Comparison of x ray computed tomography number to proton relative linear stopping power conversion functions using a standard phantom^{a)}

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Purpose: Adequate evaluation of the results from multi-institutional trials involving light ion beam treatments requires consideration of the planning margins applied to both targets and organs at risk. A major uncertainty that affects the size of these margins is the conversion of x ray computed tomography numbers (XCTNs) to relative linear stopping powers (RLSPs). Various facilities engaged in multi-institutional clinical trials involving proton beams have been applying significantly different margins in their patient planning. This study was performed to determine the variance in the conversion functions used at proton facilities in the U.S.A. wishing to participate in National Cancer Institute sponsored clinical trials.

Methods: A simplified method of determining the conversion function was developed using a standard phantom containing only water and aluminum. The new method was based on the premise that all scanners have their XCTNs for air and water calibrated daily to constant values but that the XCTNs for high density/high atomic number materials are variable with different scanning conditions. The standard phantom was taken to 10 different proton facilities and scanned with the local protocols resulting in 14 derived conversion functions which were compared to the conversion functions used at the local facilities.

Results: For tissues within ± 300 XCTN of water, all facility functions produced converted RLSP values within $\pm 6\%$ of the values produced by the standard function and within 8% of the values from any other facility's function. For XCTNs corresponding to lung tissue, converted RLSP values differed by as great as $\pm 8\%$ from the standard and up to 16% from the values of other facilities. For XCTNs corresponding to low-density immobilization foam, the maximum to minimum values differed by as much as 40% .

Conclusions: The new method greatly simplifies determination of the conversion function, reduces ambiguity, and in the future could promote standardization between facilities. Although it was not possible from these experiments to determine which conversion function is most appropriate, the variation between facilities suggests that the margins used in some facilities to account for the uncertainty in converting XCTNs to RLSPs may be too small. © 2014 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4870956>]

Key words: proton, computed tomography, phantom

1. INTRODUCTION

A major uncertainty that affects the margins to apply in planning treatments with proton and other light ion beams is the function that converts x ray computed tomography numbers (XCTNs) to light ion relative linear stopping powers (RLSPs). Determination of this conversion function has been difficult in the past because: (1) real tissues are difficult to form into shapes conducive to high accuracy measurements; (2) real tissues are difficult to maintain in a state found in live bodies; (3) more than one material may be represented by a given XCTN; and (4) the radiological properties of tissue substitutes do not match tissues with sufficient accuracy for light ions. Most facilities currently derive the conversion function by making measurements of many tissue substitutes and using complicated fitting procedures. These tedious measurements and complicated fitting procedures are also required for verification of the conversion function for routine quality assurance procedures. The lack of accurate tissue equivalent substitute

materials has resulted in each light ion facility devising their own methods and phantoms for determining the conversion function.

The accuracy of obtaining the correct RLSP for a given XCTN from these conversion functions has typically been stated in the open literature as being approximately $\pm 3.2\%$ at the 2 s.d. level.¹⁻³ On the other hand, because each facility uses different methods and phantoms, a comparison of the conversion functions obtained at different facilities has never been performed. For evaluation of results from multi-institutional treatment protocols, the uncertainty values for these conversion functions and the resulting margins applied in patient treatment plans is required. During 2010 and 2011, the National Cancer Institute (NCI), in conjunction with the Massachusetts General Hospital (MGH) Federal Share funds, sponsored a proton treatment facility site review program, conducted by the University of Texas M.D. Anderson Radiological Physics Center (RPC), to approve proton facilities to use protons in NCI funded clinical trials. Site visits were

performed at eight proton facilities in the U.S.A. and included reviews of dosimetry, treatment planning practices, and imaging capabilities. During each site visit an XCTN to proton RLSP function was generated using a standard phantom which was then compared to the function used by the facility's treatment planning system (TPS). Some facilities used more than one XCT scanner for proton patients and some used more than one protocol with a particular scanner. Three additional conversion functions were obtained using scanners at two additional proton facilities using the exact same procedure but not during official RPC site visits. A separate conversion function was measured for each scanner and protocol used clinically resulting in a total of 14 conversion functions for comparison. This report describes the measurements and results from these site visits.

2. METHODS AND MATERIALS

A method and standard phantom were designed and built to make determination of the conversion function simple and quick.⁴ The design was based upon the premises that: (1) all XCT scanners are calibrated daily for air and water values; (2) XCTNs are variable with scanning conditions for high density/high atomic number ($H\rho Z$) materials; and (3) most conversion functions in the past have been linear above an XCTN/RLSP of 1050/1.05. A conversion function can therefore be established using only air, water, and a single $H\rho Z$ sample material. Elaboration of these premises is given in the following paragraphs.

Kijewski and Bjärngard⁵ postulated that any tissue, except fat, could be considered a mix of air, "water-equivalent" material, and bone mineral in different proportions. For any tissue with an XCTN less than that of water, the atomic number of the tissue could be considered to be equivalent to that of water. The XCTNs for these tissues would therefore be different only because of different average physical densities due to the presence of air, such as in the cavities of the lung. Since the XCTNs of air and water are calibrated at all kVps to yield values of 0 and 1000, then any tissue mix of air and water-equivalent material must therefore have an XCTN that is independent of kVp. This kVp independence may not hold, however, for fatty tissue or tissue substitute materials that have a high carbon concentration and low oxygen concentration compared to water. To check the kVp independence assumption for materials with an XCTN less than water, XCT scans of a Gammex, Inc. Model 467 phantom (Middleton, WI) that contained multiple hydrocarbon-based tissue substitute materials were acquired using a General Electric Medical Optima CT590 RT scanner (Milwaukee, WI) that produced a conventional polyenergetic x ray spectrum. Scans were acquired at 80, 100, 120, and 140 kVp and the XCTNs checked for four of the tissue substitute materials contained within the phantom: LN-300 (lung), LN-450 (lung), BR12 (breast), and AP6 (adipose).

For tissues with XCTNs above the XCTN corresponding to water (in the standard model presented here tissues with XCTNs above the XCTN corresponding to muscle), the tissue is considered a mix of water (muscle) and bone mineral. Due

to the high atomic number component of the bone mineral that has an enhanced photoelectric effect, the XCTN of these tissues is kVp dependent. Fortunately, most published XCTN to RLSP conversion functions have shown that the function is linear above an XCTN of 1050 such that a measurement for a single $H\rho Z$ material can be used to parameterize the conversion function (see Fig. 5 of Ref. 7 for a comparison of several conversion functions).

Requirements for the phantom were that the diameter should be similar to a patient, the shape should minimize artifacts, and the size of the $H\rho Z$ sample should be small enough not to cause perturbations in the generated image. The phantom consisted of a 300 mm diameter wood ring with a back of wood and a front of clear polycarbonate for viewing of proper filling with water. The total thickness of the phantom was 58 mm with the thickness of the contained water being 35 mm. A port and plug were provided at the top of the phantom for filling and emptying. A 9.5 mm diameter cylindrical aluminum plug was inserted near but slightly below the center of the phantom. Figure 1 shows a typical image acquired of the standard test phantom.

The function to be used with this phantom was derived through a series of steps. First, calculated light ion RLSPs and calculated XCTNs at a single kVp for various tissues were examined and compared to values measured or calculated by previous investigators. Next, the variation of XCTNs for these tissues and aluminum as a function of the effective photon energy (keV_{eff}) was calculated and thus the variation in the conversion function as a function of the keV_{eff} was determined. Finally, a single parameter was derived to define the shape of the conversion function as a variable of the XCTN of aluminum. This parameter is the RLSP value for an XCTN value of 4095 as given by Eq. (1) taken from Ref. 4,

$$\begin{aligned} RLSP_{4095} = & 16.616 - (1.0323 \times 10^{-2} * SXCTN_{Al}) \\ & + (2.5181 \times 10^{-6} * SXCTN_{Al}^2) \\ & - (2.1339 \times 10^{-10} * SXCTN_{Al}^3), \end{aligned} \quad (1)$$

where $SXCTN_{Al}$ is the XCTN of the aluminum plug after all the XCTNs in the image have been rescaled to give $SXCTNs$

FIG. 1. XCT image of phantom.

TABLE I. Values for SXCTN to RLSP conversion function.

SXCTN	RLSP	Comment
0	0.000	Air
800	0.800	...
900	0.950	Fat
1000	1.000	Water
1050	1.050	Muscle
4095	RLSP ₄₀₉₅	Maximum

for air and water of 0 and 1000, respectively. Rescaling of the XCTNs within the scan images was accomplished by determining the average value for air at numerous locations outside the phantom and the average value for water at various locations inside the phantom and then applying Eq. (2) taken from Wrightstone *et al.*⁶ and reproduced in Moyers *et al.*⁷ The complete conversion function after scaling the XCTNs is given in Table I where straight line segments connect the data points. The data point representing adipose tissue (SXCTN of 900; RLSP of 950) was taken from Refs. 2 and 3,

$$\text{SXCTN}_{\text{mat}} = \left(\frac{\text{XCTN}_{\text{mat}} - \text{XCTN}_{\text{wat}}}{\text{XCTN}_{\text{wat}} - \text{XCTN}_{\text{air}}} \right) \times 1000. \quad (2)$$

After construction of the phantom, the validity of its use was tested by performing XCT scans at multiple kVps at one institution and deriving keV_{eff} and RLSP₄₀₉₅ values. These measurements were performed with a General Electric Medical HiSpeed CT/i scanner (Milwaukee, WI) that produced a conventional polyenergetic spectrum.

For the multi-institutional comparison of conversion functions, the phantom was taken to each facility and scanned with the local XCT scanner using the same protocol(s) used to scan patients being prepared for proton beam treatments. The images were then loaded into a TPS and measurements of the XCTN of water and air were sampled at several locations inside and outside the phantom, respectively, being careful to avoid any regions with image artifacts. The sampled values were then scaled and used to generate a conversion function for each scanner and protocol. These conversion functions were then compared to the conversion functions used by the local TPS as reported by the local staff.

3. RESULTS AND DISCUSSION

Table II gives the results of the hydrocarbon-based tissue substitute phantom tests at different kVps. The difference in SXCTNs between 80 and 140 kVp was less than or equal to 6.0% for all four materials. In this intercomparison study, however, facilities only used kVps of 120 and 140 kVp. The difference in SXCTNs between these two clinically-used kVp values was less than 1.4% for all four hydrocarbon-based materials. The difference for water-based materials, including all soft tissues except for fat, is expected to be negligible. The standard conversion function between SXCTN of 0 and 1000, as given in Table I, was thus validated for use in this intercomparison.

TABLE II. Results from hydrocarbon tissue substitute phantom kVp investigation.

kVp set	SXCTN LN-300	SXCTN LN-450	SXCTN AP6	SXCTN BR12
80	301	464	893	956
100	291	461	905	956
120	286	454	912	956
140	284	448	915	960

Table III gives the results of the initial tests of the standard phantom at different kVps. As expected, the results show that the converted RLSP for very large SXCTN is quite sensitive to the kVp used for the scan. If a facility uses different protocols during scanning of patients for treatment planning, then multiple conversion functions should be generated and applied appropriately. It should be noted that the RLSP₄₀₉₅ fitting parameter was only tested with an XCT scanner beam having a conventional polyenergetic spectrum. The fitting parameter may not be appropriate for use with monoenergetic beams such as from synchrotron sources or heavily filtered XCT beams used to separate low-energy and high-energy photons for dual-energy scanning.

Figures 2(a)–2(n) show comparisons of the facility reported and site visit measured conversion functions for each scanner and protocol. The functions used by the facility TPSs are shown as solid (black) curves, while the functions measured during the site visits are shown as dashed (red) curves. For each graph, the RLSP values are given on the axis at the left. The percentage difference between the facility and standard functions are plotted as solid (green) curves with the values given on the axis on the right. Percentage differences for an SXCTN of 0 could not be calculated because of the 0 value in the denominator. The scanner number given in the legend of each graph indicates the anonymized facility and the scanner or scanning protocol.

Figure 2(a) shows that the facility function and standard function for scanner 1.1 were within about $\pm 4\%$ for all XCTNs except for values above 3500. According to facility staff, the TPS at this facility does not allow direct assignment of RLSP values to voxels of a RLSP image as is typically required for metallic implants. Instead, this facility's TPS requires the user to reassign XCTNs to voxels within the XCT image and then apply a stored conversion function using RLSP values previously assigned to the XCTNs. This procedure resulted in the artificial rapid increase of the conversion function for high XCTNs.

TABLE III. Results from standard phantom kVp investigation.

kVp set	Meas SXCTN _{AI}	Derived keV_{eff}	Derived RLSP ₄₀₉₅
80	3515	64	2.18
100	3201	72	2.38
120	2983	81	2.57
140	2866	87	2.69

FIG. 2. SXCTN to RLSP conversion functions for various scanners and scanning protocols. In each graph, the solid (black) curve represents the function used clinically at the facility. The dashed (red) curve represents the standard conversion function derived during the site visit. The solid (green) curve represents the percentage difference between the facility and the site visit derived standard conversion functions.

FIG. 2. (Continued.)

The results shown in Fig. 2(b) for scanner 2.1 indicate there are three separate regions of XCTNs to discuss; low XCTNs representative of immobilization foams and lung tissue, XCTNs corresponding to fat, and high XCTNs corresponding to bone and implants. According to the staff at this facility, the TPS supports entry of RLSP values into the conversion function using only two digits beyond the decimal point. This restricts the value entered for air to either 0 or 0.01. This facility chose to enter a value of 0.01. This results in deviations from the measured standard function for low XCTNs. These values will not significantly affect the RLSPs of soft tissues but, if a treatment beam passed through a large amount of immobilization foam, the depth of penetration could be different than given in the plan. As an ex-

ample, if a beam passed through 200 mm of immobilization foam with a RLSP of 0.04, then this difference would equate to a difference in penetration of 0.7 mm. In the second region, for XCTNs between 850 and 1000, the differences are due to differences in the way the functions are modeled. The standard function assumes that tissues in this region consist of fat (SXCTN of 900 yields RLSP of 0.950), while the facility's function assumes that tissues are a mix of air and water (SXCTN of 900 yields RLSP of 0.901). Both cases could occur in real patients but the standard function assumed that in most situations there will be many more voxels containing fat than an air/water combination. One might imagine that increased accuracy could be obtained if a facility used one conversion function containing a specific point

for fat for scans of the abdomen where fat is abundant and a different conversion function that does not contain a specific point for fat for scans of the head where there is less fat but many partial voxel volumes consisting of air, muscle, and bone. On the other hand, Schaffner and Pedroni³ showed that very few voxels of a head scan have XCTNs in the range of fat so using a conversion function with a point specifically for fat for a body region containing very little fat may make little difference in optimizing the beam penetration. In the future, dual-energy XCT may eliminate this dilemma of which model to choose for the conversion function. In the third region, for XCTNs above 1 050, the two functions are seen to diverge. An investigation showed that the phantom was scanned with a facility approved protocol that uses 140 kVp, while the facility conversion function was generated at 120 kVp.

Figures 2(c) and 2(d) show results from two different scanners (3.1 and 3.2) located at one facility. The TPS at this facility does not allow scaling of XCTNs for individual patients, in other words it does not force the XCTN of air to be 0 and the XCTN of water to be 1000. Facilities with such systems customarily generate conversion functions with the XCTNs for air and water slightly offset from the scanner calibrated values to accommodate the values expected for an “average” patient. When a patient is significantly different than the average patient, errors in prescribed range could result. For both scanners 3.1 and 3.2 and for low XCTNs, such as encountered with immobilization foam, differences between the standard and facility RLSP values were as large as +27%. To put this difference into perspective, if a beam passed through 200 mm of immobilization foam with a RLSP of 0.04, then this difference would equate to a difference in penetration of 2.2 mm. For scanner 3.1, above an XCTN of 1 050 the facility and standard functions diverged. This divergence currently remains unexplained. For scanner 3.2, a divergence between the facility and standard functions also existed but in an opposite direction from that for scanner 3.1. After the site visit, the facility generated a new function for scanner 3.2 that was closer to the standard function measured by the RPC.

Figures 2(e) and 2(f) for scanners 4.1 and 4.2 compare conversion functions for one scanner but operated at two different kVps. Both graphs show excellent agreement between the facility and standard functions in the region with XCTNs greater than 1 500. On the other hand, significant deviations ($\approx 7\%$) were found around XCTNs corresponding to lung tissue. This facility used a hydrocarbon-based tissue substitute phantom for generating the conversion function so the difference between the RLSPs for the lung substitute and real lung tissue is the suspected cause for the difference in conversion functions. To put this difference into perspective, if a beam were to traverse 100 mm of lung tissue with a RLSP of 0.3, then this difference would equate to a difference in penetration of 2.1 mm.

Figure 2(g) shows the results for scanner 5.1. This facility uses a TPS that does not allow scaling of XCTNs for individual patients. Only small deviations were found in the region of XCTNs between air and water but above an XCTN of 1 050, significant deviations between the standard function and the

facility function were found. This facility was requested to further investigate their conversion function.

Figure 2(h) shows the results for scanner 6.1. Large deviations between the standard and facility functions were found for low XCTNs but in an opposite direction from that seen for scanners 2.1, 3.1, and 3.2. Although the TPS used at this facility has the same restriction of two digits past the decimal point for RLSP values as does the TPS used at the facility of scanner 2.1, the conversion curve used at this facility has an inflection point at an XCTN of 100 making the percentage difference drop to -10% . Above an XCTN of 1050 the standard and facility functions diverged reaching a value of -10% for the highest XCTN. For an XCTN representing hard bone the difference in RLSP was only about 3%.

Figure 2(i) shows the results for scanner 7.1. The graph and comparison is very similar to that for scanner 6.1 except at the highest XCTN where the difference is seen to reach almost -15% .

Figures 2(j) and 2(k) for scanners 8.1 and 8.2 are for a single scanner but operated in axial and helical modes, respectively, and both at 120 kVp. The axial mode was performed with a 2.5 mm wide detector, whereas the helical mode was performed with a total collimation width of 40 mm using 16 detectors each with a width of 2.5 mm. When operated in axial mode, the standard and facility functions match very well. When operated in helical mode, the standard and facility functions diverge above an XCTN of 1050 reaching a difference of about -3.5% for hard bone and -8.1% for the maximum XCTN. The derived standard function is similar to what would be obtained by a scanner operating at 140 kVp but a check of the DICOM header of the image files verified that 120 kVp was used.

Figure 2(l) shows the results for scanner 9.1. The percentage difference curve has a different shape than all of the other scanners with a rather constant offset for XCTN less than that of fat. For all XCTN however, the maximum difference is less than $\pm 6\%$.

Figures 2(m) and 2(n) for scanners 10.1 and 10.2 are for a single scanner but operated in helical and axial mode, respectively, and both at 120 kVp. For this scanner, the helical and axial modes gave essentially identical results. This is in contrast to that seen for scanner 8. One difference between the helical scans for scanners 8 and 10 is that the scan with scanner 8 was performed with a total collimation width of 40 mm, whereas the scan with scanner 10 was performed with a total collimation width of 10 mm (8×1.25 mm). It should be noted that several of the other site visit facilities that used helical scans used smaller widths between 4.5 mm (6×0.75 mm) and 10 mm (16×0.625 mm). Although the XCTNs were extracted from slices near the middle of the water contained within the test phantom, the test phantom is only 58 mm long in the table scan direction and the large total collimation width for scanner number 8.2 cannot be discounted from having an influence on the derived conversion function. Future studies of the effect of the total collimation width on the conversion function for use with narrow test phantoms and, more importantly, for patients with rapidly changing diameters with respect to the table scan direction, are therefore

FIG. 3. Summary of differences between facility and site visit derived standard conversion functions.

warranted. Examples of rapidly changing external patient diameters are at the superior end of the head and the transition from the neck region to the shoulders region. An example of a rapidly changing water equivalent diameter is at the transition from the chest region containing multiple air cavities to the abdomen region which is full of near unit density soft tissues. Until careful investigations have been performed concerning the effect of large total collimation widths on the values of XCTNs in these transition scan regions, it may be prudent to limit the total collimation width to small widths known to have minimal effects. Below an XCTN of 500, the percentage difference curves for scanners 10.1 and 10.2 are similar to scanners 6.1 and 7.1 which were at facilities that use the same TPS. The typical fat bump normally seen around an XCTN of 900 is seen to be shifted down to around an XCTN of 800 for this function. For XCTNs greater than water, the percentage difference curve first decreases to a minimum around XCTNs corresponding to hard bone and then increases for higher XCTN. For very large XCTNs above 4000, the facility has inserted artificial RLSPs to accommodate titanium implants.

Figure 3 plots all of the percentage difference results together on one graph. For tissues having XCTN values within ± 300 that of water, the conversion functions for all scanners and modes produced converted RLSP values within $\pm 6\%$ of the values produced by the standard functions and within 8% of the values from any other function. For XCTNs corresponding to lung tissue, some functions had differences in converted RLSP values as great as $\pm 8\%$ from the standard functions and up to 16% different from the values of other facilities. For XCTNs corresponding to low-density immobilization foam, the maximum-to-minimum differences in RLSP values were as great as 40%. It was not possible from these experiments to determine which conversion function is the most appropriate for use but the median percentage differences between the facility and standard derived RLSPs over all XCTNs, scanner functions, and site visits is approximately zero indicating that the standard function is a good baseline match to the collective U.S.A. proton experience. Experiments with real tissues would need to be carefully performed

to determine if the standard function needs to be adjusted. The RLSP values determined by the conversion function at some XCTNs for some facilities differ largely ($\pm 3\%$ – $\pm 25\%$) from the collective experience indicating that the uncertainty associated with converting XCTN to RLSP might be larger than experiments performed at individual facilities have predicted.

The margins that planners place around targets and organs-at-risk to optimize beam shaping are dependent upon many factors, the XCTN to RLSP conversion function being just one of those factors. These factors are typically categorized into one of two groups, penetration uncertainties due to physical characterization (PUPC) and penetration uncertainties due to beam delivery (PUBD).⁸ The margin due to PUPC, which may have nine or more components, is generally applied as a percentage of the water equivalent thickness through which the beam passes and planners typically use values between 2.5% and 5.0% at the 1.5–2 s.d. level. The margin due to PUBD is generally applied as a fixed water equivalent thickness and planners typically use values between 1 and 3 mm at the 1.5–2 s.d. level. Although the magnitudes of the various components that make up the PUPC have been assigned different values by different investigators, the largest component has generally been accepted to be the uncertainty in the XCTNs themselves at around 2.5%.^{9,10} This study suggests that, at least for some facilities, the XCTN to RLSP conversion function uncertainty may be larger than the XCTN accuracy thereby necessarily increasing the total PUPC margin that should be applied. Facilities that apply PUPC margins that do not take into account all of the various uncertainties, including a realistic XCTN to RLSP conversion function uncertainty, risk geometric misses thereby underdosing targets and/or overdosing critical organs-at-risk.

4. CONCLUSIONS

Several conclusions can be extracted from this study. Separate conversion functions are required for scanners operating at different kVps. The scanner calibration, particularly the value for air, can have a significant affect on the conversion function. Scaling of XCTNs for individual patients can allow increased accuracy in beam penetration when using a facility determined conversion function but incorrect scaling could lead to decreased accuracy. TPS manufacturers should provide three digits beyond the decimal point for entry of RLSP values to allow proper conversion of low-value XCTNs. The new calibration method and phantom greatly simplifies determination of the conversion function, reduces ambiguity, and in the future could promote standardization between facilities and reduction of uncertainties. Development of more accurate tissue-substitute materials for generating conversion functions also has the potential to reduce uncertainties. Careful investigations should be performed on the accuracy of XCTNs in regions of the patient with rapidly changing water equivalent diameters prior to using helical mode with large total collimation widths. For the present, the variation in conversion functions between facilities suggests that the margins applied around targets and organs-at-risk by some facilities to account for the uncertainty in converting XCTNs to

RLSPs may be too small; the impact of the uncertainty being dependent upon the water equivalent thickness of the materials traversed by the beam and the water equivalent thickness between targets and neighboring organs-at-risk. Although an error in the conversion function may have a smaller effect on beam penetration than other factors, such as the accuracy of the XCTNs, the contribution of an error in the conversion function on beam penetration cannot be ignored. Conversion functions should therefore be examined carefully to avoid deviations between planned and delivered beam penetrations.

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