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Incidence and prediction of seed migration to the chest after iodine-125 brachytherapy for hepatocellular carcinoma

Junqing Lin[1], Weizhu Yang[1], Na Jiang[1], Qubin Zheng[1], Jingyao Huang[1], Ning Huang[1], Ang Li[2], Han Jiang[2,*]

[1]*Department of Interventional Radiology, Fujian Medical University Union Hospital, Fuzhou, China*
[2]*Department of Nuclear Medicine, Fujian Medical University Union Hospital, Fuzhou, China*

ABSTRACT

PURPOSE: The aims were to determine the incidence of seed migration to the chest and to analyze the predictive factors after iodine-125 brachytherapy for hepatocellular carcinoma.

METHODS AND MATERIALS: Three hundred ninety-nine patients with hepatocellular carcinoma underwent iodine-125 seed brachytherapy. After seed implantation, chest X-ray radiograph or computerized tomography were undertaken to assess the occurrence and location of seed migration at 3 months after brachytherapy. The incidence of seed migration to the lung and heart was calculated. A statistical analysis of the influences of seed loss to the chest was performed between patients with and without seed migration.

RESULTS: A total of 13,977 seeds were implanted in 399 patients. One hundred fifty of the 13,977 (1.07%) seeds migrated to the chest in 81 of the 399 (20.30%) patients. Of all the migrated seeds, 112 (74.67%) migrated to the lungs in 59 (67.82%) patients, and 38 (25.33%) seeds migrated to the heart in 28 (47.46%) patients. No case exhibited clinical symptoms related to the migrated seeds. The number of seeds implanted and the number of seed implantations were significantly associated with seed migration.

CONCLUSIONS: The occurrence of seed migration to the lungs and heart was evaluated. Furthermore, the number of seeds implanted and the number of seed implantation procedures are significant predictors of seed migration.

Keywords: Iodine-125; Seed; Migration; Brachytherapy; Hepatocellular carcinoma

Introduction

Brachytherapy with permanent low-dose seed implant has been employed for decades and has gained popularity for a variety of malignant tumors. Iodine-125 (^{125}I) seed, which has a low average energy of 28.5 keV and long half-life of 59.4−60.2 days, has been widely used and has achieved satisfactory clinical outcomes (1−5). ^{125}I seed brachytherapy is a well-established treatment option for prostate cancer (1, 3, 5). In addition, ^{125}I implantation has become an increasingly used method in the management of various cancers, including hepatocellular carcinoma (HCC) (2), pulmonary (4) and pancreatic cancers (6), glioblastoma (7), and ocular (8) and rectal (9) malignant tumors.

HCC is one of the most prevalent malignancies worldwide. The incidence of HCC continues to increase rapidly by approximately 4% per year in men and 3% per year in women (10). For patients with HCC, permanent ^{125}I seed implantation is considered an effective modality to deliver a high radiation dose to the tumor while reducing the collateral damage to normal tissues. This approach has demonstrated favorable therapeutic outcomes (2, 11−13).

Seed migration is a well-recognized event that is associated with prostate brachytherapy for prostate cancer. This event is often observed in the period of the first postoperative day to the third month after seed implantation (14). In addition to decreasing the dose to the targeted region, seed migration has some potential adverse effects, such as lung

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* Corresponding author. Han Jiang, Department of Nuclear Medicine, Fujian Medical University Union Hospital, 29 Xinquan Road, Fuzhou 350001, Fujian Province, China. Tel./fax: +86-591-86218245.

E-mail address: jianghan0123@163.com (H. Jiang).

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cancer (15), acute myocardial infarction (16), angina (17), and fatal arrhythmia (17). To avoid these clinical complications, it is important to evaluate the occurrence of seed migration.

The incidence of seed migration is reported to be between 1.7% and 69.4% (14). Various locations as sites of seed movement have been documented, including the lungs (14, 18), heart (19, 20), urine (20, 21), abdomen (20–22), pelvis (20, 22), vertebral venous plexus (23, 24), sacrum (20), seminal vesicles (22), and testicular veins (25). However, the most frequent site is the chest.

To date, there is little information on the migration of ^{125}I seeds used for the HCC brachytherapy. The present study evaluated the seed loss and movement to the thorax in patients with loose ^{125}I seeds. Furthermore, both clinical and treatment-related factors associated with the occurrence of migration were analyzed.

Methods and materials

This retrospective study was conducted from January 2010 to August 2016 and was approved by the institutional research ethics committee. Three hundred ninety-nine patients diagnosed with HCC were treated with permanent ^{125}I seed brachytherapy. The patients' characteristics are provided in Table 1.

One week before treatment, preoperative planning was performed by means of a three-dimensional conformal radiation therapy treatment planning system (Astro Technology Company Limited, Beijing, China) with which conventional X-ray CT image data of the lesions were transmitted. Next, the gross tumor volume and clinical target volume were calculated. The target location, mapping of the path, and the number of seeds for implantation were determined using treatment planning system. The prescribed radiation doses were set at 120 Gy. With the guidance of CT, ^{125}I seeds were implanted into the target tumor employing 18G particle needles. All patients received loose ^{125}I seeds with an interval of 0.5–1.0 cm in the tumor according to the pretreatment planning. One type of ^{125}I seed was used during the study period (Jaco Pharmaceuticals Company Limited, Ningbo, China).

Table 1
Patient characteristics

Characteristic	Value
Age	58.1 ± 0.56 (27–84)
Gender (F/M)	59/340
HBsAg (+/−)	288/111
Child-Pugh	
A	288
B	111
AFP (ng/mL)	
≥400	270
<400	129
PLT	
≥100 × 10^9/L	260
<100 × 10^9/L	139
Number of implantations	2.23 ± 0.08 (1–13)
Number of seeds implanted	35 ± 1.57 (2–214)

HBsAg = hepatitis B; AFP = alpha-fetoprotein; PLT = platelets.

Postoperatively, the migration of ^{125}I seeds to the chest was assessed. Three months after seed implantation, all patients underwent chest radiography (with the posterior-anterior and lateral views) or CT to document the occurrence and sites of the seeds. The ^{125}I seeds were scored as migrated if they were radiographically visualized in the lung or heart. Two radiologists manually counted the numbers of the migration seeds and described the locations including the lungs and hearts. The date of the initial implantation, the number of seeds inserted, the number of seeds that moved, and the locations of the migrated seeds were recorded.

All parameters were evaluated for both groups, that is, migration-positive and migration-negative groups. Variables including age, gender, Child-Pugh, initial alpha-fetoprotein (AFP), platelets (PLT), hepatitis B (HBsAg), the number of implantations, the number of seeds implanted, and patient treatment order in the two groups were statistically compared using Mann–Whitney U tests and regression analysis. Statistical significance was defined as a p value <0.05.

The significance of the selected variables in terms of affecting seed loss was assessed based on receiver operating characteristic curves, which are defined as plots of a test sensitivity vs. 1-specificity or the false positive rate using all possible cutoff values.

Results

In total, 13,977 seeds were implanted in 399 patients (median 35, range 2–214). All HCC patients underwent chest X-rays (in the anterior-posterior or lateral view) or CT scanning to evaluate seed loss to the lungs and hearts after 3 months of seed implantation. One hundred fifty of the 13,977 (1.07%) seed migrated in 81 of the 399 (20.30%) patients, including the following: six seeds were lost in 1 patient, five in 2 patients, four in 7 patients, three in 5 patients, and two in 25 patients. In the remaining 41 (50.62%) patients, only a single seed migrated to the chest. Of all the migrated seeds, 112 (74.67%) seeds were visualized migrating to the lungs in 59 (67.82%) patients, and migration to the right lung was more common. There were 38 (25.33%) seeds migrating to the hearts of 28 (47.46%) patients. Moreover, in six patients, seeds were detected migrating to both the lungs and heart. The distribution and numbers are illustrated in Table 2. Examples of seed migration to the lungs and heart are provided in Figs. 1 and 2.

Univariate analyses of all cases in this study were performed. The results demonstrated that the number of seeds implanted and the number of implantations