

ORIGINAL ARTICLE

Influence of different image-guided tracking methods upon the local efficacy of CyberKnife treatment in lung tumors

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Introduction

Real-time tracking is one of the important advantages of CyberKnife treatment of lung tumors. In clinical practice, tracking is accomplished either using Synchrony respiratory tracking, which allows the radiation beam to be moved along with the movement of the lung tumor, or Xsight spine, which allows the position of the tumor to be assessed and corrected

Abstract

Background: The aim of this study was to explore the influence of image-guided tumor localization modality (Synchrony tracking vs. Xsight spine-based localization) on the local efficacy of CyberKnife treatment in lung cancer and lung metastases.

Methods: Retrospective analysis of 64 patients with pulmonary metastases and primary tumor cases (72 targets) treated with stereotactic body radiotherapy using CyberKnife was conducted. Synchrony respiratory tracking was used to treat 45 targets, and the remaining 27 targets were treated using Xsight spine (with an extended margin to account for positional uncertainty). The median (80%) isodose line (70–94%) covered the planning target volume at a total dose of 6000 cGy delivered in three fractions. Local efficacy was evaluated by Response Evaluation Criteria in Solid Tumors, accompanied by the follow-up of local recurrence cases and analysis of tracking methods.

Results: Short-term local control was superior for targets tracked with Synchrony than for targets localized with Xsight spine. There was no statistical difference for targets in the upper lung, but for targets in the lower lung Synchrony tracking was better. Small targets (less than 15 mL) were better controlled when Synchrony was used, but there was no difference for treatment volumes larger than 15 mL. Treatment failures were more likely in the lower lung and for small tumors localized with Xsight spine.

Conclusions: The local efficacy of CyberKnife treatment in lung cancer and lung metastases was influenced by image-guided localization method, target location within the lung, and tumor volume.

based on its location relative to the spine.^{1–4} Synchrony tracking is typically accomplished based on implanting gold markers. In most cases, doctors are accustomed to implanting these markers. In cases in which the marker is not advised, we usually adopt a localization method based on Xsight spine. The general view is that synchrony tracking is more accurate with better clinical efficacy than Xsight spine. However, the efficacy of clinical practice is the sole criterion and the specific

differences between synchrony tracking and Xsight spine have not been studied. A question has arisen as to whether differences in tracking modality can affect clinical outcomes. This question has neither been studied nor reported. Here we summarize our findings from the CyberKnife Center of the Tianjin Cancer Hospital to share with our counterparts.

Materials and methods

Patients

A retrospective analysis of 64 patients (37 men and 27 women) with lung tumors (72 targets) from September 2006 to December 2011 were carried out, including 40 patients with primary tumors (41 targets) and 24 with pulmonary metastases (31 targets). Synchrony tracking was used for 45 targets and Xsight spine for the remaining 27 targets. Synchrony was used when the requirement of gold marker implantation could be met (Table 1). The median age was 64 years (33–89 years). Targets included: 33 primary lung cancer cases; nine intrapulmonary lung cancer metastases; seven pulmonary nodules without pathological confirmation (final diagnosis by positron emission tomography); six metastases from hepatocellular carcinoma; two from thyroid carcinoma; six colorectal; one breast; one parotid gland; one rhabdomyosarcoma; two adenoid cystic carcinoma (ACC) of the salivary glands; and four renal cell carcinoma (RCC). The Kernal Patch Statistic (KPS) of all cases was above 80.

Table 1 Baseline features of patients

Features	Number
Patients	64
Targets	72
Gender	
Male	37
Female	27
Age	
Range	33–87 years
Median	64 years
Primary targets	41
Metastatic targets	31
Treatment volume	
Range	1.71–60.13 mL
Median	13.35 mL
Tracking manner	
Synchrony with gold markers	45
Xsight spine	27
Isodose (%)	
Range	70–94
Median	80
Dose/Fraction	6 000 cGy/3
Biologically effective dose	18 000 cGy

Treatment methods

Patients were fixed by body-pad according to treatment posture. We adopted the conventional contrast-enhanced computed tomography (CT) scan (1.5 mm thick), which covered 15 upper and lower targets, including the target volume and the evaluated organs at risk. For Synchrony-treated patients a single gold marker was implanted into the tumor by CT guidance. If the gold marker migrated, the implantation procedure was repeated. During treatment, the location of the gold markers was assessed using the CyberKnife image-guidance system. Xsight spine was used for tumors within 5 cm of the spine; the ability of the spine to serve as a targeting structure was confirmed by X-ray simulator fluoroscopy or rebuilt images of tumor respiratory mobility under the CT scan. Based on a registration of in-room X-rays to synthetic radiographs constructed from the treatment-planning CT scans, patients were setup and the treatment began. The median (80%) isodose line (70–94%) of all the patients covered the planning target volume (PTV), which encompassed 3–8 mm outside the gross tumor volume (Table 1). All targets received 2000 cGy in each of three fractions.^{5–8}

Follow-up observation and evaluation

All patients under CyberKnife treatment had local and systemic physical check-ups to evaluate local efficacy. In the first year of follow-up, re-examination was conducted once, at most, every three months. The following countercheck period was determined by the local efficacy. The local efficacy and tumor progress were the primary point for observation. Local efficacy was evaluated as a complete or partial response (CR, PR), stable disease (SD) or progressive disease (PD), according to Response Evaluation Criteria in Solid Tumors (RECIST).^{9–12}

Statistical methods

Data were processed by SPSS 17.0 software. A chi-square test was used to assess differences in tumor responses across groups (tracking method, tumor location, tumor size). $P < 0.05$ was defined as the standard of statistical difference.

Results

Overall comparison of short-term efficacy between tumors tracked with Synchrony and Xsight spine

At a median follow-up of 22 months (range: 2–67 months), local tumor response was superior for tumors tracked with Synchrony than with Xsight spine. Overall response rate

Table 2 Overall comparison of short-term efficacy between Synchrony and Xsight spine

	CR	PR	SD	ORR
Synchrony	20 (44.44%)	22 (48.89%)	3 (6.67%)	42 (93.33%)
Xsight spine	6 (22.22%)	14 (51.85%)	7 (25.93%)	20 (74.07%)
<i>P</i> -value	$\chi^2 = 6.84, P = 0.033$			

(ORR), including CR and PR, was 93.33% for Synchrony-tracked and 74.07% for Xsight-tracked lesions ($P = 0.033$). Differences in tumor response are detailed in Table 2.

Comparisons between tracking methods in the upper and lower lung

Lungs were divided into upper and lower portions using the carinal ridge as the boundary. Tracking modality did not influence tumor response for targets in the upper lung. For targets in lower lung, Synchrony tracking yielded better local efficacy (see Table 3 for details).

Comparisons between tracking methods for smaller and larger tumors

A treatment volume of 15 mL (diameter close to 3 cm) was the boundary for this analysis. For treatment volumes less than 15 mL local efficacy depended on tracking method, with Synchrony-tracked lesions showing a better response.

However, for treatment volumes greater than or equal to 15 mL there was no difference between tracking methods (Table 4).

The influence of different tracking methods upon the short-term efficacy of primary and metastatic targets

No differences in short-term efficacy, depending on tracking modality, were observed for primary targets, but metastatic targets responded better when treated using Synchrony tracking (Table 5).

Analysis of locally advanced targets in follow-up

At a median follow-up period of 22 months, there were, in total, six locally progressed targets (local control rate 92.67%), among which five were in the lower lung and were localized with Xsight spine (statistically significant for track-

Table 3 Comparison of short-term efficacy between upper and lower lung tracking methods

Upper lung	CR	PR	SD	ORR
Synchrony	17 (53.13%)	11 (34.38%)	4 (12.50%)	28 (87.50%)
Xsight spine	5 (31.25%)	7 (43.75%)	4 (25.00%)	12 (75.00%)
<i>P</i> -value	$\chi^2 = 2.36, P = 0.31$			
Lower lung	CR	PR	SD	ORR
Synchrony	4 (26.67%)	11 (73.33%)	0 (0.00%)	15 (100.00%)
Xsight spine	1 (9.09%)	7 (63.64%)	3 (27.27%)	8 (72.73%)
<i>P</i> -value	$\chi^2 = 4.63, P = 0.032$			

Table 4 Comparison of short-term efficacy of treatment volume between the two methods

Treatment volume <15 mL	CR	PR	SD	ORR
Synchrony	13 (48.15%)	12 (44.44%)	2 (7.41%)	25 (92.59%)
Xsight spine	2 (11.77%)	10 (58.82%)	5 (29.41%)	12 (70.59%)
<i>P</i> -value	$\chi^2 = 6.53, P = 0.038$			
Treatment volume ≥15 mL	CR	PR	SD	ORR
Synchrony	7 (38.89%)	10 (55.56%)	1 (5.56%)	17 (94.44%)
Xsight spine	4 (40.00%)	4 (40.00%)	2 (20.00%)	8 (80.00%)
<i>P</i> -value	$\chi^2 = 1.57, P = 0.46$			

Table 5 The comparison of short-term efficacy between primary and metastatic targets under different tracking methods

Primary targets	CR	PR	SD	ORR
Synchrony	11 (39.29%)	15 (53.57%)	2 (7.14%)	26 (92.86%)
Xsight spine	4 (30.77%)	7 (53.85%)	2 (15.38%)	11 (84.62%)
<i>P</i> -value	$\chi^2 = 0.79, P = 0.67$			
Metastatic targets	CR	PR	SD	ORR
Synchrony	9 (52.94%)	7 (41.18%)	1 (5.88%)	16 (94.12%)
Xsight spine	2 (14.29%)	7 (50.00%)	5 (35.71%)	9 (64.29%)
<i>P</i> -value	$\chi^2 = 6.90, P = 0.032$			

ing method and lung location based on the chi-square test). In addition, the treatment volume of targets that progressed (2.66–14.47 mL, median 4.26 mL) and were treated with Xsight spine tracking was comparatively smaller than that of targets that progressed and were treated with Synchrony (Table 6).

Discussion

This study suggested that the local efficacy of CyberKnife treatment in lung cancer and lung metastases was influenced by image-guided localization method, target location within the lung, and tumor volume.

The difference in curative effect between Synchrony tracking and Xsight spine tracking is the limitation of Xsight spine, which cannot completely track the movement of the tumor, and, thus, therapy cannot be consistent with the treatment plan. At the same time, the relevant mobility of different tumor size and tumor location impacts on the curative effect of local control. Because of the lower mobility of upper lung targets, we can adopt an appropriate external treatment plan to get a good result using Xsight spine tracking. However, for lower lung targets with greater mobility at breath, Xsight cannot guarantee that the actual dose is consistent with the planning dose, which affects the efficacy of therapy. The same is true when considering the volume of the tumor. A larger tumor is implicated by the surrounding tissue, and, therefore, has less motility, while a smaller tumor has greater motility.

Table 6 Features of locally progressed targets

	X-sight spine	Synchrony
Locally progressed targets/total targets	5/27	1/45
Upper lung targets	1	1
Lower lung targets	4	0
Treatment volume	Median: 4.26 (2.66–14.47)	31.62

These factors distinguish why the two kinds of tracking method have different curative effects.

For this study we selected targets treated with the same dose and fractionation (6000 cGy in 3 fractions) and in relatively uniform locations. As a result, local failure caused by target delineations could be avoided and other adverse factors could be reduced as much as possible. The results showed that, in general, Synchrony was superior to X-sight spine tracking. Statistical analysis showed that there were no significant differences in upper lung targets; however, tracking modality did have an effect on lower lung targets. The influence of tracking methods was also greater for smaller tumors. Different tracking methods have little influence on primary and metastatic tumors for single high-doses and short-term treatment is dependent upon pathology and radiosensitivity.^{13,14} The statistical difference found in our study was actually a result of the locations of the targets, the image-guided localization method, and tumor volume. Therefore, we could infer that for upper lung targets, especially those with a larger volume, gold marker implantation need not be used and the associated penetrating trauma can be avoided. For lower lung targets, especially those with small volume tumors, gold marker implantation may improve outcomes. Given that the short-term efficacy of stereotactic body radiation therapy (SBRT) may be influenced by RECIST, tumor regression speed, and fibrosis (though limited to minor cases), we analyzed and followed up the locally progressed targets, which supported our conclusions (Table 6).

Local efficacy was poorer for small targets treated with Xsight spine. This does not mean that small targets are more difficult to control. They were well controlled in patients treated with Synchrony. However, Xsight spine can be employed to avoid gold marker implantation, which can be a risky procedure requiring greater technical skill of the doctor. In cases where gold marker implantation cannot be completed or the procedure is too risky, Xsight spine could be used, including the extension of the PTV target volume to assure tumor coverage.

Prior studies have explored CyberKnife tracking methods largely in a theoretic manner, or by using measurements in phantoms.^{15–19} However, clinical practice experience is

lacking. This study focuses on the influence of different image-guided tracking methods upon the local efficacy of Cyberknife treatment in lung cancer and lung metastases, which do not only offer guidance to CyberKnife users for the selection of tracking method, but may also further improve the efficacy of CyberKnife treatment.

The data of this study is from a single centre, therefore, further research using larger sample sizes in order to validate our conclusions is recommended.

Conclusion

In summary, this study has suggested that tracking method could influence the local efficacy of SBRT depending on both the location and volume of lung tumors treated. Our study, therefore, provides a basis for a case-by-case approach that takes each of these factors into account. Although CyberKnife treatment has some problems, as long as we communicate, exchange, and share experiences and ideas with our counterparts, CyberKnife will improve the level of treatment in lung cancer and serve human health better in the future.

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Disclosure

No authors report any conflict of interest.

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