

# Design optimization of a Digital Tracking Calorimeter for proton CT purposes

---

H. E. S. Pettersen<sup>1,2\*</sup>, I. Meric<sup>3</sup>, O. H. Odland<sup>1</sup>, J. R. Sølve<sup>3</sup>, D. Röhrich<sup>2</sup>

<sup>a</sup>*Department of Oncology and Medical Physics, Haukeland University Hospital, Norway*

<sup>b</sup>*Department of Physics and Technology, University of Bergen, Norway*

<sup>d</sup>*Department of Electrical Engineering, Western Norway University of Applied Sciences, Norway*

\*Corresponding author: [helge.pettersen@helse-bergen.no](mailto:helge.pettersen@helse-bergen.no)

INSERT PAGE BREAK HERE

## Abstract

Max 300 ord

## 1 Introduction

This should be concise and describe the nature of the problem under investigation and its background. It should also set your work in the context of previous research, citing relevant references. Introductions should expand on highly specialised terms and abbreviations used in the article to make it accessible for readers.

This introductory text is copied directly from the PTCOG poster abstract, and should be revised.

The Bergen Proton CT group has for a time been working with benchmarking a proof-of-concept Digital Tracking Calorimeter (DTC) assembly for use as a tracking calorimeter in a proton CT setup. The proof-of-concept DTC consists of 24 Monolithic Active Pixel Sensor layers interleaved with tungsten absorbers, originally built for the reconstruction of electromagnetic showers induced by gamma radiation in high energy physics experiments. As such, the original design does not reflect the requirements of a proton CT calorimeter, regarding precision measurements of the ranges of protons with energies up to 250 MeV. The next prototype of our DTC, optimized for use in a proton CT setup, is currently in a design optimization phase where iterations of the design is assisted by Monte Carlo simulations. The results from this work will provide valuable input to the final design optimization process.

Should include (Lee et al. 2016)!

## 2 Methods

The goal of this study is to optimize the geometrical and material design of the DTC. The target for such a design is the simultaneous optimization of the following metrics: high accuracy of the range determination, limited by a non-existent systematic bias; low uncertainty (standard deviation) in the range determination, limited by the proton beam's range straggling; high track reconstruction efficiency, i.e. the ability to disentangle and reconstruct all the protons in a single readout frame; and secondary constraints such as economy (number of layers), cooling and mechanical stability.

The range accuracy ensures that the patient's Stopping Power Ratio map is correctly identified, while a high range uncertainty and an efficient track reconstruction enables that fewer protons are needed during the scan, i.e. a lower dose to the patient and a faster scan time.

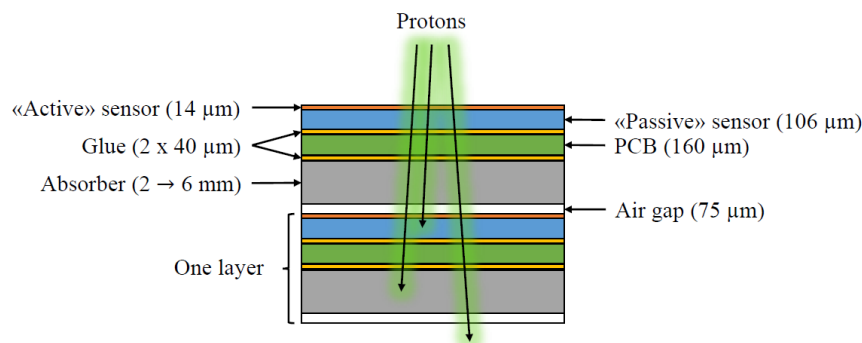
42 The following section will describe the analysis needed to obtain the accuracy, uncertainty and  
 43 efficiency as introduced above. In short, a water phantom of variable thickness is used for degrading  
 44 the beam to different energies. Each primary proton is tracked through the detector and its most likely  
 45 Bragg Curve is found. The range accuracy is then calculated from the spread of the resulting Bragg  
 46 Peak depth distribution, and is compared for the different geometries under study.

47 Note that in order to obtain the best possible estimates of the performance of the different DTC  
 48 designs, the different parts of the analysis are treated separately: The track reconstruction step is  
 49 omitted during the evaluation of the residual range calculation, where the tracks are obtained directly  
 50 from the MC truth.

## 51 2.1 Monte Carlo simulations and geometry input files

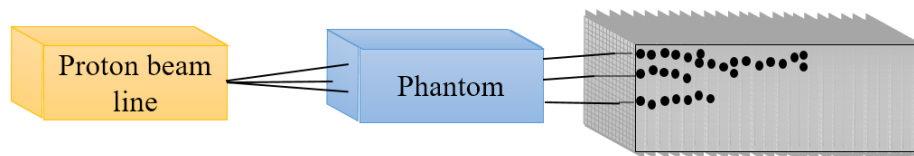
52 In this study, the MC software GATE version 7.2 has been applied, together with the physics builder  
 53 list QGSP\_BIC\_EMY, using default settings for step length and particle threshold (Grevillot et al.  
 54 2010). The mean ionization potential for water is set to 75 eV in order to facilitate comparisons with  
 55 the PSTAR database (Berger et al. 2005).

56 Several geometrical configurations are needed to evaluate how the desired detector metrics: such as  
 57 range accuracy, range uncertainty and track reconstruction efficiency, depends on the design. It is  
 58 possible to define a large number of potential designs for the DTC, and some constraints must be put  
 59 on the degrees of freedom. A baseline design based upon the original prototype of the DTC (Pettersen  
 60 et al. 2017) is shown in **Figure 1**: While the geometry of the sensor chips and electronic components  
 61 are kept, the energy degrading part of the sampling calorimeter, here called the *absorbers*, are chosen  
 62 to be between 2 mm and 6 mm of either aluminum or carbon. The proposed design use an upgraded  
 63 sensor chip compared to the original prototype, and as such the detector thickness might be decreased.



64

65 **Figure 1:** Design to be optimized: Different thicknesses (2 to 6 mm) and materials (aluminum and  
 66 carbon) for the energy absorbers are considered, and evaluated through the MC simulations. Only the  
 67 “active” sensor part is readout in the MC simulations.



68

69 **Figure 2:** Schematic setup of the variable geometry used for the design optimization. In order to  
 70 obtain a spectrum of different proton beams to hit the DTC, the thickness of the energy degrading  
 71 water phantom is modulated from 0 cm to the maximum range of the 250 MeV beam, which is  
 72 approximately 38 cm.

73 When the GATE software has been configured for a single geometry configuration, a number of  
 74 scenarios are defined by varying the thickness of an energy degrading water phantom. By performing  
 75 this step, a monoenergetic 250 MeV beam is modulated as to represent realistic energy spectra with

76 residual ranges that span the complete DTC in depth. The water phantom thicknesses vary from 0 cm  
77 to the maximum water equivalent range of the beam, approximately 38 cm, in steps of 1 mm. This fine  
78 thickness segmentation has been chosen in order to characterize the linearity of the range  
79 determination accuracy. The beam is placed distal to the water phantom, uniformly distributed from a  
80 plane, with an area of 100 cm<sup>2</sup>, parallel to the sensor area. In **Figure 2** the placement of the water  
81 phantom is shown.

## 82 2.2 Proton range from Monte Carlo truth

83 The final range calculations that emerge from the following sections need to be compared to a ground  
84 truth, in this separate MC simulations are made for this purpose. A look-up-table between phantom  
85 thicknesses and residual DTC range is created, by using the geometrical input file as described above  
86 and recording the interactions in all volumes. This is repeated for all design variants and water  
87 phantom thicknesses. The look-up-table is then used in conjunction with spline interpolation, as this  
88 method is very accurate (Pettersen et al., n.d.).

89 A look-up-table for proton ranges in pure water is also created in order to calculate the Water  
90 Equivalent Thickness from a given proton range in the DTC: This is done by calculating the energy  
91 from the proton range, and then the WET from the energy. Note that this procedure is more accurate  
92 compared to using a constant stopping power ratio between water and the detector materials.

## 93 2.3 Track reconstruction

94 One of the strengths of the DTC design is its ability to untangle and reconstruct a large number of  
95 concurrent traversing proton tracks. To this end, a track reconstruction algorithm must be defined. For  
96 more details on the track reconstruction applied in this context, see (Pettersen et al. 2017).

### 97 2.3.1 Track-following scheme

98 The track reconstruction is based upon a track-following scheme (Strandlie and Frühwirth 2010). A *hit*  
99 is here defined to be a single, or a cluster of, pixels activated by a traversing proton. A *track* is a  
100 collection of hits, and should represent the path of the original proton. The track-following scheme is  
101 then: For a given hit in the first layer of the DTC, the angular change  $\theta$  (assuming a parallel incoming  
102 proton) is calculated for all hits in the next layer. If the angular change is smaller than a reference  
103 value  $f_i\theta_R$ , the hit is appended to the growing track. The procedure is then continued until no more  
104 hits can be found to be appended to the growing track. The value  $\theta_R$  is defined as the “ $3\sigma$ ” value of  
105 the angular change distribution in the tracks obtained from the MC truth. The track-following scheme  
106 is performed two consecutive times using different values for  $f_i$ :  $f_1 = 2$  and  $f_2 = 3$ . Due to the fact  
107 that the tracks have a higher scattering power towards the Bragg Peak, the track reconstruction is  
108 performed two more times starting at the last identified hit towards the Bragg Peak: This time the  
109 values  $f_3 = 5$  and  $f_4 = 7$  are chosen as to include proton paths with high amounts of scattering.

### 110 2.3.2 The correctly reconstructed track

111 In order to benchmark the quality and efficiency of the track reconstruction algorithm as described  
112 above, a definition of the correctly reconstructed track must be made. The constraints are therefore:  
113 The first and last entry in a track must originate from the same proton history, and the last hit from a  
114 proton history must be included. By following this definition, the track objects have correct incoming  
115 vector and residual range, which is the required values for volumetric reconstruction of the stopping  
116 power map in proton CT.

117 The efficiency of the track reconstruction is then the ratio of correctly reconstructed tracks to the total  
118 number of identified tracks. Tracks stopping due to inelastic collisions do not degrade the efficiency;  
119 they can be identified due to a lack of an increase in the deposited energy at the distal part of the track  
120 due from the Bragg Peak. The efficiency is found for an increasing number of protons reconstructed  
121 simultaneously.

## 122 2.4 Bragg Curve fitting

123 It is possible to perform least-square fits of the Bragg Curve to the track's energy loss measurements  
 124 in each sensor layer. This procedure increases the range determination accuracy compared to using the  
 125 depth of the last recorded hit. While direct measurement of the energy loss is not possible using the  
 126 proposed digital sensor readout ("hit" or "no hit"), it is possible to estimate the energy loss by  
 127 counting the number of connected hits originating from the proton path, as described in detail in  
 128 (Pettersen et al. 2017), and as such this kind of model fitting is performed.

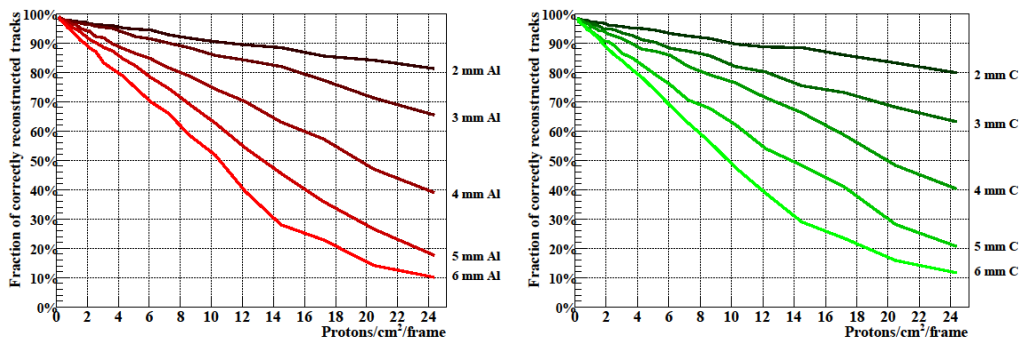
## 129 2.5 Residual range and range straggling calculation

130 The distribution of true proton ranges, having the same initial energy, is approximately gaussian.  
 131 However, the output range distribution originating from the Bragg Curve fitting is not gaussian, and it  
 132 is not trivial to describe the variations analytically due to the nature of the sparse measurements from  
 133 each sensor layer. However, a simple histogram calculation of the empirical mean value and standard  
 134 deviation yields accurate results for the residual range  $\langle R_0 \rangle$  and range straggling  $\langle \sigma \rangle$ , respectively. The  
 135 procedure is described in detail in (Pettersen et al. 2017): A gaussian fit  $(\mu', \sigma')$  to the whole range  
 136 distribution histogram with weights  $w_i$  and depth values  $x_i$  yields the summation limits for the bin  
 137 counting from  $x_1 = \mu' - 4\sigma'$  to  $x_2 = \mu' + 4\sigma'$ . Then,

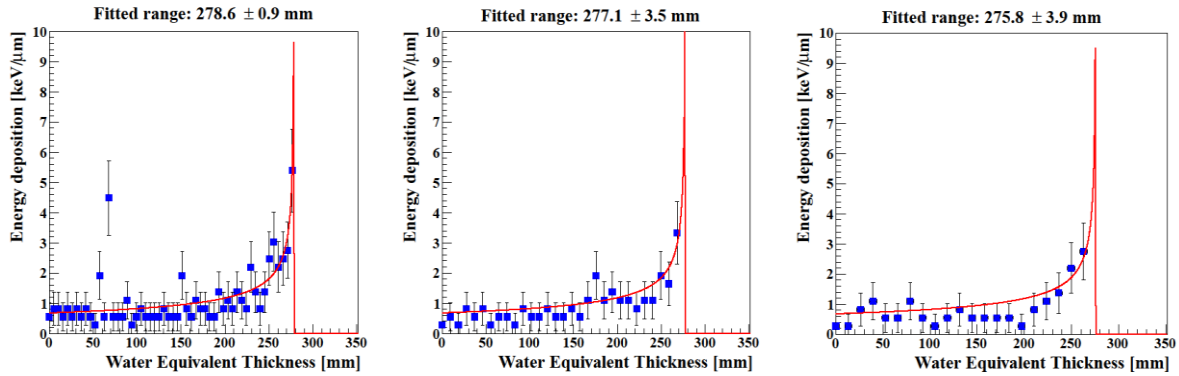
$$138 \quad \langle R_0 \rangle = \frac{\sum_{i=x_1}^{x_2} w_i x_i}{\sum_{i=x_1}^{x_2} w_i}, \quad \langle \sigma \rangle = \frac{\sqrt{\sum_{i=x_1}^{x_2} w_i (x_i - \langle R_0 \rangle)^2}}{\left[ \sum_{i=x_1}^{x_2} w_i \right] - 1}.$$

139 The results of these calculations should be comparable to the ground truth obtained from separate MC  
 140 simulations. However, it is expected that the values should be degraded somewhat. First, in terms of a  
 141 systematic error, or bias, leading to deviations in  $\langle R_0 \rangle$  compared to the nominal residual range.  
 142 Second, in terms of an increase in the measurement uncertainty  $\langle \sigma \rangle$  compared to the range straggling.  
 143 These degradations may originate from the design of the DTC setup and from how the data analysis is  
 144 performed. By comparing the measured values to their ground truth counterparts, the bias in  $\langle R_0 \rangle$  is  
 145 trivial to calculate in different phase space scenarios.

## 146 3 Results

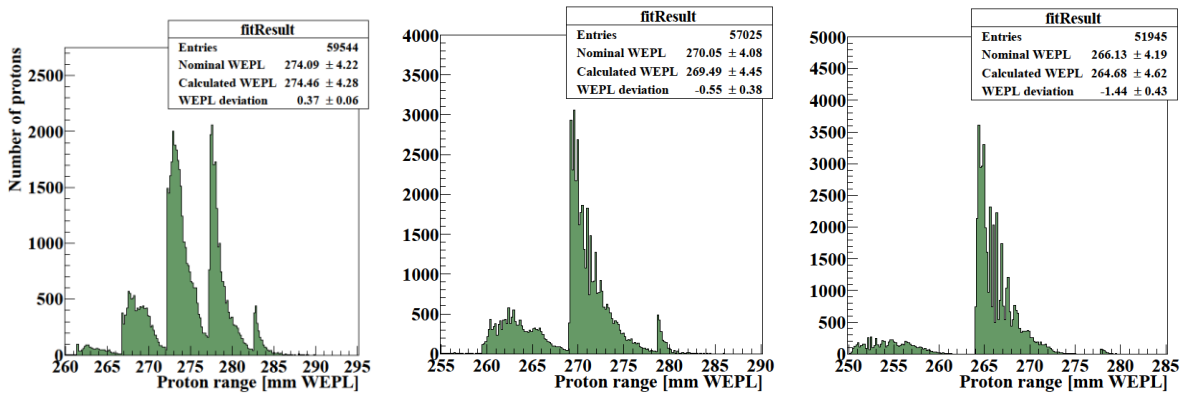


147  
 148 **Figure 3:** The tracking efficiency for different geometries. Each proton track must be fully  
 149 reconstructed, and the start- and endpoint must originate from the same incoming proton. The results  
 150 from the designs using aluminum and carbon absorbers are similar. Note that in many cases, the effect  
 151 of a wrongly reconstructed track might be small due to the nature of the error: Parallel tracks  
 152 originating from similar incoming vectors are easily confused.



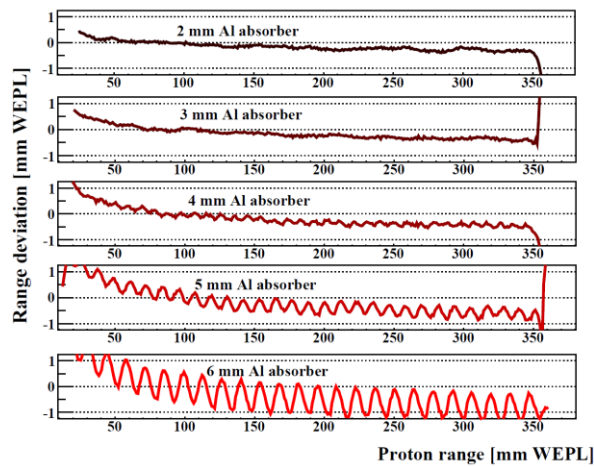
153

154 **Figure 4:** Individual proton tracks with Bragg Curve fit. Note that the range found using thinner  
 155 absorber designs yields a higher range determination accuracy. The displayed accuracy is the output  
 156 from the least-square method for an individual proton, and is not representative for an ensemble of  
 157 protons. From a 250 MeV beam degraded using a 10 cm water phantom. **Left:** 2 mm Al absorber,  
 158 **Middle:** 4 mm Al absorber, **Right:** 6 mm Al absorber.



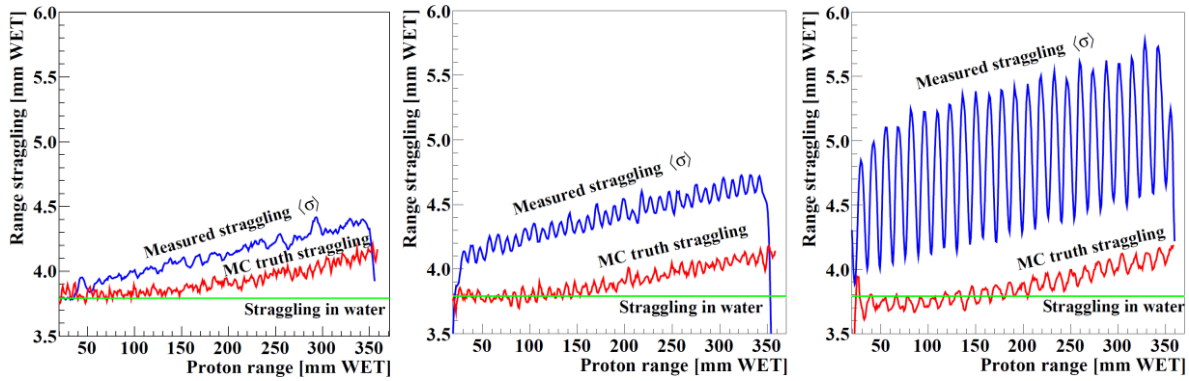
159

160 **Figure 5:** The distribution of many individual fitted ranges. From this distribution the residual range  
 161  $\langle R_0 \rangle$  and range straggling  $\langle \sigma \rangle$  of a proton ensemble is calculated, shown here as  $\langle R_0 \rangle \pm \langle \sigma \rangle$ . Each  
 162 rise in the distribution coincides with the beam reaching a new sensor layer. From a 250 MeV beam  
 163 degraded using a 10 cm water phantom. **Left:** 2 mm Al absorber, **Middle:** 4 mm Al absorber,  
 164 **Right:** 6 mm Al absorber.

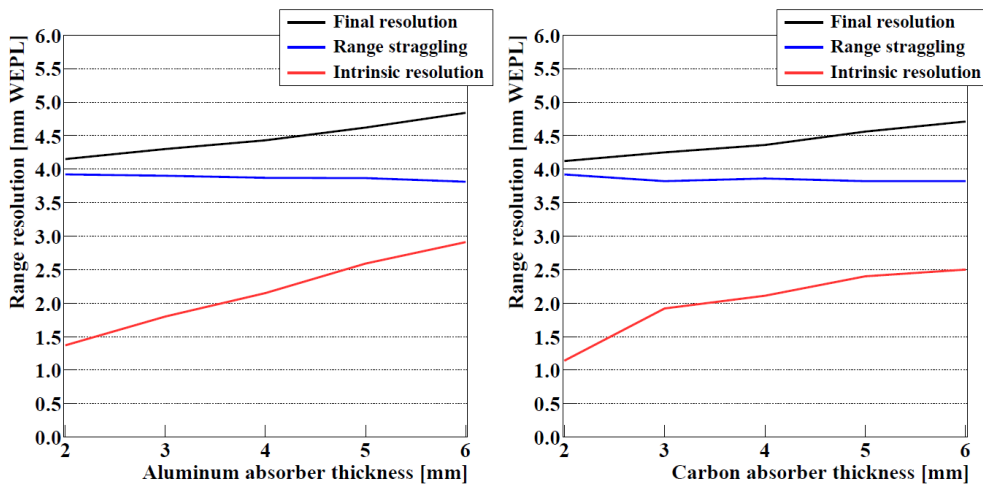


165

166 **Figure 6:** Range determination accuracy shown as the deviation between the true (MC) range, and the  
 167 reconstructed range  $\langle R_0 \rangle$  for each water degrader thickness. **In general the systematic errors are kept**  
 168 **within 0.5 mm WET.** An oscillating systematic error occurs when using thick absorbers due to the  
 169 large spacing between the measurements in subsequent layers. **TO BE UPDATED**



170  
 171 **Figure 7:** The measured range straggling ( $\sigma$ ), shown here together with the MC truth range  
 172 straggling and the “baseline” range straggling in water. An oscillating systematic error occurs when  
 173 using thick absorbers due to the large spacing between the measurements in subsequent layers. **Left:** 2  
 174 mm Al absorber, **Middle:** 4 mm Al absorber, **Right:** 6 mm Al absorber. **TO BE UPDATED**



175  
 176 **Figure 8:** Range resolution of the different configurations. Shown is the total resolution (measured as  
 177 the mean value of  $\langle\sigma\rangle$  in **Figure 6**), the range straggling from the MC truth as well as the intrinsic  
 178 resolution which is the quadratic difference between the two. **TO BE UPDATED. SWITCH COLORS:**  
 179  **$\langle S \rangle$  SHOULD BE BLUE TO MATCH FIGURE 7, RANGE STRAGGLING SHOULD BE RED!**

### 180 3.1 Efficiency of track reconstruction

181 The efficiency of the track reconstruction, as defined in Section 2.3.2, is shown in **Figure 3** for the 12  
 182 different designs under consideration. It is calculated using a 100 cm<sup>2</sup> irradiation field and by varying  
 183 the number of protons reconstructed simultaneously. For the 4 mm design, both using aluminum and  
 184 carbon, the efficiency is 90% at 4 protons per cm<sup>2</sup> per reconstruction frame, and 80% if the proton  
 185 density is doubled.

### 186 3.2 Accuracy of the range calculation

187 In **Figure 6** the range determination accuracy throughout the DTC is shown for the different designs.  
 188 Some key aspects can be seen in the figure: The *systematic errors* are kept within **0.5 mm WET**  
 189 throughout the DTC for the designs having a 4 mm Al absorber or less, and **higher for the designs with**  
 190 **more than 4 mm** Al absorbers. The *dynamic range* of the DTC, given by the region with uniform range  
 191 uncertainty and uniform range accuracy, is approximately between **20 mm WET and 350 mm WET** in  
 192 the detector, or in terms of energy between **50 MeV and 240 MeV**. There is a certain oscillation  
 193 artefact in the range determination to be observed, especially at the designs with more than 4 mm and  
 194 thicker absorbers. It is characterized by a sinusoidal perturbation of the range accuracy due to the  
 195 sparse sampling of the layer measurements in depth. A spectral analysis of the range accuracy has

196 shown that this oscillation becomes significant (having a peak-to-peak amplitude of more than 0.25  
197 mm WET) when an aluminum absorber thickness above 4.5 mm is used.

### 198 3.3 Uncertainty of the range calculation

199 The uncertainty of the range determination is highly dependent on its lower limit, which is the  
200 statistical range straggling of the proton beam. The resulting range uncertainty is a quadratic sum  
201 between the range straggling and the additional smearing due to detector and analysis. As is apparent  
202 in **Figure 7**, the range straggling is dominated by the straggling induced by interactions in the water  
203 phantom, with an increase in the uncertainty for high energy protons traversing a higher fraction of the  
204 DTC material. The range straggling inhibits an oscillating systematic error with a period matching the  
205 spacing of the sensor layers, similar to the effects described in **Section 3.2**.

### 206 3.4 Comparison of different geometries

207 It is possible to calculate the “intrinsic” or additional uncertainty of the setup by subtracting the range  
208 straggling from the measured range spread ( $\sigma$ ) in quadrature. In **Figure 8** the range straggling,  
209 intrinsic uncertainty as well as the total measured uncertainty of two designs are shown. **SOME OF**  
210 **THE RESULTS HERE WHEN THEY ARRIVE.**

### 211 3.5 Required number of sensor layers

212 Due to economical and size constraints, the number of layers required to contain the complete beam  
213 has been found for the different designs. A 230 MeV mono-energetic beam has been considered here,  
214 its range plus 5 times the range straggling leads to the following number of layers: For the 2 mm  
215 configuration, 67 layers are needed. For 3 mm, 49 layers are needed. For 4 mm, 38 layers are needed.  
216 Only 32 (27) layers are needed for the 5 (6) mm configuration, although it has been shown that these  
217 designs lead to excessive range determination errors.

## 218 4 Discussion

219 **This should discuss the significance of the results and compare them with**  
220 **previous work using relevant references.**

221 The design, analysis framework and capabilities of the original DTC were detailed in (Pettersen et al.  
222 2017). Among its key features are a “all-in-one” design where the entrance of the calorimeters can  
223 double as the proton tracker and a high rate capability due to the possibility of the tracking and  
224 reconstruction of hundreds of simultaneous proton tracks. The calorimeter performed above  
225 expectations but did not meet the requirements for a proton CT calorimeter as suggested in  
226 (Poludniowski, Allinson, and Evans 2015). Its main limitation for proton CT purposes were shown to  
227 be the utilization of 3.3 mm tungsten absorbers between each sensor layer, roughly equivalent to 15.5  
228 mm aluminum. The resulting range uncertainty for both experimental data and MC simulations was  
229 above 8 mm WET in addition to oscillating systematic errors of up to 8 mm.

230 The next generation DTC, as described in this study, is designed with proton CT as the main purpose.  
231 While the analysis framework and design philosophy remains, energy absorbers of less dense  
232 materials facilitate the track reconstruction as well as the range calculation. A comparison of the  
233 results presented here to the results of the original prototype shows that both systematic errors and  
234 range uncertainties are close to their theoretical limits of, respectively, zero and the inherent range  
235 straggling for several of the proposed designs. These capabilities are matched by current proton CT  
236 prototypes based on staged scintillators (Bashkurov et al. 2016) and parallel plate ionization chambers  
237 (Rinaldi et al. 2014).

238 This analysis was performed on a water phantom of varying thickness, however it is trivial to extend it  
239 to realistic phantoms since the incoming proton vector is well defined by the first two layers of the  
240 DTC, which are defined without the absorber material: Reducing the beam energy by less than 0.5

241 MeV. In terms of cooling and mechanical stability, a 4 mm aluminum absorber should provide the  
242 required support, and increasing air gap of 2 mm might enable an air-cooled design.

243 Using realistic assumptions about the geometry (350 cm<sup>2</sup>) and electronics capabilities (10 μs readout  
244 cycle) of the DTC design under consideration, and under the assumption that a large-area proton  
245 irradiation field can be delivered, this proton density corresponding to a 90% reconstruction efficiency  
246 converts to a proton rate capability of the DTC of 140 million protons per second. This number is  
247 above the minimum requirements of a proton CT, and of current prototypes (Scaringella et al. 2014;  
248 Bashkirov et al. 2016; Taylor et al. 2016; Naimuddin et al. 2016), and may enable scan times limited  
249 by gantry rotation speeds.

250 Another use case of such a readout scheme is the reconstruction of thousands of almost coincident  
251 protons, such as protons accelerated by the proposed Laser Accelerated Proton methods (Masood et al.  
252 2014; Hofmann et al. 2015). If a large-area irradiation field is not available or not desired (e.g. by  
253 omitting the proximal tracker and using a thin pencil beam in order to simplify the design (K. M.  
254 Hanson et al. 1978)), the rate capability will decrease.

## 255 5 Conclusion

256 This section should be used to highlight the novelty and significance of the  
257 work, and any plans for future relevant work.

258 In this work we have benchmarked different designs of the next generation Digital Tracking  
259 Calorimeter (DTC) using MC simulations together with the analysis framework developed for the  
260 proof-of-concept DTC prototype (Pettersen et al. 2017).

261 The analysis is performed by combining individual proton tracking in a high-granularity pixel range  
262 telescope and Bragg Curve modeling of each proton's energy loss. The DTC has the capability of  
263 tracking more than 100 million protons/s at 90% reconstruction efficiency, assuming realistic  
264 electronics- and design proposals as well as a uniform large-area proton field. The range uncertainties  
265 are close to the range straggling limit, and systematic errors in the range determination are kept below  
266 0.3 mm WET throughout the complete detector.

267 By considering the presented results, the optimal design in terms of the systematic and stochastic  
268 errors is 4 mm, with similar results between carbon and aluminum. The improvement achieved by  
269 using 3 mm or less absorbers is negligent due to the inherent range straggling limit to the range  
270 uncertainty. Thicker absorbers, however, yield a systematic oscillating artefact in the range  
271 determination accuracy and at 5 mm and higher this effect is degrading. In terms of the reconstruction  
272 efficiency, the smaller absorber the better: The thickness should not be far above 3 mm in order to  
273 obtain the optimal efficiency. However, when considering the realistic construction constraints, a 4  
274 mm absorber leads to far fewer required sensor layers compared to the 3 mm design, respectively 48  
275 and 39 needed layers, which might be a deciding factor between the two near-optimal alternatives.

276 This work provides input to the design of the next generation DTC in a proton CT setting, to be  
277 constructed by the Bergen Proton CT group. In addition, the Bragg Peak-guided range reconstruction  
278 presented here and in (Pettersen et al. 2017) might be of interest to similar projects.

## 279 6 Acknowledgements

280 This work was supported by Helse Vest RHF grant [911933], and is part of the main author's PhD  
281 project.



## 282 7 References

- 283 Bashkirov, V. A., R. W. Schulte, R. F. Hurley, R. P. Johnson, H. F.-W. Sadrozinski, A. Zatserklyaniy,  
284 T. Plautz, and V. Giacometti. 2016. “Novel Scintillation Detector Design and Performance for  
285 Proton Radiography and Computed Tomography.” *Medical Physics* 43 (2): 664–74.  
286 doi:10.1118/1.4939255.
- 287 Berger, M. J., J.S. Coursey, M.A. Zucker, and J. Chang. 2005. *ESTAR, PSTAR, and ASTAR: Computer*  
288 *Programs for Calculating Stopping-Power and Range Tables for Electrons, Protons, and*  
289 *Helium Ions* (version 1.2.3). Gaithersburg, MD: National Institute of Standards and  
290 Technology. <http://physics.nist.gov/Star>.
- 291 Grevillot, Loïc, Thibault Frisson, Nabil Zahra, Damien Bertrand, Frédéric Stichelbaut, Nicolas Freud,  
292 and David Sarrut. 2010. “Optimization of GEANT4 Settings for Proton Pencil Beam Scanning  
293 Simulations Using GATE.” *Nuclear Instruments and Methods in Physics Research Section B:*  
294 *Beam Interactions with Materials and Atoms* 268 (20): 3295–3305.  
295 doi:10.1016/j.nimb.2010.07.011.
- 296 Hofmann, Kerstin M., Umar Masood, Joerg Pawelke, and Jan J. Wilkens. 2015. “A Treatment  
297 Planning Study to Assess the Feasibility of Laser-Driven Proton Therapy Using a Compact  
298 Gantry Design.” *Medical Physics* 42 (9): 5120–5129. doi:10.1118/1.4927717.
- 299 K. M. Hanson, J. N. Bradbury, T. M. Cannon, R. L. Hutson, D. B. Laubacher, R. Macek, M. A.  
300 Paciotti, and C. A. Taylor. 1978. “The Application of Protons to Computed Tomography.”  
301 *IEEE Transactions on Nuclear Science* 25 (1): 657–60. doi:10.1109/TNS.1978.4329389.
- 302 Lee, Chae Young, Hankyeol Song, Chan Woo Park, Yong Hyun Chung, Jin Sung Kim, and Justin C.  
303 Park. 2016. “Optimization of Proton CT Detector System and Image Reconstruction  
304 Algorithm for On-Line Proton Therapy.” Edited by Li Zeng. *PLOS ONE* 11 (5): e0156226.  
305 doi:10.1371/journal.pone.0156226.
- 306 Masood, U., M. Bussmann, T. E. Cowan, W. Enghardt, L. Karsch, F. Kroll, U. Schramm, and J.  
307 Pawelke. 2014. “A Compact Solution for Ion Beam Therapy with Laser Accelerated Protons.”  
308 *Applied Physics B* 117 (1): 41–52. doi:10.1007/s00340-014-5796-z.
- 309 Naimuddin, Md, G. Coutrakon, G. Blazey, S. Boi, A. Dyshkant, B. Erdelyi, D. Hedin, et al. 2016.  
310 “Development of a Proton Computed Tomography Detector System.” *Journal of*  
311 *Instrumentation* 11 (02): C02012.
- 312 Pettersen, H. E. S., M. Chaar, I. Meric, O. H. Odland, J. R. Sølief, and D. Röhrich. n.d. “Accuracy of  
313 Parameterized Proton Range Models; a Comparison.” *Radiation Physics and Chemistry*  
314 Submitted.
- 315 Pettersen, H.E.S., J. Alme, A. Biegun, A. van den Brink, M. Chaar, D. Fehlker, I. Meric, et al. 2017.  
316 “Proton Tracking in a High-Granularity Digital Tracking Calorimeter for Proton CT  
317 Purposes.” *Nuclear Instruments and Methods in Physics Research Section A: Accelerators,*  
318 *Spectrometers, Detectors and Associated Equipment* 860C: 51–61.  
319 doi:10.1016/j.nima.2017.02.007.
- 320 Poludniowski, G, N M Allinson, and P M Evans. 2015. “Proton Radiography and Tomography with  
321 Application to Proton Therapy.” *The British Journal of Radiology* 88 (1053): 20150134.  
322 doi:10.1259/bjr.20150134.
- 323 Rinaldi, I, S Brons, O Jäkel, B Voss, and K Parodi. 2014. “A Method to Increase the Nominal Range  
324 Resolution of a Stack of Parallel-Plate Ionization Chambers.” *Physics in Medicine and*  
325 *Biology* 59 (18): 5501–15. doi:10.1088/0031-9155/59/18/5501.
- 326 Scaringella, M, M Bruzzi, M Bucciolini, M Carpinelli, G A P Cirrone, C Civinini, G Cuttone, et al.  
327 2014. “A Proton Computed Tomography Based Medical Imaging System.” *Journal of*  
328 *Instrumentation* 9 (12): C12009–C12009. doi:10.1088/1748-0221/9/12/C12009.
- 329 Strandlie, Are, and Rudolf Frühwirth. 2010. “Track and Vertex Reconstruction: From Classical to  
330 Adaptive Methods.” *Reviews of Modern Physics* 82 (2): 1419–58.  
331 doi:10.1103/RevModPhys.82.1419.
- 332 Taylor, J. T., G. Poludniowski, T. Price, C. Waltham, P. P. Allport, G. L. Casse, M. Esposito, et al.  
333 2016. “An Experimental Demonstration of a New Type of Proton Computed Tomography  
334 Using a Novel Silicon Tracking Detector.” *Medical Physics* 43 (11): 6129–6136.  
335