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FULL PAPER

Evaluation of a template-based algorithm for markerless lung tumour localization on single- and dual-energy kilovoltage images

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Objective: To evaluate a template-based matching algorithm on single-energy (SE) and dual-energy (DE) radiographs for markerless localization of lung tumours.

Methods: A total of 74 images from 17 patients with Stages IA–IV lung cancer were considered. At the time of radiotherapy treatment, gated end-expiration SE radiographs were obtained at 60 and 120 kVp at different gantry angles (33° anterior and 41° oblique), from which soft-tissue-enhanced DE images were created. A template-based matching algorithm was used to localize individual tumours on both SE and DE radiographs. Tumour centroid co-ordinates obtained from the template-matching software on both SE and DE images were compared with co-ordinates defined by physicians.

Results: The template-based matching algorithm was able to successfully localize the gross tumor volume within 5 mm on 70% (52/74) of the SE images vs 91% (66/74) of the DE images ($p < 0.01$). The mean vector differences between the co-ordinates of the template matched by the algorithm and the co-ordinates of the physician-defined ground truth were 3.2 ± 2.8 mm for SE images vs 2.3 ± 1.7 mm for DE images ($p = 0.03$).

Conclusion: Template-based matching on DE images was more accurate and precise than using SE images.

Advances in knowledge: This represents, to the authors' knowledge, the largest study evaluating template matching on clinical SE and DE images, considering not only anterior gantry angles but also oblique angles, suggesting a novel lung tumour matching technique using DE subtraction that is reliable, accurate and precise.

INTRODUCTION

In recent years, stereotactic body radiotherapy (SBRT) has become increasingly utilized for the treatment of early-stage lung tumours.^{1–7} Because of the high doses per fraction, accurate patient setup and tumour localization are essential for safe delivery using this modality.^{8–11} One of the most confounding technical factors associated with SBRT is respiratory motion. A number of approaches have been utilized to incorporate respiratory motion into the treatment planning and delivery process. The simplest approach involves utilizing an internal target volume.^{12–16} For tumours near the apex of the lung where motion is minimal, this approach may be adequate. However, for tumours near the diaphragm, the internal target volume dimensions can be significant, resulting in the irradiation of a relatively large volume of healthy lung. For these cases, methods to reduce respiratory motion may be required. Such methods include compression, gating, active breathing control and breath-hold.^{17–20} Although all approaches involve some degree of

external monitoring, it is desirable to monitor the position of tumour during treatment using an independent mean.

One method for real-time verification utilizes implantation of radio-opaque fiducial markers.^{21–23} However, such an approach involves an invasive procedure and carries risks of pneumothorax and exacerbation of underlying chronic obstructive pulmonary disease.¹¹ Although earlier studies have shown that displacement of the markers in the lung may be significant,^{21–23} migration will be dependent on the type of marker used.^{24–26} Another method utilizes external markers as surrogates for respiratory motion.²⁷ However, external markers rely on the assumption of a direct correlation between external anatomy and internal tumour position. This correlation is not always accurate, especially when using abdominal displacement surrogates.²⁷

An independent means of tumour position verification involves using radiography throughout the course of

Table 1. Patient/tumour characteristics

Patient	Group stage	Location	Volume (cm ³)	A/P dimension (cm)	R/L dimension (cm)	S/I dimension (cm)	Distance from mediastinum (cm)	Range of motion on 4D-CT (cm)
1	IIIA	Right upper	243.3	8.9	7.4	8.5	0	0.7
2	IB	Left upper	27.9	3.7	3.3	3.9	3.6	0.8
3 ^a	IA	Left upper	13.9	2.1	1.7	2.9	0	0.5
3 ^a	IB	Right lower	54.5	4.0	5.3	3.9	2.5	0.6
4	IIIA	Right upper	13.8	2.7	3.2	3.8	3.3	0.3
5	IA	Left upper	4.3	2.7	1.6	2.0	1.7	0.2
6	IB	Right lower	97.5	5.1	5.9	6.5	3.4	0.9
7	IA	Left lower	3.8	2.1	1.9	1.8	6.0	0.9
8	IIA	Right upper	54.9	4.7	3.5	4.8	2.4	0.4
9	IA	Right upper	0.3	1.0	1.3	0.4	2.5	1.1
10	IB	Left upper	12.7	4.0	3.6	2.5	0	1.1
11	IB	Right upper	4.1	2.1	1.8	1.7	1.8	0.5
12	IB	Right lower	70.8	6.0	5.3	4.4	3.0	1.7
13	IB	Right lower	2.2	2.2	1.2	1.6	6.2	0.3
14	IV	Left upper	0.7	1.2	1.6	0.7	5.9	0.9
15	IA	Right upper	0.5	0.6	1.1	0.6	7.2	0.4
16	IA	Right middle	0.2	0.8	0.8	0.7	0	0.9
17	IA	Right lower	3.5	1.8	2.0	1.9	6.5	1.4

4D, four-dimensional; A/P, anterior-posterior; R/L, right-left; S/I, superior-inferior.

^aThe same patient was treated with two separate courses for two separate primary lung cancers.

treatment.^{28,29} A number of vendors currently provide software to obtain kilovoltage (kV) images during the course of treatment either at fixed angles or while the gantry is rotating during volumetric modulated arc therapy. Using these radiographs with a template-matching algorithm may allow for a quantitative measure of the tumour location relative to its expected position. However, in lung tumours, this method may fail when the boundary of the tumour is obscured by overlying bones. One method that may improve the visualization of these tumours is dual-energy (DE) imaging.

In this present study, our purpose was to evaluate a template-based matching algorithm on single-energy (SE) and DE radiographs to localize lung tumours of patients undergoing image-guided radiation therapy using either SBRT or three-dimensional conformal radiation therapy (3DCRT). DE imaging enhances visualization of soft-tissue abnormalities, such as lung tumours, in chest radiographs by taking advantage of the different degrees to which tissues attenuate high- and low-energy photons.^{30–42} The DE process involves obtaining two different radiographs, one at low energy (such as 60 kVp) and one at high energy (such as 120 kVp). Using these images, a weighted logarithmic subtraction is performed that removes obscuring bony anatomy (ribs and vertebral bodies), thus creating a third image that highlights soft tissue, such as lung tumours.^{30,43,44} Recently, Sherertz et al³⁰ published a prospective feasibility study investigating tumour visibility in DE radiographs compared with conventional kV radiographs used in image-guided radiation therapy of patients with lung cancer. In that study, obscuring bony anatomy was successfully removed in all analyzed DE images, and tumour visibility was improved when compared with conventional radiographs.³⁰ The DE process is unique in that it takes advantage of already widely available and relatively inexpensive kV image guidance systems.

METHODS AND MATERIALS

Patients and treatment

Patients with lung cancer scheduled to receive SBRT or 3DCRT were enrolled in a DE imaging trial under an institutional review board-approved prospective protocol at our centre. Eligible patients had no implanted fiducials and a Karnofsky Performance Status of 70 or greater. Patient and tumour characteristics are summarized in Table 1. 17 patients were recruited for this study with a total of 18 tumour sites that were treated and imaged. 15 of the tumours were treated with SBRT and 3 with 3DCRT. The tumours varied considerably in size (0.21–243.3 cm³) with a mean GTV of 33.8 ± 59.7 cm³.

CT simulation and treatment planning

All patients underwent CT simulation and radiation therapy planning according to our standard institutional protocol. Patients were simulated in the supine position and immobilized using a body mould (Alpha Cradle®; Smithers Medical Products Inc., Canton, OH) indexed to the treatment table. A four-dimensional CT simulation was acquired using the Real-Time Position Management™ (RPM) System (Varian Medical Systems, Palo Alto, CA) on a dedicated CT scanner (Brilliance Big Bore; Philips Medical Systems, Andover, MA). Target delineation, prescription dose and treatment technique were determined by the treating radiation oncologist.

Image acquisition

Patients were treated with each fraction according to a standard protocol. Following treatment, 60 and 120 kVp end-expiration gated images were acquired using the RPM system. Energies for DE imaging were selected based on previous studies where image quality and dose were optimized.^{30,43–45} A prior study demonstrated that the estimated mean dose at the skin per DE image pair was approximately 0.44 ± 0.03 mGy, comparable with the expected skin dose from conventional SE imaging.³⁰ Image pairs were acquired once per treatment fraction with a maximum of five sets per patient. Images were obtained at several angles used for treatment with at least one image set taken at an anteroposterior gantry angle. In total, 74 image pairs were acquired with 33 anterior images and 41 oblique. A total of 33 image pairs were obtained using the Varian TrueBeam™ Integrated Imaging Solution in conjunction with the Varian iTools Capture (Varian Medical Systems Inc., Palo Alto, CA) software and a Matrox Imaging (Dorval, QC) frame grabber card and 41 image pairs were obtained using the Varian iX (Varian Medical Systems Inc., Palo Alto, CA).

Image processing

The raw image data were exported and processed offline to create DE images. Images were imported into MATLAB® (MathWorks®, Natick, MA) for processing. The 60- and 120-kVp images were initially aligned by amplitude and phase using the data captured by the RPM system. Subsequently, a rigid registration was performed to further reduce misregistration artefacts. The registration algorithm focused on a manually selected region of interest (ROI) centred on the tumour. The size of the ROI was related to the tumour size, with larger tumours having larger ROIs. The low-energy image was then translated such that the bony anatomy in the ROI was aligned in both the high- and low-energy images. The optimal alignment was determined by maximizing the normalized cross-correlation (NCC) over the ROI. Once the images were registered, a weighted logarithmic subtraction was performed, on a pixel-by-pixel basis, to create a DE image with suppressed bony anatomy.⁴⁵

$$\ln(I_{\text{Soft}}^{\text{DE}}) = \ln(I^{\text{High}}) - w_s \ln(I^{\text{Low}}) \quad (1)$$

where I^{High} and I^{Low} are the intensities of individual pixels produced from the high- and low-energy images, respectively; $\ln$ is the natural logarithm; and w_s is the relative weight required to produce the soft-tissue image pixels ($I_{\text{Soft}}^{\text{DE}}$). The 120-kVp images were used as the standard SE images to which the DE images were compared.

Matching algorithm

Template matching was performed using a non-commercial version of Varian RapidTrack™ software.⁴⁶ In brief, the software creates a template from physician contours of the tumour on planning CT scans performed prior to treatment. The treating physician contoured the gross tumor volume (GTV) on the 50% phase scan (end expiration) which corresponds to the same phase as the acquired high- and low-energy images. It was empirically determined that the mediastinal window provided the best overall agreement between the template and the GTV as

observed on the radiographs. The software determined the GTV match location on the image by shifting the template across the image and calculating the NCC between the template and the acquired image at different two-dimensional offsets within the search region for the DE or SE image. Calculation of NCC at different two-dimensional offsets within a search region results in a match score surface. The offset at which NCC has the maximum value (*i.e.* the position of the peak of the match score surface) represents the potential target position within the search region. The strength of this peak relative to NCC values away from the peak, called sidelobe values, is quantified by the peak-to-sidelobe ratio (PSR) and is calculated by:⁴⁶

$$\text{PSR} = \frac{[\text{peak value} - \text{mean sidelobe}]}{[\text{sidelobe standard deviation}]} \quad (2)$$

Successful template matching was defined as any instance in which the algorithm matched the template on the image.

For each of the SE and DE images, two physicians manually placed the software-created template on the visualized tumour. The average of the co-ordinates from the manually placed templates by each physician was considered ground truth for each individual image pair. The matched co-ordinates were subsequently compared with the ground truth values.

Statistical analysis

The differences between the algorithm's detection rate, false detection rate and accuracy using SE and DE images were evaluated statistically using a Fisher's exact test and Student's two-sided *t*-test. The detection rate was defined as the percentage of images that the algorithm was able to produce template-matching co-ordinates for the tumour. The false detection rate was defined as differences of >5 mm between the template co-ordinates and the ground truth co-ordinates. Accuracy was defined as the difference in the template-matched co-ordinates and physician-defined ground truth co-ordinates. *p*-values <0.05 were considered statistically significant.

RESULTS

74 image pairs from 17 patients with a total of 18 discrete lung tumours were examined in this study. These results are summarized in Table 2. Of the 74 image pairs analyzed, the algorithm successfully matched the template in 61 (82%) of the SE

images and 74 (100%) of the DE images ($p < 0.01$). The mean distance between the GTV centroid co-ordinates (x, y) of the matched template and physician-defined ground truth co-ordinates was 3.2 ± 2.8 mm for SE compared with 2.3 ± 1.7 mm for DE, respectively ($p = 0.03$). The false detection rate (fraction of images with >5 mm matching errors) was 7/74 (9.4%) for DE images vs 9/74 (12.1%) for SE images ($p = 0.79$). A further analysis was performed to determine if the PSR value was predictive of template-matching accuracy. For PSR <3, the matching accuracy was 3.3 ± 3.1 mm vs 2.2 ± 1.3 mm for PSR ≥ 3 ($p = 0.02$). Furthermore, the false detection rate was 20.9% (PSR <3) vs 4.0% (PSR ≥ 3) ($p < 0.01$).

Figure 1 demonstrates differences in template-matching accuracy using DE imaging vs SE imaging for an 80-year-old male (Table 1—Patient 5) with a left upper-lobe adenocarcinoma measuring $2.1 \times 1.7 \times 2.9$ cm. These images are taken at a 0° anteroposterior angle. Figure 1a is a SE image in which the ribs are obscuring the borders of the tumour, particularly in this challenging case at the apex of the lung. The algorithm matched the template (green) on the image, at a distance >6 mm from the physician-defined ground truth. In the DE subtracted image (Figure 1b), the obscuring bony anatomy is removed, the borders of the tumour are more easily defined and the algorithm matched the tumour to within 1 mm.

A similar case is presented in Figure 2 in which the tumour is obscured by the overlying bony anatomy. In this case of a 70-year-old female (Table 1—Patient 16) with a right upper lobe adenocarcinoma measuring $0.5 \times 0.6 \times 1.1$ cm, the images were also taken at a 0° anteroposterior angle. Although the lesion was at the apex in the previous case, for Figure 2, the tumour is more inferior and at the periphery. In many cases, one would expect peripheral lesions to be more easily visualized than those closer to the apices or mediastinum. Owing to the overlying rib, however, in Figure 2a, for SE, the algorithm did not accurately place the template over the tumour (>5 mm from ground truth). Once the ribs were removed using DE, Figure 2b demonstrates sharper borders of the tumour, allowing for sub-millimetre template matching.

Figure 3 shows an example of comparing SE with DE at an oblique 63° gantry angle. These images are from a 67-year-old female (Table 1—Patient 8) with a $2.1 \times 1.9 \times 1.8$ -cm left lower lobe adenocarcinoma. The lesion is situated in an area that

Table 2. Template-matching results and distance from ground truth

Parameter	SE (120 kVp)	DE
Total images ($n = 74$) with successful template matching	61	74
Percentage of images matched	82%	100%
Mean $\pm$ SD x co-ordinate differences (mm) from ground truth	-0.3 ± 3.3	0.2 ± 2.0
Mean $\pm$ SD y co-ordinate differences (mm) from ground truth	-0.8 ± 2.4	-0.5 ± 2.0
Mean $\pm$ SD distance (mm) from ground truth	3.2 ± 2.8	2.3 ± 1.7
False detection rate (template-matching error >5 mm)	12%	9%

DE, dual-energy images; kVp, peak kilovoltage; *n*, number of images; SE, single-energy images obtained at 120 kVp; SD, standard deviation.

Figure 1. Left upper-lobe lung tumour template matching at 0° (anterior/posterior) using single energy at 120 kVp (a) and dual energy subtraction (b). Matched template appears in solid line and ground truth in black dashes. Bar = 1 cm.

presents challenges in imaging due to the left lateral lower ribs and diaphragm. In this case, with SE in Figure 3a, the algorithm was unable to match the template on the tumour. In the DE subtracted image (Figure 3b), the algorithm is again able to template match the tumour with submillimetre accuracy.

DISCUSSION

The results of this study suggest that automated markerless template matching using a novel template-based matching algorithm on planar radiographs is feasible and that DE images may offer an advantage over SE images, both in terms of accuracy and precision. The significance of this study is that to our knowledge, it is the largest study evaluating template matching on clinical SE and DE images, considering not only anterior gantry angles but also oblique angles. Although both DE and SE images had a similar false detection rate, when combined with the ability of the algorithm to detect the tumour on the image, the overall success of DE template matching was 91% (67/74) vs 70% (52/74) for SE images ($p < 0.01$). The lower percentage of SE images for which template matching was successful was due to the presence of ribs and other bones which obscure the tumour on SE radiographs, making it difficult for the algorithm to match the template.

An important clinical question is how does one know that the template match is accurate? In this analysis, the PSR value was evaluated as a predictor of this accuracy. We observed a statistically significant increase in accuracy for $\text{PSR} \geq 3$ vs $\text{PSR} < 3$. Specifically, the false detection rate was only 4% for $\text{PSR} \geq 3$ vs 20.9% of values for $\text{PSR} < 3$. Moreover, for $\text{PSR} \geq 3$, the maximum deviation from ground truth was 6.7 vs 16.6 mm for $\text{PSR} < 3$. Thus, when using such an approach clinically, template matches should have a $\text{PSR} \geq 3$ to minimize the false detection rate.

We are currently investigating the role that CT image quality plays on template-matching accuracy and the false detection rate, with the goal of optimizing imaging parameters. In the present study, a CT slice thickness of 3 mm was utilized. A smaller slice thickness may lead to higher resolution templates that improve the matching accuracy. Another area of ongoing research is the optimal window/level (W/L) for template generation. Template matching requires the physician to outline the tumour on planning CT scan. Although a lung W/L is often used for contouring the tumour for planning purposes, we have found that using a mediastinal window is better for template

Figure 2. Right upper-lobe lung tumour template matching at 0° (anterior/posterior) using single energy at 120 kVp (a) and dual energy subtraction (b). Matched template appears in solid line and ground truth in black dashes. Bar = 1 cm.

Figure 3. Left lower-lobe lung tumour template matching at 63° oblique angle using single energy at 120 kVp (a) and dual energy subtraction (b). Matched template appears in solid line and ground truth in black dashes. With single energy (a), template could not be successfully matched and only ground truth is shown. Bar = 1cm.

matching. A study to systematically evaluate the W/L for template matching is being designed.

The results of this study using template matching compare favourably with others presented in the literature. In a study by Menten *et al*,⁴² SE and DE images were produced from an anthropomorphic phantom and Monte Carlo simulations using data from patients with lung cancer. Using an automated template-matching algorithm, the mean tumour localization errors ranged from 3.3 to 5.2 mm on a limited data set. Interestingly, they noted that template matching was not possible in 9/24 (38%) of the images due to poor soft-tissue contrast. Although our tracking rate was significantly higher, the imaging angles used were primarily anteroposterior and those corresponding to treatment angles. As such, these tended to have less soft-tissue overlap with the tumour. It is important to note that despite removing bone from the image, DE subtraction will not improve tumour contrast when there is overlap with soft tissue (*i.e.* heart). In a separate study, Tanaka *et al*⁴⁰ used a commercially available bone suppression algorithm to remove overlying bony anatomy from SE radiographs. Using a matching algorithm, they observed mean errors of 3.3 ± 3.3 vs 1.3 ± 1.1 mm on bone-suppressed images. However, a limitation of their study is that the bone suppression algorithm can only be applied to anteroposterior images and thus may have limited use in the radiotherapy setting.

Despite the value in the current study, there are some limitations. First, ground truth was defined independently by only two physicians and the average of those co-ordinates was used to

compare to the location of the template matched by the algorithm. Our previous study showed that the average displacement between the two physician's ground truth co-ordinates was 1.0 ± 0.8 mm.⁴⁴ If more physicians were involved in the process, a more precise determination of ground truth may be possible. Additionally, this study uses a template-matching algorithm that is not yet commercially available and therefore this system cannot yet be employed in clinics without access to the software. Finally, this study tested the DE process in conjunction with the novel template-matching algorithm on static kV images only. Future studies are anticipated that will extend this work to markerless tracking on DE fluoroscopy images^{41,42,44} using a fast-switching kV X-ray generator. A limited version of the fast-kV-switching real-time DE imaging system has been implemented for a pilot study in 20 patients undergoing lung tumour RT.⁴⁷

CONCLUSION

In summary, we have presented a template-based lung tumour-matching technique using DE subtraction that is reliable, accurate and precise, and that can be employed using currently available linear accelerators and onboard imagers without the need for hardware upgrades. Going forward, by combining the template-based matching algorithm and DE method with fluoroscopy, this technique may allow for real-time tracking of lung tumours.

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