

# Short-term outcomes of CyberKnife therapy for advanced high-risk tumors: A report of 160 cases

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**Abstract.** The objective of the present study was to evaluate short-term outcomes of CyberKnife therapy in patients with advanced high-risk tumors. A total of 201 target areas from 341 advanced high-risk tumor lesions in 160 patients were treated with CyberKnife. A prescribed dose of 18-60 Gy to the gross tumor volume was delivered in 1-6 fractions to complete the entire treatment in 1 week. Radiographic studies and clinical examinations were performed at 1- to 3-month follow-up intervals, and the results were compared to outcomes of 160 similar advanced high-risk tumor patients who were treated by conformal radiotherapy (CRT). After CyberKnife therapy, the short-term improvement in the quality of life was significant according to radiographic study, radioimmunoassay and ZPS scores of these patients. The total rates of objective efficacy and alleviation of ascities were as high as 66.88 and 67.90%. The short-term outcomes in our series of patients with advanced high-risk tumors treated with CyberKnife appeared to be better compared to conventional CRT. CyberKnife may be an option for patients with incurable advanced high-risk tumors, although further studies of the long-term outcomes are required to confirm the validity.

## Introduction

Most advanced high-risk tumors are contraindicated for conventional treatments, such as surgery, chemotherapy and radiotherapy, due to the following characteristics: post-operative recurrence and metastasis (1); significant functional central organ invasion (2); local lymph node nerve cell infiltration or multiple metastases (3-5). On this occasion, symptomatic palliative therapy is preferable in clinical treatment (6). Due to direct invasion, tumors oppress neighboring tissues; thus,

the accompanying tumor oppression syndrome leads to great patient suffering (7-9).

In order to improve therapeutic efficacy for advanced high-risk tumors, we tried to eliminate the local lesion by CyberKnife, which was combined with hyperthermia therapy. In the present study, a retrospective evaluation of short-term outcomes of patients treated consecutively with CyberKnife was performed to demonstrate the clinical applicability of CyberKnife for incurable advanced high-risk tumors. Through CyberKnife therapy, we controlled the development of tumors, alleviated the clinical symptoms of patients and reduced adverse reactions.

## Patients and methods

**Patient characteristics.** One hundred and sixty patients with 341 tumor lesions were recruited; all of them were patients with advanced high-risk tumors who came to the Center for Tumor Treatment, The People's Liberation Army 107th Hospital, for palliative treatment between November 2010 and June 2011. The inclusion criteria were: i) pathological or radiographic confirmation of stage III-IV high-risk tumors; ii) performance status (PS) of 1-4 according to the Eastern Cooperative Oncology Group (ECOG) scale; iii) all the inclusive patients provided informed consent for detection and treatment.

One hundred and one patients were male and 59 were female. All patients were from 6 to 81 years of age, with a mean age of 53.7. The locations of tumors were 55 head and neck cases, 54 chest cases, 34 abdomen cases and 17 vertebral cases. Included were a total of 341 lesions and 201 target area plans among all patients. The number of lesions for each patient ranged from 1 to 24. The largest tumor lesion was 15x9.5x18 cm, while the smallest was 1x0.5x0.5 cm. Twenty-eight cases were combined with moderate to severe hydrothorax or ascites, and 49 cases had cerebral edema of different degrees.

**Methods.** CT scans (1.25-mm) were conducted soon after the patients were hospitalized. MRI, PET-CT or DSA image fusion was performed when necessary. For the organs which usually make large respiratory amplitude, 1-3 gold markers were placed into the lung, liver and pancreas, to definitely mark the target areas. We then outlined the target areas and determined the treatment plan and therapeutic doses according to the number, volume, location and stage of the tumor, which

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were usually delivered in 1-6 fractions, and the entire treatment was completed in 1 week. The whole doses ranged from 18 to 60 Gy, with a fractional dose of 4-18 Gy. For patients with somatic tumors, we subjoined radiofrequency ablation diathermy of 2 fractions per week after the CyberKnife therapy, with an equivalent hot dose of 40°C/min.

**Outcome evaluation and statistical analyses.** The outcomes were evaluated based on radiographic examination, radioimmunoassay, ZPS (Zubrod-ECOG-WHO) scores, changes in ascities and the Objective Efficacy Evaluation Criteria. Comparisons between short-term outcomes of CyberKnife therapy and conformal radiotherapy (CRT) were made. Chi-square test was used for the comparison of the rate between the two samples. Differences were considered statistically significant with a P-value <0.05. SPSS 13.0 software was used for statistical analysis.

## Results

**Radiographic observation.** Radiographic study showed tumor shrinkage of different degrees and even disappearance after CyberKnife therapy (18 disappeared, 99 exhibited shrinkage, 35 were unchanged and 8 were enlarged). The recent curative effect of CyberKnife therapy in the radiographic study was 73.13%, and was obviously superior to CRT (3 disappeared, 65 exhibited shrinkage, 70 were unchanged and 22 were enlarged) according to the statistical analysis.

**Radioimmunoassay (RIA).** In 40 patients, the tumor marker reversed trend and was positively heightened. After CyberKnife therapy, 5 cases became negative, 15 cases decreased to different degrees and 17 cases were unchanged, while 3 cases became more positive.

**ZPS scores before and after treatment.** After CyberKnife therapy, the ZPS scores of all patients decreased, accompanied by alleviation of tumor oppression syndrome and apparent improvement of the quality of life. The comparison of ZPS scores before and after CyberKnife therapy was performed using the Wilcoxon's test ( $P < 0.05$ ). Apparent improvement of ZPS scores occurred after CyberKnife therapy.

**Changes in ascities.** There were 28 patients who presented with different degrees of ascites among the 160 cases. Regarding the alleviation of ascites, CyberKnife treatment was significantly effective in 8 cases (ascites disappeared completely), effective in 11 cases (>60% ascites disappeared after treatment and no new complication appeared), while CyberKnife treatment was ineffective in 9 cases. The total efficacy rate was 67.9%.

**Objective efficacy assessment.** For patients with advanced high-risk tumors who received repeated treatment, there was still high palliative efficacy after CyberKnife therapy. What should be emphasized is that, although there were no significant changes in radiography, these patients experienced complete improvement in the quality of life after CyberKnife therapy. According to the statistical analysis, CyberKnife therapy is superior to CRT in the aspect of objective effect assessment.

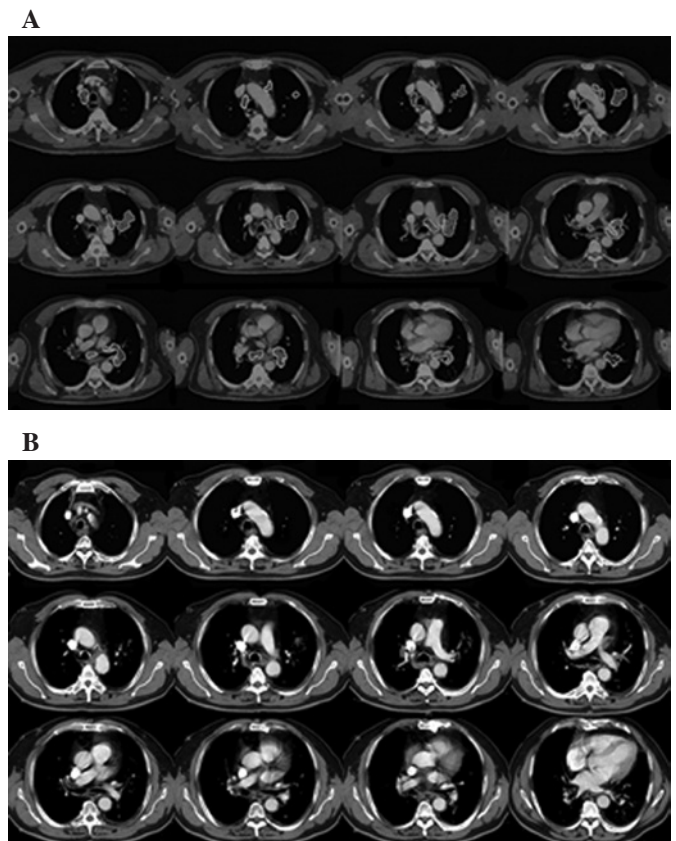


Figure 1. Lung cancer with mediastinal lymph node metastases (15 lesions). CT revealed that tumor lesions completely disappeared after CyberKnife therapy. (A) CT before CyberKnife therapy (2011-01-28); (B) CT after CyberKnife therapy (2011-03-11).

## Discussion

With substantial improvements in radiotherapy technology, stereotactic body radiotherapy, which allows dose-intensification, has led to promising treatment outcomes (10). Cyberknife, the robotic stereotactic radiosurgery system, which is able to precisely deliver a high dose of radiation using an excellent synthesis of modern image-guided localization and a compact robotically positioned linear accelerator, has unique advantages that make it dramatically suited for stereotactic radiotherapy of advanced high-risk tumors (11,13).

However, due to the realization of hypofractions, larger doses and shorter treatment courses when using CyberKnife therapy, numerous studies have consequently placed too much emphasis on the lack of need for patient hospitalization, the short treatment course and non-toxic side effects (12-14). We believe that CyberKnife, due to its precision and flexibility, should be highly individualized, and the blind pursuit of a rapid treatment course and early discharge from the hospital should be avoided (15). During the present study, we found it was extremely necessary to prevent an early tumor-dissolving response and abnormal bilirubin metabolism due to the rapid, short-course killing of tumor cells. The study also discovered that patient neutrophil levels suddenly decreased 2 weeks after CyberKnife therapy. If this had not been discovered in time and treated efficiently, there would have been serious consequences for the patients. Therefore, it is necessary for patients with multiple or large tumors to be hospitalized.

Using a combination of CyberKnife with a variety of imaging techniques, such as CT, MRI, PET-CT and DSA, an actual three-dimensional image of tumors or vascular lesions can be obtained. This provides a good foundation for target area sketching (16,17). However, to date, most experts still refer to the traditional radiobiology model (18); a new biological model has yet to be established. Because of this delay, in China, no uniform treatment exists even for the same disease (19-21). Based on the dosage plan, which was designed according to the linear quadratic model, with the  $\alpha/\beta$  value of early response tissues set as 10, late response tissue as 3 and converted by conventional 2 Gy fractionated radiation, we arrived at a dosage which was close to the clinical experienced dose. Yet, a difference with both the clinical practice and foreign reports was noted (22,23). As a more precise therapy modality, CyberKnife realizes hypofractionated stereotactic treatment and abandons the strict limitation of taking biological effect into consideration, which is different from ordinary radiotherapy. (24-27).

We conclude that CyberKnife is undoubtedly a safer treatment modality for high-risk or highly difficult cases. One patient in our study who had lung cancer with mediastinal lymph node metastases (15 lesions) was definitely a highly difficulty case. After treatment using CyberKnife, the tumor lesions completely disappeared (Fig. 1). After the applied research of CyberKnife in 160 advanced high-risk (or difficult) tumor cases, we believe that CyberKnife cannot only quickly improve the clinical symptoms of patients and obtain satisfactory short-term curative effects, but it is also suitable for the treatment of high-risk tumors, thus curing the incurable tumors.

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