Preliminary clinical efficacy of iodine-125 seed implantation for the treatment of advanced malignant lung tumors

ABSTRACT

Aims: This study aims to observe the preliminary clinical efficacy of percutaneous interstitial brachytherapy using iodine-125 seeds for the treatment of advanced malignant lung tumors.

Subjects and Methods: This retrospective study enrolled 24 patients in our hospital with advanced malignant lung tumors between June 2013 and November 2017. Computed tomography (CT)-guided iodine-125 seed implantation therapy was administered to these patients. All patients were followed up at 3, 6, and 12 months after the operation. The clinical efficacy was evaluated by CT.

Results: Among the 24 patients, the objective response rates at 3, 6, and 12 months after the procedure were 50.0%, 50.0%, and 33.3%, respectively. Recent occurrence of adverse reactions were observed, including four cases of pneumothorax, three cases of hemoptysis, and two cases of particle displacement.

Conclusions: CT-guided percutaneous interstitial brachytherapy with iodine-125 seeds can be used for the treatment of lung malignant tumors. Its clinical curative effect is remarkable and it results in limited trauma, reducing the incidence of adverse reactions and improving patient quality of life.

KEY WORDS: Brachytherapy, computed tomography guided, iodine-125 seed, malignant lung tumor

INTRODUCTION

Malignant tumors are the second leading cause of death in China. Malignant lung tumors are among the most common malignant tumors, with high incidence rates. The incidence and mortality of primary lung cancer are the highest among malignant tumors worldwide.[1] When diagnosed, the disease has generally progressed to the middle and late stages; thus, patients have lost the chance for radical surgery and have a poor prognosis. At the same time, the lung is a common site for tumor metastasis. More than 60% of malignant tumors have distant metastasis at the first visit, 30%–50% of which metastasize to the lungs. The most common primary tumors include thyroid cancer, breast cancer, kidney cancer, choriocarcinoma, osteosarcoma, liver cancer, stomach cancer, colorectal cancer, and prostate cancer. Conventional treatment includes surgery, chemotherapy, radiation therapy, and targeted therapy. In recent years, therapeutic methods have been increasing, and the implantation of radioactive particles as a form of brachytherapy has been widely performed in clinical practice. Studies have demonstrated the advantages of this treatment, including its safety, effectiveness, reduced complications, and reproducibility.[2-5] This method has been applied to a variety of solid tumors, including liver cancer, pancreatic cancer, reproductive system tumors, and brain tumors.[6-10] It also achieves better results in the treatment of malignant lung tumors.[11-19]

This article retrospectively analyzed the clinical data and evaluated the preliminary efficacy of iodine-125 seed implantation in patients with lung malignancy. The report is as follows.
Subjects and Methods

Patients
The individuals included 24 patients with advanced lung malignancies treated in our hospital between June 2013 and November 2017 who provided written informed consent. The cases included 19 with primary lung cancer and five with lung metastases. There were 19 men and 5 women with an age range of 46–79 years and average age of 67.6 ± 12.0 years. The tumor size ranged from 20 to 81 mm with an average of 38.9 ± 14.0 mm. Among primary lung cancer cases, 13 were squamous cell carcinoma (SCC), two were adenocarcinoma, two were adenosquamous carcinoma, one was small cell lung cancer, and one was atypical carcinoid; 12 cases were central type and seven were peripheral type. All cases were Stage IIIA and above. The lung metastases included three cases of hepatocellular carcinoma (HCC) and two cases of colon cancer, all of which were Stage IV [Tables 1 and 2].

Instrumentation
Iodine-125 seed implantation was guided by a Siemens Miyabi Angio-computed tomography (CT) scanner (64-slice) and a Siemens Symbia T16 Single photon emission CT/CT with an interval of 5 mm. Chest CT was performed for all patients to evaluate the tumor characteristics 2 weeks before the procedure. A treatment planning system (TPS; KL-SIRPS-3D of Beijing Tianhang Kelin Technology Development Co., Ltd.) was used to calculate the number and distribution of seeds based on the preoperative CT images. The TPS ensured a prescription dose of 145 Gy to the target volume. The implantation needle (18 G), turnable implantation gun, and iodine-125 seeds were all provided by Beijing ZHIBO Hi-Tech Biotechnology Co., Ltd. The diameter of each seed was 0.8 mm, and the length was 4.5 mm. The half-life of each seed was 59.6 days, and the tissue penetration distance was 1.7 cm. The activity of each iodine-125 seed was 0.5–0.8 mCi.

Procedure
Before the procedure, all patients were scanned by 5-mm thin slice chest CT to measure the tumor volume. The CT scan images were transferred to TPS. The matched peripheral dose was calculated based on the target volume and iodine-125 seed activity, the position of the implantation needle, and the number of seeds. The implantation procedure was performed under local anesthesia (2% lidocaine) in the CT room. The implantation needle was inserted into the tumor tissue under CT guidance while avoiding puncturing the nearby vessels and other organs. The seeds were then implanted using a turntable implantation gun, with a center-to-center space between seeds of 0.5–1.0 cm. After the procedure, the entire lung was scanned routinely to observe seed distribution and to assess complications such as pneumothorax and bleeding. The patients were kept in the interventional ward for 1–2 days after the procedure.

Follow-up and efficacy evaluation
Each patient underwent follow-up examinations at 3, 6, and 12 months after the procedure. Chest CT was performed at each follow-up. The physical status of the patients and the tumor diameters were recorded during the follow-up period. Solid tumor efficacy evaluation criteria (RECIST 1.1) were used to assess the therapeutic efficacy.

Complete response (CR) was defined as the complete disappearance of a lesion for >4 weeks. Partial response (PR) was defined as a decrease in lesion by ≥30% that then remained unchanged for 4 weeks. Stable disease (SD) was defined as a decrease in tumor size by <30% or increase by <20%. Progressive disease (PD) defined as an increase in lesion size by ≥20%. The local tumor objective response rate (ORR) was defined as the sum of CR and PR, and the disease control rate (DCR) was defined as the absence of tumor progression (CR and PR and SD).

Results
All patients tolerated the brachytherapy well with no operation-related deaths. Three months after the procedure, three cases (12.5%) achieved a CR, nine cases (37.5%) achieved a PR, 12 cases (50.0%) had SD, and there was no PD, resulting in an ORR of 50.0% and DCR of 100%. The 6- and 12-month ORRs were 50.0% and 91.7%, respectively, while the DCRs were 33.3% and 75.0%, respectively [Table 3].

Complications
Among all cases, after brachytherapy, three patients experienced hemoptysis, which was relieved after hemostasis treatment; four patients developed pneumothorax, three of which had a minor pneumothorax and one had a massive pneumothorax, which improved after 1 week of closed thoracic drainage; and two cases experienced seed shifting.

Typical cases
A 49-year-old male with HCC and metastasis in the right lower lung showed CR to brachytherapy [Figure 1]. Iodine-125 seeds were implanted in his right lower lung tumor region for
brachytherapy. The right lower lung tumor had completely disappeared at 3, 6, and 12 months after the procedure.

A 78-year-old male with moderately differentiated squamous cell lung carcinoma in his left lower lung and progression after chemotherapy and radiotherapy showed a significant reduction in tumor size after iodine-125 seed implantation [Figure 2].

A 73-year-old woman with a poorly differentiated adenosquamous carcinoma in her right lung that had progressed after multicourse treatment showed a significant reduction in tumor size after iodine-125 seed implantation [Figure 3].

A 77-year-old male with a moderately differentiated squamous cell lung carcinoma in his right lung and progression after chemotherapy and radiotherapy showed a significant reduction in tumor size after iodine-125 seed implantation [Figure 4].

A 74-year-old male with local recurrence after surgery for moderately differentiated SCC in his right lower lung exhibited a significant reduction in tumor size after iodine-125 seed implantation [Figure 5].

**DISCUSSION**

CT-guided iodine-125 seed implantation is a minimally invasive treatment and form of interstitial brachytherapy. Iodine-125
is a low-energy radionuclide that continuously releases radiation and emits X-rays and gamma rays of 27.4–31.5 keV. It can kill tumor cells by continuously destroying the DNA double strands and making them lose their proliferative ability. The radiation directly acts on the tumor tissue, and its physical half-life is 59.6 days. The effective continuous

Figure 2: (a) Computed tomography image showing moderately differentiated squamous cell carcinoma in the left lower lung. (b) Computed tomography image 3 months after iodine-125 seed implantation. (c) Computed tomography image 6 months after the procedure. (d) Computed tomography image 12 months after the procedure. (e) Dose-volume histogram calculated for treatment planning. (f and g) Postoperative verification images

Figure 3: (a) Computed tomography image showing a poorly differentiated adenosquamous carcinoma in the right lung. (b) Computed tomography image 3 months after iodine-125 seed implantation. (c) Dose-volume histogram calculated for treatment planning. (d and e) Postoperative verification images
irradiation period for the tumor is up to 200 days, which increases the effect of radiotherapy. Meanwhile, the radiation penetration is extremely weak: as short as 17 mm. Therefore, the damage to the surrounding normal tissue is minimal. This treatment method results in a significant reduction in tumor reproliferation due to continuous irradiation; the continuous low-dose irradiation inhibits mitosis of the tumor cells arresting them in the G2 phase. Therefore, the treatment can maximally inactivate tumor cells to achieve the therapeutic purpose. Studies have shown that interstitial brachytherapy using iodine-125 seeds can provide good results in the treatment of malignant lung tumors. In our study, 24 patients had satisfactory results with an ORR of 50.0% and a DCR of 100% at 3 months postoperatively; 50.0% ORR and 91.7% DCR at 6 months...
postoperatively; and 33.3% ORR and 75.0% DCR at 12 months postoperatively. Most of the patients in this group had progressed after systemic chemotherapy and radiotherapy. The tumor cells were dormant or resistant to various chemotherapeutic drugs. They were not sensitive to chemotherapy. The radioactive seeds can kill tumor cells in large numbers and damage active cells within the implanted range. The treatment may also increase the sensitivity of active tumor cells to chemotherapeutic drugs due to the reduced tumor burden, which is conducive to further comprehensive treatment of cancer patients. In addition, the efficacy of radiotherapy for lung metastases is closely related to whether the primary tumor is sensitive to radiation.[25]

In this group of patients, four developed pneumothorax, including one case of massive pneumothorax, which was remitted after thoracic drainage closure; three patients developed hemothysis and received hemostasis treatment; and two patients showed particle displacement without obvious discomfort.

The preliminary results were satisfactory. Compared to other treatment methods, the method described in the present study can improve patient quality of life and has good value for clinical application. However, the indications should be strictly controlled, the characteristics of chest anatomy and imaging should be mastered, and CT positioning should be skillfully applied. Moreover, the preoperative preparation should be sufficient, and the procedure should be performed according to the preoperative plan. Finally, complications should be diagnosed and treated promptly.

Our study has several limitations, including the limited number of patients and lack of assessment of long-term clinical efficacy. Therefore, large-scale studies with long-term follow-up periods are needed to confirm the clinical efficacy of this method.

CONCLUSIONS

CT-guided percutaneous interstitial brachytherapy using iodine-125 seeds for the treatment of malignant lung tumors is safe and effective, has few side effects, and can be repeated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017;67:7-30.
2. Bagshaw MA, Cox RS, Rambach JE. Radiation therapy for localized prostate cancer. Justification by long-term follow-up. Urol Clin North Am 1990;17:787-802.
3. Wang H, Wang J, Jiang Y, Li J, Tian S, Ran W, et al. The investigation of 125I seed implantation as a salvage modality for unresectable pancreatic carcinoma. J Exp Clin Cancer Res 2013;32:106.
4. Zhang FJ, Wu PH, Gu YK, Zhao M, Zhang L, Tan ZB, et al. CT guided radioactive seed 125I implantation in treating lung metastasis. Chin J Radiol 2004;38:906-9.
5. Hu XK, Wang MY, Yang ZG, Qiu CD, Li DF, Li XD, et al. The study of curing central-type lung cancer by CT guided percutaneous embedding of 125I seeds. Chin J Radiol 2004;38:910-5.
6. Jin Z, Du Y, Li Z, Jiang Y, Chen J, Liu Y. Endoscopic ultrasonography-guided interstitial implantation of iodine-125 seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: A prospective pilot study. Endoscopy 2008;40:314-20.
7. Lin ZY, Lin J, Lin C, Li YG, Chen SM, Hu JP, et al. 1.5T conventional MR-guided iodine-125 interstitial implants for hepatocellular carcinoma: Feasibility and preliminary clinical experience. Eur J Radiol 2012;81:1420-5.
8. Hu X, Qiu H, Zhang L, Zhang W, Ma Y, Qiao Z, et al. Recurrent gliomas: Comparison of computed tomography (CT)-guided 125I seed implantation therapy and traditional radiotherapy. Cancer Biol Ther 2012;13:840-7.
9. Zhu L, Jiang Y, Wang J, Ran W, Yuan H, Liu C, et al. An investigation of 125I seed permanent implantation for recurrent carcinoma in the head and neck after surgery and external beam radiotherapy. World J Surg Oncol 2013;11:60.
10. Han L, Li C, Wang J, He X, Zhang X, Yang J, et al. Iodine-125 radioactive seed tissue implantation as a remedy treatment for recurrent cervical cancer. J Cancer Res Ther 2016;12:C176-80.
11. Zhang W, Li J, Li K, Zhang Y, Han M, Ma W. Efficacy and safety of iodine-125 radioactive seeds brachytherapy for advanced non-small cell lung cancer-A meta-analysis. Brachytherapy 2018;17:439-48.
12. Jiang G, Li Z, Ding A, Zhou F, Jiao W, Tang D, et al. Computed tomography-guided iodine-125 interstitial implantation as an alternative treatment option for lung cancer. Indian J Cancer 2015;51 Suppl 2:e9-12.
13. Li R, Ying Z, Yuan Y, Lin Q, Dai J, Xu R, et al. Comparison of two iodine-125 brachytherapy implant techniques for the treatment of lung tumor: Preplanning and intraoperative planning. Brachytherapy 2019;18:87-94.
14. Li RF, Wang YD, Yan Y, Yang P, Sha F, Li W, et al. Implantation of 125I seeds for the treatment of non-small cell lung cancer: Evaluation of short-term effect. J Interv Radiol 2014;23:65-8.
15. Zhang T, Lu M, Peng S, Zhang W, Yang G, Liu Z, et al. CT-guided implantation of radioactive 125I seed in advanced non-small-cell lung cancer after failure of first-line chemotherapy. J Cancer Res Clin Oncol 2014;140:1383-90.
16. Chen Y, Li Y, Jia Y, Lei K, Zhang X, Cao Y, et al. Bronchial artery chemoembolization combined with radioactive iodine-125 seed implantation in the treatment of advanced nonsmall cell lung cancer. J Cancer Res Ther 2017;13:636-41.
17. Yu X, Li J, Zhong X, He J. Combination of iodine-125 brachytherapy and chemotherapy for locally recurrent stage III non-small cell lung cancer after concurrent chemoradiodtherapy. BMC Cancer 2015;15:656.
18. Wu C, Li B, Sun G, Peng C, Xiang D. Efficacy and safety of iodine-125 brachytherapy combined with chemotherapy in the treatment of advanced NSCLC in the elderly. Onco Targets Ther 2018;11:6617-24.
19. Huo X, Huo B, Wang H, Wang L, Cao Q, Zheng G, et al. Implantation of computed tomography-guided iodine-125 seeds in combination...
20. Wu LB, Liu G, Liu JJ. Clinical efficacy of radioactive 125I seed implantation in the treatment of severe cancer pain. Hainan Med J 2016;27:398-400.

21. Jiao DC, Zhang FJ, Lu LG, Wu YX. CT guided radioactive 125I seed implantation in treating lung malignant tumors. J Interv Radiol 2008;17:190-3.

22. Martinez-Monge R, Nag S, Martin EW. 125Iodine brachytherapy for colorectal adenocarcinoma recurrent in the pelvis and paraaortics. Int J Radiat Oncol Biol Phys 1998;42:445-50.