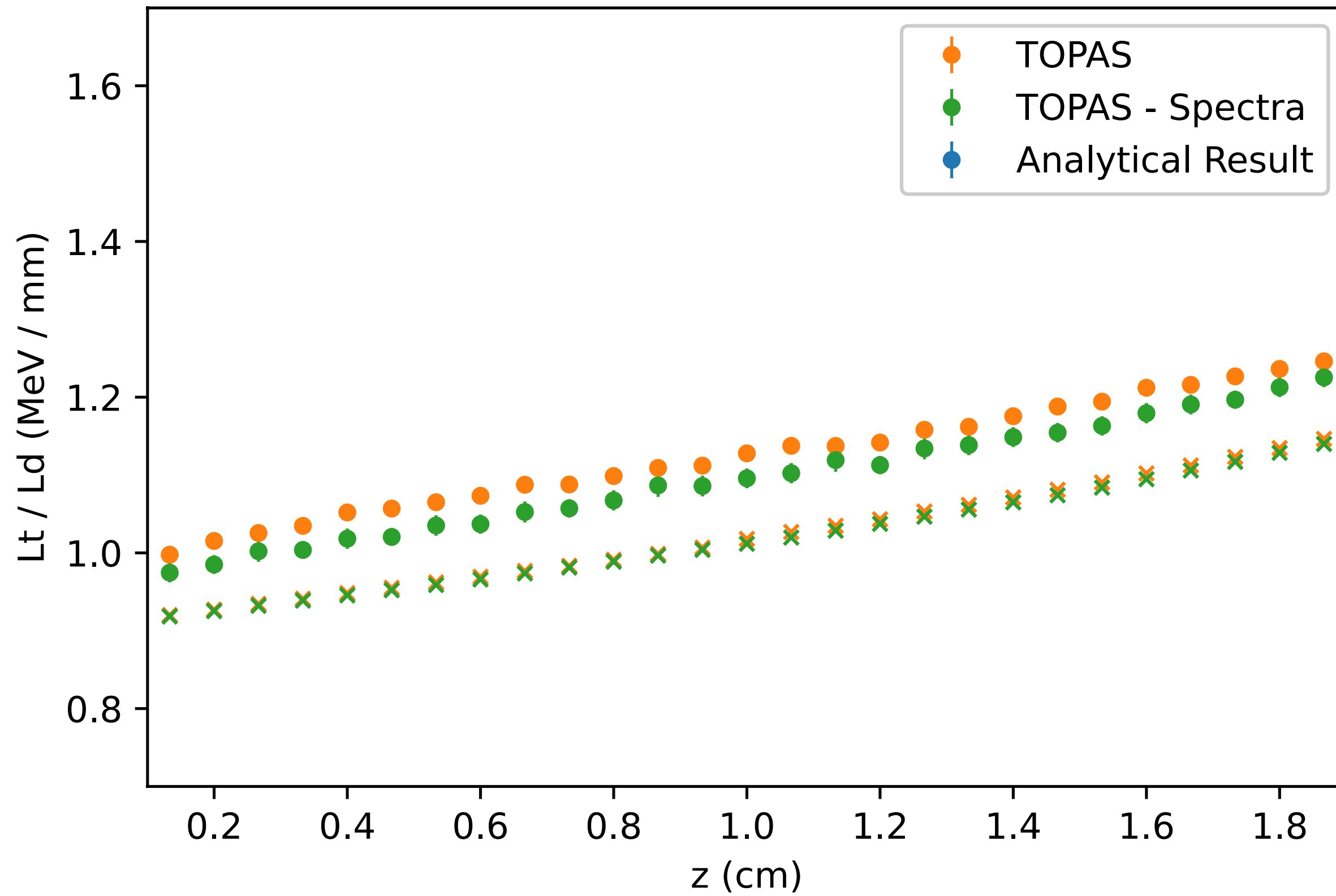
LET Distribution in PENH - 250 MeV



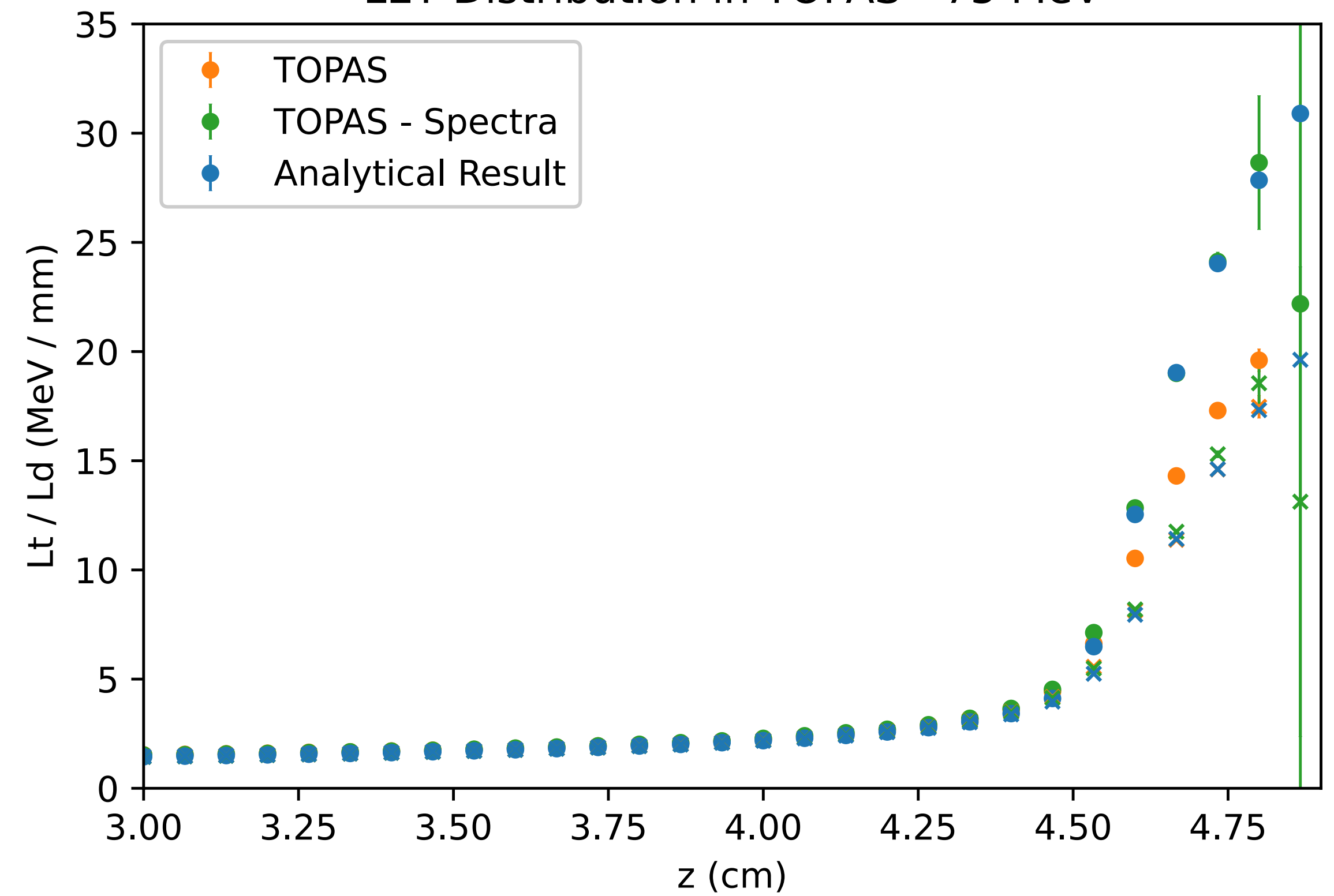
# Full Calculations

# 75 MeV

LET Distribution in TOPAS - 75 MeV

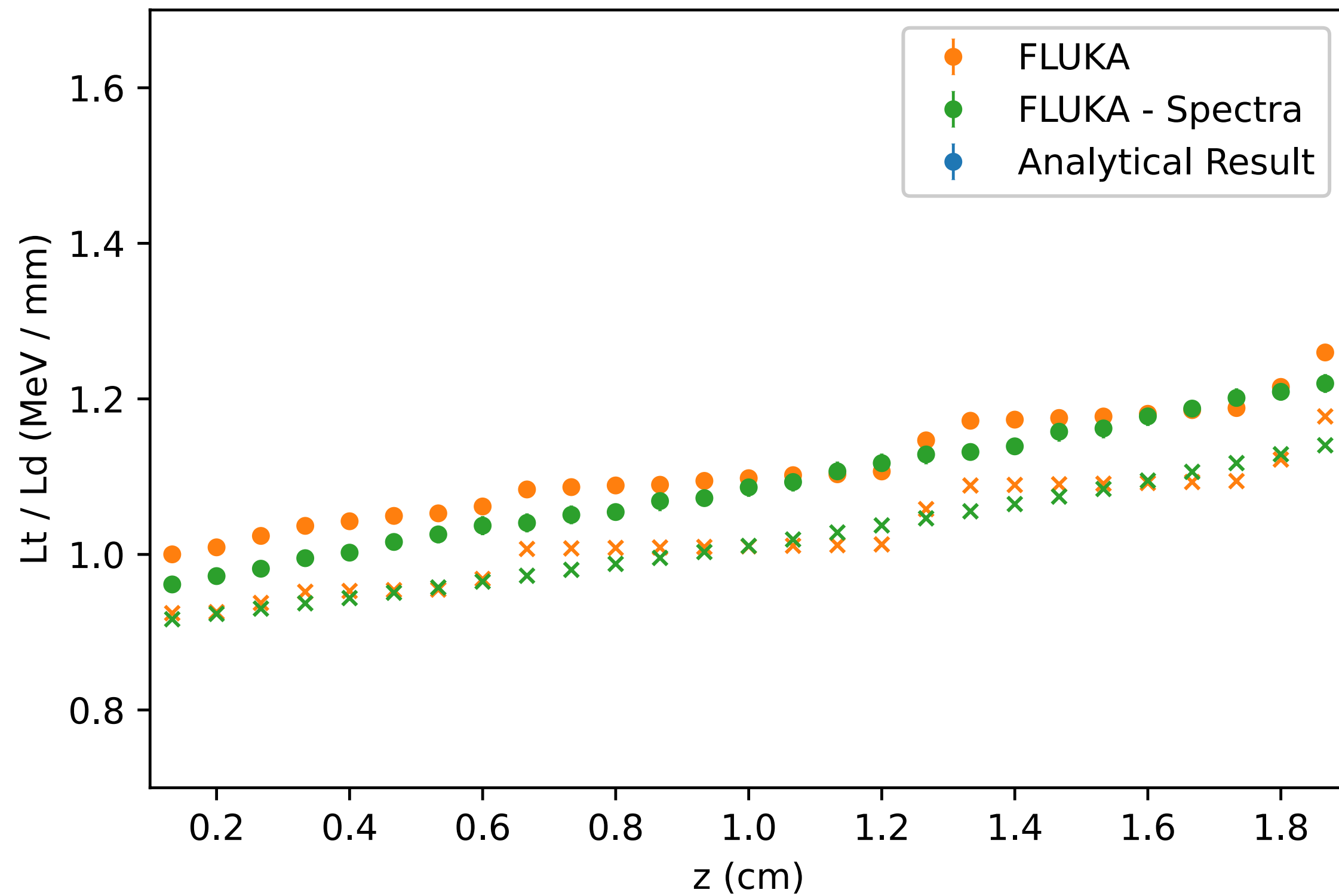


LET Distribution in TOPAS - 75 MeV

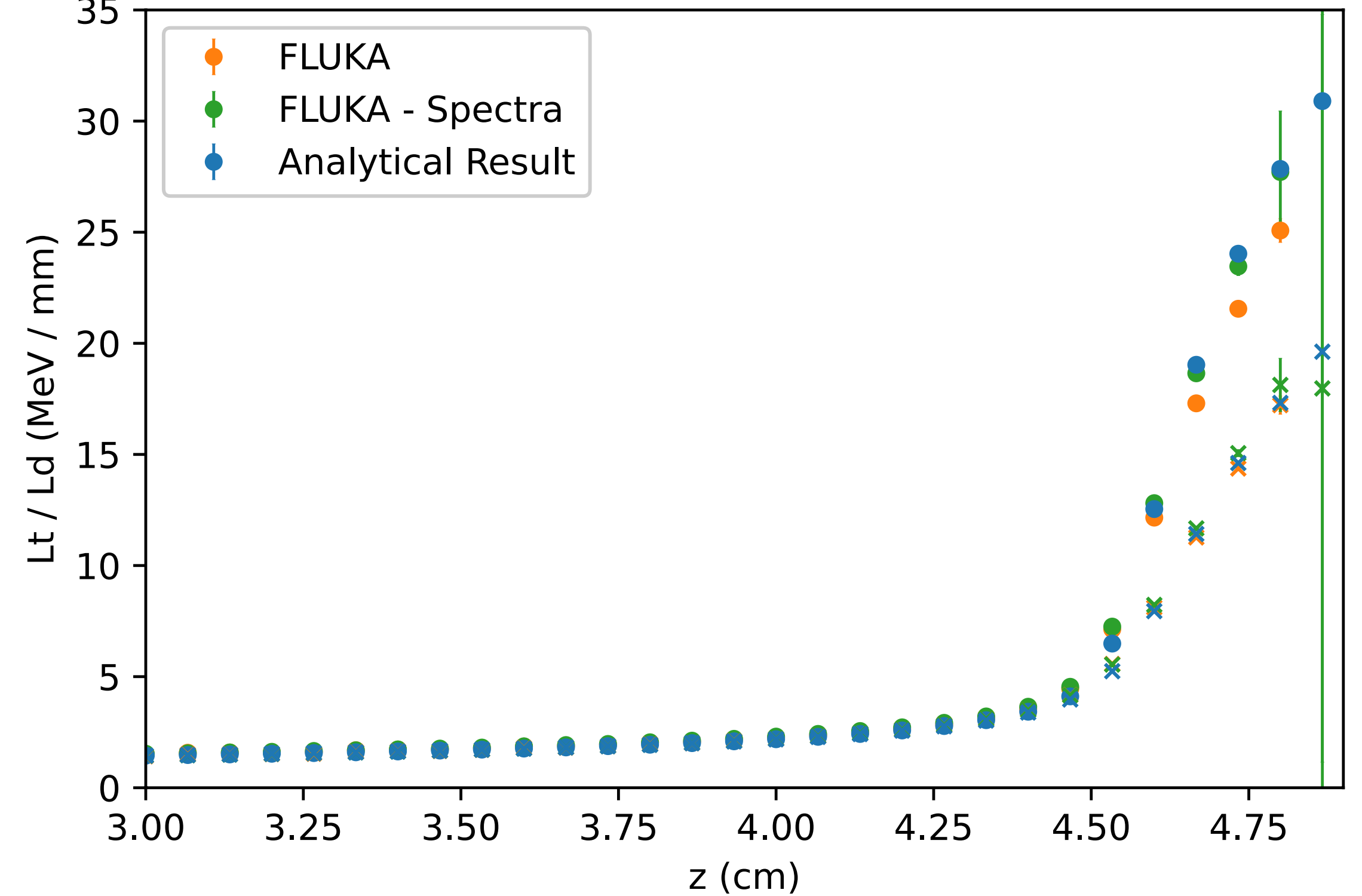


# 75 MeV

LET Distribution in FLUKA - 75 MeV

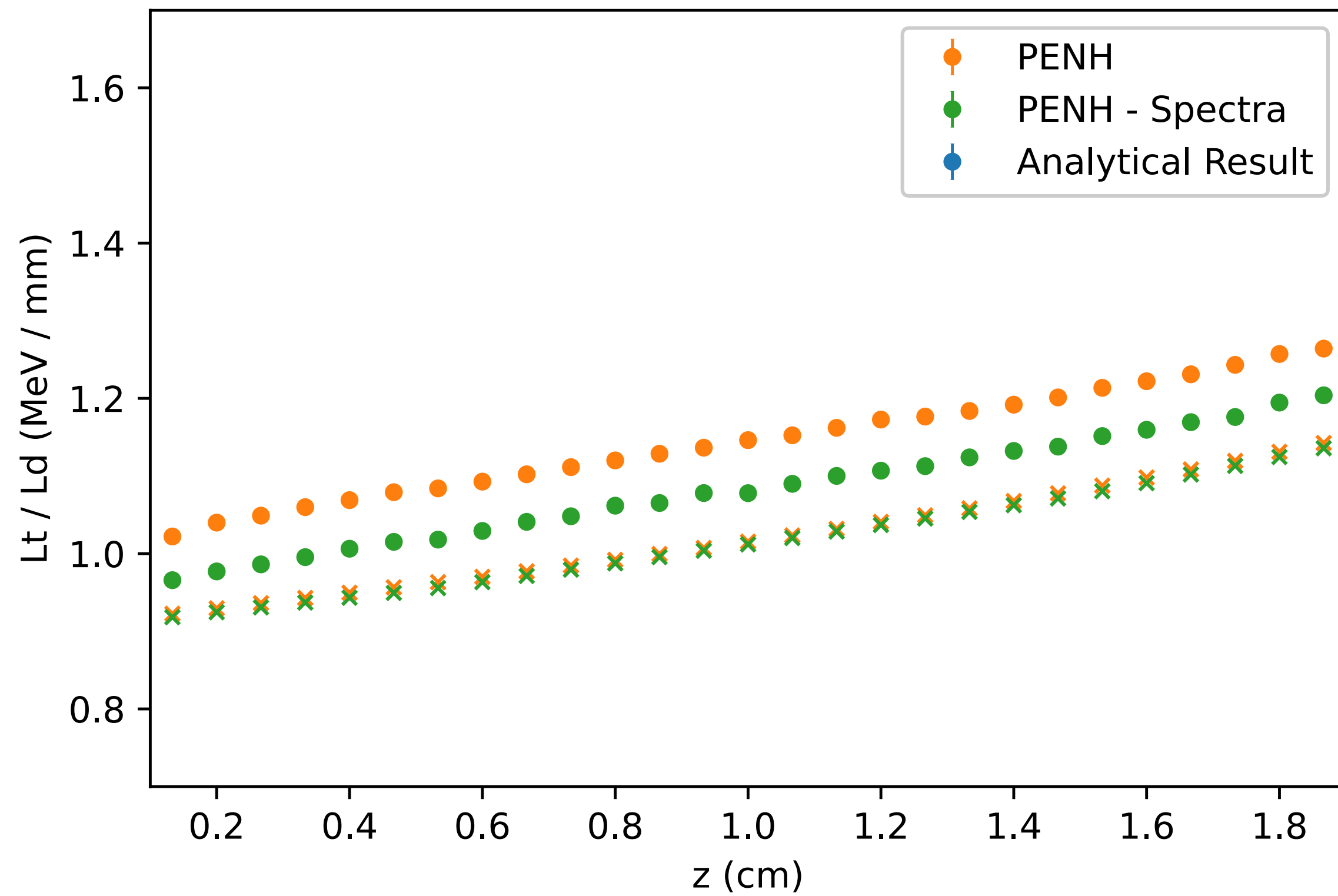


LET Distribution in FLUKA - 75 MeV

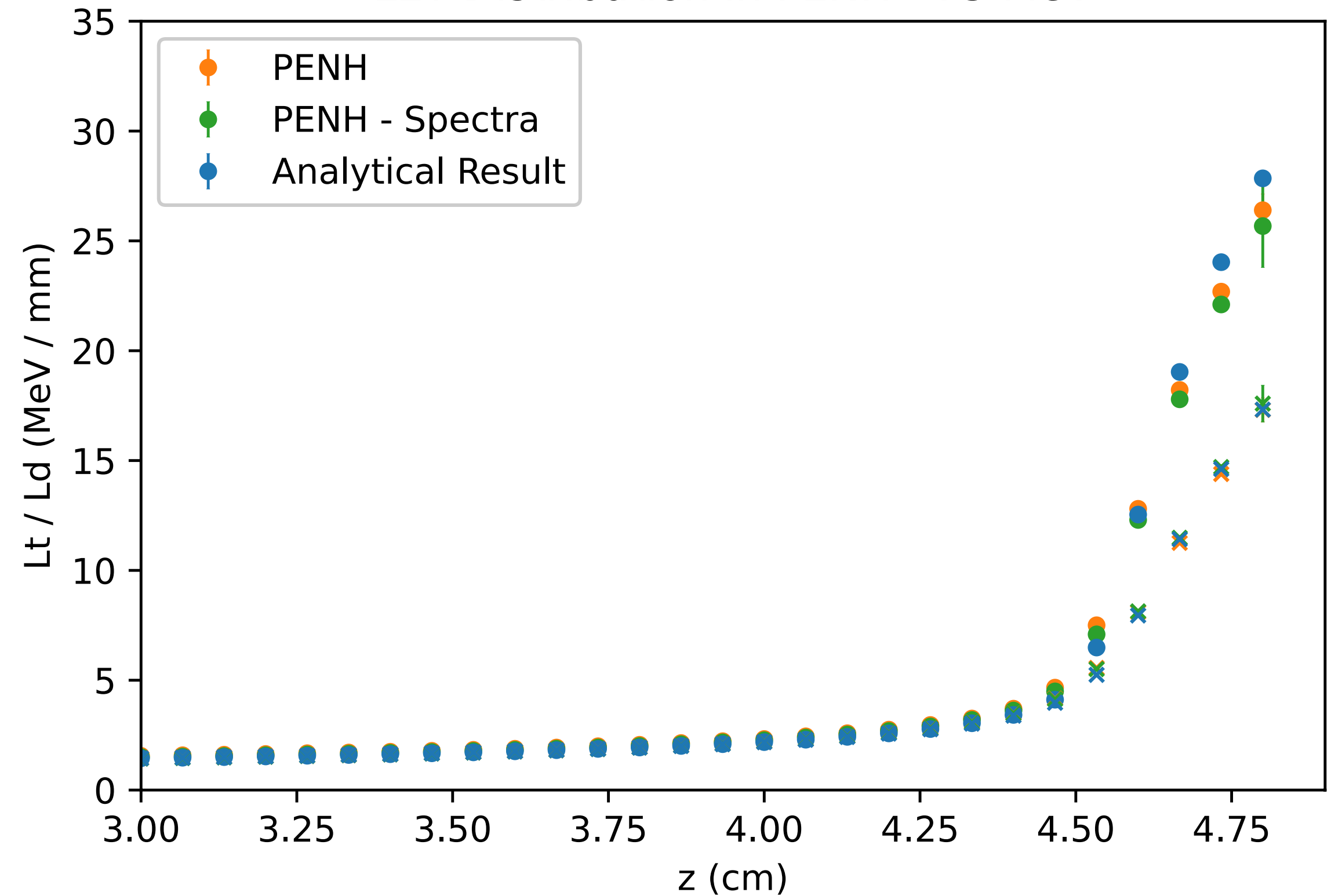


# 75 MeV

LET Distribution in PENH - 75 MeV



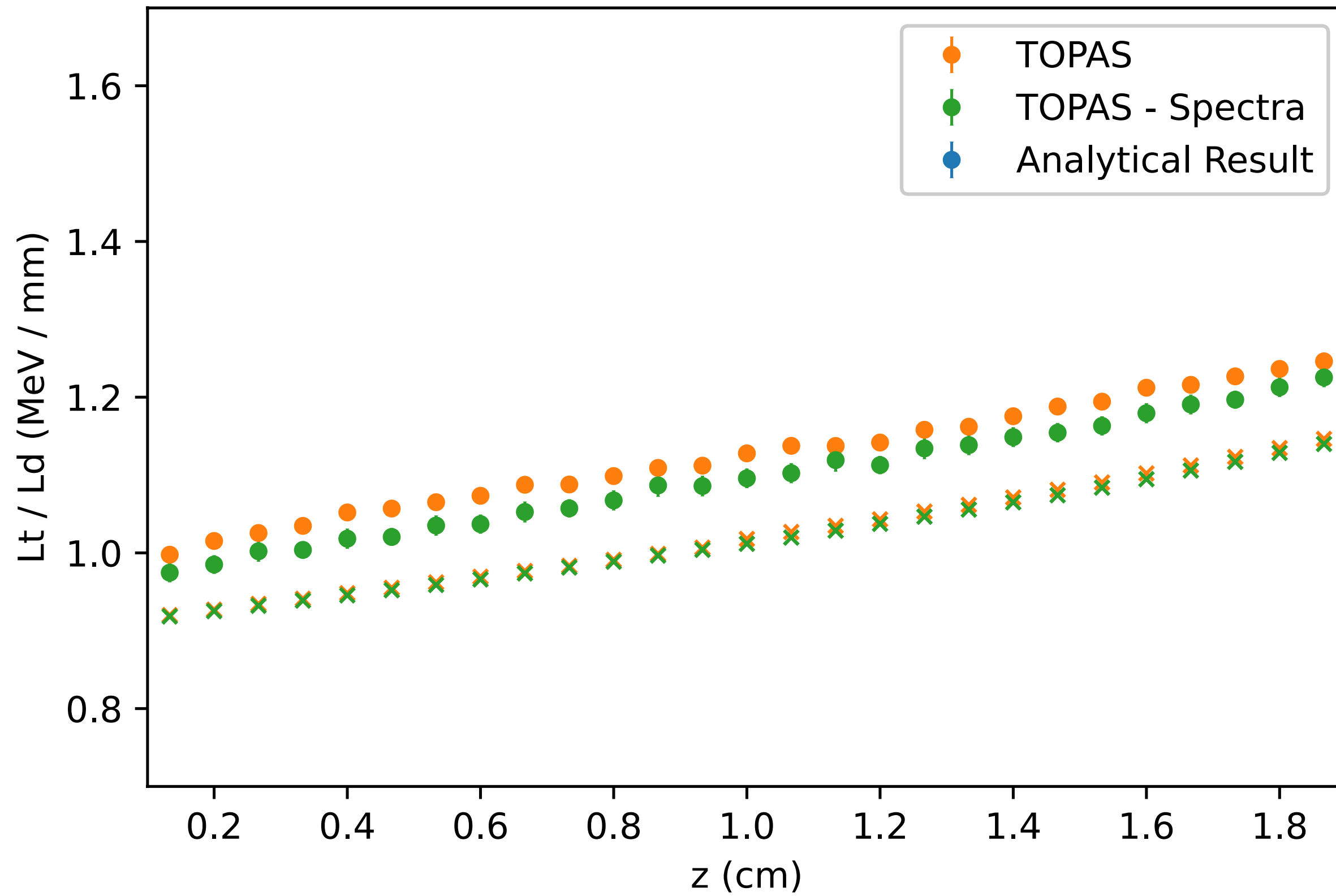
LET Distribution in PENH - 75 MeV



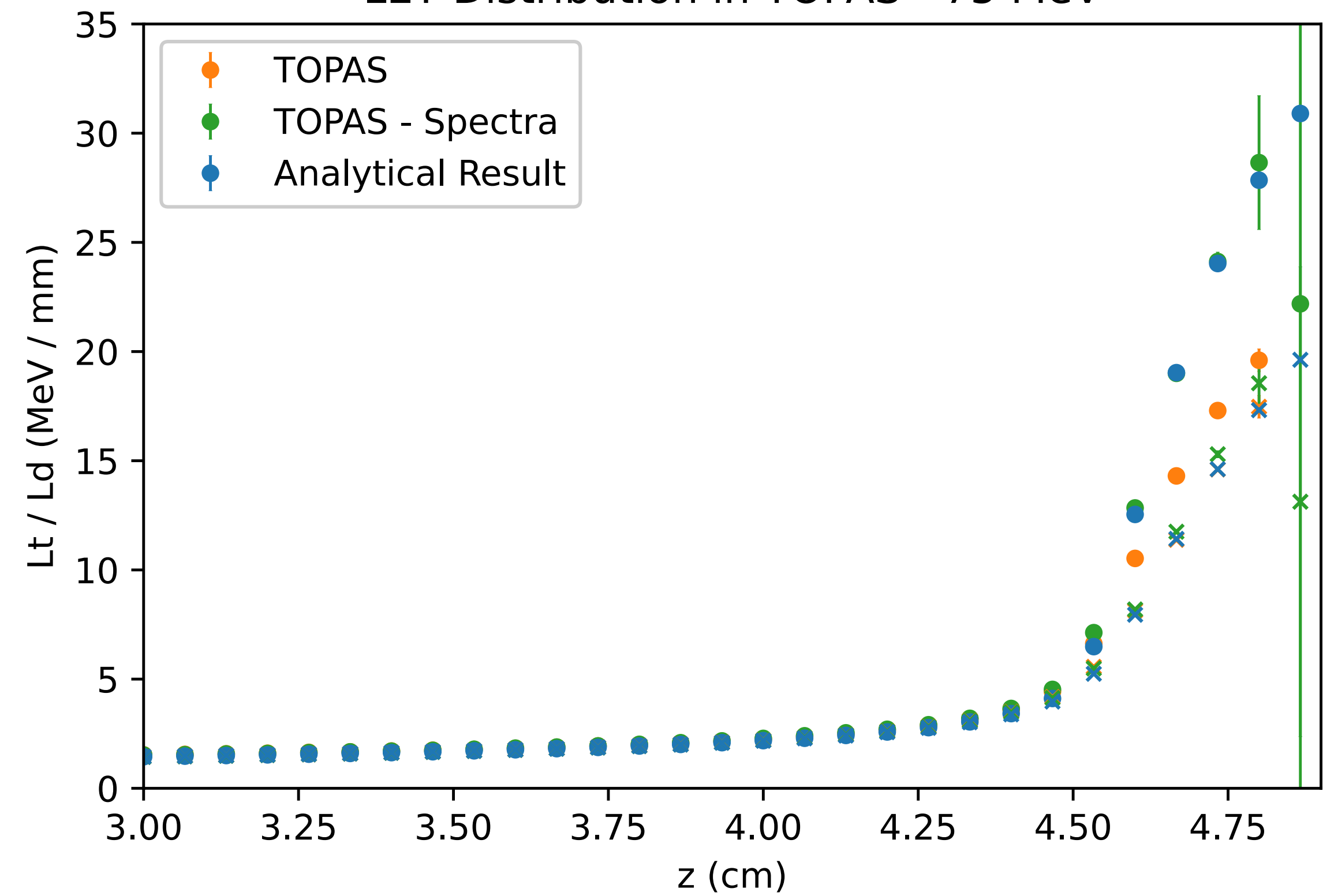


# 75 MeV

LET Distribution in TOPAS - 75 MeV

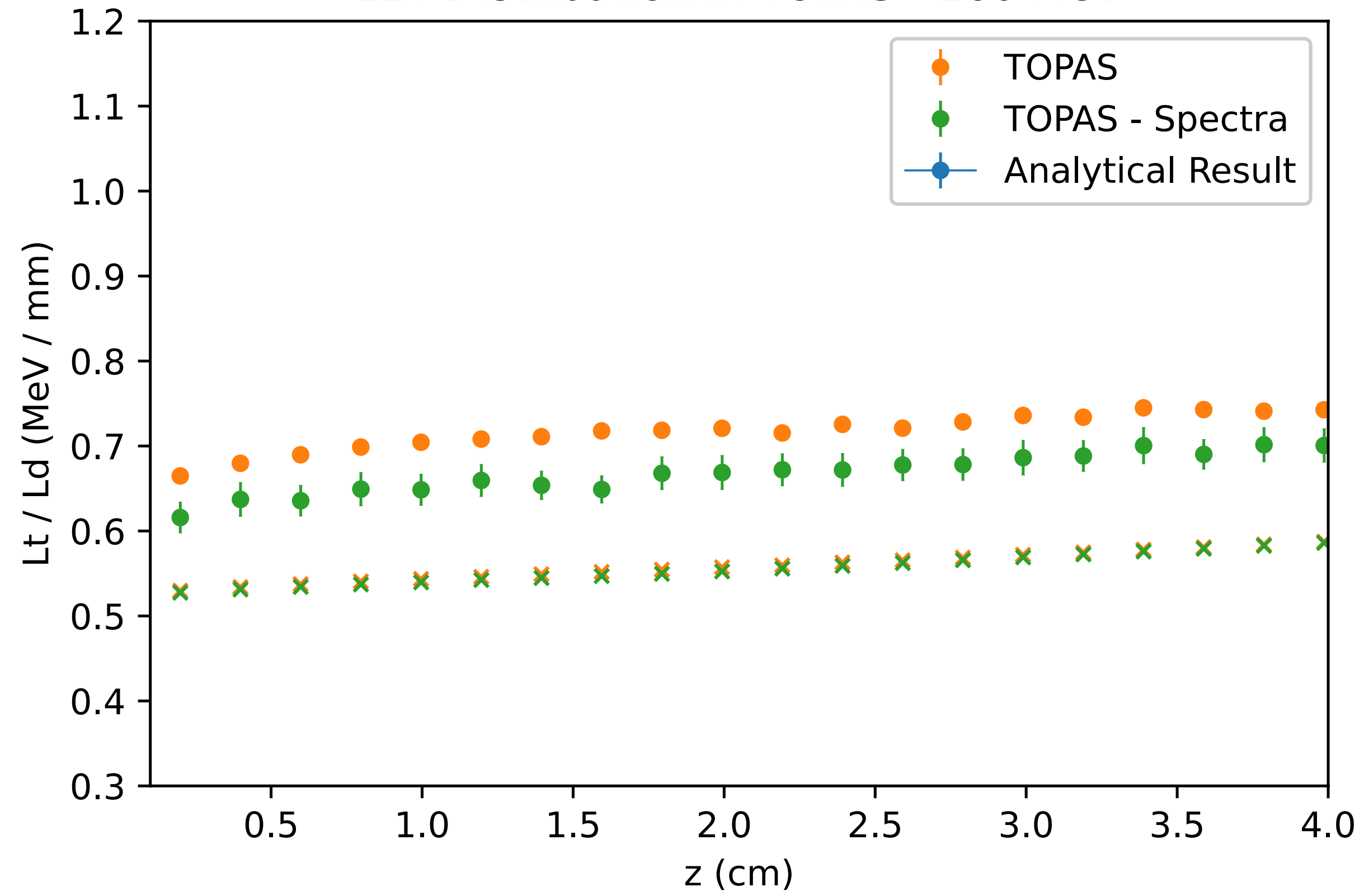


LET Distribution in TOPAS - 75 MeV

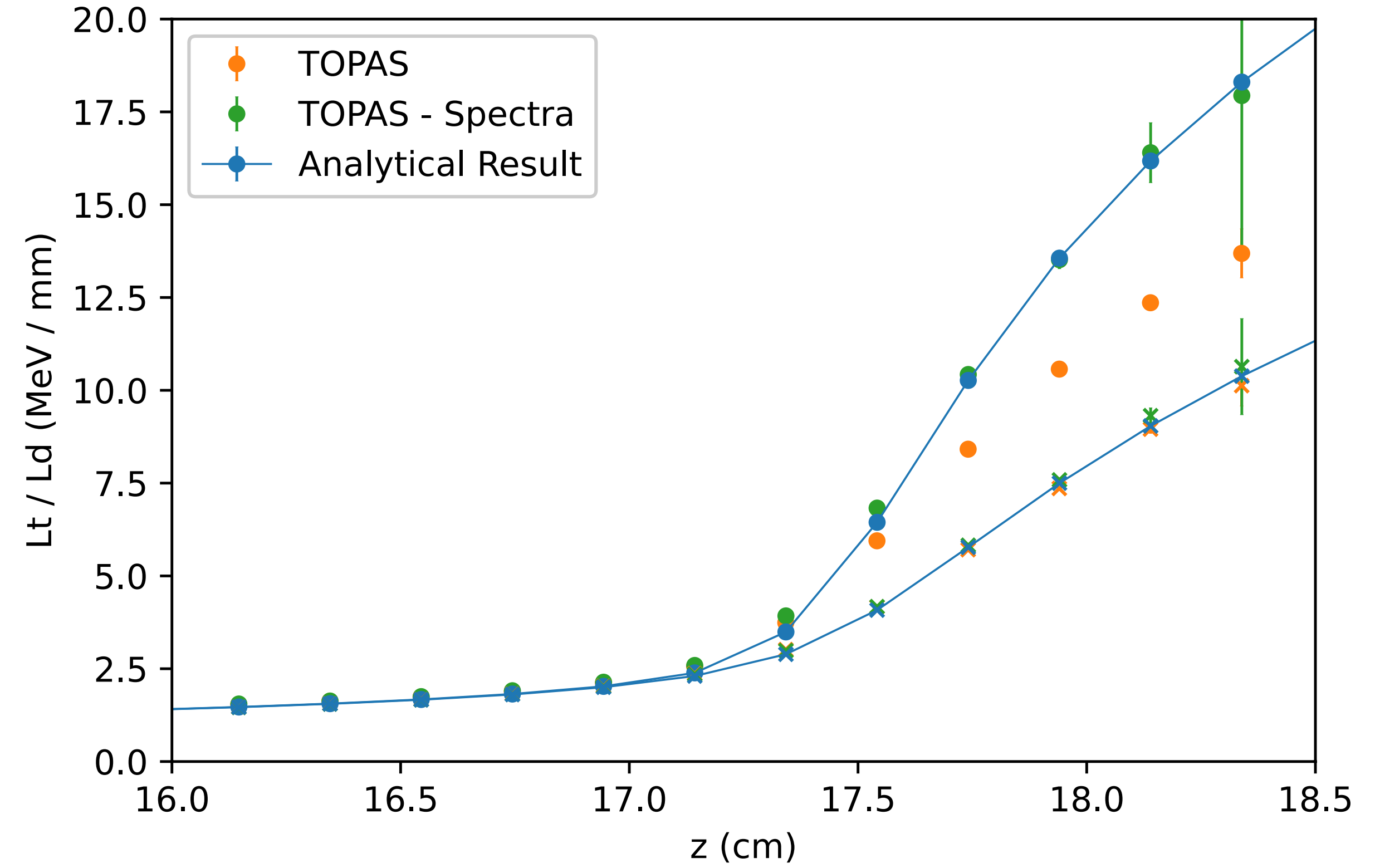


# 160 MeV

LET Distribution in TOPAS - 160 MeV

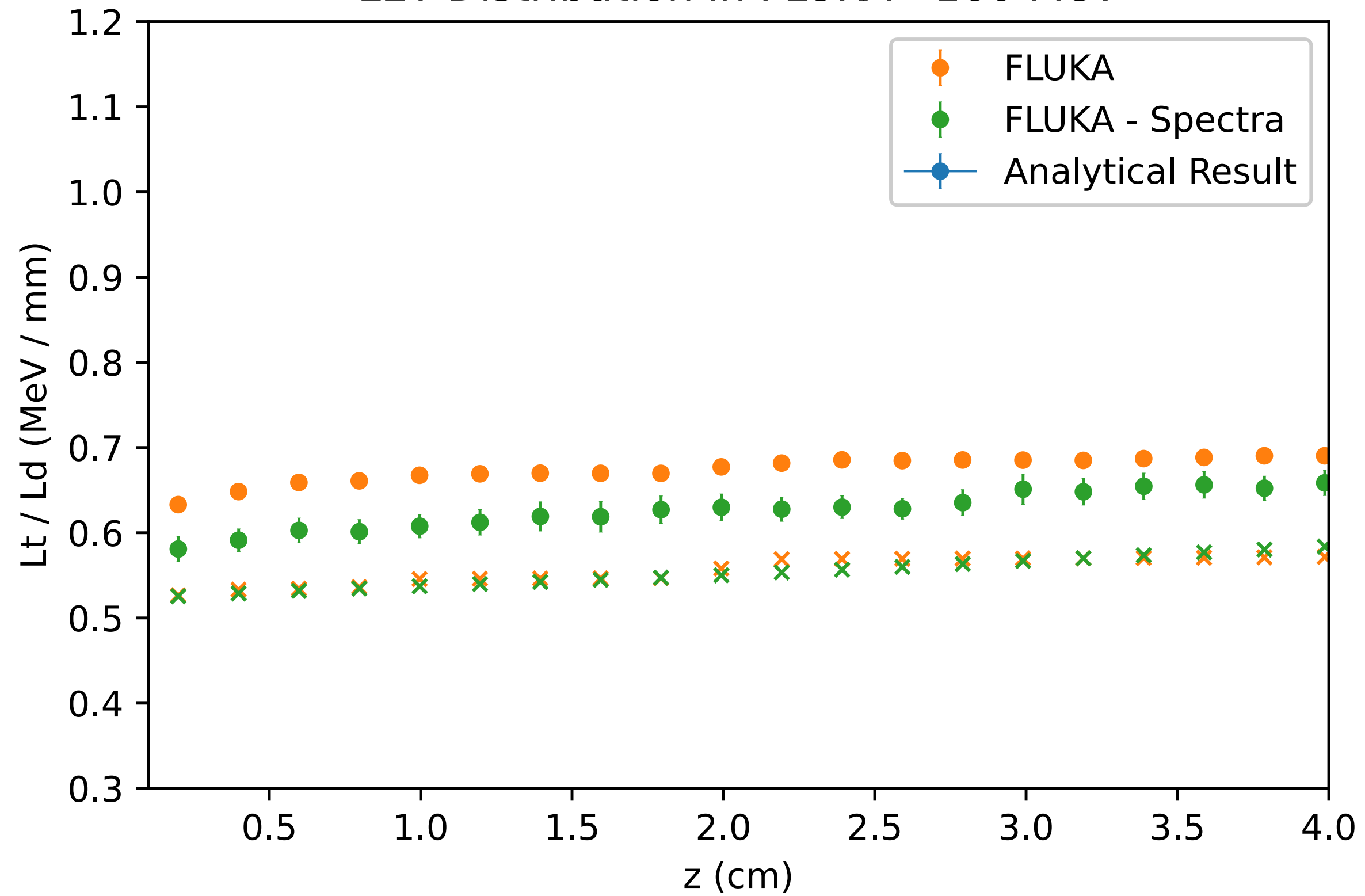


LET Distribution in TOPAS - 160 MeV

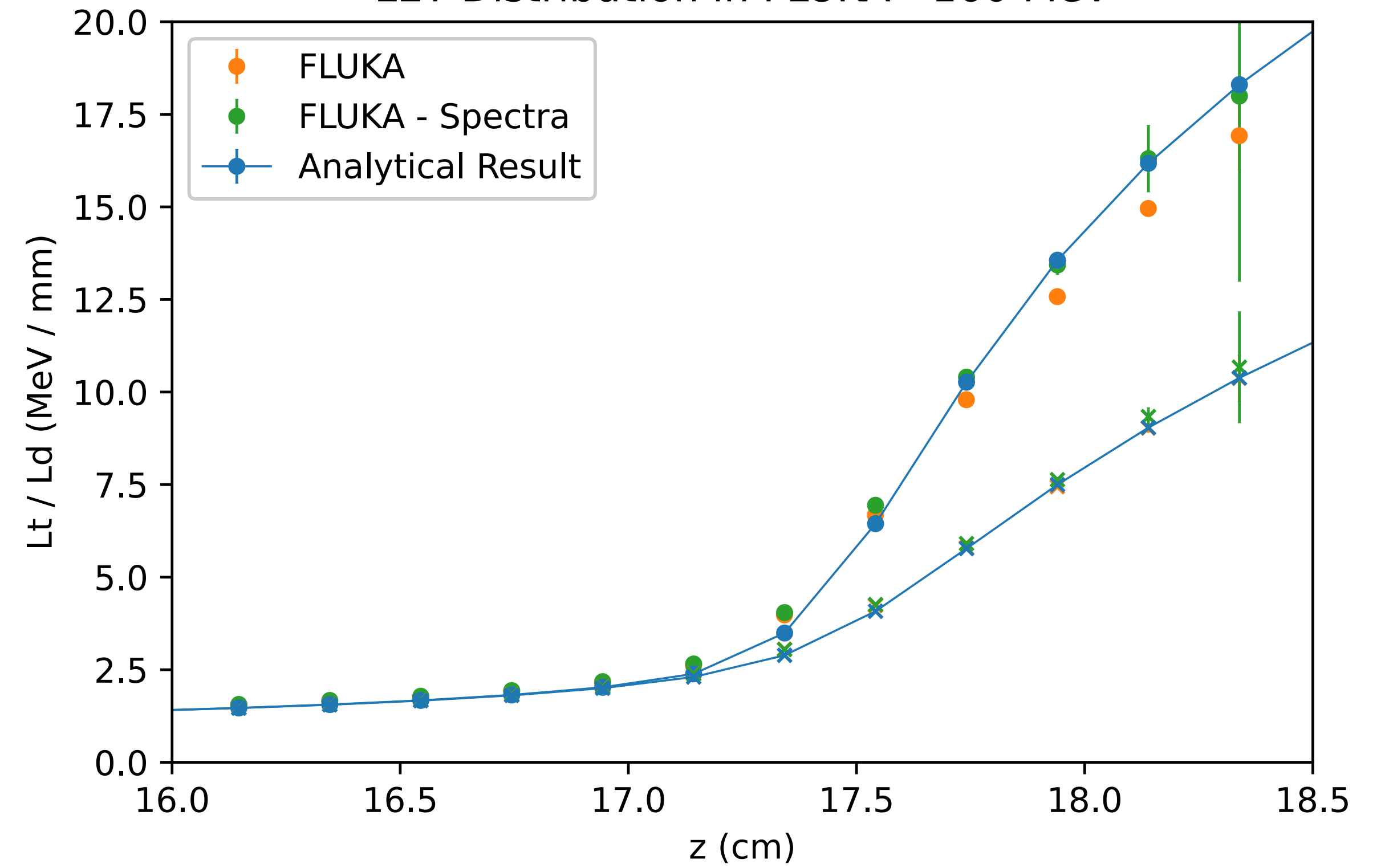


# 160 MeV

LET Distribution in FLUKA - 160 MeV

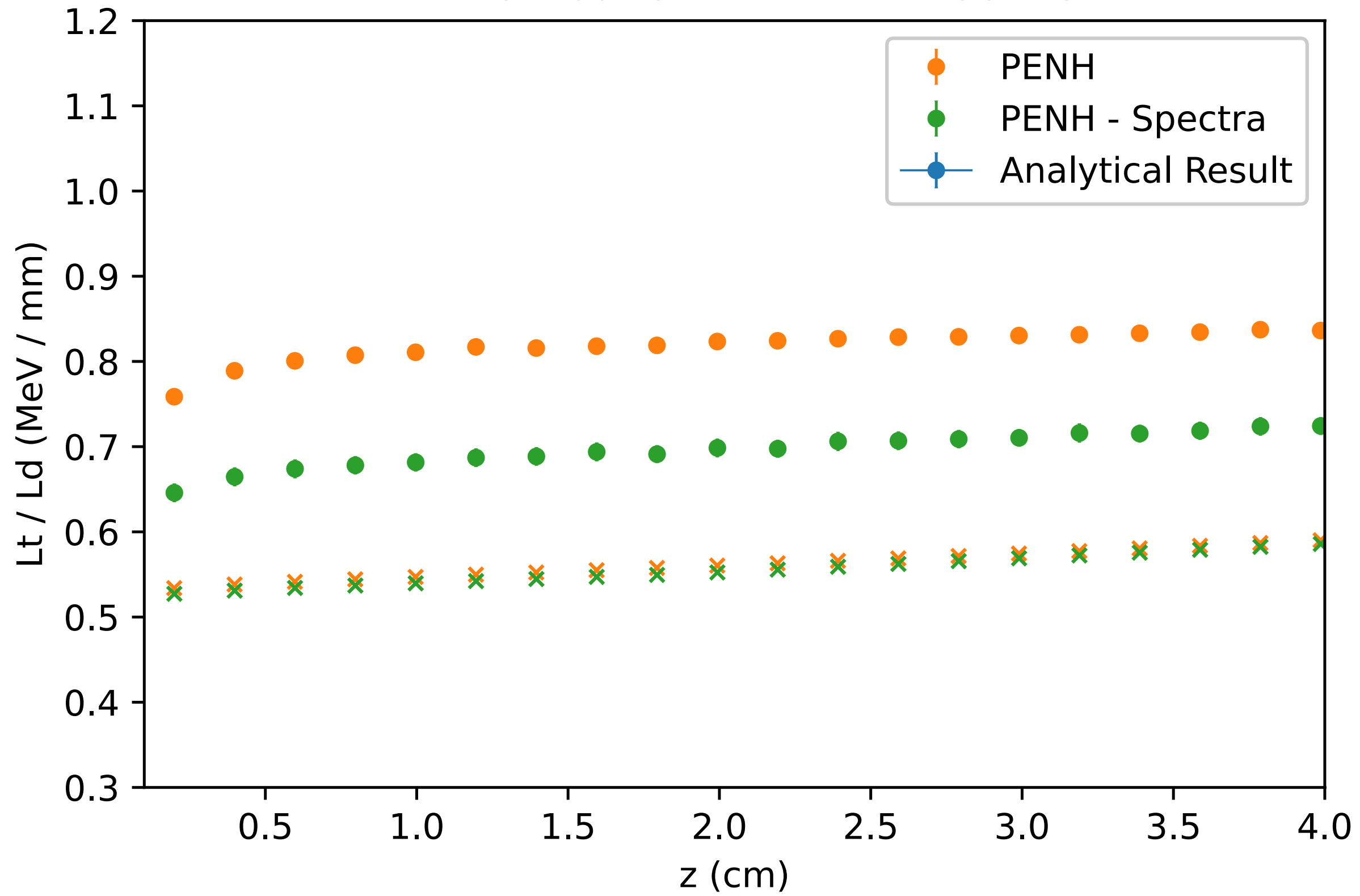


LET Distribution in FLUKA - 160 MeV

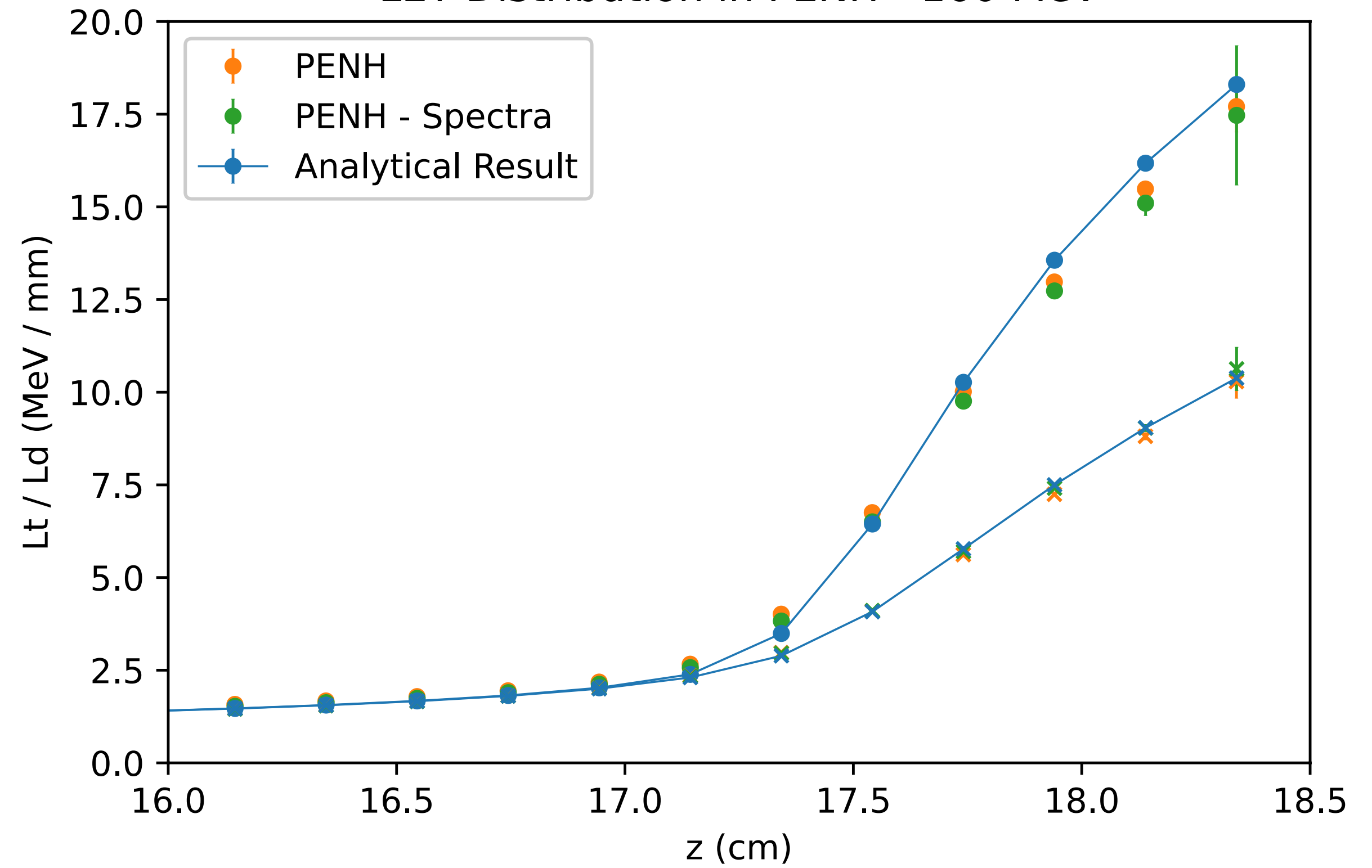


# 160 MeV

LET Distribution in PENH - 160 MeV

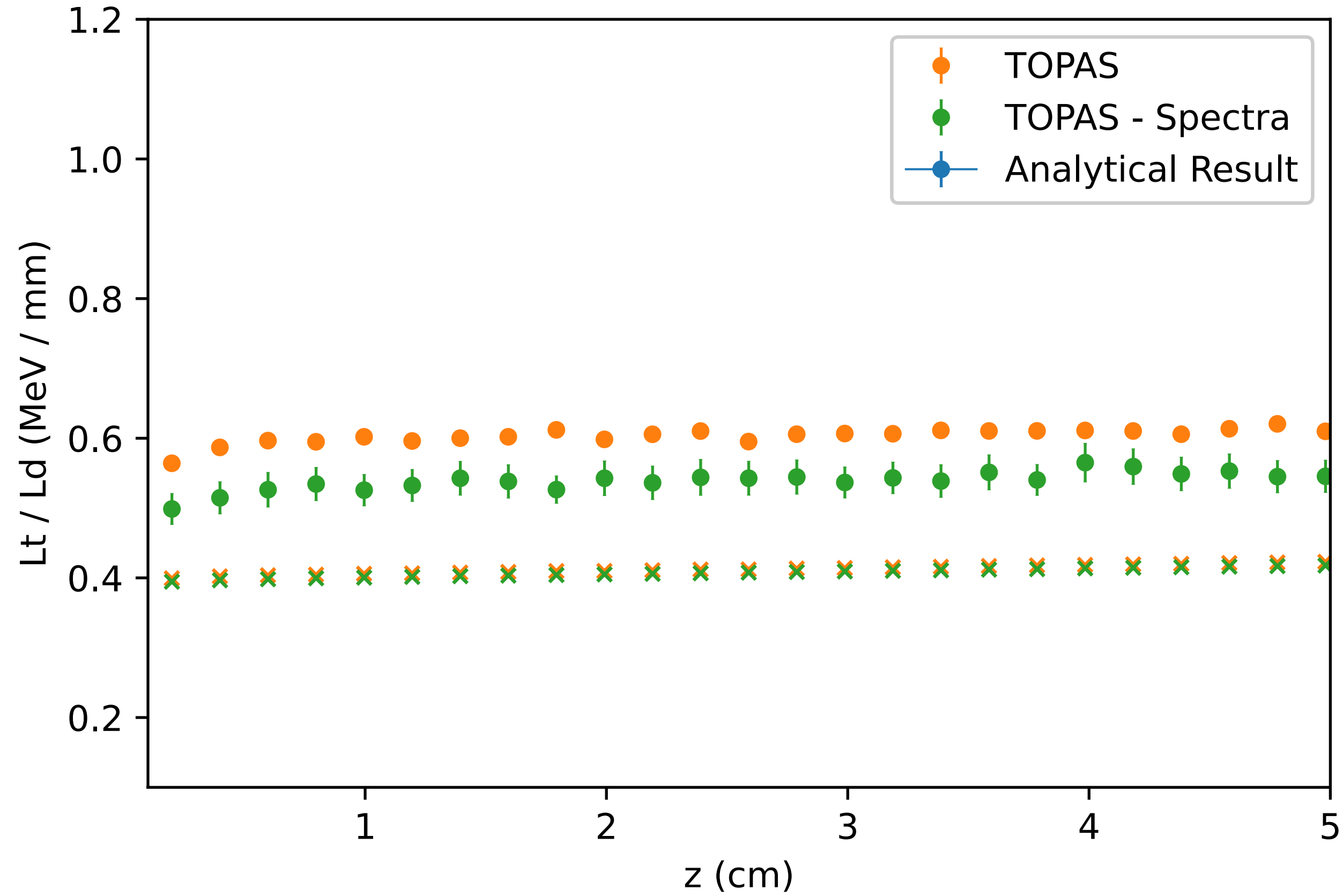


LET Distribution in PENH - 160 MeV

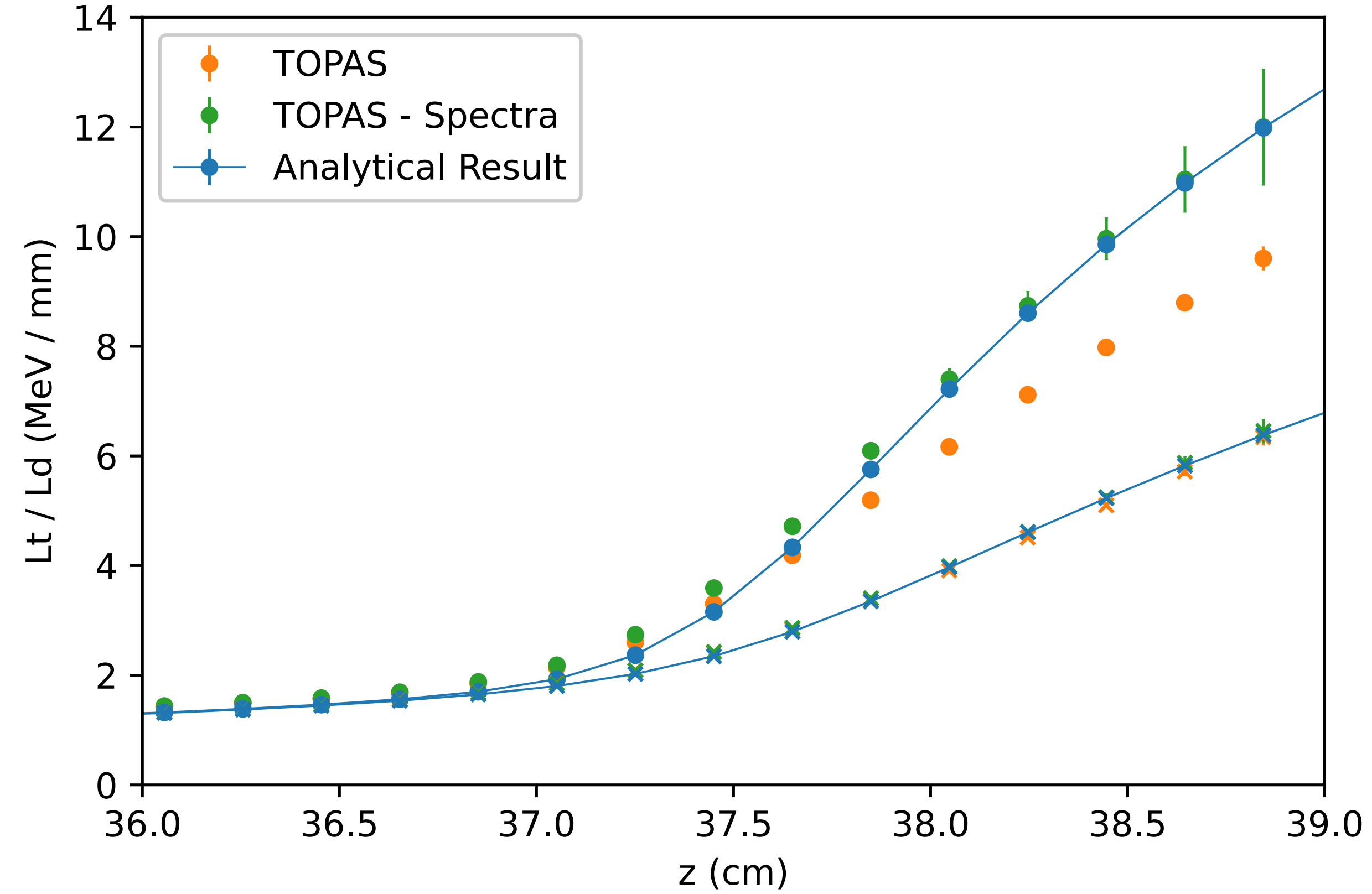


# 250 MeV

LET Distribution in TOPAS - 250 MeV

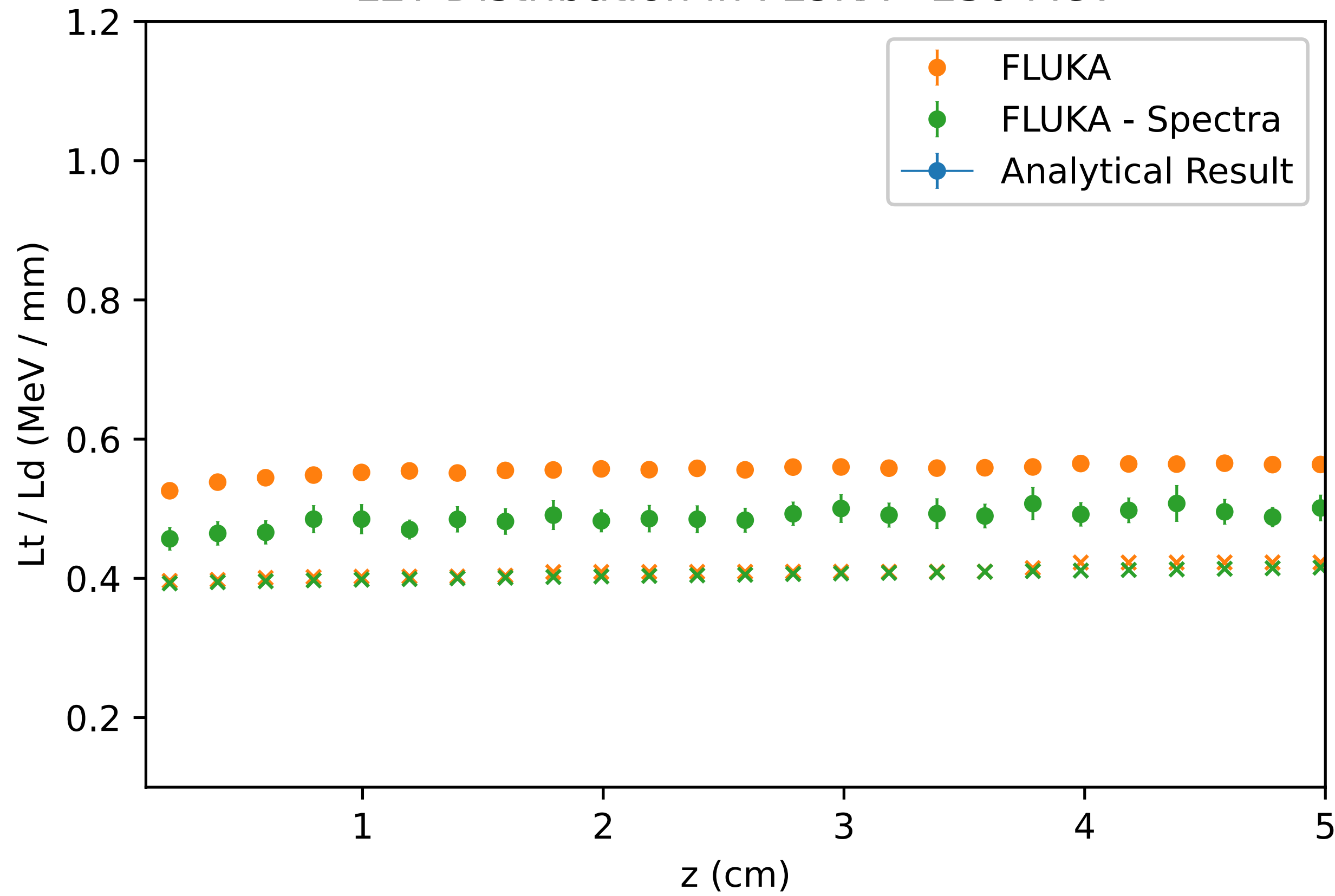


LET Distribution in TOPAS - 250 MeV

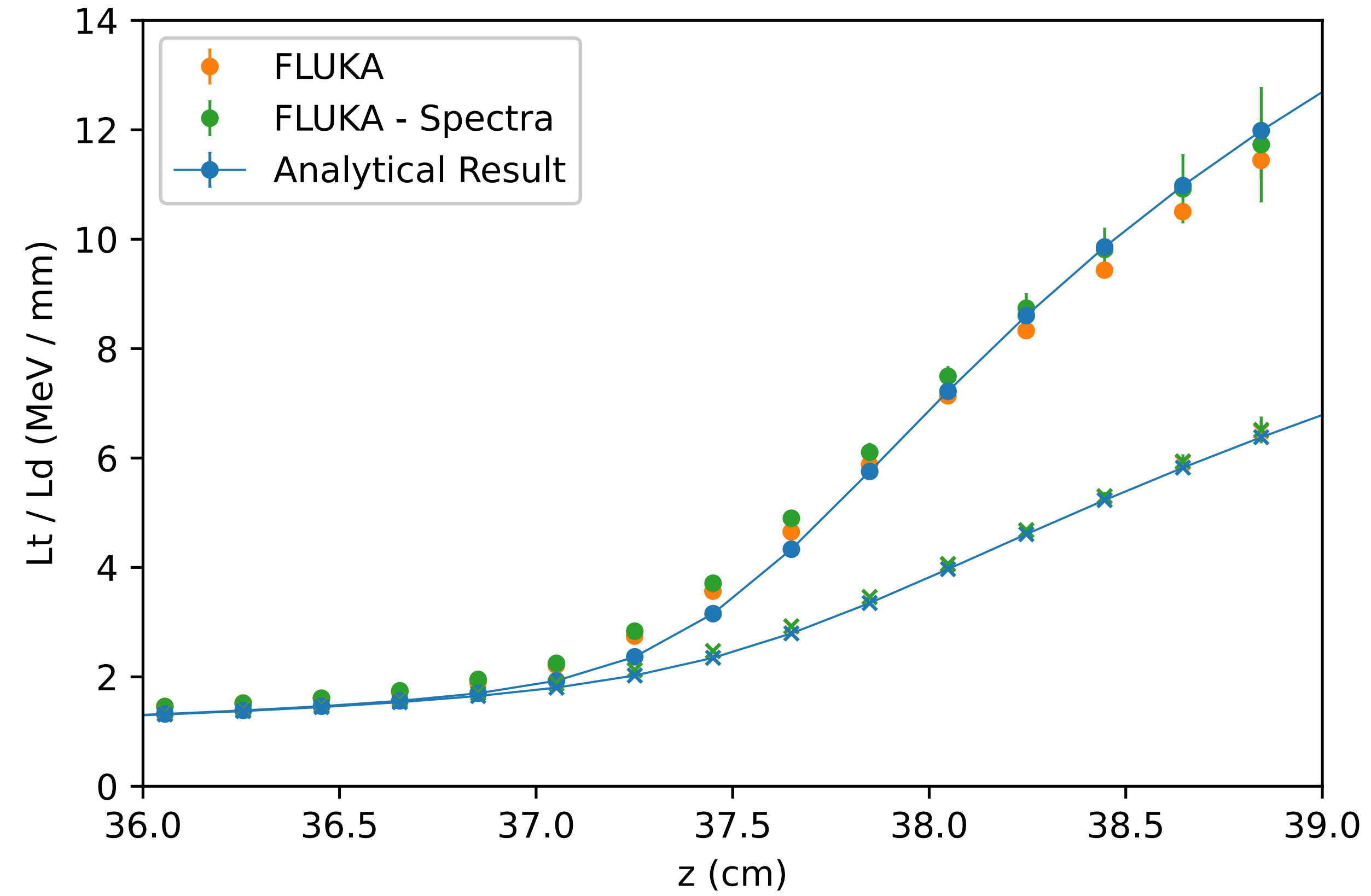


# 250 MeV

LET Distribution in FLUKA - 250 MeV

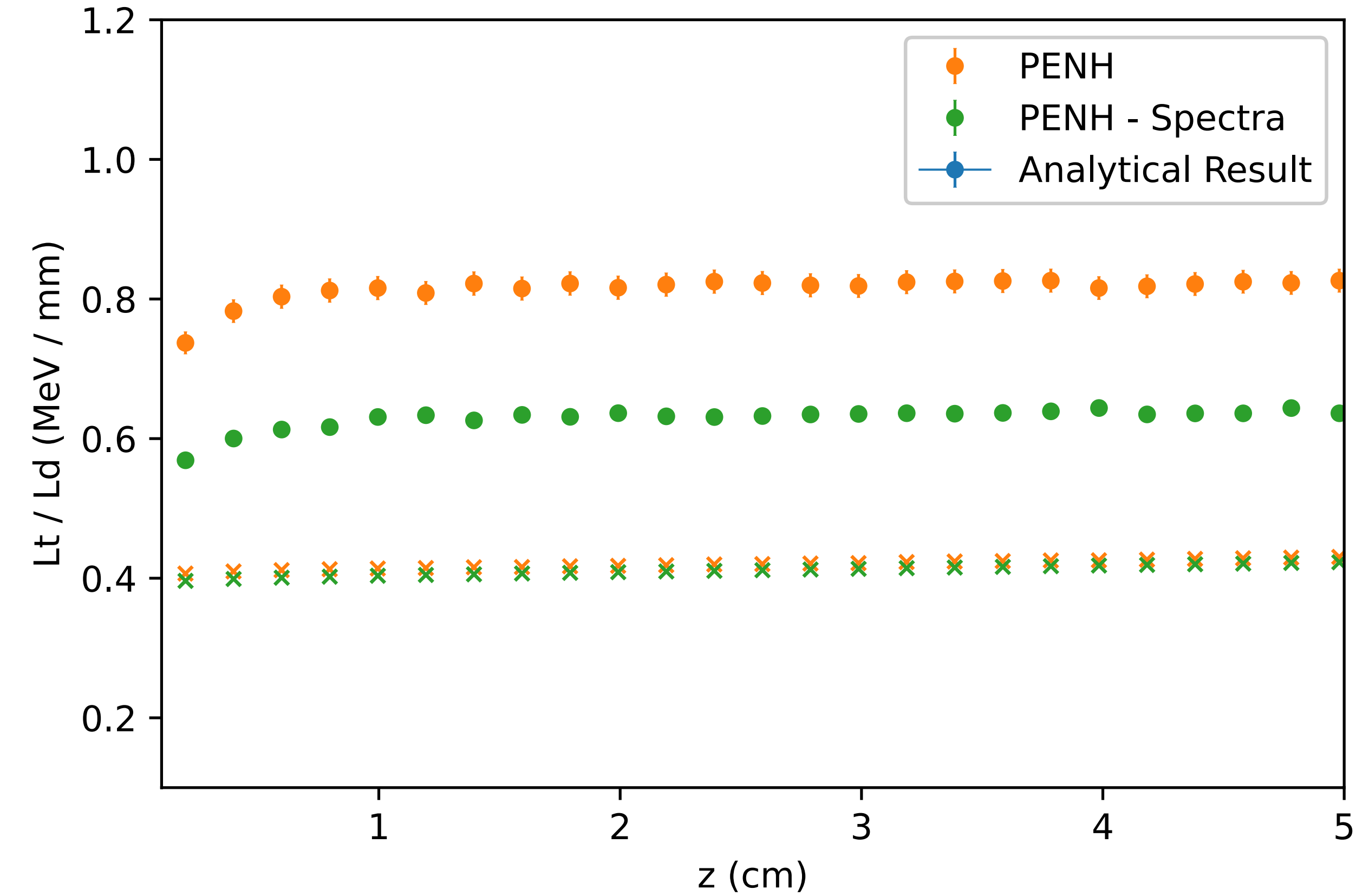


LET Distribution in FLUKA - 250 MeV



# 250 MeV

LET Distribution in PENH - 250 MeV



LET Distribution in PENH - 250 MeV

