ISSUE WITH HADRONIC PHYSICS AIIHP

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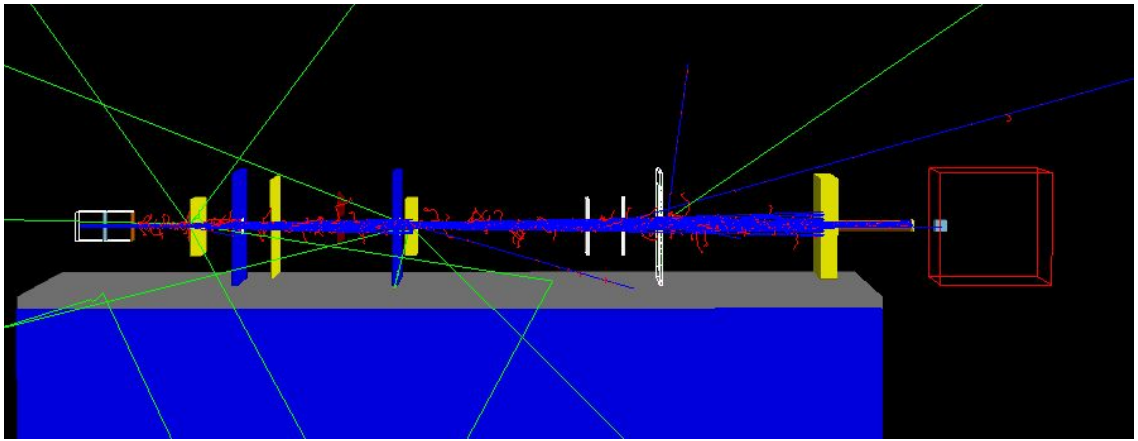
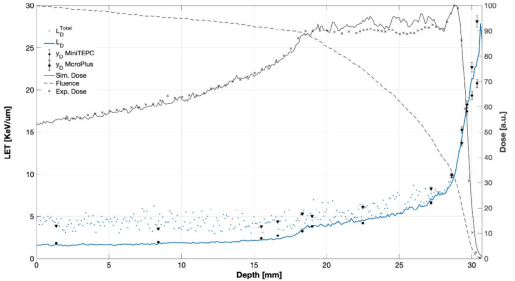
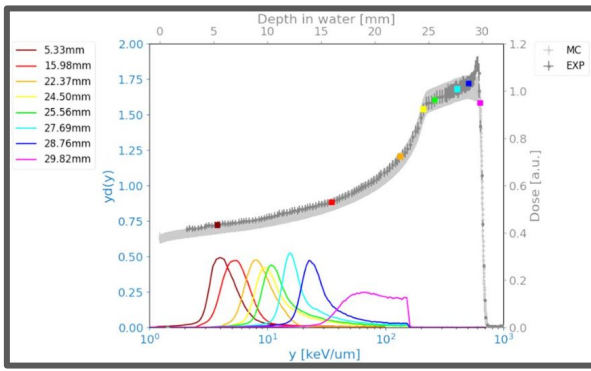
Hadrontherapy advanced example

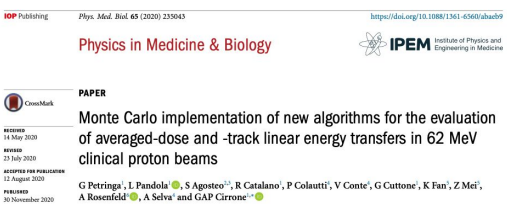


- Dose
- LET
- RBE

Benchmarked several times against experimental data






IOP Publishing Phys. Med. Biol. 65 (2020) 235043 https://doi.org/10.1088/1361-6560/abaeb9

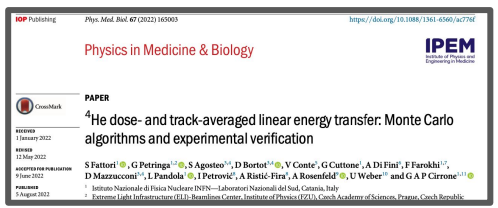
Physics in Medicine & Biology

IPEM Institute of Physics and Engineering in Medicine

PAPER

Monte Carlo implementation of new algorithms for the evaluation of averaged-dose and -track linear energy transfers in 62 MeV clinical proton beams

G Petringa, L Pandola, S Agosteo, R Catalano, P Colautti, V Conte, G Cuttone, K Fan, Z Mei, A Rosenfeld, A Selva and GAP Cirrone


IOP Publishing Phys. Med. Biol. 67 (2022) 165003 https://doi.org/10.1088/1361-6560/ac776f

Physics in Medicine & Biology

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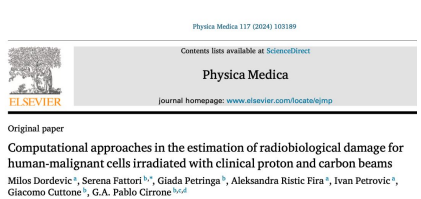
PAPER

^{4}He dose- and track-averaged linear energy transfer: Monte Carlo algorithms and experimental verification

S Fattori, G Petringa, S Agosteo, D Bortot, V Conte, G Cuttone, A Di Fini, F Farokhi, D Mazzucconi, L Pandola, I Petrović, A Ristić-Fira, A Rosenfeld, U Weber and G A P Cirrone


Physica Medica 117 (2024) 103189

Contents lists available at ScienceDirect

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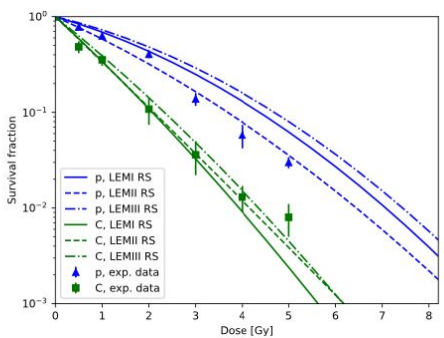
journal homepage: www.elsevier.com/locate/ejmp

Original paper

Computational approaches in the estimation of radiobiological damage for human-malignant cells irradiated with clinical proton and carbon beams

Milos Dordevic, Serena Fattori, Giada Petringa, Aleksandra Ristic Fira, Ivan Petrovic, Giacomo Cuttone, G.A. Pablo Cirrone



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S Fattori et al 2022 Phys. Med. Biol. 67 165003 https://doi.org/10.1088/1361-6560/ac776f

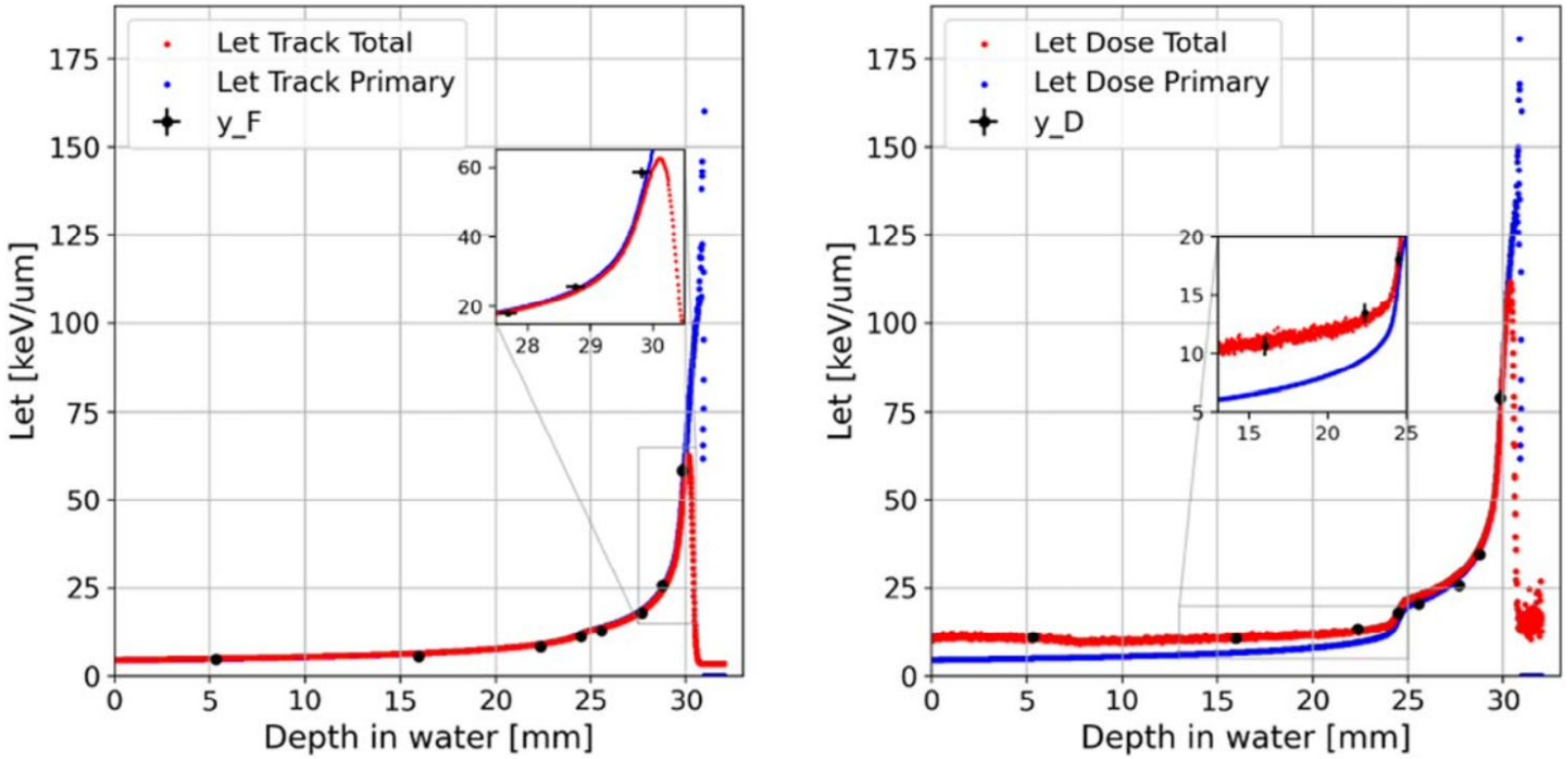

Figure 5. Configuration B: $\bar{y}_F$ values in comparison with the $\bar{L}_t$ values (image on the left), and $\bar{y}_D$ values in comparison with $\bar{L}_d$ values (image on the right): in red $\bar{L}_{t/d}^{Total}$, in blue $\bar{L}_{t/d}$ of the primary, and in black the corresponding microdosimetric quantities $\bar{y}_{F/D}$.

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Hadrontherapy Physics Lists used

HADRONTHERAPY_1

- standard_opt4
- G4DecayPhysics()
- G4RadioactiveDecayPhysics()
- G4IonBinaryCascadePhysics()

- G4EmExtraPhysics()
- G4HadronElasticPhysics**HP**()
- G4StoppingPhysics()
- G4HadronPhysicsQGSP_BIC_**HP**()
- G4NeutronTrackingCut()

HADRONTHERAPY_2

- standard_opt4
- G4DecayPhysics()
- G4RadioactiveDecayPhysics()
- G4IonBinaryCascadePhysics()

- G4EmExtraPhysics()
- G4HadronElasticPhysics()
- G4StoppingPhysics()
- G4HadronPhysicsQGSP_BIC()
- G4NeutronTrackingCut()

HADRONTHERAPY_3

- standard_opt4
- G4DecayPhysics()
- G4RadioactiveDecayPhysics()
- G4IonElasticPhysics()
- **G4IonPhysicsPHP()**
- G4EmExtraPhysics()
- **G4HadronElasticPhysicsHP()**
- G4StoppingPhysics()
- **G4HadronPhysicsQGSP_BIC_AllHP()**
- G4NeutronTrackingCut()

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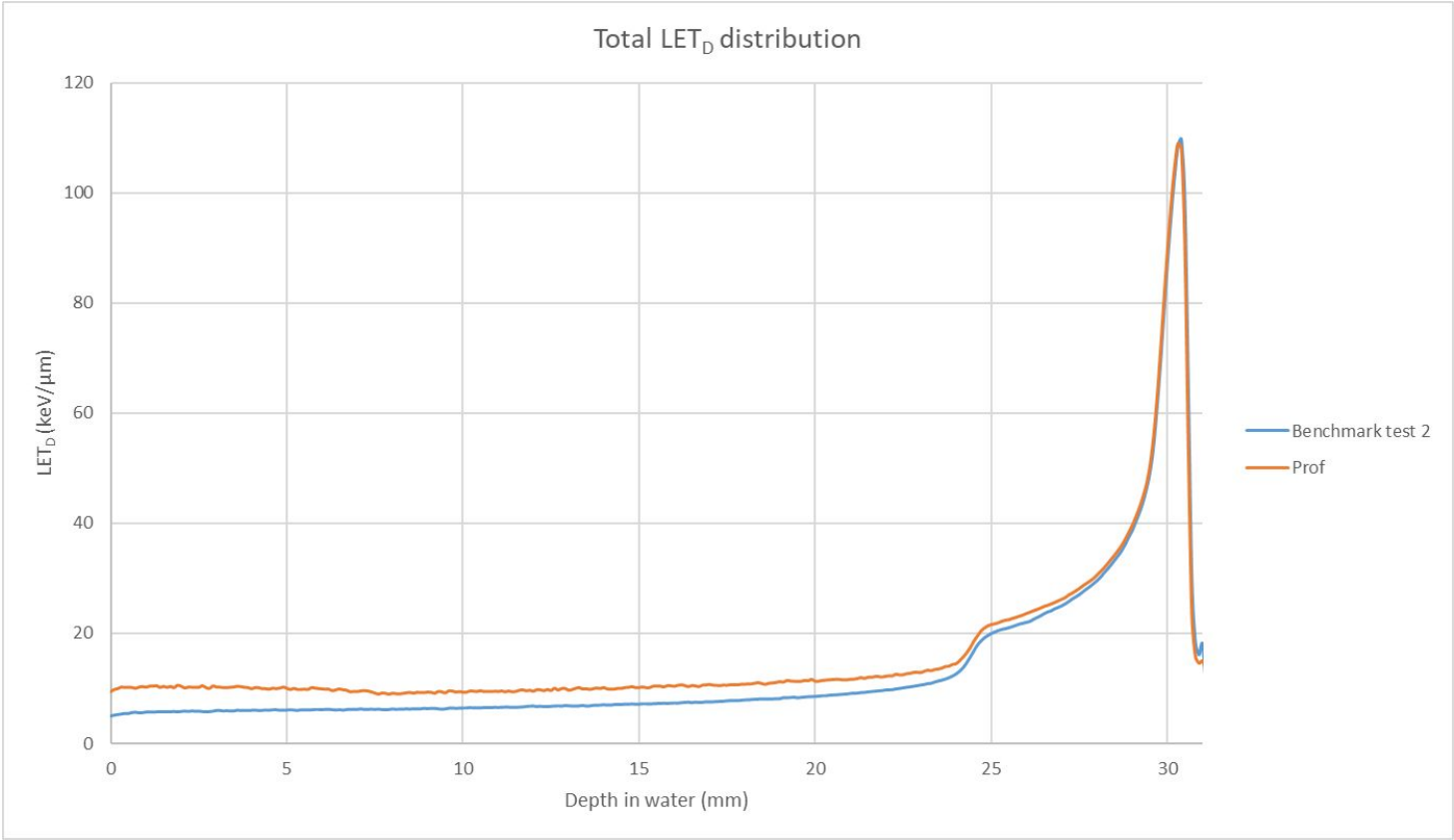
Comparison of Let_dose total

- Master Thesis on Geant4 code development
- Geant4 **11.2.1**
- Benchmark activity of comparison with results of **10.6.2**



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SEQUENCE OF TESTS:

1. LET_dose total was reproducing experimental data in version 10.6.2 with AllHP
   https://doi.org/10.1088/1361-6560/ac776f

2. We noticed LET_dose total with AllHP totally changed in version 11.2.1. The problem does NOT involve:
   - LET_dose of the primary (tested with He4)
   - LET_track total and of the primary

3. TENDL table (1.3.2 in 10.6.2 and 1.4 in 11.2.0) were exchanged (used 1.3.2 with 11.2.1) but the problem remained → **the issue is not caused by the change in the TENDL data tables**

4. Several hadrontherapy versions were compiled and run with their corresponding version of geant4 to identify when the change started to show up:
   - until version **11.1.3 of 10 Nov 2023 it was OK**
   - from version **11.2.0 of 08 Dec 2023 the problem started**

5. Hadrontherpy downloaded from version 11.1.3 was compiled and run with geant4 version 11.2.0: the result is **NOT OK** → **the issue is not inside the example**

6. Also the versions subsequent to 11.2.1 were tested to verify the issue was not solved in the newest releases:
   - 11.2.2: the problem is still there
   - 11.3.0.beta: the problem is still there

7. Hadrontherapy from 11.3.0.beta was compiled with geant4 **11.3.0.beta** and was run with **another hadronic physics model** and the result was compatible with that one of versions from 11.1.3 and older and so **OK**

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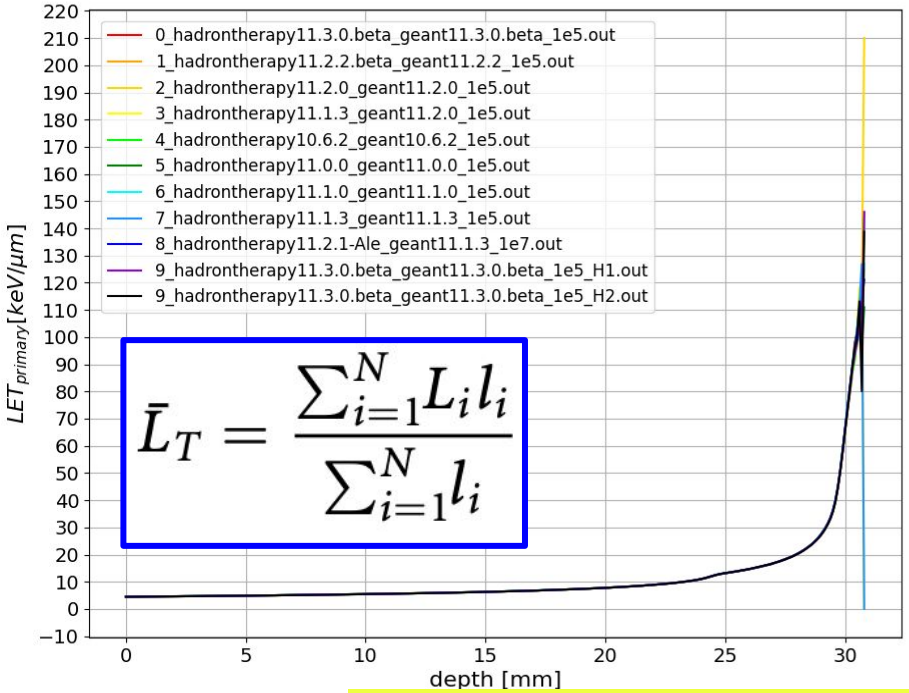
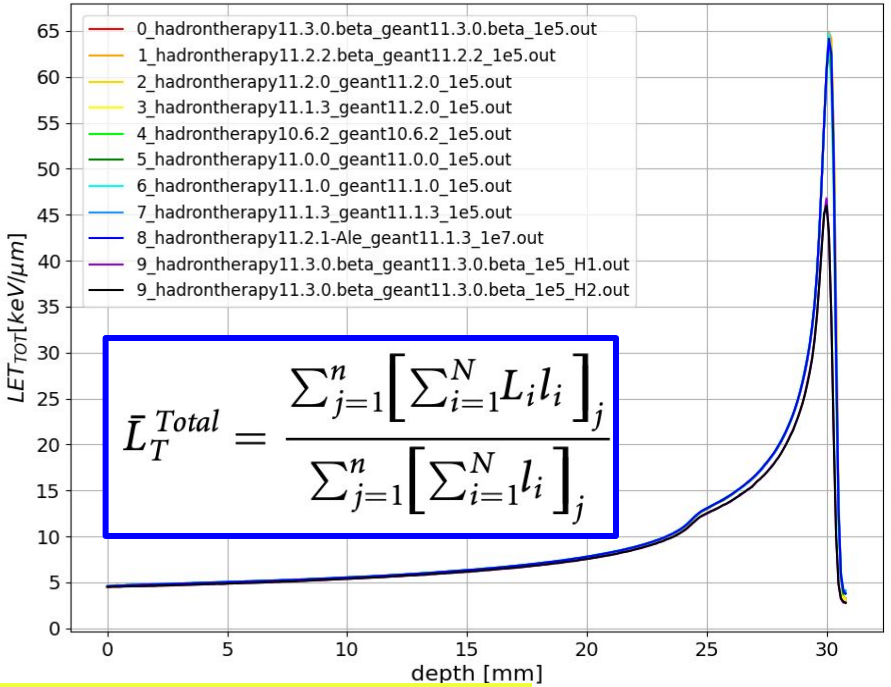
LET_track: track-averaged Electronic Stopping Power:

- **Li** is the tabulated electronic stopping power at a given energy in the given medium, directly retrieved from Monte Carlo;
- **li** is the the track length of the particle in the given volume;
- The index **i** runs over the total number of steps N carried out by the particle in the volume considered;
- The index **j** runs over all the particles travelling in that volume, including the secondary ions

LET_{TRACK}





As mentioned the issue does **not affect the LET_track**

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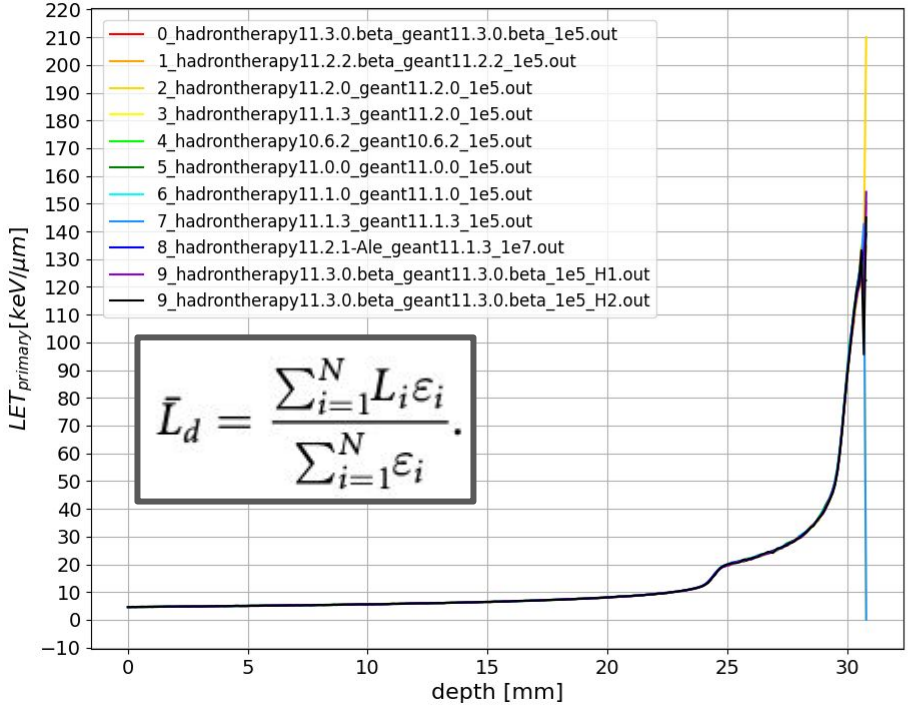
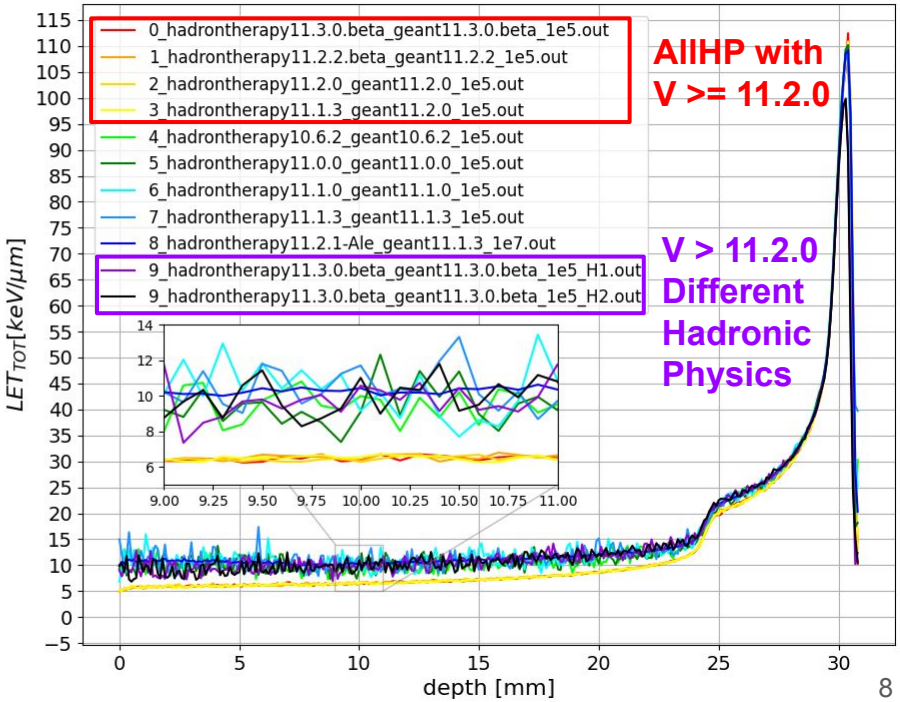
LET_dose: dose-averaged Electronic Stopping Power: ε is the energy loss of the particle in the given volume

Another evident anomaly, beside the absolute value, is represented by the **statistical fluctuations**: all versions are run with a 10^5 histories and results are expected to be very noisy for LET_dose total, and so it is for versions before 11.2.0, while for the subsequent versions (**red**, **orange**, **gold** and yellow curves) the **fluctuations are unbelievably tiny**, **comparable with** statistics of the order of 10^7 histories (run represented with **blue** curve)

LET_{DOSE}





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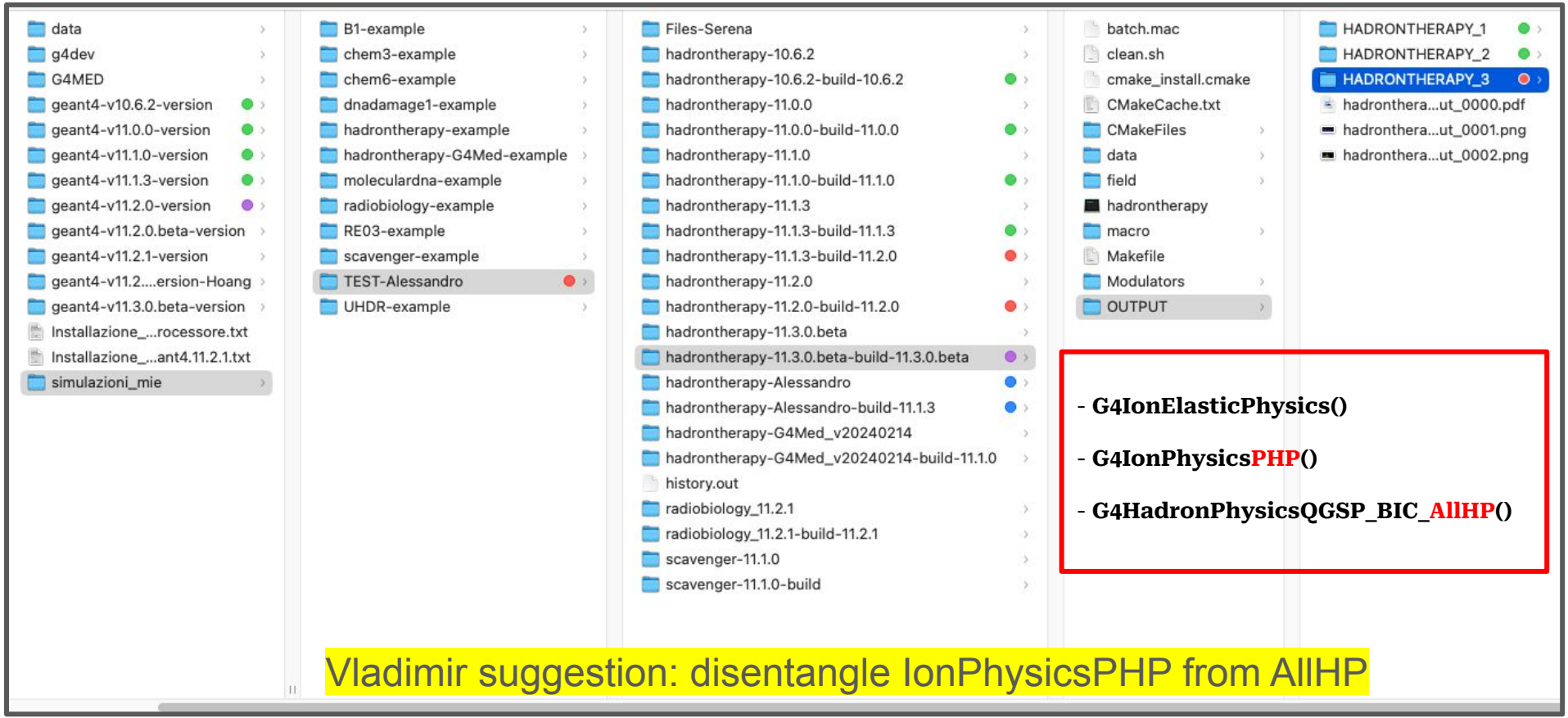
Summary (before CM in Catania)



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```
// SF ************************************************************
else if (name == "HADRONTHERAPY_3") {
        // HP models are switched ON
        AddPhysicsList("standard_opt4");
        hadronPhys.push_back( new G4DecayPhysics());
        hadronPhys.push_back( new G4RadioactiveDecayPhysics());

        // ION PHYSICS************************************
        hadronPhys.push_back(new G4IonElasticPhysics());            // <---------
        hadronPhys.push_back( new G4IonPhysicsPHP());               // <---------
        // ************************************************

        hadronPhys.push_back( new G4EmExtraPhysics());
        hadronPhys.push_back( new G4HadronElasticPhysicsHP());
        hadronPhys.push_back( new G4StoppingPhysics());
        hadronPhys.push_back( new G4HadronPhysicsQGSP_BIC_AllHP());//<---------
        hadronPhys.push_back( new G4NeutronTrackingCut());

    G4cout << "HADRONTHERAPY_3 PHYSICS LIST has been activated" << G4endl;    }
```

```
else if (name == "HADRONTHERAPY_4") {
        // HP models are switched ON
        AddPhysicsList("standard_opt4");
        hadronPhys.push_back( new G4DecayPhysics());
        hadronPhys.push_back( new G4RadioactiveDecayPhysics());

        hadronPhys.push_back( new G4IonBinaryCascadePhysics());     //<---------

        hadronPhys.push_back( new G4EmExtraPhysics());
        hadronPhys.push_back( new G4HadronElasticPhysicsHP());
        hadronPhys.push_back( new G4StoppingPhysics());
        hadronPhys.push_back( new G4HadronPhysicsQGSP_BIC_AllHP());  //<---------
        hadronPhys.push_back( new G4NeutronTrackingCut());

    G4cout << "HADRONTHERAPY_4 PHYSICS LIST has been activated" << G4endl;    }
```

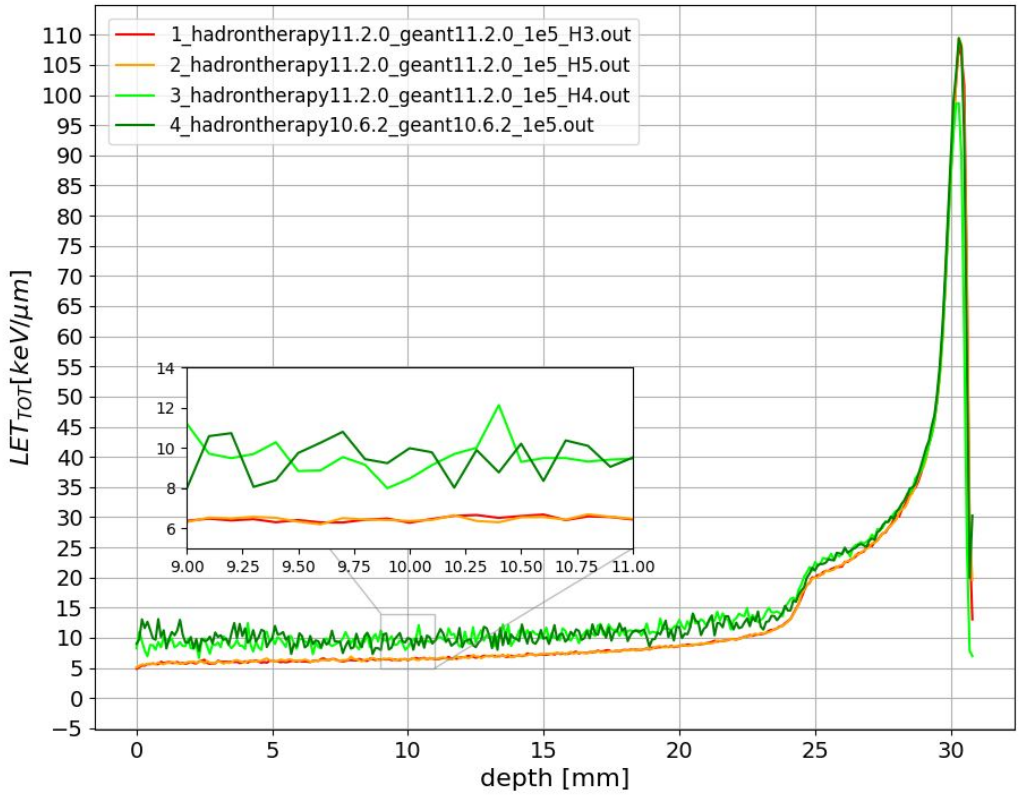
```
else if (name == "HADRONTHERAPY_5") {
        // HP models are switched ON
        AddPhysicsList("standard_opt4");
        hadronPhys.push_back( new G4DecayPhysics());
        hadronPhys.push_back( new G4RadioactiveDecayPhysics());

        // ION PHYSICS************************************
        hadronPhys.push_back(new G4IonElasticPhysics());            // <---------
        hadronPhys.push_back( new G4IonPhysicsPHP());               // <---------
        // ************************************************

        hadronPhys.push_back( new G4EmExtraPhysics());
        hadronPhys.push_back( new G4HadronElasticPhysicsHP());
        hadronPhys.push_back( new G4StoppingPhysics());
        hadronPhys.push_back( new G4HadronPhysicsQGSP_BIC_HP());     //<---------
        hadronPhys.push_back( new G4NeutronTrackingCut());

    G4cout << "HADRONTHERAPY_5 PHYSICS LIST has been activated" << G4endl;    }
```

Check for HP of protons and ions



The problem is with HP of ions

Additional Tests suggested from Alberto e Vladimir:

1. There is a change concerning the **EM ionization of ions**
   (replacing _G4IonParametrisedLossModel_ with _G4LindhardSorensenIonModel_)
   which occurred between G4 11.1 and 11.2, which would be worth to check:
   In G4EmStandardPhysics_option4 → G4EmStandardPhysics_option4::ConstructProcess()
   *// generic ion_*
   _ particle = G4GenericIon::GenericIon();_
   _ G4ionIonisation ionIoni = new G4ionIonisation();_*
   _ __ //__ionIoni->SetEmModel(new __G4LindhardSorensenIonModel()__) // 11.2._
   → (new __G4IonParametrisedLossModel()__) // 11.1._

2. In the current **ParticleHP** code in **several places** there is a **check if energy below 20 MeV**.
   This may mean that there is no nuclear fragmentation for alpha particles between 20 and 200 MeV.
   The cross section exists but no final state is produced.
   Edit G4IonPhysicsPHP.cc lines 99, 100:
   const G4double maxPHP = ***200.0*MeV*** → ***20.0*MeV***
   const G4double overlapPHP_BIC = ***10.0*MeV*** → ***2.0*MeV***

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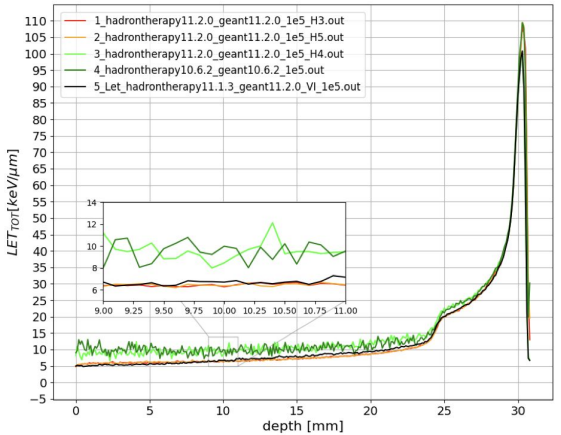
Results of those additional Tests:

1. I have found that:
   - version 11.0.0 uses G4IonParametrisedLossModel
   - version 11.2.0 uses G4LindhardSorensenIonModel
   - BUT versions **11.1.0** --> **11.1.3** **already use G4LindhardSorensenIonModel**

   And since by compiling the hadrontherapy example with 11.1.0 and 11.1.3 I did not encounter the issue, I think the G4LindhardSorensenIonModel is not causing the problem.

2. I tried the suggested change in G4IonPhysicsPHP.cc lines 99, 100:
   const G4double maxPHP = ***200.0*MeV → 20.0*MeV***
   const G4double overlapPHP_BIC = ***10.0*MeV → 2.0*MeV***
   and recompiled Geant4.
   Unfortunately, the change did not impact the result
   i.e. it did not solve the issue :(
   Just to remember: in this LET curve it is considered:
   - a ***wrong*** *result when this curve is low at the entrance, i.e.* ***5 keV/um****, and* ***no noisy***
   - a high, ***10 keV/um****,* ***noisy*** *curve at the entrance is* ***OK***



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@Today:

Discussing with Alberto and Vladimir, to who I sent a file of the std output of this last simulation, they noticed plenty of warnings about duplication of the Decay process, such as:

```
-------- WWWW ------- G4Exception-START -------- WWWW -------
*** G4Exception : Run0111
      issued by : G4PhysicsListHelper::RegisterProcess
Duplication of processes
*** This is just a warning message. ***
-------- WWWW -------- G4Exception-END --------- WWWW -------

G4PhysicsListHelper::RegisterProcess :Decay for xi(2030)0 with  type/
subtype =6/201  is has same subType as Decay for xi(2030)0
It will not be added !!

-------- WWWW ------- G4Exception-START -------- WWWW -------
*** G4Exception : Run0111
      issued by : G4PhysicsListHelper::RegisterProcess
Duplication of processes
*** This is just a warning message. ***
-------- WWWW -------- G4Exception-END --------- WWWW -------

G4PhysicsListHelper::RegisterProcess :Decay for xi- with  type/subtype
=6/201  is has same subType as Decay for xi-
It will not be added !!
```

And they are wondering if I have seen similar warnings also for **G4 11.1.3**,
i.e. when the results are good and reasonable:
CHECK THE LOG FILE IN THIS CASE

M

1. Are you using the hydrotherapy example "out-of-the-box", or do you use something slightly different?
   If we compile hadrontherapy advance example using the current master G4 and run the default macro hadrontherapy.in will it work out of the box or **we need to add extra environment variables an do other manipulations**?

2. **What macro give a problem**, **what macro (if exist) work properly**?

And also about "**full analysis**"

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@Today:

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UNDER CONSTRUCTION

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@Today:

1. Ok it is true: the example is the one released BUT with these additions:
   In the “HadrontherapyPhysicsList” Class must be added the Physics List “cocktail” →
   That produces the issue

```
else if (name == "HADRONTHERAPY_5") {
        // HP models are switched ON
        AddPhysicsList("standard_opt4");
        hadronPhys.push_back( new G4DecayPhysics());
        hadronPhys.push_back( new G4RadioactiveDecayPhysics());

        // ION PHYSICS**********************************
        hadronPhys.push_back(new G4IonElasticPhysics());            // <---------
        hadronPhys.push_back( new G4IonPhysicsPHP());               // <---------
        // *********************************************

        hadronPhys.push_back( new G4EmExtraPhysics());
        hadronPhys.push_back( new G4HadronElasticPhysicsHP());
        hadronPhys.push_back( new G4StoppingPhysics());
        hadronPhys.push_back( new G4HadronPhysicsQGSP_BIC_HP());    //<---------
        hadronPhys.push_back( new G4NeutronTrackingCut());

    G4cout << "HADRONTHERAPY_5 PHYSICS LIST has been activated" << G4endl;    }
```

2. The macro to be use is “**carbon_beamline.mac**”.
   To reproduce the issue: /Physics/addPhysics HADRONTHERAPY_1 → /Physics/addPhysics **HADRONTHERAPY_5**
   Macro **working properly**: the same one with **/Physics/addPhysics HADRONTHERAPY_1**

   Additional information about this macro:

   - In the released version it shoots by default carbon ions:
     /gps/ion 6 12 6
     /gps/ene/mono 744 MeV
     /gps/ene/sigma 0.740 MeV

   - In my study I was using He4:
     /gps/ion 2 4 2
     /gps/ene/mono 247.7 MeV
     /gps/ene/sigma 0.248 MeV

   Moreover:
   - I have just noticed comparing the release macro and mine, that in the released one there is, in addition, this command:
     # Set a very high time threshold to allow all decays to happen
     /process/had/rdm/thresholdForVeryLongDecayTime 1.0e+60 year

     - In my macro I added the commands to produce the LET output:
     /analysis/secondary true
     /analysis/computeLet

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@Today:

About “**full analysis**”: not really necessary. It is quite simple to spot the issue by looking at the LDT column, first ~100 rows, in the Let.out file

Let_hadrontherapy11.2.0_geant11.2.0_1e5_H4.out

```
  1 i    j    k    LDT LTT proton_D    proton_T    deuteron_D  deuteron_T
         triton_D    triton_T    He3_D    He3_T    alpha_1_D   alpha_1_T   alpha_D
         alpha_T He5_D    He5_T    He6_D    He6_T    Li6_D    Li6_T    Li7_D    Li7_T
         Li8_D    Li8_T    Li9_D    Li9_T    Be6_D    Be6_T    Be7_D    Be7_T    Be9_D
         Be9_T    Be10_D   Be10_T   B8_D     B8_T     B10_D    B10_T    B11_D    B11_T
         B12_D    B12_T    B14_D    B14_T    C10_D    C10_T    C11_D    C11_T    C12_D
         C12_T    C13_D    C13_T    C14_D    C14_T    C15_D    C15_T    N12_D    N12_T
         N13_D    N13_T    N14_D    N14_T    N15_D    N15_T    N16_D    N16_T    N17_D
         N17_T    O14_D    O14_T    O15_D    O15_T    O16_D    O16_T    O17_D    O17_T
         O18_D    O18_T    O19_D    O19_T    F17_D    F17_T    F18_D    F18_T    F19_D
         F19_T    Ne18_D   Ne18_T   Ne19_D   Ne19_T   Ne20_D   Ne20_T
  2 0    0    0    8.23741 4.50817 11.6799 4.37139 16.5101 4.93918 24.9548 4.71565
         4.59521 4.57891 4.67967 4.47441 110.352 60.7016 0    0    0    0    142.304
         116.472 94.2035 93.3802 0    0    0    0    0    0    0    0    0    0
         0    0    0    0    418.361 393.38  0    0    0    0    0    0    594.2   558.604
         565.283 534.62  0    0    492.485 469.003 0    0    0    0    0    0    671.006
         624.45  754.355 686.153 0    0    0    0    0    0    831.35  739.863 815.572
         505.15  0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0
  3 1    0    0    11.0195 4.53155 10.7848 4.46688 13.7583 4.40238 23.7719 4.90676
         60.4555 11.3236 4.65807 4.47968 111.814 51.1462 0    0    0    0    113.577
         110.618 167.847 156.868 199.198 193.64  0    0    0    0    0    0    0
         0    0    0    0    0    0    346.924 329.02  0    0    0    0    0    555.129
         502.752 603.742 535.732 503.291 478.594 0    0    0    0    0    0    558.901
         533.103 663.754 616.757 847.417 678.719 696.061 650.562 856.242 698.215
         0    0    188.855 188.855 767.216 602.824 0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    0
  4 2    0    0    9.41401 4.52301 10.6261 4.58082 16.2109 4.25112 5.18518 1.76225
         68.8212 13.1721 4.58468 4.48407 98.5844 49.2256 0    0    0    0    187.977
         178.194 1.99763 1.99763 0    0    0    0    0    0    387.451 322.444 0    0
         0    0    0    0    0    0    408.74  389.303 0    0    0    0    0    0    0
         533.426 481.99  3.25755 3.25755 0    0    0    0    0    0    291.665 261.329
         676.68  612.152 747.321 670.719 0    0    0    0    0    0    899.117 743.587
         867.87  724.965 0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0
  5 3    0    0    7.91562 4.51967 11.1852 4.8485  14.4162 3.81702 6.25837 2.12282
         28.8875 5.70937 4.59797 4.49121 112.473 38.8016 0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    0    0    0    0    0
```

3 characters

Let_hadrontherapy11.2.0_geant11.2.0_1e5_H5.out

```
  1 i    j    k    LDT LTT proton_D    proton_T    deuteron_D  deuteron_T  triton_D
         triton_T    alpha_D alpha_T alpha_1_D   alpha_1_T   Li6_D    Li6_T    Li7_D    Li7_T
         Be9_D    Be9_T    B10_D    B10_T    B11_D    B11_T    C11_D    C11_T    C12_D    C12_T
         C13_D    C13_T    C14_D    C14_T    N14_D    N14_T    N15_D    N15_T    N16_D    N16_T
         O15_D    O15_T    O16_D    O16_T    O17_D    O17_T    O18_D    O18_T    F17_D    F17_T
  2 0    0    0    5.1009  4.50188 15.5833 7.36291 13.2879 7.29504 0    0    72.8336 43.7909
         4.612   4.47194 0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    436.54  316.132 0    0    0    0    0
  3 1    0    0    5.32964 4.53103 13.9702 6.97955 15.832  8.212   0    0    69.8231 41.5382
         4.60091 4.47846 0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    384.601 306.043 0    0    0    0    0
  4 2    0    0    5.57632 4.54784 14.0726 7.05694 17.4454 7.67148 0    0    78.404  47.8962
         4.61104 4.48501 0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    447.562 301.513 0    0    0    0    0
  5 3    0    0    5.53638 4.55347 12.791  6.77537 15.5399 7.73611 0    0    73.6965 42.0198
         4.58235 4.4917  0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    550.451 360.75  0    0    0    0    0
  6 4    0    0    5.684   4.56175 11.9756 6.17905 16.5062 7.51051 0    0    62.0862 37.7959
         4.64107 4.50045 0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    806.333 483.976 0    0    0    0    0
  7 5    0    0    5.73293 4.5823  12.0719 6.00799 16.0831 7.08271 0    0    73.0941 42.2392
         4.64017 4.50727 0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    305.769 242.574 0    0    0    0    0
  8 6    0    0    5.62449 4.58444 11.5423 6.01997 13.1323 6.63164 0    0    67.9962 39.2669
         4.67884 4.5156  0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    376.708 289.014 0    0    0    0    0
  9 7    0    0    5.68774 4.59634 11.7561 5.99654 16.0103 7.57143 0    0    63.0288 36.5315
         4.66765 4.52216 0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    571.079 355.72  0    0    0    0    0
 10 8    0    0    5.87899 4.61222 11.9487 5.81734 18.0307 7.92337 0    0    71.076  39.9702
         4.68177 4.52798 0    0    0    0    0    0    0    0    0    0    0    0    615.331 498.637 0
         0    0    0    0    0    0    0    0    0    0    0    371.908 309.894 0    0    0    0    0
 11 9    0    0    5.70403 4.61149 12.7617 6.01535 12.2227 6.72528 0    0    71.7443 39.048
         4.60203 4.53287 0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    365.137 283.961 0    0    0    0    0
 12 10   0    0    5.60451 4.61141 11.0845 5.4366  15.421  7.49523 0    0    59.8955 34.0967
         4.62649 4.5412  0    0    0    0    0    0    0    0    0    0    0    0    0    0
         0    0    0    0    0    0    0    0    0    632.504 421.873 0    0    215.916 215.916 0    0
```

3 characters

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