RANGES OF IONS IN BIOLOGICAL TARGETS

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1. Introduction

Ion therapy is a promising cancer treatment modality for specific types of tumours. Its application requires technological development in the field of accelerator technology [1-3], beam transport [4-7], radiobiology, dosimetry, treatment planning, *etc*. Many of these development fields are based on the physics of ion interaction with matter, which is tightly connected to the precise knowledge of ion ranges in different biological targets.

The present paper deals with systematic calculation of therapeutic proton-beam ranges in different human tissues. The ranges are calculated by the Monte Carlo module of the SRIM-2013 code (SRIM=Stopping and Ranges of Ions in Matter) [8]. The human tissues that are selected from the SRIM-2013 built-in compound dictionary are characterized by their density. The tissue density is used as the only variable in the range-fitting formula at a given proton-beam energy. The range-to-density data are collected for proton beams at several energies covering the clinically relevant energy interval from 60 MeV to 220 MeV. The collected data are processed in such a way that a fitting formula for the proton-beam range that is as merely a function of the tissue density is found. The paper shows that the therapeutic proton-beam ranges can be satisfactorily, *i.e.* with the accuracy within the natural range straggling, assessed by an extremely simple function of the tissue density. The result can be used for quick assessment of the proton-beam range in human tissues at many clinical and research applications like phantom design and phantom experiments, design and preparation of quality-assurance set-ups, design and preparation of *in-vitro* biological experiments with human tissues irradiated by proton beams, *in-vivo* animal experiments, *etc*.

2. Materials and Methods

The well-established and widely recognized computer program SRIM-2013 (SRIM=Stopping and Ranges of Ions in Matter) [8] was used to calculate proton ranges in the energy interval from 60 MeV to 220 MeV [9] in 28 different biological targets taken from the built-in SRIM compound dictionary. The targets were selected from the category called "Biological materials – Human". The SRIM compound dictionary provides information about chemical composition of each material and its density. We were looking for the range-to-density dependence without taking into account the target chemical composition, because the exact chemical composition of individual tissues and organ structures varies in time and can never be precisely known in clinical practice at the particular moment of patient irradiation. The density is a material parameter that is more stable and can be better correlated with the so-called CT numbers (Hounsfield units) gained from the CT images [10]. Hence the main question of interest is: "Is it possible to predict the ion range as a function of the target density in a material with unknown chemical composition?" It should, however, be pointed out that this "unknown" chemical composition is meant within a group of materials with similar chemical composition, like different human tissues.

Table 1 summarizes the results of all simulations.

Tab. 1. *Proton-beam ranges in different human tissues taken from the SRIM built-in compound dictionary. Range straggling represents one standard deviation (square root of the variance) of the range distribution.*

Tissue	Density [g/cm^3]	Proton-beam kinetic energy [MeV]							
		60	100	120	140	150	180	200	220
		Average range straggling [% of the range]							
		1.43	1.38	1.36	1.36	1.36	1.35	1.33	1.32
		SRIM Monte Carlo range [mm]							
Water (liquid)	1.000	30.4	76.1	105	138	155	213	256	301
Human blood, ICRU	1.060	29.0	72.5	100	131	148	203	244	287
Human skin	1.090	28.2	70.4	97.3	127	144	198	237	279
Skeletal muscle	1.050	29.3	73.2	101	132	149	205	246	290
Skeleton-cartilage	1.100	28.3	70.7	97.7	128	144	198	238	280
Skeleton-spongiosa	1.180	26.7	66.7	92.2	120	136	187	224	264
Skeleton-red marrow	1.030	29.5	73.8	102	133	151	207	248	292
Skeleton-yellow marrow	0.980	30.4	76.2	105	138	156	214	257	302
Cortical bone, adult	1.920	18.1	45.2	62.4	81.8	92.2	126	151	178
Cortical bone, age 6-13	1.830	18.9	47.0	64.8	85	95.9	131	157	185
Cortical bone, age 2-5	1.800	19.1	47.7	65.8	86.2	97.3	133	160	188
Perinatal rhesus monk	1.400	23.3	58.2	80.4	105	119	163	195	230
Mammary gland, #1	0.990	30.5	76.2	105	138	156	214	257	302
Mammary gland, #2	1.020	29.8	74.5	103	135	152	209	251	296
Mammary gland, #3	1.060	29.0	72.4	100	131	148	203	244	287
Spleen	1.090	28.2	70.5	97.4	127	144	198	237	279
Testis	1.040	29.4	73.6	101	133	150	206	248	291
Thyroid	1.050	29.2	73.0	100	132	149	205	246	289
Trachea	1.060	29.0	72.6	100	131	148	204	244	287
Ovary	1.050	29.2	73.0	100	132	149	205	245	289
Pancreas	1.040	29.1	72.7	100	131	148	204	245	288
Prostate	1.040	29.5	73.7	101	133	150	207	248	292
Urinary bladder-urine	1.020	29.9	74.9	103	135	153	210	252	296
Urinary bladder, empty	1.040	29.5	73.7	101	133	150	207	248	292
Urinary bladder, full	1.030	29.7	74.2	102	134	151	208	250	294
Adipose tissue	0.920	32.2	80.7	111	146	165	227	272	320
Bone-cortical, ICRP	1.850	18.5	46.0	63.5	83.2	93.9	128	154	181
Muscle-skeletal, ICRP	1.040	29.6	74.1	102	134	151	208	249	293

3. Results

Data collected in Table 1 are presented in graphical form in Figure 1. The data points represent the ranges calculated by SRIM. Let us call them Monte Carlo ranges, R_{MC}. The vertical error bars represent the range straggling defined as the square root of the variance of the range distribution. Let us call it natural range straggling. This parameter is automatically calculated by SRIM during the Monte Carlo simulation. That is why we will use notation S_{MC} for the natural range straggling. The natural range straggling can be expressed either directly in millimeters (this is the case of Figure 1) or in percentage of the Monte Carlo range, $S_{MC}/R_{MC}\times 100\%$ (this is the case of Table 1). The relative natural range straggling is almost the same at all proton-beam energies ranging from 1.43% to 1.32% at 60 MeV and 220 MeV, respectively.

The data sets corresponding to different energies (60 MeV, 100 MeV, 120 MeV, 140 MeV, 150 MeV, 180 MeV, 200 MeV, and 220 MeV) can be clearly recognized.

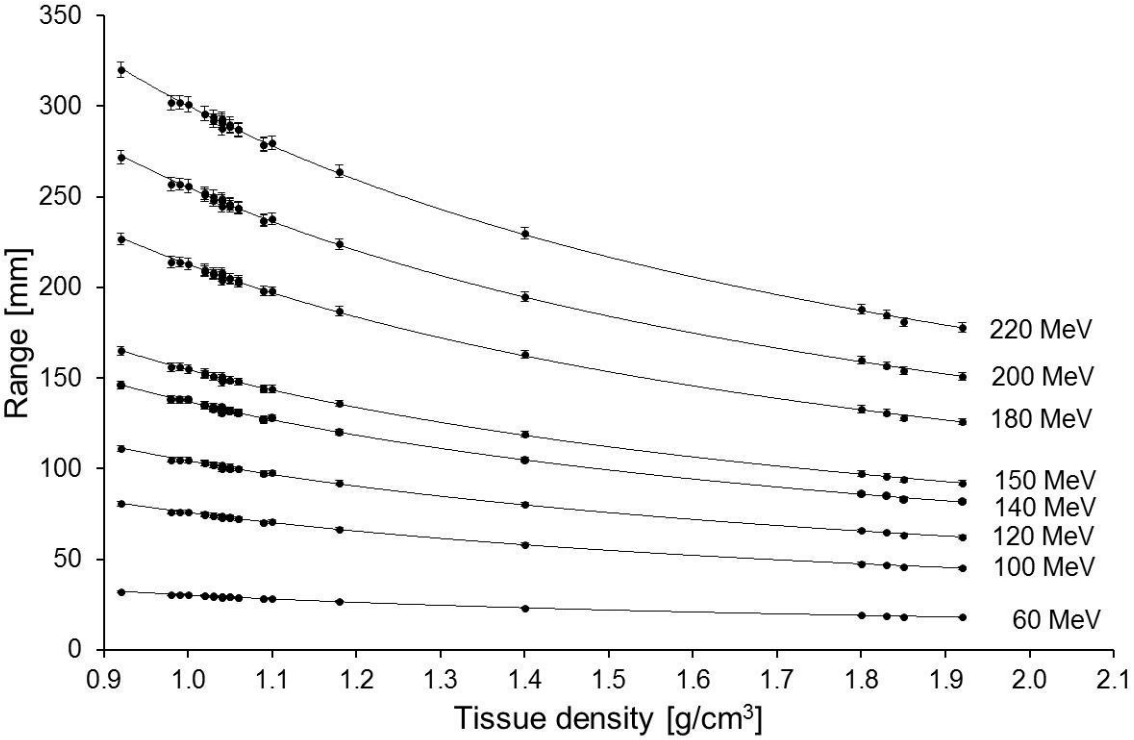

Fig.1: *Proton-beam ranges as a function of target density calculated by SRIM for different proton-beam energies from 60 MeV to 220 MeV.*

The solid lines represent the best analytical fit of the Monte Carlo ranges at given energy. We found out that the best fit was achieved by a power function in the form:

$$R_{FIT} = \frac{A}{\rho^{B}} \tag{1}$$

where R_{FIT} is the fitted range in mm, ρ is the tissue density in g/cm^3, *A* is a coefficient and *B* is an exponent. The values of the *A* and *B* fit-parameters are listed in Table 2 together with the statistical R^2-parameter characterizing the fit quality. These parameters were gained by the "Trendline" routine of MS-EXCEL. It can be seen from Table 2, that according to the R^2-criterion, the worst fit was achieved for the 120 MeV data set. This data is shown in Figure 2.

Tab. 2. *The fit parameters of the power function fitting the Monte Carlo proton-beam ranges.*

Parameter	Proton-beam kinetic energy [MeV]			
	60	**100**	**120**	**140**
A	30.3102717	75.8141408	104.39231068	136.960798
B	0.78836442	0.79454471	0.79028262	0.793905
R^2	0.99915362	0.99914064	0.99898486	0.99900546
	Proton-beam kinetic energy [MeV]			
	150	**180**	**200**	**220**
A	154.70037116	212.81489695	255.27184339	300.33838498
B	0.79465875	0.80605214	0.80533004	0.80411715
R^2	0.99931858	0.99916285	0.9992679	0.99918418

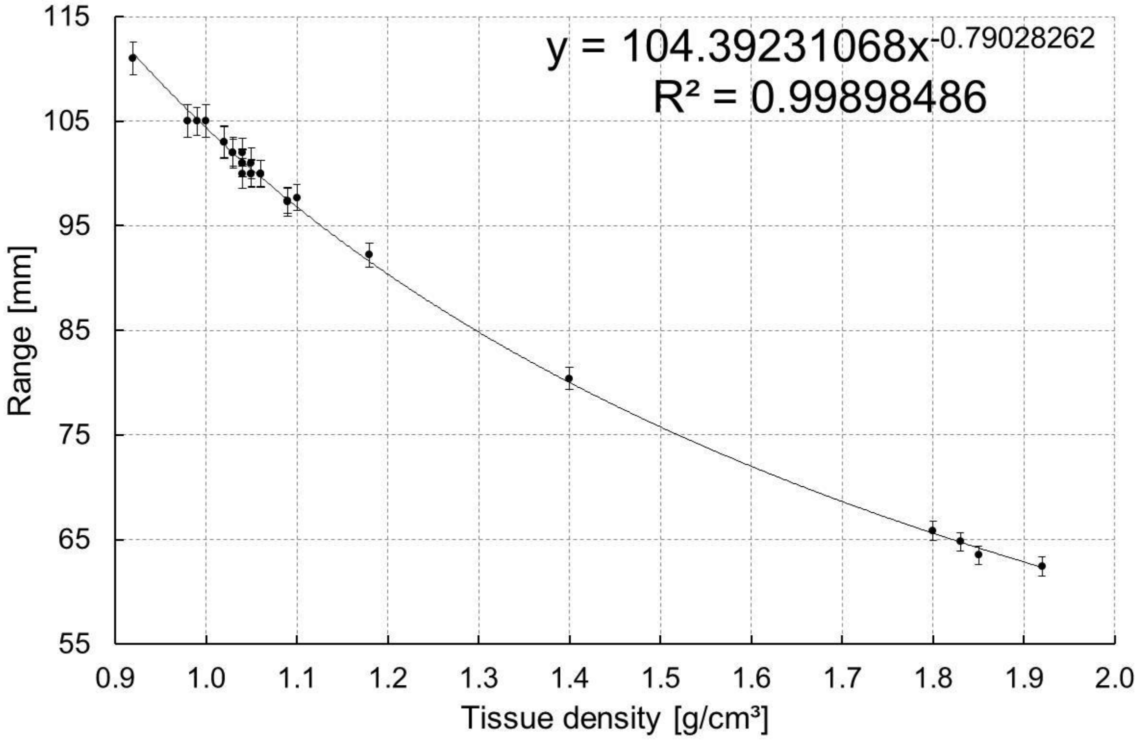

Fig.2: *Proton-beam ranges as a function of target density calculated by SRIM for the proton-beam energy of 120 MeV. This data set represents the worst fit according to the R^2-criterion. Nevertheless, the fitted ranges stay within the natural range straggling at all data points.*

4. Discussion

Although the R^2-parameter is commonly used to characterize the fit-quality, we were looking for a physics-based criterion and decided to test whether the fitting function stayed within the natural range straggling. Each Monte Carlo range is accompanied by its individual value of the natural range straggling, S_{MC} (the values quoted in Table 1 are averaged over all data-points belonging to the same proton-beam energy). For each Monte Carlo range, we calculated the corresponding fitted value, R_{FIT}, using Eq. (1) and values from Table 2. After that, the deviation of the fitted range from the Monte Carlo range, *D*, was calculated for each data point as:

$$D = \frac{|R_{MC} - R_{FIT}|}{R_{MC}} 100\% \qquad (2)$$

Finally, the deviation, *D*, was compared with the relative natural range straggling, S_{MC} as $S_{MC} - D$. In case of the positive result, the fitting function stays inside the “error bars” representing the natural range straggling. In case of the negative result, the fitting function extends out of the natural range straggling. Results of the above described test are summarized in Table 3.

Tab. 3. *Results of the fitting test in terms of fit-deviation versus the natural range straggling.*

Energy [MeV]	Number of points failed	Average relative S_{MC} [%]	Average deviation, *D* [%]	The worst data-point		
				Individual S_{MC} [%]	Individual *D* [%]	$S_{MC} - D$
60	0	1.434	0.382	1.539	1.306	0.233
100	0	1.377	0.388	1.365	1.091	0.274
120	0	1.358	0.416	1.450	1.206	0.244
140	0	1.360	0.397	1.420	1.345	0.075
150	0	1.362	0.305	1.473	1.320	0.153
180	0	1.350	0.372	1.367	1.260	0.107
200	0	1.333	0.368	1.403	1.000	0.403
220	0	1.320	0.374	1.331	1.180	0.151

5. Conclusions

It has been shown that for a group of biological materials and human tissues, the proton-beam range can be satisfactorily assed by an analytical function with the only variable – the target density. The best form of this analytical function is a power function with two parameters: the coefficient and the exponent. These parameters were found for 8 energies in the clinically relevant energy interval from 60 MeV to 220 MeV corresponding to the proton-beam range in a water-equivalent tissue from 30.4 mm up to 301 mm, respectively. The fitting was done with the aid of the built-in “Trendline” routine of MS-EXCEL. The ranges were calculated with the SRIM-2013 code and the biological materials were selected from its compound dictionary – Biological materials – Human.

The fit quality was evaluated by the statistical R^2-parameter that is listed in Table 2. The average value of the R^2-parameter is 0.99915226. The worst value is 0.99898486 at the proton-beam energy of 120 MeV.

In addition to this, we tested the analytical fitting function with respect to the natural range straggling representing 1-sigma value of the range distribution. The fitting function stays inside the natural range straggling at all data points. The average range straggling for all data points is 1.362 % of the range. The average deviation of the fitted range from the Monte Carlo range is 0.375 % of the Monte Carlo range. This means that on average, the fitting function stays inside 28 % of the natural range straggling, which is an excellent agreement. The worst data-point is contained in the energy-set belonging to 180 MeV. The natural range straggling of this particular point is 1.367 % of the Monte Carlo range. The deviation of the fitted range from the Monte Carlo range is 1.260 % of the Monte Carlo range. The difference between the natural range straggling and the deviation is 0.107 % of the Monte Carlo range.

At this stage of our work, the parameters of the analytical fitting-function must be found individually for each proton-beam energy-set. However, it shall be possible to found an energy-scaling based on some correlation between the fitting parameters and the proton-beam energy. This work is presently in progress and will be included in the extended version of this paper [11].

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