Proton Beam Therapy

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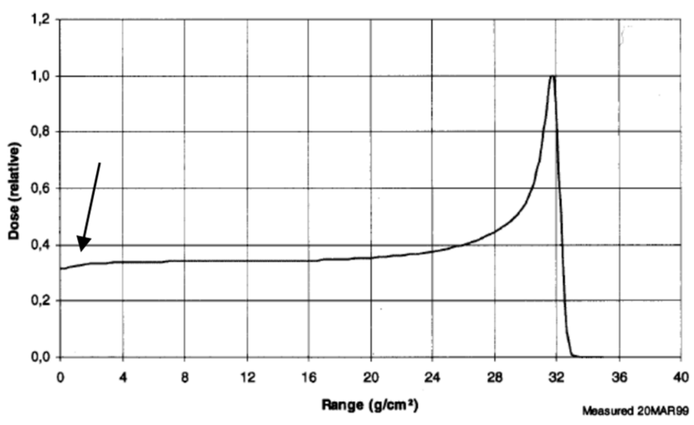
HYPOTHESIS



The bragg peak characteristics of protons help them minimise normal tissue damage. This has many benefits of minimising side effects, especially in children who have growing cells. They also, however, mean proton beams are more sensitive to uncertainties such that they could cause damage to vital organs such as the spinal cord, or provide sub-optimal treatment, if the conformation of the beam to the target volume or the dose are miscalculated. This has proven especially challenging in the treatment of lung cancer. However, other factors such as cost and availability of proton centres are also setbacks avoiding it from becoming a leading treatment method despite its high theoretical potential. [1] Picture source [2]

THEORETICAL BACKGROUND

The two major sources of uncertainty discussed in this research paper are those arising from the conversion of CT (Computed Tomography) numbers to stopping powers (SPRs) and those arising from MCS (Multiple Coulomb Scattering).

CT numbers are calculated using Stoichiometric Calibration which works by finding tissue substitutes of known chemical composition to find scanner specific parameters. Several formulae are then used to calculate Hounsfield Units (HUs) for tissues . Mean excitation energies (I-values) and electron densities are used to calculate relative proton stopping powers. Any uncertainties in this estimation also increase the uncertainties of proton range. [3 (also the source for the graph below)][4]

MCS is modeled using several theories like the Moliere theory which helps determine the distribution of scattering angles of a proton beam interacting with matter using several parameters like the characteristic and multiple scattering angles, screening and reduced angles along with concepts of gaussian distribution. The range degradation caused by MCS affects dose calculations while neutrons created by the interaction of protons with materials leads to higher contribution to the patient's whole body dose. Hence it is necessary to study and implement it. [5]

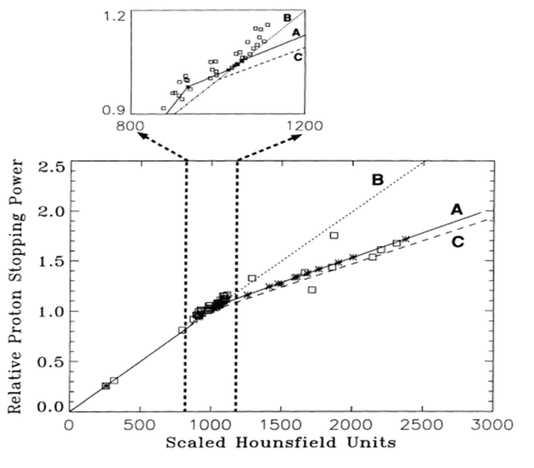


Figure 2. Calibration curves for the transformation of Hounsfield values into relative proton stopping power (ρ_e). The solid line shows the stoichiometric calibration (A) for biological tissues, the dotted line the tissue substitute calibration for Mylar/Melinex/PTFE (B) and the dashed line the tissue substitute calibration for B110/SB5 (C). The squares represent calculations for tissue substitutes and the stars are calculations based on the chemical composition of real tissues. The small plot shows in detail the Hounsfield number range corresponding to soft tissue.

SUPPORTING DATA

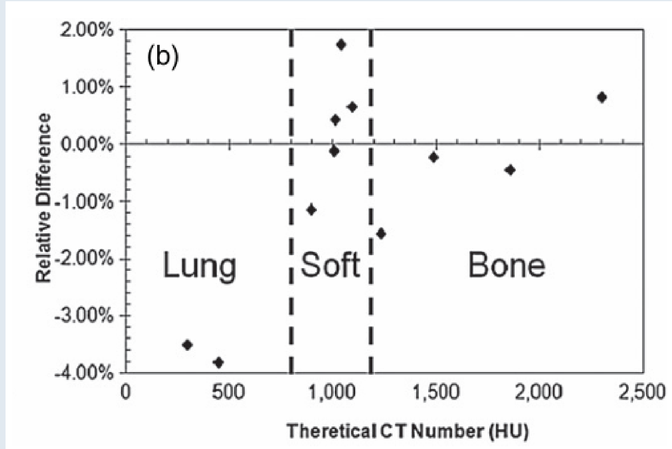


Table 1. Estimated proton range uncertainties and their sources and the potential of Monte Carlo for reducing the uncertainty. Paganetti and Goitein (2000), Robertson *et al* (1975) and Wouters *et al* (1996). The estimations are average numbers based on 1.5 standard deviations. Extreme cases, such as lung treatments, might show bigger uncertainties.

Source of range uncertainty in the patient	Range uncertainty without Monte Carlo	Range uncertainty with Monte Carlo
Independent of dose calculation		
Measurement uncertainty in water for commissioning	±0.3 mm	±0.3 mm
Compensator design	±0.2 mm	±0.2 mm
Beam reproducibility	±0.2 mm	±0.2 mm
Patient setup	±0.7 mm	±0.7 mm
Dose calculation		
Biology (always positive) ˆ	+∼0.8%	+∼0.8%
CT imaging and calibration	±0.5%[a]	±0.5%[a]
CT conversion to tissue (excluding I-values)	±0.5%[b]	±0.2%[g]
CT grid size	±0.3%[c]	±0.3%[c]
Mean excitation energy (I-values) in tissues	±1.5%[d]	±1.5%[d]
Range degradation; complex inhomogeneities	−0.7%[e]	±0.1%
Range degradation; local lateral inhomogeneities *	±2.5%[f]	±0.1%
Total (excluding *, ˆ)	2.7% + 1.2 mm	2.4% + 1.2 mm
Total (excluding ˆ)	4.6% + 1.2 mm	2.4% + 1.2 mm

The number are estimations based on finding by
[a] Chvetsov and Paige (2010).
[b] Schaffner and Pedroni (1998) and Matsufuji *et al* (1998).
[c] Espana and Paganetti (2011).
[d] ICRU (1993), Bichsel and Hiraoka (1992) and Kumazaki *et al* (2007).
[e] Sawakuchi *et al* (2008), Bednarz *et al* (2010) and Urie *et al* (1986).
[f] Bednarz *et al* (2010).
[g] Espana and Paganetti (2010).

The graph is borrowed from [4] and shows the relative difference between the calculated and measured CT numbers for **tissue substitutes** (which do not show as high correlation with proton stopping powers as real tissues as shown in graph on bottom left). This is the highest for lung as can be seen.

Since there is no perfect one to one correlation between CT numbers and SPRs, their calibration has posed a challenge in proton beam therapy. They lead to an uncertainty of about 3.0%-3.4% in the proton range. [5] HUs can be average over a voxel for heterogenous geometries with varying densities, e.g. in lung causing problems. [9] Although CT scanners could provide SPRs, as of 2019, such a system that would be commercially viable has not been developed. Using dual-energy CT (DECT), another method has been developed which uses a proprietary algorithm to calculate relative electron density and an effective atomic number image, which are then used to determine I-values. However, since they dealt with tissues of well defined composition with not much mixing of tissues involved, this method may not work for real human tissues. CT artifacts from metal implants can also lead to significant uncertainties if their incorrect Hounsfield units are not overwritten. [5]

Since analytic algorithms are unable to incorporate the effects of range degradation (caused by MCS), they lead to underestimation of doses provided to critical structures at the distal end of the target volume. [5] This, along with the vast number of theories considered to model events during proton interaction with matter in Monte Carlo Algorithms, has led to overwhelming evidence in the favour of their use for dose calculations and study of proton scattering behaviour. [6] [7] One example is an inter-institutional study conducted in 2017. Of the 5 institutions that participate in the test of irradiating lung phantoms to compare their calculated and measured dose, only 1 passed when using analytical algorithms while 4 passed when using Monte Carlo, despite the criteria for success being very low. [8] The table above also shows a quantitative analysis of their uncertainties summarised from several different papers. [9] Despite Monte Carlo being considered the gold standard for dose calculations, they still suffer from uncertainties. These algorithms were designed for study of high energy physics, hence specific physics settings are more accurate for specific energy ranges such that the codes need to be tailored for proton beam therapy. Uncertainties in the mean excitation energy values also affect them. Modelling of treatment head with sufficient accuracy is also a challenge. [9]

CONCLUSION

The issues of uncertainties raised in the hypothesis are indeed a huge problem in delivering proton beam therapy as there are many complicated theories coming into play when protons interact with matter, each with its own sources of uncertainties. Though development of technology and methods by the hard work of researchers and companies has led to significant advancement in tackling these uncertainties (such as in the case of Monte Carlo algorithm development to tackle uncertainties due to MCS and the use of DECT to tackle the uncertainties arising from the conversion of CT numbers to SPRs), there is still much room for improvement. The case for lung is often mentioned as the worst case scenario due to its heterogeneous geometry such that it is difficult to implement these methods to the lung case. These uncertainties, along with the high cost of development and the resulting low availability of proton therapy centres are the major problems faced by proton beam therapy.

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