


A Case of Iodine I25 Seeds (I-125) Responding to Lung Squamous Cell Carcinoma

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Abstract

Lung squamous cell cancer (SCC) and accounts for approximately 20%–30% of all lung cancers. Surgery, chemotherapy and radiotherapy are the main treatments for lung SCC patients. A case with lung SCC patient who was treated using iodine I25 seeds (I-125) because the location of the tumor was adjacent to the great vessels. I-125 is an ideal brachytherapy for lung SCC patients with large masses who lost the chance of operation. I-125 is an adjuvant therapy, combined with chemotherapy and molecular targeting therapy might serve to improve the prognosis of lung SCC patients.

Keywords

lung squamous cell carcinoma, iodine I25 seeds, chemotherapy, targeted therapy, integrated therapy

Introduction

Lung cancer is a disease with high frequency and lethality. According to data from the American Cancer Society, approximately 25% of all cancer deaths are died from lung cancer in the United States in 2020.¹ Non-small cell lung cancer (NSCLC) is the predominant subtype of lung cancers, which accounts for ~85%.² Lung squamous cell cancer (LUSC) is a subtype of NSCLC and accounts for approximately 20%–30% of all lung cancers.³ Over the past decades, molecularly targeted therapies have been applied in routine clinical to treat lung adenocarcinoma (LADC) patients with gene alterations such as EGFR and ALK,⁴ while there are no targeted therapies for LUSC.⁵ Therefore, LUSC patients have a worse prognosis than LADC patients.⁶ Surgery, chemotherapy, and radiotherapy are the main treatments for LUSC patients.

Implantation of iodine-125 (I-125) seeds into tumors has been an important treatment tool for many malignant tumors by radiating low-energy gamma rays to damage DNA.⁷ Implantation of I-125 seeds maximize the reduction dose in surrounding normal tissue of cancer, due to I-125 is inversely proportional to the square of the distance from implanted location.⁸ The absorbed dose rate of internal exposure (0.81 mGy/day) was higher than that of external irradiation (0.21 mGy/day).⁹ It has been reported that I-125 seeds was

safe and effective in a variety of different tumors, such as head and neck cancer,¹⁰ parotid adenoid cystic carcinoma,¹¹ high-grade gliomas,¹² papillary thyroid carcinoma recurrence,¹³ and even in vulvar squamous cell cancer.¹⁴ In this article, we described a case with LUSC patient who was treated using I-125 seeds in our department in recent years.

Case Report

Here, we present the case of an 86-year-old man who developed chronic cough for 3 months. Chest Computed Tomography (CT) scan showed that cancer in the lower left lung field with concomitant intrapulmonary, mediastinal under carina metastasis from outside institutes in June, 2019.

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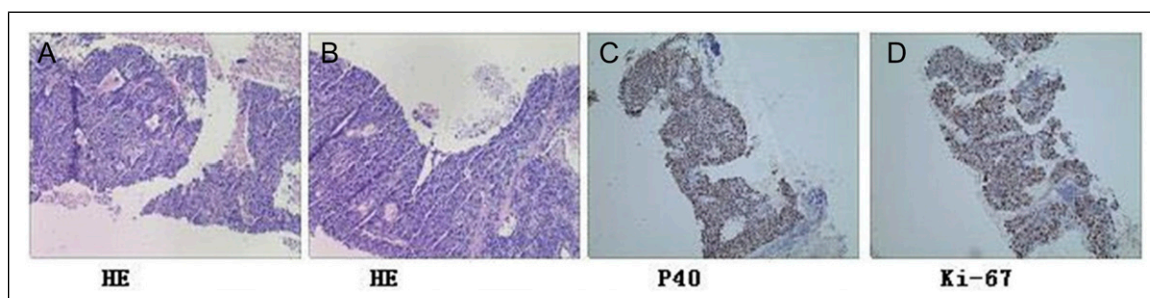


Figure 1. Histopathologic specimen. (A) (B) H&E staining, $\times 100$. (C) P40 staining, $\times 100$. (D) Ki67 staining, $\times 100$. H&E, hematoxylin and eosin.

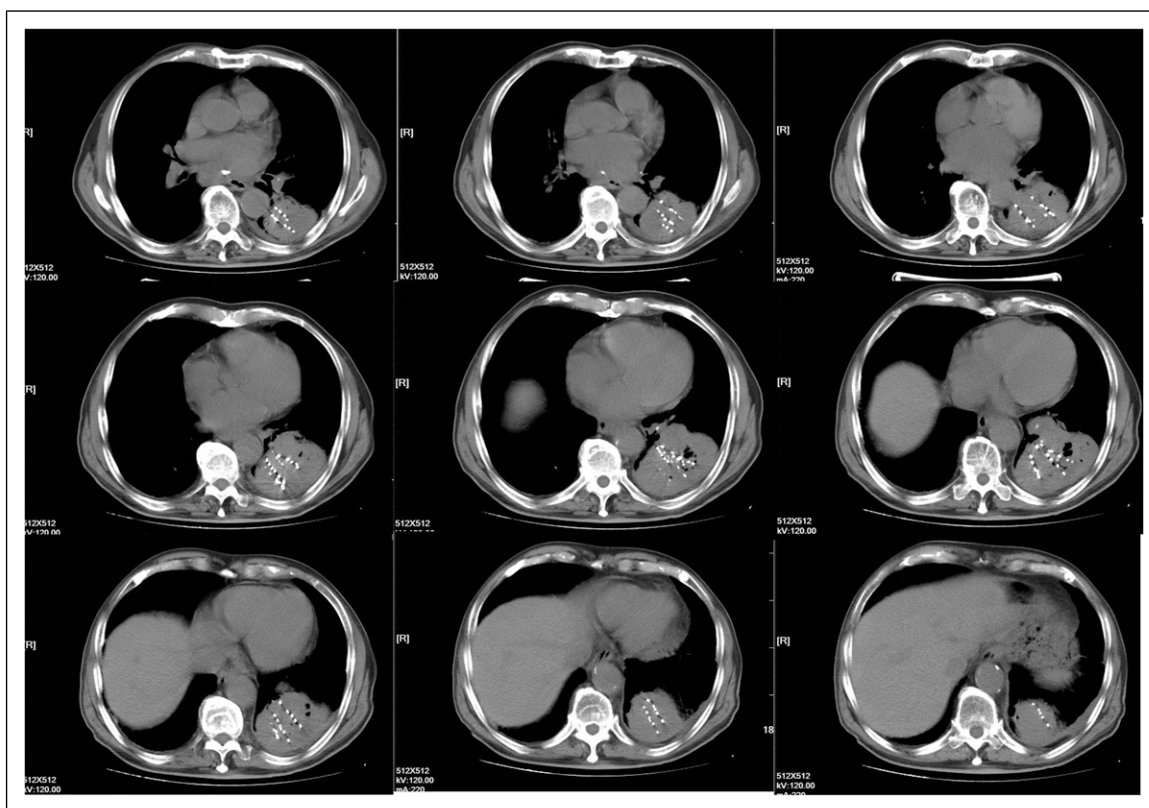


Figure 2. I-125 seeds homogenously spread in lesion on chest CT.

Laboratory tests were within normal limits. The patient had smoking history with a 10-pack 50-year (smoking index: 500) and never smoked 20 years after quitting. A CT guided lung biopsy was performed on August 2nd, 2019 in our hospital. The biopsy pathology result showed poorly differentiated and non-keratinizing carcinomas (Figure 1A and 1B). Immunohistochemical staining results (Figure 1C and 1D) were as follows: Cytokeratin7 (CK7) (–), CK20 (–), CK5/6 (weak +), P40 (+), gA (–), P16 (–), and the expression of mutation type P53, Ki-67 (+, approximately 80%). Based on HE morphology and immunohistochemical results, this patient was hospitalized with a diagnosis of LUSC. According to the 8th edition of AJCC/UICC TNM staging system, this patient was

considered as cT4N3M0 (IIIB).¹⁵ The location of the tumor was adjacent to the great vessels, surgery was not the preferred approach. Moreover, due to a fear of common side-reaction of chemo/radiotherapy, chemo/radiotherapy was not considered by the patient's family. They were hopeless about this disease and its treatment. The indications for immunotherapy were only for advanced lung cancer at that time. And the price of immunotherapy was very high. I-125 seeds were perhaps one option. The patient and his family agreed with this treatment with attempt optimism. Therefore, the patient was treated with 150 I-125 seeds in the lesion under the guidance of ultrasound on August 21th, 2019. The biological effective dose of I-125 seed is nearly 100 Gy. The chest CT showed I-125 seeds

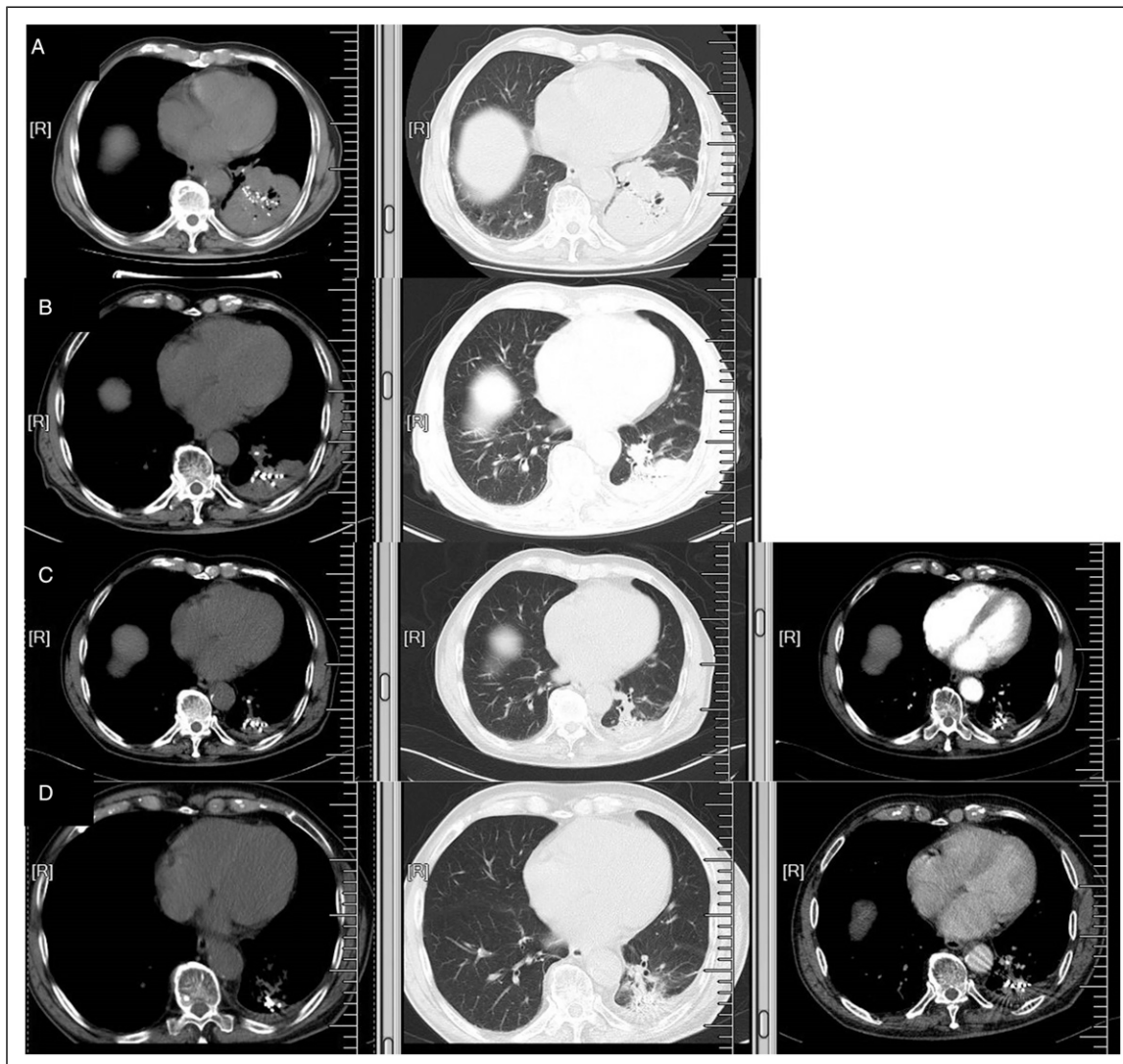


Figure 3. The lesion on chest CT during chemotherapy. **(A)** The maximal cross-section of lesion was 87 mm*63 mm and the maximal mediastinal lymph node was 43 mm on chest CT on August 22th, 2019. **(B)** The maximal cross-section of lesion was 46 mm*30 mm and the maximal mediastinal lymph node was 30 mm on November 11th, 2019. **(C)** The maximal cross-section of lesion was 40 mm*25 mm and the maximal mediastinal lymph node was 30 mm on March 2nd, 2020. **(D)** The maximal cross-section of lesion was 40 mm*25 mm and the maximal mediastinal lymph node was 30 mm on June 4th, 2020.

homogeneously spread in lesion on August 22th, 2019 (Figure 2). The symptoms of cough had improved markedly, which improving the confidence of family members to continue treatment. They agreed to receive chemotherapy. From November 20th, 2019, to June 5th, 2020, the patient received 6 cycles of chemotherapy with the “paclitaxel 130 mg d1,8 and carboplatin 0.3 g d1” regimen as first-line therapy. During that time, the lesion gradually decreased (Figure 3). Unfortunately, chest CT scan indicated that the lesion was larger on August 17th, 2020, than that on June 4th, 2020, (Figure 4A). Therefore, local radiotherapy with DT60 Gy/30F was performed from August 24th, 2020. The scope of radiotherapy includes left hilar and mediastinal lymph node. After radiation therapy, the patient underwent a regular comprehensive

review. The lesion was no significant change in tumor size of chest CT scan (Figure 4B and C).

However, after 7 months, the lesion was larger again than that on March 4th, 2021 (Figure 5A). The patient was treated with 70 I-125 seeds in the lung lesions on March 10th, 2021. The chemotherapy with the “gemcitabine 1.2 g d1,8” regimen was also performed to arrest the progression of the condition. Unfortunately, grade IV myelosuppression was observed after chemotherapy. The patient refused immunotherapy for economic reasons. After that, this patient was received anlotinib (12 mg po qd) as rescue therapy. The size of the lesions was stable in the following reexamination (Figure 5B and C). A time flow chart of treatment for this patient is summarized in Figure 6.

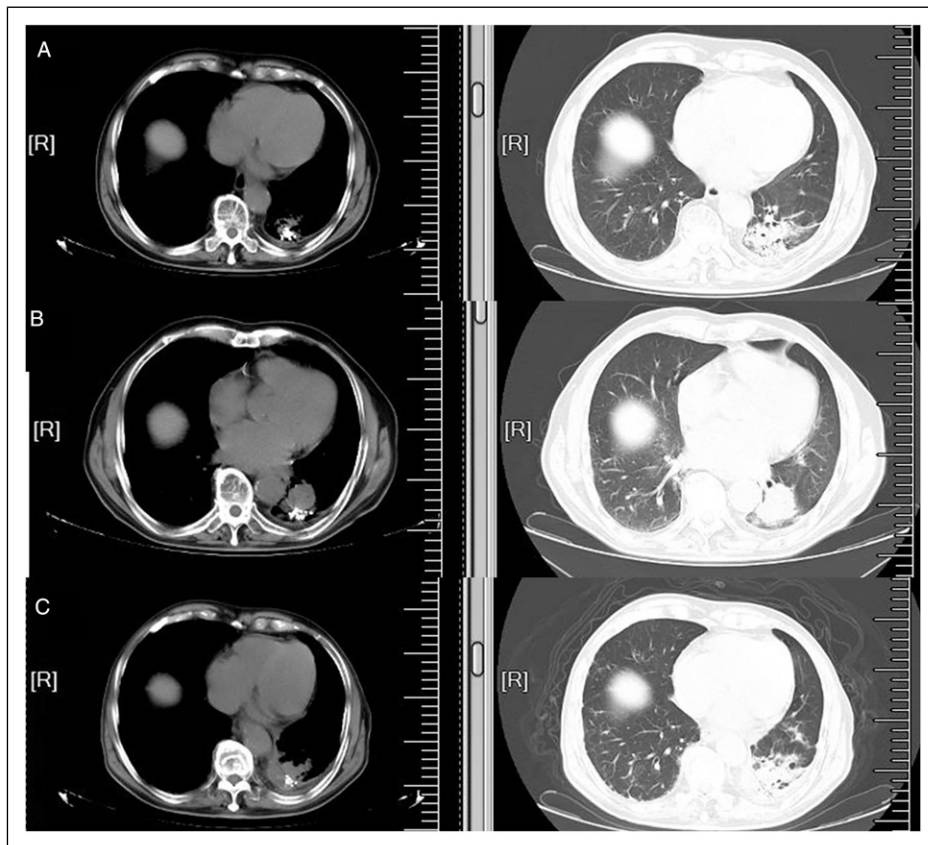


Figure 4. The lesion on chest CT during local radiotherapy. **(A)** The maximal cross-section of lesion was 45 mm*35 mm on chest CT on August 17th, 2020. **(B)** The maximal cross-section of lesion was 32 mm*35 mm on October 12th, 2020. **(C)** The maximal cross-section of lesion was 37 mm*32 mm on January 18th, 2021.

To date, this patient continues to be followed and no signs of relapsing disease. The survival time was more than 2 years.

Discussion

Here, we report a case of LUSC in a 86-year-old man, who had smoking index scores higher than 400. Surgery is normally the first choice for cancer patients. However, surgery is not appropriate for this case, because of and the tumor was large and adjacent to the great vessels. Moreover, major surgery would have risked significant complications or even death for elder patient.¹⁶ And this patient feared chemo/radiotherapy. The implantation of I-125 seeds is relative simple and less traumatic. Therefore, implanting of I-125 seeds was used to reduce of tumor size for subsequent treatment. The choice of I-125 seeds seems nonstandard but it was the most suitable for this patient, relecting the concept of “individualized therapy.” Implantation of I-125 seeds has long effective time but low dosage, and accurate treatment positioning compared with conventional external beam radiotherapy.¹⁴ It offers more treatment options for solid tumor patients who lost the chance of surgical resection and fear chemo/radiotherapy, as an ideal brachytherapy and option. Implantation of I-125 seeds may be

used again several times and has no limit of cumulative dose, comparing with external irradiation therapy. It combining with other treatments may complement each other in the treatment of cancer patients. On the other hand, implantation of I-125 seeds can be applied to patients while allowing for individualization with distinct locations or different numbers of I-125 seeds. The effective diameter of I-125 seeds is only 17 mm.¹⁷ Low-dose rate brachytherapy showed excellent outcomes in a well selected patient population.¹⁸ Therefore, I-125 seeds work incredibly well and have high security for the patients with large tumor. In this patient, following treatment with I-125 seeds, and combined with chemotherapy, the lesion in lung rapidly shrunk without discomfort or pain sensation. The outcome was encouraging, I-125 seeds offered good therapeutic effect. Therefore, I-125 is an adjuvant therapy, which improving the confidence of treatment for advanced patient.

However, after 14-month progression-free survival (PFS), the lesion in lung was larger than that of reexamine CT last time. External irradiation was performed to control the development of the lesion. It was reported that I-125 seeds combined three-dimensional conformal radiotherapy had more higher local control rate than stereotactic ablative

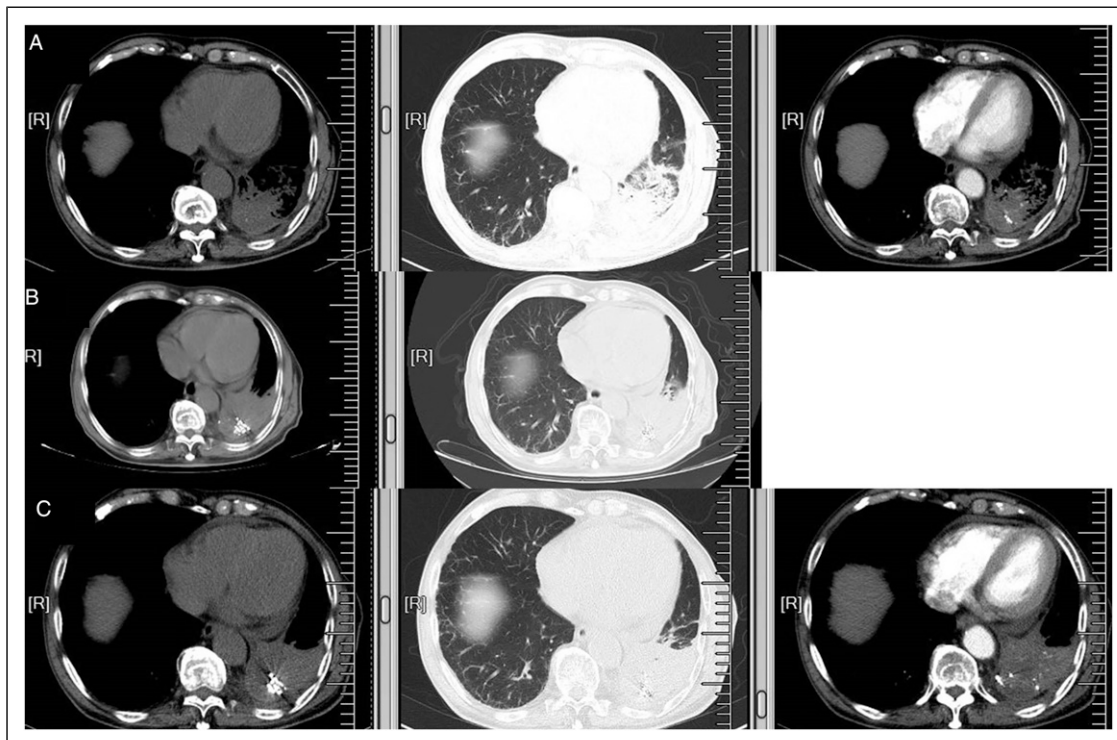


Figure 5. The lesion on chest CT during I-125 seeds, chemotherapy and targeted therapy. (A) The maximal cross-section of lesion was 64 mm*41 mm on March 4th, 2021. (B) The maximal cross-section of lesion was 64 mm*65 mm on April 19th, 2021. (C) The maximal cross-section of lesion was 64 mm*65 mm on May 21th, 2021.

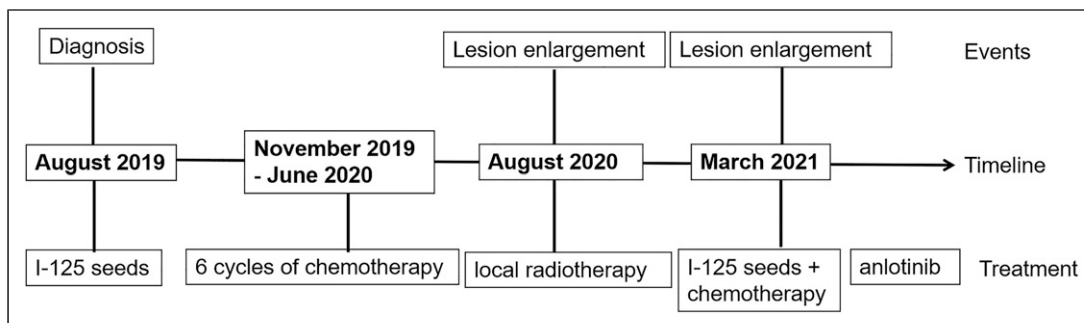


Figure 6. The flow of this patient receiving treatment over a period of years.

radiotherapy on NSCLC^{19,20}. Unfortunately, PFS after external irradiation was relatively short with 7 months. I-125 seeds could be a salvage therapy for recurrent head and neck squamous carcinoma after external beam radiotherapy or surgery.²¹ Therefore, I-125 seeds were implanted into the lung lesion on March 10th, 2021. Chemotherapy was also performed subsequently. Nevertheless, due to grade IV myelosuppression, chemotherapy was undertaken only once. Anlotinib was used as rescue therapy. Anlotinib is a multi-target tyrosine kinase inhibitor (TKI) by blocking the tyrosine kinase receptors, such as platelet-derived growth factor receptors (PDGFR) α and β , VEGFRs 1-3, and fibroblast growth factor receptors (FGFRs) 1-4^{22,23}. The clinic application of

anlotinib has not been adopted in advanced NSCLC²⁴ and soft tissue sarcoma.²⁵ It was reported that anlotinib has a tendency to prolong survival in LUSC patients.²⁶ At present, the condition of this patient remains stable with anlotinib. The survival time of this patient was more than 2 years. It is longer than lung cancer at same stage.²⁷ Therefore, comprehensive treatment might serve to improve the prognosis of LUSC patients.

Conclusion

I-125 is an ideal brachytherapy and option for LUSC patients with large masses who lost the chance of operation and fear

chemo/radiotherapy. I-125 is an adjuvant therapy, which improving the confidence of treatment for advanced patient. Comprehensive treatment might serve to improve the prognosis of LUSC patients.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Declaration of conflicting interests

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Ethical approval

The study was approved by the Human Ethics Review Committee of Jiangsu Taizhou People's Hospital.

Informed consent

Written informed consent to publish this report and the associated medical images was provided by the patient.

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References

- Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021;71:209-249.
- Ma J, Lu Y, Zhang S, et al. β -Trop ubiquitin ligase and RSK2 kinase-mediated degradation of FOXN2 promotes tumorigenesis and radioresistance in lung cancer. *Cell Death Differ.* 2018;25:1473-1485.
- Taniguchi H, Yamaguchi H, Dotsu Y, et al. Phase II study of nedaplatin and amrubicin as first-line treatment for advanced squamous cell lung cancer. *Thorac Cancer.* 2019;10:1764-1769.
- Kim Y, Hammerman PS, Kim J, et al. Integrative and comparative genomic analysis of lung squamous cell carcinomas in East Asian patients. *J Clin Oncol.* 2014;32:121-128.
- Xu C, Fillmore CM, Koyama S, et al. Loss of Lkb1 and Pten leads to lung squamous cell carcinoma with elevated PD-L1 expression. *Cancer Cell.* 2014;25:590-604.
- Momcilovic M, Bailey ST, Lee JT, et al. The GSK3 signaling axis regulates adaptive glutamine metabolism in lung squamous cell carcinoma. *Cancer Cell.* 2018;33:905.
- Chen L, Sun T, Kan X, et al. Transarterial chemoembolization combined with iodine-125 seed implantation for patients with hepatocellular carcinoma: A retrospective controlled study. *J Int Med Res.* 2020;48:1220743861.
- Ma X, Yang Z, Jiang S, et al. Hybrid optimization based on non-coplanar needles for brachytherapy dose planning. *J Contemp Brachytherapy.* 2019;11:267-279.
- Tanaka S, Kinouchi T, Fujii T, et al. Observation of morphological abnormalities in silkworm pupae after feeding $^{137}\text{CsCl}$ -supplemented diet to evaluate the effects of low dose-rate exposure. *Sci Rep.* 2020;10:16055.
- Qiu B, Jiang Y, Ji Z, et al. The accuracy of individualized 3D-printing template-assisted I125 radioactive seed implantation for recurrent/metastatic head and neck cancer. *Front Oncol.* 2021;11:664996.
- Gao Y, Zheng L, Zhang JJG, et al. Surgery combined with iodine-125 interstitial brachytherapy for treatment of parotid adenoid cystic carcinoma: A single-institution experience. *Brachytherapy.* 2021;20:383-392.
- Wang C, Liu S, Peng L, et al. Correction to: Permanent iodine-125 brachytherapy for patients with progressive or recurrent high-grade gliomas. *BMC Cancer.* 2020;20:736.
- Vilar TA, Ajuria O, Rioja ME, Cabañas Montero J. Selective neck dissection guided by a radioactive I125 seed for papillary thyroid carcinoma recurrence. *Cir Esp.* 2020;98:478-481.
- Ni Q, Pan C, Guo Q, et al. Success of ^{125}I -seed treatment in vulvar squamous-cell carcinoma with aplastic anemia: A case report. *Onco Targets Ther.* 2020;13:12561-12566.
- Feng SH, Yang ST. The new 8th TNM staging system of lung cancer and its potential imaging interpretation pitfalls and limitations with CT image demonstrations. *Diagn Interv Radiol.* 2019;25:270-279.
- Han B, Li Q, Chen X. Frailty and postoperative complications in older chinese adults undergoing major thoracic and abdominal surgery. *Clin Interv Aging.* 2019;14:947-957.
- Wang W, Liu Z, Zhu J, et al. Brachytherapy with iodine 125 seeds for bone metastases. *J Cancer Res Ther.* 2017;13:742-747.
- Logghe P, Verlinde R, Bouttens F, et al. Long term outcome and side effects in patients receiving low-dose I125 brachytherapy: A retrospective analysis. *Int Braz J Urol.* 2016;42:906-917.
- Zhang Z, Mao H, Wang X, Sheng W. Comparison of I125 seed brachytherapy (radioactive seed brachytherapy) joint three-dimensional conformal radiotherapy and stereotactic ablative radiotherapy on early nonsmall cell lung cancer. *J Cancer Res Ther.* 2020;16:1560-1568.
- Li W, Dan G, Jiang J, Zheng Y, Zheng X, Deng D. Repeated iodine-125 seed implantations combined with external beam radiotherapy for the treatment of locally recurrent or metastatic

- stage III/IV non-small cell lung cancer: a retrospective study. *Radiat Oncol.* 2016;11:119.
21. Jiang Y, Zhen P, Dai J, et al. Long-term safety and efficacy of CT-guided I125 radioactive seed implantation as a salvage therapy for recurrent head and neck squamous carcinoma: A multicenter retrospective study. *Front Oncol.* 2021;11:645077.
 22. Li S. Anlotinib: A novel targeted drug for bone and soft tissue sarcoma. *Front Oncol.* 2021;11:664853.
 23. Lu C, Zhang Q, Zhang H, et al. A small molecular multi-targeting tyrosine kinase inhibitor, anlotinib, inhibits pathological ocular neovascularization. *Biomed Pharmacother.* 2021; 138:111493.
 24. Han B, Li K, Wang Q, et al. Effect of anlotinib as a third-line or further treatment on overall survival of patients with advanced non-small cell lung cancer: The ALTER 0303 phase 3 randomized clinical trial. *JAMA Oncol.* 2018;4:1569-1575.
 25. Chi Y, Fang Z, Hong X, et al. Safety and efficacy of anlotinib, a multikinase angiogenesis inhibitor, in patients with refractory metastatic soft-tissue sarcoma. *Clin Cancer Res.* 2018;24: 5233-5238.
 26. Pouteau E, Kabir-Ahmadi M, Noah L, et al. Superiority of magnesium and vitamin B6 over magnesium alone on severe stress in healthy adults with low magnesemia: A randomized, single-blind clinical trial. *PLoS One.* 2018;13:e208454.
 27. David EA, Daly ME, Li CS, et al. Increasing rates of no treatment in advanced-stage non-small cell lung cancer patients: A propensity-matched analysis. *J Thorac Oncol.* 2017;12: 437-445.