A multicenter prospective study on quality of life and pain relief for cancer patient after $^{125}$I seed implantation

Jingxuan Zhang, Qiuyu Sun, Lan Gao, Lijuan Sun, Chunxue Wang, Baohua Li, Junjie Wang, Panfeng Wang

Radiation Oncology Department, Peking University Third Hospital, Beijing, China
Interventional and Vascular Surgery Department, Southeast University Zhongda Hospital, Nanjing, China
Oncology Department, Affiliated Zhongshan Hospital of Dalian University, Dalian, Liaoning, China
Neurology Department, Peking University Third Hospital, Beijing, China

ARTICLE INFO

Keywords:
- Pain
- Quality of life
- $^{125}$I seed implantation
- Cancer
- Nursing

ABSTRACT

Objective: To prospectively explore the efficacy of $^{125}$I seed implantation on quality of life and pain relief in cancer patient.

Methods: Consecutive cancer patients who underwent $^{125}$I seed implantation in three centers in China between October 1, 2020 and March 31, 2021, were assessed. The Functional Assessment of Cancer Therapy and Brief Pain Inventory were used to evaluate patients’ quality of life and pain relief on the day before, 1 week, 1 month, and 3 months after seed implantation.

Results: A total of 104 cancer patients were enrolled. Total score of quality of life was not statistically different 3 months after seed implantation compared with before implantation, while patients’ quality of life was worse one week after seed implantation but then recovered. A total of 43 (41.3%) patients had pain before seed implantation, of which 16 (37.2%) patients had severe pain and 27 (62.8%) had mild-to-moderate pain. In patients with severe pain, the worst pain scores decreased significantly 3 months after implantation. In patients with mild-to-moderate pain, pain severity and pain interference score increased significantly after implantation compared with pre-implantation. Compared with pain before implantation, patients’ quality of life of patients without pain was higher.

Conclusions: $^{125}$I seed implantation maintains the quality of life of patients within 3 months. For patients with severe pain, seed implantation has obvious pain relief, which improves the quality of life of the patients. Nurses should provide personalized guidance for patients with different degrees of pain.

Introduction

Pain is one of the most common symptoms of cancer patients. Regardless of the stage of cancer, the proportion of pain in cancer patients was about 51% and 66% in advanced and metastatic patients, of which 38% was moderate or severe. Pain can cause a severe stress reaction in the body, lead to the release of stress hormones, affect the function of many-body systems, accelerate the deterioration of the disease, and seriously affect the patient’s quality of life. The influence of pain on mood, sleep, normal work, and quality of life in cancer patients was significantly higher than that in patients without pain. Radioactive $^{125}$I seed implantation is a safe and effective form of brachytherapy, which is minimally invasive with radioactive seeds implanted into the tumors. Low-dose $\gamma$ rays are continuously released by radionuclide decay, which damages the DNA of tumor cells, induces apoptosis of tumor cells, and kills tumor tissues. The reduction in tumor volume can relieve the compression of peripheral nerves and tissues and, at the same time, reduce the secretion of inflammatory mediators related to pain, such as 5-hydroxytryptamine and prostaglandin, to relieve pain and improve the functional status of patients.

$^{125}$I seed implantation has been widely used in the treatment of prostate cancer, liver cancer, lung cancer, pancreatic cancer, rectal cancer, and other solid tumors. Previous prospective studies have indicated that quality of life was maintained after $^{125}$I seed implantation in patients with prostate cancer. It is also effective on pain relief for patients with cancers, such as metastatic bone cancer and pancreatic cancer. However, the efficacy of $^{125}$I seed implantation on both the quality of life and pain relief for patients with various kinds of cancer was...
limited. The purpose of this study was to explore prospectively the efficacy of $^{125}$I seed implantation on quality of life and pain relief for cancer patients.

**Methods**

**Participants and study design**

Cancer patients who underwent $^{125}$I seed implantation were assessed between October 1, 2020, and March 31, 2021, from Peking University Third Hospital, the Affiliated Zhongshan Hospital of Dalian University, and the Affiliated Zhongda Hospital of Southeast University, all in China. The inclusion criteria were as follows: expected survival > 3 months; over the age of 18; and providing informed consent. The exclusion criteria were as follows: previous history of mental illness or cognitive impairment; those who cannot understand and communicate with each other; or complications from chronic diseases, such as severe heart, liver, and renal insufficiency.

Clinical data of the enrolled patients were obtained from the medical records. The pain and quality of life of the enroled patients were evaluated by questionnaire the day before, 1 week, 1 month, and 3 months after $^{125}$I seed implantation. The quality of life and pain of the patients before seed implantation were investigated face to face by the researchers after informed consent was obtained and by telephone conversation during follow-up.

**Functional assessment of Cancer Therapy-Generic**

The Functional Assessment of Cancer Therapy-Generic (FACT-G) was used to evaluate the patients’ quality of life. The four domains of the scale were: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB). The four domains were formulated in separate subscales that made up a series of 27 Likert-type items. Patients were asked to respond to each item on a scale of 0–4, with 0 meaning “not at all” and 4 meaning “very much.” The scores for each item were added to the total for quality of life. A higher score indicated a better quality of life. The scale is widely used to evaluate the therapeutic effect of cancer patients and has good reliability and validity. The test-retest reliability of the four domains was above 0.85. The values of Cronbach’s $\alpha$ for each domain were above 0.8.15

**Brief Pain Inventory**

The Brief Pain Inventory (BPI) was used to evaluate pain. The evaluation included the pain severity score and the pain interference score. The value of Cronbach’s alpha for the two aspects were 0.894 and 0.915, respectively. The pain severity score was calculated from the four items relating to pain intensity (worst pain, least pain, average pain, and pain right now). Each item was rated from 0, no pain, to 10, pain as bad as you can imagine. The pain interference, with seven sub-items (general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life) were rated from 0, does not interfere, to 10, completely interferes. The scores of the worst pain score before seed implantation were divided into mild pain (1–3), moderate pain (4–6), and severe pain (7–10).

**Seed implantation**

Contrast-enhanced computed tomography (CT) was performed within 1–2 days before operation to obtain the target area and endangered organs. Then the brachytherapy treatment planning system was used to determine the prescribed dose and seed activity, design the needle access, simulate the spatial distribution of the seeds, and calculate the dose distribution. Seed implantation was performed according to the plan. The three-dimensional printing noncoplanar template (3D-PNCT) was aligned to the surface of the therapeutic region, and the implantation needles were percutaneously punctured to the predetermined depth through the template guide hole. The dose verification after operation showed that the prescription dose of seeds implantation was 118.93 ± 22.29 Gy, and the range was 60–180 Gy. The number of implanted seeds was 40.00 (30.00, 68.00), the range was 9–220, and the activity of particles was 0.40–0.80 mCi.

**Data analysis**

The Statistical Package for Social Sciences (SPSS) version 26 software program was used for data management and analysis. The continuous variables’ conformity to the normal distribution is expressed by mean ± standard deviation (Mean ± SD). Those that did not conform to normal distribution were represented by a median (M) (P25, P75). Classified variables were expressed as percentages. Generalized estimation equation was used to analyze the interaction between various factors. Repeated measures ANOVAs were used for measurement data consistent with normal distribution and homogeneity of variance. The Friedman test was used for measurement data that do not conform to normal distribution. A non-parametric test was used for comparison between groups that did not conform to normal distribution.

**Ethical considerations**

Written informed consent was obtained from each patient before they participated in this study. This study was approved by the Ethics Committee of the Peking University Third Hospital (Approval No. IRB00006761-M2019243).

**Results**

Patient accrual started on October 1, 2020 and closed on March 31, 2021. The final analysis data were followed up until June 31, 2021. A total of 110 patients were assessed. Three patients were lost to follow-up, and three patients died during follow-up. A total of 104 patients were enrolled. Among them, 55 were from the Southeast University Zhongda Hospital, 41 from Peking University Third Hospital, and nine from the Affiliated Zhongshan Hospital of Dalian University (Fig. 1). Most of the patients presented with chest, lumbar, and abdominal tumors: There were 33 cases (31.7%) of chest tumors, including lung cancer, breast cancer, and thymic malignant tumors. There were 54 cases (51.9%) of lumbar and abdominal tumors, including cervical, bladder, pancreatic, gastric, liver, and rectal cancers. There were eight cases (7.7%) of head and neck tumors, including nasopharyngeal, maxillary sinus, parotid, laryngeal, and tongue carcinomas. There were nine cases (8.7%) of other types of tumors, including lymphoma, skin cancer, and sarcoma. The age of the patients was 59.73 ± 10.10 years old, ranging from 32 to 82 years old. During the follow-up period, 59 patients (56.7%) received other treatments, such as chemotherapy, radiotherapy, and interventional therapy. The characteristics of the patients are shown in Table 1.

**Quality of life**

Total score of quality of life was not statistically changed in the 3 months after seed implantation compared with before seed implantation, while patients’ PWB, SWB, EWB, and FWB were worse one week after seed implantation and then recovered (Table 2); PWB scores decreased one week after implantation compared with the preoperative scores, and then increased 1 month and 3 months after implantation compared with one week after implantation ($P = 0.047$ and 0.020, respectively). There were significant differences in SWB scores before and after seed implantation ($P = 0.043$), but there was no significant difference in pairwise comparisons at different time points. EWB scores improved one week after implantation compared with before implantation ($P = 0.009$). FWB scores improved three weeks after implantation compared with one week after implantation ($P = 0.004$). The trend of quality of life is shown in Figure 2.
Interactive factors affecting of quality of life

The total score of quality of life and four domains were taken as dependent variables, and patient characteristics, pain degree, and pain effects were taken as independent variables. Table 3 shows the significant influencing factors in all dimensions of quality of life. With the exception of the factors in the table, there was no relationship between age, sex, settlement, tumor type, and other clinical characteristics of the patient's quality of life.

Pain relief

A total of 43 (41.3%) patients had pain before seeds implantation, of which 16 (37.2%) patients had severe pain and 27 (62.8%) had mild-to-moderate pain.

For patients with severe pain, the scores of the worst pain decreased significantly from 8.00 (7.00, 10.00) before implantation to 5.00 (3.00, 7.20) ($P = 0.002$) 3 months after implantation. The degree of pain 1 month and 3 months after implantation was significantly lower than that before implantation ($P = 0.010$ and 0.016, respectively). Although there was no significant difference in seven pain interference sub-items of general activity, mood, walking ability, normal work, relationships with other people, sleep, and enjoyment of life before and after particle implantation (Table 4), the pain interference score showed a downward trend (Fig. 3).

For patients with mild-to-moderate pain, both scores of the four pain severity categories and the seven pain interference sub-items of general activity, mood, walking ability, normal work, relationships with other people, sleep, and enjoyment increased significantly after implantation compared with pre-implantation, including the worst pain, the least pain, average pain, and pain right now (Fig. 4).
Table 2.
Quality of life (n = 104).

| Quality of life | Pre          | Post-1 week | Post-1 month | Post-3 months | χ² | P     |
|----------------|--------------|-------------|--------------|---------------|----|-------|
| Total score    | 69.67 ± 14.96| 68.89 ± 15.69| 71.19 ± 16.57| 71.47 ± 16.19| 1.086 | 0.350|
| PWB            | 23.00 (18.00, 27.00) | 21.00 (18.00, 25.00) | 23.00 (20.00, 26.00) | 23.00 (20.00, 26.00) | 13.125 | 0.004|
| SWB            | 17.00 (13.25, 20.00) | 15.50 (12.25, 20.00) | 17.00 (13.00, 21.00) | 17.50 (13.75, 20.00) | 8.133 | 0.043|
| EWB            | 17.00 (13.25, 20.00) | 18.00 (16.00, 20.00) | 18.00 (15.00, 20.00) | 17.00 (15.00, 20.00) | 13.026 | 0.023|
| FWB            | 14.00 (10.00, 17.75) | 13.00 (10.00, 17.00) | 14.00 (10.00, 18.00) | 15.00 (10.75, 19.00) | 13.445 | 0.004|

1. Repeated measures ANOVA; F. 2. Friedman test χ²; Compared with Pre, aP < 0.05; compared with post-1 week, bP < 0.05; compared with post-1 month, cP < 0.05; compared with post-3 months, dP < 0.05

EBW: emotional well-being; FWB: functional well-being; PWB: physical well-being; SWB: social/family well-being

Fig. 2. Quality of life (n = 104).

Table 3.
Analysis of influencing factors of quality of life.

| Quality of life | Factors                | B    | SE     | 95% CI      | Wald χ² | P     |
|----------------|------------------------|------|--------|-------------|---------|-------|
| Total score    | The worst pain         | 2.689| 0.977  | 0.774–4.603 | 7.576   | 0.006|
|                | The pain right now     | 2.325| 1.047  | 0.273–4.377 | 4.929   | 0.026|
|                | Normal work            | 2.475| 0.871  | 1.671–3.617 | 8.064   | 0.005|
|                | Intervventional therapy| 1.415| 1.003  | –0.551–3.381| 1.990   | 0.158|
|                | Chemotherapy           | –1.712| 2.525  | –6.660–3.266| 0.460   | 0.498|
|                | Radiotherapy           | 2.131| 2.089  | –1.965–6.227| 1.040   | 0.308|
| SWB            | General activity       | 1.457| 0.281  | 0.905–2.008 | 26.809  | < 0.001|
|                | Mood                   | 0.826| 0.280  | 0.278–1.375 | 8.708   | 0.003|
|                | Walking ability        | 1.007| 0.322  | 0.375–1.639 | 9.749   | 0.002|
|                | EWB                    | 1.057| 0.222  | 0.620–1.494 | 22.480  | < 0.001|
|                | Enjoyment of life      | 0.956| 0.205  | 0.553–1.358 | 21.675  | < 0.001|
| SWB            | The average pain       | 0.720| 0.354  | 0.025–1.416 | 4.122   | 0.042|
|                | General activity       | 0.651| 0.291  | 0.082–1.221 | 5.019   | 0.025|
|                | Intervventional therapy| –1.451| 1.937  | –7.947–0.354| 4.591   | 0.032|
|                | Chemotherapy           | –0.149| 2.091  | –4.247–3.949| 0.005   | 0.943|
|                | Radiotherapy           | –2.056| 1.789  | 1.452–3.120 | 0.251   | 0.616|

0° means this is the control.

EBW, emotional well-being; FWB, functional well-being; PWB, physical well-being; SWB, social/family well-being.

Table 4.
Pain intensity and pain interference in patients with severe pain (n = 16).

| Pain              | Pre          | Post-1 week | Post-1 month | Post-3 months | χ² | P     |
|-------------------|--------------|-------------|--------------|---------------|----|-------|
| The worst pain    | 8.00 (7.00, 10.00) | 5.00 (4.00, 7.00) | 5.00 (4.00, 7.00) | 5.00 (3.00, 7.25) | 14.951 | 0.002|
| The least pain    | 2.00 (1.25, 3.00) | 2.00 (0.25, 2.75) | 2.00 (0.25, 2.75) | 1.50 (0.00, 2.00) | 7.387 | 0.061|
| The average pain  | 4.50 (4.00, 5.75) | 3.50 (2.00, 5.00) | 4.00 (2.25, 5.00) | 2.50 (1.00, 3.52) | 5.828 | 0.120|
| The pain right now| 3.50 (3.00, 5.00) | 2.00 (1.00, 4.75) | 2.50 (1.00, 5.00) | 2.00 (1.00, 5.25) | 2.383 | 0.497|
| General activity  | 8.00 (4.50, 8.00) | 4.50 (2.55, 7.75) | 5.00 (2.55, 7.75) | 4.00 (2.50, 8.00) | 6.125 | 0.016|
| Mood              | 6.50 (4.25, 8.75) | 5.50 (3.25, 7.00) | 5.00 (0.00, 7.75) | 4.00 (0.75, 8.00) | 5.304 | 0.151|
| Walking ability   | 4.50 (2.25, 2.75) | 5.00 (0.00, 6.75) | 4.50 (0.00, 8.00) | 2.50 (0.75, 6.25) | 2.487 | 0.478|
| Normal work       | 5.00 (2.00, 7.75) | 4.00 (2.55, 7.75) | 4.00 (2.55, 7.75) | 3.00 (0.00, 8.00) | 3.796 | 0.284|
| Relationships with other people | 5.00 (0.00, 6.75) | 2.00 (0.00, 5.75) | 0.00 (0.00, 8.50) | 0.00 (0.00, 7.25) | 0.824 | 0.444|
| Sleep             | 7.50 (4.75, 10.00) | 6.00 (1.50, 10.00) | 6.00 (1.75, 9.00) | 3.00 (1.00, 8.00) | 6.078 | 0.108|
| Enjoyment of life | 6.00 (1.00, 8.00) | 3.50 (0.00,8.00) | 2.00 (0.00, 7.25) | 2.50 (0.00, 8.00) | 3.264 | 0.353|

Compared with Pre, aP < 0.05; compared with post-1 month, bP < 0.05; compared with post-3 months, cP < 0.05; χ²: Friedman test.
Discussion

This study focused on the pain relief and the quality of life of patients with different degrees of pain treated with 125I seed implantation. Overall, quality of life for patients decreased 1 week after implantation but increased 1 month and 3 months after implantation. Similarly, a retrospective study of patients with advanced pancreatic cancer showed no significant change in quality of life 3 months after seed implantation. However, Koga et al. reported that quality of life in patients with prostate cancer at third month after seed implantation was worse after treatment, and then improved to baseline 12th month after treatment, while, in this study, the same tendency was observed at 1 week and recovered 3 months after seed implantation, respectively. This may be due to the invasive nature of seed implantation, which leads to a temporary worse quality of life.

As a new treatment method for advanced tumors, 125I seed implantation has demonstrated a remarkable clinical effect even for pain control. Wang, et al. and Yao, et al. reported that brachytherapy with 125I seeds for bone metastases relieved severe pain significantly and all the quality of life measures significantly improved, including appetite, sleep, fatigue, and mental state. Similar to the above studies, in this study, 3 months after seed implantation in patients with severe pain, the degree of pain significantly decreased and quality of life significantly improved. The effects of pain on general activity, mood, walking ability, normal work, relationships with other people, sleep, and enjoyment of life was also alleviated. The physical well-being of the patients significantly improved. For patients with mild-to-moderate pain, the pain intensity and pain interference scores increased after 125I seed implantation. This may be because the pain symptoms result mostly directly from the invasive growth of the tumor but can also result from therapeutic interventions, such as chemotherapy, radiation, and interventional therapy. After seed implantation, some patients will receive further chemotherapy, radiotherapy, or intervention, and treatment-related adverse reactions can also lead to increased pain. Therefore, for patients with mild-to-moderate pain before implantation, targeted education on pain-related knowledge should be provided for patients and their families to improve their pain coping skills.

Among the most common causes for physical distress in cancer patients is pain symptoms, which has a negative impact on quality of life. Studies have shown that neuropathic pain in cancer patients affects daily life more severely, and that improvement in the quality of life is more pronounced after its treatment. The results of this study confirmed that before 125I seed implantation, quality of life of pain-free patients was higher than that of patients with pain. After seed implantation, the quality of life in patients with pain improved more significantly, especially for patients with severe pain. Good symptom management is associated with improved patient quality of life. Overall, the results show that 125I seed implantation maintains patients’ quality of life and can significantly improve the quality of life for patients with pain. For patients with severe pain, the pain was significantly relieved after seed implantation, and the improvement of the quality of life of patients was even more significant.

Table 5.

| Quality of life | Group | No. | Pre | Post-1 week | Post-1 month | Post-3 months | \(F/\chi^2\) | \(P\) | \(F/\chi^2\) | \(P\) |
|----------------|-------|-----|-----|-------------|-------------|--------------|----------------|-----|----------------|-----|
| Total score    | Pain  | 43  | 61.21 ± 13.23 | 63.24 ± 14.05 | 68.97 ± 11.46 | 63.45 ± 16.30 | 3.315<sup>a</sup> | 0.030 | 18.173         | <0.001 |
|                | Painless | 61  | 75.03 ± 13.52 | 72.47 ± 15.72 | 72.60 ± 16.57 | 70.56 ± 14.03 | 1.719<sup>b</sup> | 0.176 |                |       |
| PWB            | Pain  | 43  | 19.00 (13.00, 23.00) | 20.00 (14.00, 21.00) | 21.00 (17.50, 24.00) | 20.00 (14.00, 23.00) | 5.060<sup>b</sup> | 0.167 | 8.846         | <0.001 |
|                | Painless | 61  | 25.00 (22.50, 27.00) | 24.00 (19.50, 26.00) | 25.50 (22.00, 27.00) | 24.50 (22.00, 27.00) | 8.077<sup>b</sup> | 0.013 |                |       |
| SWB            | Pain  | 43  | 16.34 ± 4.18 | 15.76 ± 4.45 | 16.24 ± 5.33 | 15.55 ± 4.91 | 0.961<sup>a</sup> | 0.414 | 2.344         | 0.130 |
|                | Painless | 61  | 17.37 ± 4.55 | 16.67 ± 4.34 | 17.50 ± 4.59 | 17.82 ± 4.24 | 2.255<sup>a</sup> | 0.093 |                |       |
| EWB            | Pain  | 43  | 16.00 (10.00, 18.00) | 17.00 (15.00, 19.00) | 16.00 (14.00, 18.00) | 16.50 (14.00, 18.25) | 16.009<sup>b</sup> | 0.001 | 6.796         | <0.001 |
|                | Painless | 61  | 19.00 (16.00, 20.00) | 20.00 (17.00, 20.00) | 19.00 (16.25, 20.00) | 19.50 (16.00, 20.00) | 1.782<sup>b</sup> | 0.19 | 6.195        | <0.001 |
| FWB            | Pain  | 43  | 11.00 (8.00, 16.00) | 11.00 (9.00, 14.00) | 11.00 (10.00, 15.00) | 13.00 (8.00, 16.00) | 3.126<sup>b</sup> | 0.373 | 7.256         | <0.001 |
|                | Painless | 61  | 15.00 (12.00, 19.00) | 14.00 (11.00, 20.00) | 15.00 (11.00, 19.00) | 17.00 (13.00, 20.00) | 11.230<sup>b</sup> | 0.010 |                |       |

<sup>a</sup>Repeated measures ANOVA; <sup>b</sup>Friedman test; <sup>c</sup>Comparison between groups.

EWB, emotional well-being; FWB, functional well-being; PWB, physical well-being; SWB, social/family well-being.
There were several limitations in this study. First, there was a small sample size because of the stratified analysis of patients' pain. However, future studies should expand the sample size, classify patients with different types of cancer, and extend the follow-up time to fully analyze the effects of $^{125}$I seed implantation on pain and quality of life. Second, the evaluation of patients' pain and quality of life mainly depends on patients' subjective feelings, but there are differences in patients' sensitivity to pain. Other factors, such as family relationships and social work, may also be affected by prolonged follow-up, which may lead to mixed bias. Similarly, different treatment after seeds implantation may also affect patient's pain and quality of life. Third, the follow-up was based on telephone conversations, which may lead to a certain bias. Therefore, future research should consider a detailed study on the specific dimensions of quality of life.

Conclusions

$^{125}$I seed implantation maintains the quality of life of patients within 3 months. For patients with severe pain, $^{125}$I seed implantation has obvious pain relief, and therefore, improves sleep, general activity, mood, and patients' quality of life. Nurses should focus on improving quality of life and the continuity of care after therapy and provide personalized guidance for patients with different degrees of pain.

Authors' contributions

Study conception and design: Panfeng Wang.

Data collection: Qiuyu Sun, Lan Gao, Lijuan Sun, Chunxue Wang.

Data analysis and interpretation: Jingxuan Zhang.

Drafting of the article: Jingxuan Zhang.

Critical revision of the article: Junjie Wang, Baohua Li.

Funding

This work was supported by the Nursing Research Project of Chinese Medical Association Magazine (Grant No. CMAPH-NRG2019012).

Declaration of competing interest

None declared.

Ethics statement

This study was approved by the Ethics Committee of the Peking University Third Hospital (Approval No. IRB00006761-M2019243).

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