Radiotherapy and Oncology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

A novel voxel based homogeneity index: Rationale and clinical implications for whole-brain radiation therapy

Alexander Henry Thieme [a,*], Carmen Stromberger [a], Pirus Ghadjar [a], Sophie K. Piper [b], Volker Budach [a]

[a] Department of Radiation Oncology, Charité – Universitätsmedizin Berlin, Berlin, Germany; [b] Institute of Biometry and Clinical Epidemiology, Charité – Universitätsmedizin Berlin, Berlin, Germany

ARTICLE INFO

Article history:
Received 3 July 2017
Received in revised form 30 March 2018
Accepted 6 April 2018
Available online xxxx

Keywords:
Homogeneity Index
TCP/NTCP
Treatment Planning
WBRT
Plan Quality

ABSTRACT

Purpose or objective: A homogeneity index (HI) measures the uniformity of a dose distribution within a given target volume. Traditional HIs only use a limited number of dose–volume histogram data-points for calculation. A voxel-based homogeneity index (VHI) is proposed which utilizes the entire information of the three-dimensional dose distribution. We compared the VHI with existing HIs and analyzed if VHI results were associated with treatment outcomes in patients who underwent therapeutic WBRT.

Material and methods: The VHI analyzes deviations from the prescribed dose in each voxel of the target volume. We retrospectively analyzed WBRT treatment plans. Overall survival (OS), CNS progression-free-survival (CNS PFS) and hazard rates were compared for tertile-split levels of the VHI using the Kaplan–Meier methods and multivariable Cox-regression analysis.

Results: WBRT treatment plans (n = 770) were used for HIs comparison. OS and CNS PFS were assessed for 430 patients. The VHI showed a higher sensitivity for dose inhomogeneities. Lower OS and CNS PFS were observed for higher levels of $VHI_{Underdosage}$, particularly in patients with good performance status (KPS >70%) (OS: Log-rank P = .007, HR = 1.37 95%CI [1.09, 1.72]).

Conclusion: Higher sensitivity and feasibility to assess treatment plan quality using the VHI were demonstrated. First clinical implications were found in terms of compromised OS/CNS PFS for WBRT with radiation underdosage.

The major objective of conventionally fractionated external beam radiation therapy has always been to cover the target volume by the prescribed dose as homogeneously as possible while limiting radiation exposure to the surrounding normal tissue and organs at risk. Technological advances like intensity modulated radiation therapy (IMRT) or volumetric-modulated arc therapy (VMAT) were employed to improve the three-dimensional dose distribution in order to achieve these goals. An accurate description of the dose distribution inside the target volume is important because the success of radiation therapy relies on it. While radiation underdosage correlates with a decreased tumor control probability [1], overdosage can result in harmful side effects if the target volume overlaps with or is identical to an organ at risk [2]. However, the search for a universal and easily understandable score that quantifies homogeneity of the dose distribution has not yet been fully successful. A homogeneity index (HI) should measure how well the dose distribution within the target volume complies with the prescribed dose. There have been various attempts to define HIs [3–8]. None of them have been found to be ideal [9–11]. Conventional HIs only use a limited number of data points from the dose–volume histograms for calculation (Table 1). Since values like the maximum (D_{max}) and minimum dose (D_{min}) are sensitive to calculation parameters, e.g., the voxel size, and are therefore not reliable [5,12], improved indices use the minimal dose covering a small volume of the target to represent the dose maximum (e.g., minimal dose covering 5% of the target volume, D_5) and the minimal dose covering most of the target to represent the dose minimum (e.g., D_{95}). The most commonly used HI has been suggested by Wu [5] which was slightly modified by the International Commission on Radiation Units and Measurements (ICRU) [12]. Further indices which characterize homogeneity are RTOG HI [3], RTOG Coverage [3], Radical and Moderate Dose HI [4]. In principle all conventional HIs are a ratio between the maximum and minimum dose in the target and neglect the distribution of the dose in between. Therefore, a huge amount of information is omitted which results in fundamental drawbacks which are demonstrated in Fig. 1a–d. The dose–volume histograms (DVHs) of up to four fictive plans and their HI scores are compared. Plan 1 has the best homogeneity in all examples and should receive

* Corresponding author.
E-mail addresses: alexander-henry.thieme@charite.de (A.H. Thieme), carmen.stromberger@charite.de (C. Stromberger), pirus.ghadjar@charite.de (P. Ghadjar), sophie.piper@charite.de (S.K. Piper), volker.budach@charite.de (V. Budach).

https://doi.org/10.1016/j.radonc.2018.04.007
0167-8140/

Table 1
Formulas and ideal values of established homogeneity indices.

	Formula	Ideal value
RTOG Homogeneity Index [3]	$HI_{RTOG} = \frac{D_{max}}{PD}$	1
RTOG Coverage [3]	$Coverage = \frac{D_{min}}{PD}$	1
Wu Homogeneity Index [5]	$HI_{WU} = \frac{D_2 - D_{98}}{PD}$	0
ICRU Homogeneity Index [12]	$HI_{ICRU} = \frac{D_2 - D_{98}}{D_{50}}$	0
Radical Dose Homogeneity Index [4]	$rDHI = \frac{D_{min}}{D_{max}}$	1
Moderate Dose Homogeneity Index [4]	$mDHI = \frac{D_{95}}{D_5}$	1

D_{min}: minimum dose within the target volume.
D_{max}: maximum dose within the target volume.
D_2, D_5, D_{95}, D_{98}: is the minimal dose found in 2%, 5%, 95% and 98% of the target volume.
PD: prescribed dose.

a better score than Plans 2–4 with an increasing inhomogeneity due to under- or overdosage. The examples are constructed in the sense that the same score is calculated for all presented DVHs. This indicates a general flaw in conventional indices where the same score is assigned to dose distributions which have different homogeneity. The novel HI, described and clinically evaluated in this paper, aims to improve the sensitivity for dose inhomogeneity by utilizing the entire information present in the three-dimensional dose distribution of the target volume.

Methods and materials

A voxel based homogeneity index (VHI) is proposed which analyzes the deviations from the prescribed dose in each voxel of the target volume (Fig. 1e). This score is independent of the target

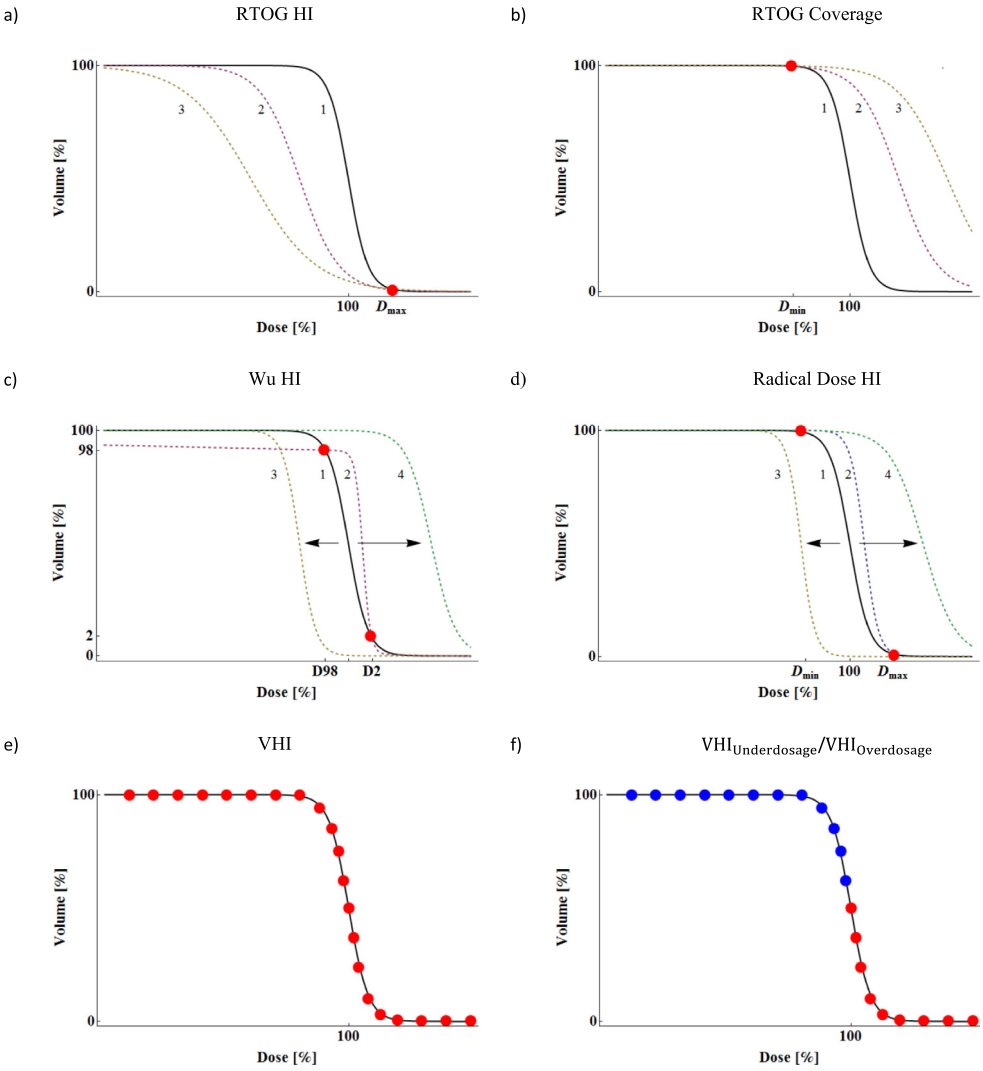

Fig. 1. (a) The DVHs for three fictive treatment plans with varying inhomogeneities have the same RTOG HI score. This index uses the dose maximum (D_{max}) for calculation which is the same for all three plans. While the target volume is adequately and homogeneously covered in DVH 1, increasing underdosage can be noticed in DVHs 2 and 3. (b) The three fictive DVHs have the same score according to the RTOG Coverage which uses the dose minimum (D_{min}) for calculation. Increasing overdosage can be noticed in DVHs 2 and 3 if compared to DVH 1. (c) Four DVHs are presented with varying inhomogeneity but identical score for the Wu HI. Under- and overdosage can be noticed in DVH 2, however the curve intersects at the same D_2 andD_{98} of DVH 1. Therefore identical scores are calculated for both DVHs. Since the difference $D_2 - D_{98}$ is used for calculation, the curves can be shifted to the left or right (DVH 3 and 4) resulting in serious under- and overdosage while still maintaining an identical score. Similar cases can be constructed for the Moderate Dose and ICRU HIs. (d) Four DVHs are demonstrated with identical Radical Dose HI score. A ratio between the dose minimum (D_{min}) and dose maximum (D_{max}) is used for calculation. Curves which intersect at the same D_{min} and D_{max} will be given the same score (DVH 2). Similar to the Wu HI the curves may also be shifted to the right and left without changes in the score, if the slope of the curve is adjusted (steeper for DVH 3, flatter for DVH 4). (e) The functional principle of the VHI is demonstrated. All voxels of the dose distribution in the target are used for calculation. Therefore deviations from the prescribed dose at an arbitrary position of the DVH are noticed and result in an increased score. (f) $VHI_{Underdosage}$ and $VHI_{Overdosage}$ only use those voxels for calculation which contribute to underdosage and overdosage. This is visualized by means of a DVH where blue points contribute to underdosage and red points to overdosage.

Please cite this article in press as: Thieme AH et al. A novel voxel based homogeneity index: Rationale and clinical implications for whole-brain radiation therapy. Radiother Oncol (2018), https://doi.org/10.1016/j.radonc.2018.04.007