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Original Research Article

An uncertainty metric to evaluate deformation vector fields for dose accumulation in radiotherapy

Akihiro Takemura[a,*], Akira Nagano[b], Hironori Kojima[c,e], Tomohiro Ikeda[d], Noriomi Yokoyama[e], Kosuke Tsukamoto[c], Kimiya Noto[c], Naoki Isomura[c], Shinichi Ueda[c], Hiroki Kawashima[a]

[a] Faculty of Health Sciences, Institution of Medical, Pharmaceutical and Health Sciences, Kanazawa University, 5-11-80 Kodatsuno, Kanazawa 920-0942, Japan
[b] Division of Radiology, Okayama University Hospital, 2-5-1 Shikatacho, Kitaku, Okayama 700-8558, Japan
[c] Department of Radiological Technology, Kanazawa University Hospital, 13-1 Takaramachi, Kanazawa 920-8641, Japan
[d] Department of Radiation Oncology, Southern Tohoku Proton Therapy Center, 7-115 Yatsuyamada, Koriyama-City, Fukushima-Pref. 963-8563, Japan
[e] Division of Health Sciences, Graduate School of Medical Sciences, Kanazawa University, 5-11-80 Kodatsuno, Kanazawa 920-0942, Japan

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ABSTRACT

Background and purpose: In adaptive radiotherapy, deformable image registration (DIR) is used to propagate delineations of tumors and organs into a new therapy plan and to calculate the accumulated total dose. Many DIR accuracy metrics have been proposed. An alternative proposed here could be a local uncertainty (LU) metric for DIR results.

Materials and methods: The LU represented the uncertainty of each DIR position and was focused on deformation evaluation in uniformly-dense regions. Four cases demonstrated LU calculations: two head and neck cancer cases, a lung cancer case, and a prostate cancer case. Each underwent two CT examinations for radiotherapy planning.

Results: LU maps were calculated from each DIR of the clinical cases. Reduced fat regions had LUs of 4.6 ± 0.9 mm, 4.8 ± 1.0 mm, and 4.5 ± 0.7 mm, while the shrunken left parotid gland had a LU of 4.1 ± 0.8 mm and the shrunken lung tumor had a LU of 3.7 ± 0.7 mm. The bowels in the pelvic region had a LU of 10.2 ± 3.7 mm. LU histograms for the cases were similar and 99% of the voxels had a LU < 3 mm.

Conclusions: LU is a new uncertainty metric for DIR that was demonstrated for clinical cases. It had a tolerance of < 3 mm.

1. Introduction

Adaptive radiotherapy (ART) is commonly employed in head and neck cancer [1–3], prostate cancer [4,5], and other sites [6,7] and modalities [8,9]. Deformable image registration (DIR) is an important ART tool because it helps to delineate organs and targets for therapy re-planning [10–13].

DIR has been used for summing dose accumulations over treatment courses. To measure daily dose distributions, structures are propagated to cone beam CT images or megavoltage CT images acquired for patient setup and dose calculations [12–19]. DIR has been used to calculate accumulated dose distributions using daily dose distributions [20–22]. Daily distributions are deformed according to the deformation vector field (DVF), and then summed to obtain a total dose distribution. This assumes that DIRs work accurately. However, issues of sliding organs [23] and uniform-density regions [24] are well known. Specifically, DIR deformation at the interface between a fixed organ and a sliding organ was inaccurate because these organs could move separately. The incorrect deformation may be visually obvious. The issue of uniform-density regions is that the interior of these regions could be deformed and incorrect deformation is difficult to identify because the pixels have the same density. There is little information on the accuracy of deformation in the interior, especially for clinical cases. Hence, an accuracy check does not work, which is more serious for dose accumulation because it may lead to incorrect dose summations.

The most frequently used metric for DIR accuracy is the Dice similarity coefficient (DCS) [25]. It indicates the similarity in volume and shape between organs in reference and deformed images, which is the resulting image of DIR [26,27]. Target registration error (TRE) quantification, which shows the distance error for fiducial markers and/or anatomical landmarks between a reference image and a deformed image, is also frequently calculated [28–32]. The Hausdorff distance and surface errors [27,33] use boundaries of organs and fiducial markers in the reference image as the ground truth, and thus only assess

* Corresponding author.
E-mail address: at@mhs.mp.kanazawa-u.ac.jp (A. Takemura).

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deformation accuracies of the boundaries and markers. If deformation in the interior of a uniform-density organ is incorrect when the organ in the resulting deformed image is grossly similar to the reference image, the evaluations will assess the result as good. DSC, Hausdorff distances, TRE, and surface errors cannot assess the correctness of interior deformation in organs. Intensity differences between two images have not been effective when a voxel in the organ is moved to a wrong place. Elsewhere, a known deformation was performed on a reference image to generate a moving image that was deformed to fit the reference image [27,28]. The deformation calculated by DIR methods and the given deformation were compared. However, it is difficult to follow anatomical motion such as respiration.

In a DVF assessment, Varadhan et al. [27] used inverse consistency error, Jacobians, and harmonic energy. The inverse consistency error revealed the difference between a DVF from image A to image B calculated with a DIR, and another DVF from image B to image A as a consistency metric [34,35]. The Jacobian and the harmonic energies indicated the deformation magnitude and DVF smoothness. Schreibmann et al. evaluated a DVF directly by using the Curl operation [36] that detected unrealistic deformation. For an accurate quantification of dose accumulation, accuracy evaluation of an individual DIR result is necessary. However, because of the lack of deformation ground truth, that assessment in clinical cases is impossible.

For DIR uncertainty evaluation, Murphy et al. [24] used randomly defined volumes of interest (VOIs) in a pair of CT image sets and obtained DVFs for the VOIs with DIR. The mean DVF was calculated from the DVFs in overlapping regions of the VOIs and the DVF error was the difference from the mean. This method required 50 repeated DIR executions for one pair of images. Another study calculated the DIR uncertainty by using at least five image sets [37]. These methods revealed variations in multiple DVFs and the comprehensive uncertainty of the DIR method. However, they could be used for DIR quality assurance and not for results.

Here, a local uncertainty (LU) metric was calculated from a moving image and a DVF; it required one DIR execution. It evaluated uncertainties in uniform-density regions and was applied to four clinical cases.

2. Methods

2.1. Local uncertainty

The LUs represented positional variations of candidates for a target position, which were calculated from surrounding organ edges after DIR. Hence, organ edges were used to determine candidate positions in organ interiors.

A moving image was defined as one of the initial images for DIR and was deformed to match a reference image. A reference image was defined as another initial image to which the moving image was matched. A deformed image was a deformed moving image and a DIR result.

To calculate the LU for target position p_0, neighboring positions p_1, p_2, p_3,…p_n were searched radially from p_0 in an initial moving image I_{src} (before DIR). The neighboring positions were set on organ edges that had sufficient contrast with the pixel density at p_0 (Eq. (1)):

$$p_i = \left\{ q \;\middle|\; \begin{array}{l} q \in I_{src}, \\ q = p_0 + k\cdot\vec{v_i} \;\; and \;\; MIN(k), \; and \\ I_{ref}(p_0) - cnt > I_{ref}(q) \;\; or \;\; I_{ref}(p_0) + cnt < I_{ref}(q) \end{array} \right\} (i = 1, 2, 3...n) \quad (1)$$

Here, $\vec{v_i}$ was a unit vector of arbitrary direction that originated on p_0, k was the minimum number to satisfy the third condition in Eq. (1), and *cnt* was the minimum contrast needed to resolve a pixel on an organ edge.

Distances from p_1, p_2, p_3,…p_n to p_0 were r_1, r_2, r_3,…r_n, respectively (Eq. (2)). The DIR mapped p_0, p_1, p_2, p_3,… p_n to p'_0, p'_1, p'_2, p'_3,… p'_n, respectively, with a DVF T in Eq. (3):

$$r_i = p_i - p_0 = |k\cdot\vec{v_i}| \; (i = 1, 2, 3...n) \quad (2)$$

$$p_i' = T\cdot p_i \quad (3)$$

Then, a candidate position c'_i in a deformed image was calculated as the intersection of the p'_i-centered sphere with radius r_i, the p'_{i+1}-centered sphere with radius r_{i+1}, and the p'_{i+2}-centered sphere with radius r_{i+2}. The p'_i-centered sphere with radius r_i was defined as:

$$f(p_i', r_i): (x - x'_{pi})^2 + (y - y'_{pi})^2 + (z - z'_{pi})^2 = r_i^2 \quad (4)$$

The intersection of the three spheres was then calculated from:

$$g_j' = \begin{cases} f(p_i', r_i) = A \\ f(p'_{i+1}, r_{i+1}) = A \\ f(p'_{i+2}, r_{i+2}) = A \end{cases} \quad (5)$$

where A was an arbitrary value. The intersection g_j could have two positions (g'_{j_0} and g'_{j_1}) at the maximum. The closer of the two positions to p'_0 was chosen as candidate c'_i (Eq. (6)):

$$c_i' = \begin{cases} g'_{j.0} \; when \; d(p_0', g'_{j0}) \leqslant d(p_0', g'_{j.1}), \\ g'_{j.1} \; else \end{cases} \quad (6)$$

where $d(p'_0, g'_{j\_0})$ and $d(p'_0, g'_{j\_1})$ was the distance between p'_0 and g'_{j_0} or g'_{j_1}.

Finally, the LU value at p'_0 was calculated from the coordinates of the candidates (Eqs. 7–10):

$$LU = \sqrt{\sigma_x^2 + \sigma_y^2 + \sigma_z^2} \quad (7)$$

$$\sigma_x = \sqrt{\frac{\sum_0^m (x_i - \overline{x})}{m-1}} \quad (8)$$

$$\sigma_y = \sqrt{\frac{\sum_0^m (y_i - \overline{y})}{m-1}} \quad (9)$$

$$\sigma_z = \sqrt{\frac{\sum_0^m (z_i - \overline{z})}{m-1}} \quad (10)$$

where m was the number of candidate positions, and $\overline{x}$, $\overline{y}$, *and* $\overline{z}$ were the mean values of the *x, y, and z* candidate coordinates. The coordinates of the i_{th} candidate were x_i, y_i, *and* z_i. Hence, the LU value represented the positional variation of a target position, shown schematically in Fig. 1 for 2D images.

In Fig. 1 of the Supplementary Material, a uniform-density region in a reference image was shifted by one pixel in a moving image. DIR software often provides a resulting DVF that exhibited deformation only in areas close to the boundary of the uniform-density region. In this case, the Dice coefficient was one because the shape of the region in the deformed image completely matched that in the reference image. However, the actual positions of the stationary portion of the uniform-

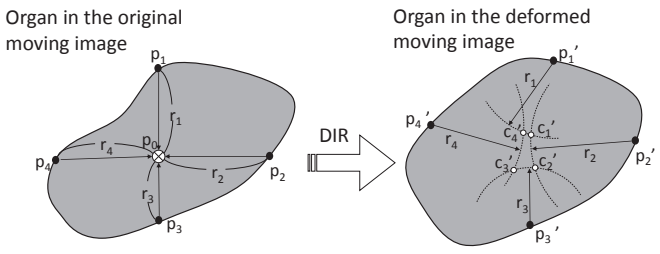

Fig. 1. Schematic of candidate position determination in two-dimensional images for a local uncertainty calculation.