consistent with the steadiness of the 3D tumor position at the expiratory phase shown in Fig. 5 and in our previous analysis (7). The relative steadiness of the speed and the position at the expiratory phase shown in this study will be important in the design of 4DRT in future. Meanwhile, intercepting radiotherapy rather than pursuing radiotherapy is safer and most cost-effective in clinical use.

Frequent correction of the treatment couch during the delivery of irradiation was as important as the setup at the start of irradiation. Any emotional change of the patient, as well as any unintentional sigh, cough, or abdominal distention, can induce a change in the tumor trajectory (8). The need for frequent and prompt correction strongly suggests the importance of fine on-line remote control of the treatment couch from outside the treatment room in intercepting radiotherapy. Otherwise, radiotherapists would be required to go into the treatment room too many times to adjust the treatment couch during the delivery of radiotherapy. The 4D setup system was useful for increasing the efficiency of gated irradiation by selecting the best position for gating. The actual efficiency of 28% in the 21 patients in our study was not detrimental, although it was less than the best achievable efficiency, 62.4%, predicted by the 4D setup. The reason why actual efficiency was lower than the predicted one may be explained by the learning curve necessary to use the 4D setup system efficiently. Otherwise, it may be due to the difference in the trajectory between the prediction and the actual treatment, because of the large intrafractional change of the trajectory. If the latter is the main reason, the 4D setup system is to be modified for increasing efficiency. However, we are not yet certain which explanation is correct, because only a few researchers have had the opportunity to use the 4D setup system so far.

Four-dimensional setup using the tumor trajectory in the RTRT system can minimize the systematic setup error between the tumor position at the planning CT and the tumor position at the actual treatment at the same respiratory phase, as long as the fiducial marker is stable. Even if there is a large interfractional change in the tumor position relative to bony landmarks, the risk of geographically missing the target volume will be reduced with the 4D setup. The main limitations of this setup are as follows: (*1*) possible migration of the fiducial marker from the implanted position, (*2*) possible deformation of the tumor during radiotherapy, and (*3*) lack of awareness about the relationship between the marker and the critical organ. The first two limitations could be reduced by using 3 fiducial markers around the tumor or by adding CT-on-rail in the treatment room. We reported earlier that the reliability of the marker position lasts for 2–4 weeks from the start of radiotherapy, beyond which the deformation of the lung due to inflammation and tumor shrinkage makes the position unreliable (23). Now at our institution, 3 or 4 markers are implanted around the tumor and used to detect the possible migration before treatment (23).

In conclusion, substantial interfractional and intrafractional changes in the absolute amplitude and speed of lung tumors were detected. Because the determination of internal target volume using 4DCT, prediction models of respiratory motion, and pursuing RT systems are all vulnerable to these changes in the absolute amplitude and speed of lung tumors, more work is required to polish 4DRT. The 4D setup using the trajectory of tumor motion with fine on-line remote control of the treatment couch was shown to be useful for reducing the uncertainty of tumor motion and for increasing the efficiency of gated irradiation.

REFERENCES

1. Shirato H, Shimizu S, Kitamura K, *et al.* Four-dimensional treatment planning and fluoroscopic real-time tumor tracking radiotherapy for moving tumor. *Int J Radiat Oncol Biol Phys* 2000;48:435–442.
2. Keall PJ, Starkschall G, Shukla H, *et al.* Acquiring 4D thoracic CT scans using a multislice helical method. *Phys Med Biol* 2004;49:2053–2067.
3. Underberg RW, Lagerwaard FJ, Cuijpers JP, *et al.* Four-dimensional CT scans for treatment planning in stereotactic radiotherapy for stage I lung cancer. *Int J Radiat Oncol Biol Phys* 2004;60:1283–1290.
4. Shirato H, Shimizu S, Kunieda T, *et al.* Physical aspects of a real-time tumor-tracking system for gated radiotherapy. *Int J Radiat Oncol Biol Phys* 2000;48:1187–1195.
5. Neicu T, Shirato H, Seppenwoolde Y, *et al.* Synchronized moving aperture radiation therapy (SMART): Average tumour trajectory for lung patients. *Phys Med Biol* 2003;48: 587–598.
6. Shimizu S, Shirato H, Ogura S, *et al.* Detection of lung tumor movement in real-time tumor-tracking radiotherapy. *Int J Radiat Oncol Biol Phys* 2001;51:304–310.
7. Seppenwoolde Y, Shirato H, Kitamura, K, *et al.* Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat, measured during radiotherapy. *Int J Radiat Oncol Biol Phys* 2002;53:822–834.
8. Shirato H, Seppenwoolde Y, Kitamura K, *et al.* Intrafractional tumor motion: Lung and liver. *Semin Radiat Oncol* 2004;14:10–18.
9. Engelsman M, Damen EM, De Jaeger K, *et al.* The effect of breathing and setup errors on the cumulative dose to a lung tumor. *Radiother Oncol* 2001;60:95–105.
10. Wijesooriya K, Bartee C, Siebers JV, *et al.* Determination of maximum leaf velocity and acceleration of a dynamic multileaf collimator: Implications for 4D radiotherapy. *Med Phys* 2005;32:932–941.
11. Van Sornsen de Koste JR, de Boer HC, Schuchhard-Schipper RH, Senan S, Heijmen BJ. Procedures for high precision setup verification and correction of lung cancer patients using CT-simulation and digitally reconstructed radiographs (DRR). *Int J Radiat Oncol Biol Phys* 2003;55:804–810.
12. Wulf J, Hadinger U, Oppitz U, *et al.* Stereotactic radiotherapy of extracranial targets: CT-simulation and accuracy of treatment in the stereotactic body frame. *Radiother Oncol* 2000; 57:225–236.
13. Fung AY, Grimm SY, Wong JR, *et al.* Computed tomography localization of radiation treatment delivery versus conventional localization with bony landmarks. *J Appl Clin Med Phys* 2003;4:112–119.
14. Shirato H, Shimizu S, Bo X, *et al.* Four-dimensional (4-D) treatment planning integrating respiratory phases and three-dimensional (3-D) movements of lung and liver tumors using

high-speed computed tomography (CT) and magnetic resonance imaging (MRI). In: Lemke MW, Inamura K, Farman A, editors. Computer assisted radiology and surgery. San Diego: Elsevier Science; 1998;265–270.

15. Vedam SS, Keall PJ, Kini VR, *et al.* Acquiring a four-dimensional computed tomography dataset using an external respiratory signal. *Phys Med Biol* 2003;48:45–62.
16. Underberg RW, Lagerwaard FJ, Cuijpers JP, *et al.* Four-dimensional CT scans for treatment planning in stereotactic radiotherapy for stage I lung cancer. *Int J Radiat Oncol Biol Phys* 2004;60:1283–1290.
17. Rietzel E, Chen GT, Choi NC, *et al.* Four-dimensional image-based treatment planning: Target volume segmentation and dose calculation in the presence of respiratory motion. *Int J Radiat Oncol Biol Phys* 2005;61:1535–1550.
18. Murphy MJ. Tracking moving organs in real time. *Semin Radiat Oncol* 2004;14:91–100.
19. Berbeco RI, Jiang SB, Sharp GC, *et al.* Integrated radiotherapy imaging system (IRIS): Design considerations of tumour tracking with linac gantry-mounted diagnostic x-ray systems with flat-panel detectors. *Phys Med Biol* 2004;49:243–255.
20. Vedam SS, Keal PJ, Docef A, *et al.* Predicting respiratory motion for four-dimensional radiotherapy. *Med Phys* 2004;31: 2274–2283.
21. Sharp GC, Jinag SB, Shimizu S, *et al.* Prediction of respiratory tumour motion for real-time image-guided radiotherapy. *Phys Med Biol* 2004;49:425–440.
22. Wu H, Sharp GC, Salzberg B, *et al.* A finite state model for respiratory motion analysis in image guided radiation therapy. *Phys Med Biol* 2004;49:5357–5372.
23. Imura M, Yamazaki K, Shirato H, *et al.* Insertion and fixation of fiducial markers for setup and tracking of lung tumors in radiotherapy. *Int J Radiat Oncol Biol Phys* 2005;63:1442–1447.