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Original Research Article

Comparison of single and dual energy CT for stopping power determination in proton therapy of head and neck cancer

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ABSTRACT

Background and purpose: Patients with head and neck (HN) cancer may benefit from proton therapy due to the potential for sparing of normal tissue. For planning of proton therapy, dual-energy CT (DECT) has been shown to provide superior stopping power ratio (SPR) determination in phantom materials and organic tissue samples, compared to single-energy CT (SECT). However, the benefit of DECT in HN cancer patients has not yet been investigated. This study therefore compared DECT- and SECT-based SPR estimation for HN cancer patients.
Materials and methods: Fourteen HN cancer patients were DECT scanned. Eight patients were scanned using a dual source DECT scanner and six were scanned with a conventional SECT scanner by acquiring two consecutive scans. SECT image sets were computed as a weighted summation of the low and high energy DECT image sets. DECT- and SECT-based SPR maps were derived. Water-equivalent path lengths (WEPLs) through the SPR maps were compared in the eight cases with dual source DECT scans. Mean SPR estimates over region-of-interests (ROIs) in the cranium, brain and eyes were analyzed for all patients.
Results: A median WEPL difference of 1.9 mm (1.5%) was found across the eight patients. Statistically significant SPR differences were seen for the ROIs in the brain and eyes, with the SPR estimates based on DECT overall lower than for SECT.
Conclusions: Clinically relevant WEPL and SPR differences were found between DECT and SECT, which could imply that the accuracy of treatment planning for proton therapy would benefit from DECT-based SPR estimation.

1. Introduction

Treatment planning of proton therapy is today typically based on stopping power ratio (SPR) estimation from single-energy CT (SECT) images. The SPR is used in treatment planning to calculate the dose distribution and the proton range [1]. SPR can be estimated from a SECT scan applying a piecewise linear fit between CT numbers and SPRs, calibrated either on literature data for human tissues [2] or on measurements for tissue substitutes with known properties [3]. Using an empirical fit, all tissues cannot be estimated correctly as some tissues can have the same CT number but different SPRs or vice versa [4]. Patient-specific tissue variations can also cause large SPR estimation errors when estimated based on SECT [5]. Dual-energy CT (DECT) has been proposed by several groups for improving the SPR accuracy compared to SECT [4–8], and DECT has been shown to be superior to SECT for organic tissue samples [9–12].

DECT has been introduced into treatment planning of proton therapy [13,14]. In this clinical workflow, virtual mono-energetic images (VMIs) are used, which are comparable to SECT images acquired at a single energy instead of the full x-ray spectrum [15]. Hudobivnik et al. have compared dose calculations based on SECT and DECT scans in the brain region [16]. They found range differences on the order of 1 mm, but concluded this result to be insignificant as their DECT-based SPR estimation had an accuracy of the same order [16].

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Treatment planning comparisons have also been performed on prostate and brain tumor patients by Wohlfahrt et al. [14]. They found that the range shifts for brain tumors was 1.1 mm (1.2% of the total range) and 4.1 mm (1.7%) for prostate-cancer patients [14].

The advantages of DECT should be investigated for all potential proton therapy indications. Treatment of patients with head and neck (HN) cancer is a particular challenge due to the many critical normal tissues close to the targeted tumor-bearing volumes. These patients may therefore benefit considerably from proton therapy due to the possibility of improved normal tissue sparing [17]. Furthermore, it has been shown that larger range margins (up to around 6% + 1 mm) were needed in the HN region [18]. Accurate SPR calculation has therefore a considerable potential for these patients. DECT- and SECT-based SPR determination for the HN region has so far only been compared in a head phantom, indicating that DECT is superior to SECT, especially in heterogeneous regions [19]. The aim of this study was to compare DECT- and SECT-based SPR estimation in a cohort of HN cancer patients, in terms of water-equivalent path lengths (WEPLs) and SPR distributions in selected anatomical regions with homogeneous density. As the superiority of DECT has already been established in theoretical, phantom and animal tissue evaluations [4–7,9–11], any SPR deviations between DECT and SECT will be considered to be in favor of DECT-based proton therapy treatment planning.

2. Material and methods

2.1. Patient cohort

This study was approved by the local ethics committee in the Central Denmark Region (ESDH 1-10-72-61-16). In total, fourteen HN cancer patients were DECT scanned after written informed consent was obtained. The first eight patients were scanned with a Dual Source CT scanner (Group A) while the last six patients were scanned using a conventional SECT scanner by acquiring two consecutive scans at different kVp-settings (Group B). All patients were treated with photon-based radiotherapy, and they were scanned approximately mid-way through their treatment course (in week three or four).

2.2. SPR calculation

For the DECT-based SPR estimation, we used the method proposed by Taasti et al. [7]; the equations used for the SPR estimation were:

$$\mathrm{SPR}^{\mathrm{est}}_{\mathrm{soft}} = (1 + x_{\mathrm{s1}})u_H - x_{\mathrm{s1}}u_L + x_{\mathrm{s2}}u_L^2 + x_{\mathrm{s3}}u_H^2 + x_{\mathrm{s4}}(u_L^3 + u_H^3) \tag{1a}$$

$$\mathrm{SPR}^{\mathrm{est}}_{\mathrm{bone}} = (1 + x_{\mathrm{b1}})u_H - x_{\mathrm{b1}}u_L + x_{\mathrm{b2}}\frac{u_L}{u_H} + x_{\mathrm{b3}}(u_L^2 - u_H^2) + x_{\mathrm{b4}}(u_L^3 + u_H^3) \tag{1b}$$

The two equations were for soft and bone tissues, respectively, with the categorization of the two tissue types based on a nearest neighbor classification [20] (three nearest neighbors; more detail is given in the Supplementary Material (SM) S1.1). The calibration of these equations is described in SM S1.2.

The x-values in Eq. (1) were fitting parameters, and the u-values were so-called reduced CT numbers, which were calculated as follows:

$$u_j = \frac{\mathscr{H}_j - B_j^{tg}}{A_j^{tg}} \tag{2}$$

Here $\mathscr{H}_j$ was the CT number for the low, $j = L$, and the high, , energy spectrum, respectively. The calibration of the A- and B-parameters is described in SM S1.3.

For the SECT-based SPR estimation the stoichiometric method proposed by Schneider et al. [2] was used. Individual conversion curves were calibrated for each scanner, but the same constraints were used, whereby only the slopes of the different line segments differed. The conversion curve used for Group A can be seen in Fig. S2.1 in SM. The scanner characterization parameters, K^{ph}, K^{coh} and K^{KN}, used for the CT number prediction [2] were obtained from virtual 120 kVp SECT scans (Section 2.4) of a calibration phantom, Gammex Cone-Beam Electron Density Phantom (Gammex Inc., Middleton, WI).

2.3. DECT and SECT comparison

We calculated water-equivalent path lengths (WEPLs) from the DECT- and SECT-based SPR maps. The WEPLs were calculated along the proton beam paths through the entire slice using the Radon transform implemented in MATLAB (The MathWorks Inc., Natick, MA), for angles in the interval from 0° to 175° in steps of 5°. The projections through the SPR maps were multiplied by the pixel size to get WEPLs in millimeter. WEPLs equal to zero (i.e. proton paths entirely outside the body outline) in the SECT-based SPR maps were removed from the WEPL comparison.

WEPL difference maps were generated by subtracting the SECT- from the DECT-based WEPL map. The WEPL differences were reported as the root-mean-square (RMS) of the difference map, as well as RMS difference relative to the RMS of the DECT-based WEPL map, and as the 2.5% and 97.5% percentiles of the WEPL difference distributions to show the variation.

To compare the SPR directly, regions-of-interest (ROIs) were placed in reasonably homogeneous tissue regions, cranium bone, brain and eyes. The cranium bone was segmented using the bone classification applied in the DECT-based SPR method (SM S1.1). Only slices in the upper part of the head were included in the analysis, from the top of the eyes and upwards. The brain was segmented by placing a circular ROI in eight consecutive slices in the homogeneous brain region above the level of the lateral ventricle, and a circular ROI was placed in each eye in 3–5 slices.

The SPR comparison between the DECT- and SECT-based methods were based on mean SPR values over the ROIs. The SPR difference was taken relative to the mean SPR in the DECT-based SPR maps:

$$\Delta\mathrm{SPR} = \frac{\langle \mathrm{SPR}_{\mathrm{DECT}} \rangle - \langle \mathrm{SPR}_{\mathrm{SECT}} \rangle}{\langle \mathrm{SPR}_{\mathrm{DECT}} \rangle} \cdot 100\% \tag{3}$$

where $\langle ... \rangle$ denoted the mean over the ROI.

To quantify the uncertainty in the calculation caused by noise in the SPR maps, the standard error of the mean (SEM) was derived based on error propagation for the standard deviation, σ:

$$\mathrm{SEM}(\Delta\mathrm{SPR}) = \frac{100\%}{\sqrt{N}} \sqrt{\left(\frac{\langle \mathrm{SPR}_{\mathrm{SECT}} \rangle}{\langle \mathrm{SPR}_{\mathrm{DECT}} \rangle^2}\right)^2 \cdot \sigma^2(\mathrm{SPR}_{\mathrm{DECT}}) + \left(\frac{1}{\langle \mathrm{SPR}_{\mathrm{DECT}} \rangle}\right)^2 \cdot \sigma^2(\mathrm{SPR}_{\mathrm{SECT}})} \tag{4}$$

As the SEM is used in the calculation of the confidence interval, CI-95% = [μ−1.96·SEM,μ + 1.96·SEM], the magnitude of SEM relative to the magnitude of the SPR difference, ΔSPR, indicates if the result is statistically significant.

2.4. CT scan protocols

SECT images were generated by linearly weighted summation of the low and high energy DECT images, to simulate a 120 kVp image. This procedure was chosen not to expose the patients to an unnecessarily increased dose by acquiring both a DECT and SECT scan. Yu et al. have showed that this procedure can provide the same image quality as regular SECT images [15].

Patients in Group A were scanned with a Siemens SOMATOM Definition Flash dual source CT scanner (Siemens Healthineers, Forchheim, Germany) with a tube potential pair of 100/Sn140 kVp (Sn: 0.4 mm extra tin filtration). The two DECT scans were acquired simultaneous using two x-ray tubes with a 95° separation. Virtual 120 kVp SECT scans were generated during the reconstruction process at the scanner. The mixing parameter was set to $M = 0.6$ (Eq. (5)) as