Application of the transosseous approach for computed tomography-guided radioactive 125-iodine seed implantation for the treatment of thoracic and abdominal lymph node metastases

ABSTRACT

Aim: This study aimed to investigate the technical procedure, safety, and clinical value of the transosseous approach for computed tomography (CT)-guided radioactive 125-iodine ($^{125}$I) seed implantation for the treatment of thoracic and abdominal lymph node metastases.

Subjects and Methods: This was a retrospective study that Nine lymph node metastases in nine patients were treated in our hospital between January 2010 and August 2018. Under CT guidance, at least one puncture path was made through the transosseous approach. The seeds were planted according to the TPS. CT/MRI scans were performed every 2 months after the treatment to evaluate local therapeutic efficacy according to the Response Evaluation Criteria in Solid Tumors.

Results: The transosseous approach was successfully established in all patients. The median follow-up time was 11 months (6–36 months). At 2, 4, 6, 10 and 12 months after operation, the objective effective rate and clinical benefit rate were 66.67%, 77.78%, 77.78%, 71.43%, 66.67% and 50.00%; and 88.89%, 88.89%, 88.89%, 71.43%, 66.67% and 50.00%, respectively. The survival rate of the patients at 6, 12, 18, 24, 30 and 36 months after operation was 53.00%, 26.00%, 26.00%, 13.00%, 13.00% and 13.00%, respectively.

Conclusions: The transosseous approach for CT-guided radioactive $^{125}$I seed implantation was safe, effective, and minimally invasive for the treatment of thoracic and abdominal lymph node metastases.

KEY WORDS: Brachytherapy, lymph node metastases, radioactive $^{125}$I seed implantation, transosseous approach, X-ray computed tomography
and abdominal lymph node metastases treated by computed tomography (CT)-guided radioactive $^{125}$I seed implantation through a transosseous approach in our hospital between January 2010 and August 2018.

**SUBJECTS AND METHODS**

**Ethics**
Informed consent was obtained from the participants, and the study was approved by the ethics committee of our university.

**Patients**
Nine patients with lymph node metastases underwent CT-guided transosseous radioactive $^{125}$I seed implantation in our hospital, including six men and three women. The patients were aged 45–77 years and the median age was 61 years. There were a total of nine lesions with an average maximum diameter of 2.83 ± 0.92 cm (1.50–4.20 cm), including seven mediastinal and two retroperitoneal lesions. The inclusion criteria were as follows: (1) all patients underwent systemic treatment and two patients failed local radiotherapy; except lymph node metastases treated with $^{125}$I seed implantation, the primary focus and other metastases were effectively controlled; (2) there was no vital structural occlusion between the lesion and the puncture required for the transosseous approach; and (3) at least one puncture needle was required through a transosseous approach, with no other safe puncture path in this area. The exclusion criteria were as follows: (1) patients with serious insufficiency of the heart, liver, lung, or kidney function; (2) patients with uncontrollable clotting disorders; and (3) lesions over 7 cm in diameter. The general information of the patients is shown in Table 1.

**Instruments**
- 64-slice CT scanner (Siemens SOMATOM Definition AS, Germany)
- 11G bone biopsy needle (GALLINI, BM 11/15, Mantova, Italy), 17G blunt tip coaxial introducer needle (BARD, C1816A, Arizona, USA), and 18G PTC puncture needle (HAKKO, B18/20, Nagano, Japan)
- HGGR 3000 CT-guided radioactive particle treatment planning systems (TPS) (Hejia Medical Video Equipment Co., Ltd., Zuhai, China). Radioactive $^{125}$I seed (Atomic High Tech, Beijing, China), with 4.5 mm length, 0.8 mm diameter, 0.8 mCi, 14.8–29.6 MBq activity, and 59.6-day half-life.

**Preoperative preparation**
The size, location, and adjacent important organs and blood vessels of the lesions were detected by conventional CT plain scans and enhanced examinations within 2 weeks before the operation. Blood routine examinations and coagulation time were evaluated to exclude hemorrhagic diseases. The patients fasted for 4 h before the operation, and the venous channels were opened. A positioning fence was placed on the body surface of the intended needle insertion location according to the preoperative imaging data, and the patients underwent breath-holding training.

**Preoperative treatment planning systems**
CT images were collected by computer with a prescription dose of 120 Gy. The needle entry point and the puncture path were as designed in the TPS to avoid important tissues and organs such as the trachea and large blood vessels; at least one needle puncture was performed through a transosseous approach. The spatial distribution and number of implanted seeds in the tumor were designed.

**Operation process**
**Operation procedure**
First routine CT scout scans were performed. The puncture path and the entry point were determined according to the preoperative enhanced CT scans and TPS. Routine sterilization was performed, with 2% lidocaine used for local anesthesia.

**Transvertebral approach**
Three lesions were located anterior to the vertebral body. The patients were placed in a prone position, and punctures were made through a transpedicular approach, avoiding the spinal canal, intervertebral foramen, and large vessels anterior to the vertebral body. A total of four transosseous paths were established. After local anesthesia, a small 0.5-cm
opening was made at the entry point of the skin and the vertebral body was drilled with an 11G bone biopsy needle with the operator pressing and rotating the bone biopsy needle into the bone. CT scans were repeatedly conducted during the drilling to ensure that the placement of the bone biopsy needle was consistent with the designed puncture path. The compression force was carefully controlled when the distal bone cortex was nearly penetrated to protect the anterior tissues and organs. After the transosseous path was established, the bone biopsy needle was removed and an 18G puncture needle was gradually inserted through the path to implant seeds to the distal end of the target lesion according to the TPS [Figure 1].

**Transsternal approach**
Six lesions were located posterior to the sternum, and six transosseous paths were established by transsternal puncture. The patients were placed in a supine position, and the transosseous path was established as described above. In four lesions, the 18G puncture needle was inserted directly through the transosseous path to place the seeds according to the TPS. The other two lesions were located behind the superior vena cava and aortic arch and anterior to the trachea, indicating that the target lymph nodes were surrounded by large vessels and the trachea. After the transosseous paths were established, a 17G blunt tip coaxial introducer needle was gradually inserted through the paths under CT guidance to the anterior edge of the superior vena cava and aortic junction and was then gently twisted and rotated for blunt dissection. The blunt tip needle was replaced with an 18G puncture needle and gradually penetrated the lesion. The seeds were implanted according to the TPS.

**Nontransosseous approach**
For other nontransosseous punctures, an 18G puncture needle was gradually inserted to the target lesion under CT guidance and the seeds were implanted according to the TPS.

**Postoperative dosimetry verification**
Immediately, after the seed implantation was completed, the distribution of the seeds (spacing uniformity, seed displacement, and shedding) was observed by CT scan and the seeds were reimplanted if necessary. According to the American Brachytherapy Society standard, CT imaging after seed implantation was introduced into the TPS for postoperative quality verification. A D90 ≥ prescribed dose (PD) indicated that the dose received by 90% of the target volume (D90) reached or exceeded the PD; a V100 ≥ 90% indicated the percentage of target volume that received 100% of the PD; V200 <50% indicated the percentage of target volume that received 200% of the PD; these were defined as technical success, indicating good implantation quality; otherwise, the implantation was considered to be unsatisfactory.

**Postoperative follow-up and curative effect evaluation**
Enhanced CT or magnetic resonance scans were performed every 2 months after the operation, and the curative effect was evaluated according to the response evaluation criteria in solid tumors. The objective response rate (RR) and clinical benefit rate (CBR) were calculated as follows: RR = (complete response [CR] + partial response [PR])/total number of lesions × 100% and CBR = (CR + PR + stable disease)/total number of lesions × 100%.

The degree of postoperative pain was evaluated using the Visual Analog Scale. The postoperative pain relief effect compared to that before the operation was evaluated as follows: significant relief, pain disappearance or pain grade decreased by 2; effective relief, pain grade decreased by 1; and invalid, pain grade did not decrease or increase. Postoperative pain relief rate = (significant relief + effective relief)/preoperative number of patients with pain × 100%.

**Statistical methods**
Data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., New York). Measurement data were
expressed as means ± standard deviation, whereas counting data were expressed as percentages and were compared by Chi-square tests. The changes in target lymph nodes before and after the operation were analyzed by paired t-tests. *P* < 0.05 was considered a statistically significant difference.

**RESULTS**

**Seed implantation**

Transosseous approaches were successfully established in all patients, and implantation of radioactive $^{125}$I seeds was successfully completed according to the TPS. The transosseous approach established by the bone drilling technique increased the average operation time by 13.9 min (7.5–18.6 min) and the number of local scans by 5.2-fold (3–8-fold). CT-guided radioactive $^{125}$I seed implantation in all nine thoracic and abdominal lymph node metastases in nine patients succeeds the first time, and an average of 18 ± 6 seeds (8–40 seeds) was implanted. The clinical target volume, D90, V100, and V200 before and after the operation are shown in Table 2. A total of 158 $^{125}$I seeds were implanted according to the preoperative TPS, and 163 $^{125}$I seeds were actually implanted. There was no significant difference in the number of seeds before and after the operation (*P* < 0.05). The satisfactory rate in postoperative dose verification was 88.89% (8/9). A total of 33 needles were removed to plant the seeds in the target lesion according to the TPS and 45 needles were actually implanted. The number of needles before and after the operation differed significantly (*P* < 0.05).

**Curative effect and pain relief**

The objective effective rate and CBR at 2, 4, 6, 8, 10, and 12 months after the operation are shown in Table 3. Among the nine patients included in this study, local symptoms such as preoperative pain occurred in three cases, including one case with chest pain and two cases with abdominal pain; after seed implantation, the pain was relieved in two cases on the 2nd day after the operation and the dose of oral analgesia was reduced, whereas the pain symptoms were significantly improved in the other case. One month after the operation, the pain symptoms of all three patients were relieved, resulting in an effective rate of pain relief of 100.00% (3/3) at 1 month after the operation.

**Complications**

All patients tolerated the surgery. One case developed small retrosternal hematoma after sternal puncture; it was not enlarged and the monitoring was released after 4 h of observation. No complications such as pneumothorax, massive bleeding, infection, hemoptysis, and fracture were observed.

**Patient survival**

The median follow-up time was 11 months (6–36 months). Seven cases died at the end of follow-up, with a median time to death of 11 months (6–24 months). The patients mainly died of multiple distant metastases and multiple organ failure, with survival rates of 53.00%, 26.00%, 26.00%, 13.00%, 13.00%, and 13.00% at 6, 12, 18, 24, 30, and 36 months postoperatively, respectively.

**DISCUSSION**

In recent years, brachytherapy with CT-guided radioactive $^{125}$I seed implantation has developed rapidly and has been widely used for the treatment of various lymph node metastases, with achieved obvious curative effects. Methods to accurately realize the preoperative TPS plans during operation have been the main focus of radioactive $^{125}$I seed implantation technology in recent years.

Our previous work applied the transosseous approach to improve the effectiveness of seed implantation therapy. In the present study, in addition to the conventional soft-tissue puncture paths, the transosseous approach was established to implant radioactive $^{125}$I seeds in the target area caused by bone

| Table 2: Comparison of postoperative validation with preoperative planned dosimetric parameters |
|-----------------------------------------------|
| **Index** | Preoperative | Postoperative | *P*
| Clinical target volume | 5.41±1.32 | 7.53±0.90 | 0.011
| D90 (Gy) | 135.23±18.13 | 139.25±15.57 | 0.507
| V100 (%) | 91.8±7.18 | 98.03±10.85 | 0.191
| V200 (%) | 41.21±2.18 | 43.42±2.47 | 0.144

| Table 3: Evaluation of computed tomography-guided radioactive $^{125}$-iodine seed implantation in the treatment of thoracic and abdominal lymph node metastases |
|------------------|------------------|------------------|------------------|------------------|
| **Follow-up time (month)** | **Number of tumors** | **Efficacy evaluation, n (%)** | **RR (%)** | **CBR (%)** |
| 2 | 9 | CR (33.33) | PR (33.33) | SD (22.22) | PD (11.11) | 66.67 | 88.89 |
| 4 | 9 | CR (55.56) | PR (22.22) | SD (11.11) | PD (11.11) | 77.78 | 88.89 |
| 6 | 9 | CR (66.67) | PR (11.11) | SD (11.11) | PD (11.11) | 77.78 | 88.89 |
| 8 | 7 | CR (71.43) | PR (0) | SD (0) | PD (28.57) | 71.43 | 71.43 |
| 10 | 6 | CR (88.89) | PR (0) | SD (0) | PD (33.33) | 66.67 | 66.67 |
| 12 | 4 | CR (50.00) | PR (0) | SD (0) | PD (50.00) | 50.00 | 50.00 |

CR=Complete response, PR=Partial response, SD=Stable disease, PD=Prescribed dose, RR=Response rate, CBR=Clinical benefit rate
occlusion. No significant differences were observed between postoperative dose verification and preoperative D90, V100, and V200, which indicated good agreement between postoperative results and the preoperative planned TPS parameters; thus, transosseous puncture could supplement the requirements for dosimetric distribution and accurately provide the preoperative planning. Huo et al.[16] performed radioactive $^{125}$I seed implantation through soft tissues such as the lung, reporting a satisfactory rate in postoperative quality verification of $<40.00\%$. In contrast, by combining the routine soft-tissue path and the transosseous approach, the satisfactory rate of postoperative dose verification in the present study was $88.89\%$, much higher than that for soft-tissue path implantation such as the lung. The unsatisfactory dose verification in one patient in the present study might have been due to the following reasons: (1) partial necrosis of the center of the target lymph node, resulting in the displacement and aggregation of partially implanted seeds, and (2) puncture path errors during the operation. The average gross tumor volume after the operation was larger than that before the operation, which may be caused by local bleeding and tissue enema in the target area during seed implantation.

Pneumothorax and bleeding are the most common complications of mediastinal lymphoid metastases by transpulmonary puncture. The incidence of pneumothorax and bleeding is significantly reduced by nontranspulmonary puncture that avoids damage to the visceral pleura and lung tissue. When no important structures exist between the bone and the lesion and there is no other safe puncture path, the seeds can be implanted through the transosseous approach. D’Agostino et al.[17] summarized their preliminary experience with mediastinal lesions biopsies through a sternal approach in seven patients, demonstrating that the method was safe, effective, and was well tolerated. In their study, seeds were implanted in seven mediastinal lesions through a transosseous approach; since the puncture needle did not pass through the visceral pleura, no postoperative iatrogenic pneumothorax and pulmonary bleeding occurred. Complex abdominal lymph node anatomy increases the risk of seed implantation, and gastrointestinal injury and massive bleeding are serious complications. In the present study, seeds were implanted in two patients through transosseous puncture, which effectively avoided the large blood vessels and other important tissues and organs around the puncture path. When implanting the seeds, all patients were punctured successfully according to the planned puncture path and the effect of seed distribution was satisfactory, thus meeting the requirements for a sufficient radiation dose. Postoperative small retrosternal hematoma occurred in only one case, which did not require special treatment. No serious postoperative complications occurred. These results indicate that this technology is safe and reliable.

$^{125}$I seeds continuously emit low-energy gamma rays to inhibit tumor cell proliferation; moreover, continuous low-dose irradiation can treat tumors by reoxidizing anoxic cells and increasing tumor sensitivity to radiation as well as inhibiting tumor mitosis, killing tumor cells in metastatic lymph nodes, and inhibiting the growth of target lymph nodes. Gao et al.[1] reported a local control rate of 75.0% at 3 months after seed implantation in 16 cases of lymph node metastases; Wang et al.[19] applied $^{125}$I seeds for the treatment of retroperitoneal lymph node metastases, reporting an objective effective rate of 80.05% and CBR of 96.00% at 2 months after the operation. In the present study, the objective effective rate and CBR at 2, 4, 6, 8, 10, and 12 months after the operation, shown in Table 3, were consistent with the above results. Our findings suggest that radioactive $^{125}$I seed implantation can inhibit further growth of metastatic lymph nodes and improve local symptoms, making it ideal for the treatment of metastatic lymph nodes.

The continuous low-dose irradiation of $^{125}$I seeds can also change cell membrane structure, block action potential formation, and inhibit and block pain conduction, resulting in pain relief. This effect may be caused by the destruction of autonomic ganglion by the rays released by the seeds or by the reduction of enlarged lymph nodes by internal irradiation, relieving tumor tension and compression of the autonomic ganglion. Wang et al.[19] applied radioactive seed implantation for the treatment of lymphoid metastases, reporting a pain relief rate of 80.00% at 2 days after the operation. In the present study, three patients had preoperative pain, which was relieved at 1 month after the operation, resulting in a pain relief rate of 100.00%.

Limitations

First, this single-center retrospective study had a small sample size, which limited the statistical significance. Second, although we performed both the transosseous approach and soft-tissue path punctures during the operation to save time, the transosseous approach through bone drilling increased the average operation time by 13.9 min and the number of local scans by 5.2-fold, which was time-consuming and increased the ionizing radiation received by patients. In addition, the follow-up of some patients was not regular. Finally, most of the patients with lymph node metastases had advanced malignant tumors; however, radioactive $^{125}$I seed implantation is performed only for the local treatment of metastatic lymph nodes, which limited the effect on prolonging the overall survival of patients.

CONCLUSIONS

The results of this study suggest that a transosseous approach for CT-guided radioactive $^{125}$I seed implantation was a safe and effective minimally invasive method for the treatment of thoracic and abdominal lymph node metastases.

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Conflicts of interest
There are no conflicts of interest.

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