Radiotherapy and Oncology xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

CT-based patient modeling for head and neck hyperthermia treatment planning: Manual versus automatic normal-tissue-segmentation

René F. Verhaart [a,*], Valerio Fortunati [b], Gerda M. Verduijn [a], Theo van Walsum [b], Jifke F. Veenland [b], Margarethus M. Paulides [a]

[a] Erasmus MC – Cancer Institute, Department of Radiation Oncology; and [b] Erasmus MC, Department of Medical Informatics and Radiology, Rotterdam, The Netherlands

ARTICLE INFO

Article history:
Received 17 June 2013
Received in revised form 10 January 2014
Accepted 25 January 2014
Available online xxxx

Keywords:
Manual segmentation
Automatic segmentation
Inter-observer variability
Intra-observer variability
Dosimetry
Sensitivity analysis

ABSTRACT

Background and purpose: Clinical trials have shown that hyperthermia, as adjuvant to radiotherapy and/or chemotherapy, improves treatment of patients with locally advanced or recurrent head and neck (H&N) carcinoma. Hyperthermia treatment planning (HTP) guided H&N hyperthermia is being investigated, which requires patient specific 3D patient models derived from Computed Tomography (CT)-images. To decide whether a recently developed automatic-segmentation algorithm can be introduced in the clinic, we compared the impact of manual- and automatic normal-tissue-segmentation variations on HTP quality.

Material and methods: CT images of seven patients were segmented automatically and manually by four observers, to study inter-observer and intra-observer geometrical variation. To determine the impact of this variation on HTP quality, HTP was performed using the automatic and manual segmentation of each observer, for each patient. This impact was compared to other sources of patient model uncertainties, i.e. varying gridsizes and dielectric tissue properties.

Results: Despite geometrical variations, manual and automatic generated 3D patient models resulted in an equal, i.e. 1%, variation in HTP quality. This variation was minor with respect to the total of other sources of patient model uncertainties, i.e. 11.7%.

Conclusions: Automatically generated 3D patient models can be introduced in the clinic for H&N HTP.

Hyperthermia, i.e. raising tissue temperature to 39–44 °C, has been shown to improve clinical outcome when added to radiotherapy or chemotherapy for several tumor sites [1–3], including the head and neck [4–6]. We recently developed a hyperthermia applicator to investigate the benefit of deep local heating of head and neck tumors [7,8]. The clinical use of this device requires hyperthermia treatment planning (HTP) based on electromagnetic simulations for pre-treatment and real-time treatment optimization and tissue dose assessment. Crucial inputs for HTP are full 3D patient models incorporating all normal tissues and the gross tumor volume (GTV). These models are generated by segmenting tissue regions on Computed Tomography (CT) images [9]. We recently developed an automatic-segmentation algorithm for head and neck HTP that has shown to be accurate, reproducible and substantially reduces operator time [10]. A clinical introduction of the algorithm requires a comparison of the impact of automatic segmentation on the hyperthermia treatment quality with the actual clinical standard, which is based on manual segmentations. Manual segmentations are prone to observer variation, and the patient model influences the accuracy of HTP for deep hyperthermia in the pelvic region [11,12]. Due to the large number of small tissue regions in the head and neck region, observer variation in tissue segmentation may have a substantial impact on the hyperthermia treatment quality, but, this impact has never been quantified.

CT-based observer variation in tissue segmentation has already been assessed for head and neck radiotherapy treatment planning [13,14]. However, while HTP requires a full 3D patient model, these studies included only a limited number of tissues, and many reported either inter-observer or intra-observer variation. But, although not complete, these studies provide an excellent reference to compare the results for separate organs.

Assessments of the exposure by electromagnetic sources of the human body also involve 3D human models. These studies often summarize causes of simulation uncertainties in an uncertainty budget, which includes uncertainties such as variations in dielectric tissue properties and variations in the gridsize [15,16]. Observer dependent tissue segmentation might also influence the

* Corresponding author. Address: Erasmus MC – Cancer Institute, Department of Radiation Oncology, Hyperthermia Unit, Groene Hilledijk 301, P.O. Box 5201, 3008 AE Rotterdam, The Netherlands.
E-mail address: r.f.verhaart@erasmusmc.nl (R.F. Verhaart).

http://dx.doi.org/10.1016/j.radonc.2014.01.027
0167-8140/

simulated electromagnetic field, however this confounding influence usually is not included in the uncertainty budget.

In this paper we report the manual and automatic CT-based segmentation variation for the tissues included in the 3D patient models for head and neck HTP. In addition, we compared the impact of the manual and automatic segmentation variation on the HTP outcomes, i.e. the planned hyperthermia dose and HTP quality. To quantify the importance of segmentation variations, we compare their influence to those of other sources of patient-modeling variation, i.e. gridsize and dielectric tissue-property uncertainties. The decision, whether or not to introduce the automatic-segmentation algorithm into the clinic, can be based on these results.

Materials and methods

Patient selection

The analysis presented in this paper covers 7 of the 34 patients treated with head and neck hyperthermia thus far. The patients were selected to represent the patient population eligible for head and neck hyperthermia, i.e. the patients included were balanced per tumor site, and both small (T2) and large (T4) tumors were included (Supplementary Table 1).

Computed Tomography (CT) images

CT scans acquired for radiotherapy treatment planning were used for HTP, leading to advantages in logistics and target region assignment. To make the group of patients for our study as representative as possible, we included CT scans of patients with distinct characteristics to span the entire patient population variability.

CT scans of the patients were obtained using a Somatom Sensation Open (Siemens AG, Erlangen, Germany), except for patient 3, who was scanned with a PQ 5000 (Philips Healthcare, Best, the Netherlands). The slice spacing varied from 1.5 to 2.5 mm and the in-plane resolution varied from 0.7×0.7 mm to 1.0×1.0 mm, with a scan matrix of 512×512. For patients 1–5, an intravenous injection of 100 ml contrast agent (Omnipaque 300, GE Healthcare Inc.) was administered with an injection rate of 1.8 ml/s, and imaging was performed 45 s after injection.

Segmentation protocol

All CT slices are segmented into several normal tissues and the target volume. We used the clinical target volume (CTV) as the hyperthermia target volume (HTV), and segmented the GTV in order to assign tumor dielectric tissue properties to this region. The list of segmented tissues was based on the visibility on CT and the dielectric (and thermal) property contrast with adjacent tissues. The brain, spinal cord and eyes were segmented since these are highly thermo-sensitive tissues. Therefore, the thermal dose should be restricted in these tissues. Note that thresholds were not used in the optimization, and are only relevant in online steering since absolute SAR level calculations require the clinically applied power.

First, an in-house developed tool (implemented in MevisLab v.2.2.1, MeVis Medical Solutions AG, Bremen, Germany) was used to remove non-patient structures, such as the patients' bed and the patients' immobilization mask. Second, Hounsfield (HU) thresholds were applied to segment bone (HU: 200–3000), muscle (HU: 0–200), fat (HU: −300 to 0), lungs and internal air (HU: −1000 to −300) [17]. The lungs were separated from the internal air by applying the threshold only to the slices that contain lung tissue. Third, the automatically segmented bone was manually corrected in case of streak artifacts, and when blood vessels were incorrectly assigned as bone due to the presence of contrast agent. Fourth, the tissues in the brain (cerebrum, cerebellum, brainstem), the spinal cord (myelum), the eyes (sclera, lens, vitreous humor, optical nerve) and the other head and neck tissues (thyroid gland, thyroid and cricoid cartilage) were segmented manually using iSeg (v.3.1, Zurich Med Tech AG, Zurich, Switzerland) and automatically using a multi-atlas approach combined with intensity modeling [10]. Fifth, the HTV and GTV were both manually segmented in Focal (v.4.64, Elekta AB, Stockholm, Sweden) by a head and neck radiation oncologist.

Hyperthermia treatment planning (HTP)

Hyperthermia treatment planning was performed as described by Rijnen et al. [18]. For electromagnetic field simulations, a uniform gridsize of 2 mm was chosen. Dielectric tissue properties, i.e. relative permittivity (ϵ_r), effective conductivity (σ_{eff}) and volume density of mass (ρ) were assigned to each tissue [19,20] (Supplementary Table 2). The commonly used 1g-averaged and 10g-averaged specific absorption rate (SAR) standards [IEEE/IEC62704-1] as calculated in SEMCAD-X (v.14.8.1, Schmid & Partner Engineering AG, Zurich, Switzerland) were used for SAR dosimetry.

For the tissue property sensitivity study, we reduced computational time twelve-fold by performing only one simulation, i.e. a simulation with all antennas exited using optimized phase and amplitude settings instead of a simulation per antenna and a subsequent weighted summation of the fields. The validity of this approximation for the sensitivity analysis was verified for three variations (ϵ_r: +6%, σ_{eff}: +6%, ρ: +3%), in which we observed an average error in HTP quality ($|\Delta HTQ|$) of only 0.2% (min–max: 0.02–0.6%).

Segmentation evaluation

Three trained medical radiation technologists (observer 1, observer 2, observer 3) and one radiation oncologist (reference) manually segmented per patient the ten tissues, see Fig. 1 for segmentation examples. The reference segmented the seven patient models only once, while the 3 other observers segmented them twice to investigate intra-observer variation. The manual tissue segmentation of one patient took on average 5–6 h, all segmentations were done within 4 weeks and the time between first and second segmentation of the same patient varied between 1–15 days. The images were anonymized and supplied in a random order to minimize bias in the manual segmentations. The automatic-segmentation algorithm took on average 1 h per patient (3.3 GHz Intel Core i7-980 processor, with 24 GB of RAM, running 64 bit Windows 7). Since the segmentation of the radiation oncologist is assumed as most accurate, variations from that segmentation are reported as segmentation inaccuracies. The observer–reference variations (inter-observer variation: reference–observer 1, reference–observer 2, reference–observer 3), the variation between two segmentations per observer (intra-observer variation: observer 1–observer 1, observer 2–observer 2, observer 3–observer 3) and the automatic-reference variations were determined. Observer variation was quantified using the Dice similarity coefficient [21] and the mean surface distance (MSD)(itkContourMeanDistanceImageFilter, www.itk.org), i.e. the average distance between two volumes. Since DSC measures the overlap between volumes, the variation is quantified using 1-DSC. We used DSC instead of 1-DSC to compare our results to other studies.

Dosimetric evaluation

As temperature dose predictions still come with high uncertainties, we quantified the effect of segmentation variation on the

Please cite this article in press as: Verhaart RF et al. CT-based patient modeling for head and neck hyperthermia treatment planning: Manual versus automatic normal-tissue-segmentation. Radiother Oncol (2014), http://dx.doi.org/10.1016/j.radonc.2014.01.027