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Radioactive seed migration following parotid gland interstitial brachytherapy

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ABSTRACT

PURPOSE: To evaluate the incidence and associated factors of pulmonary seed migration after parotid brachytherapy using a novel migrated seed detection technique.

METHODS AND MATERIALS: Patients diagnosed with parotid cancer who underwent permanent parotid brachytherapy from January 2006 to December 2011 were reviewed retrospectively. Head and neck CT scans and chest X-rays were evaluated during routine follow-up. Mimics software and Geomagic Studio software were used for seed reconstruction and migrated seed detection from the original implanted region, respectively. Postimplant dosimetry analysis was performed after seeds migration if the seeds were still in their emitting count. Adverse clinical sequelae from seed embolization to the lung were documented.

RESULTS: The radioactive seed implants were identified on chest X-rays in 6 patients. The incidence rate of seed migration in 321 parotid brachytherapy patients was 1.87% (6/321) and that of individual seed migration was 0.04% (6/15218 seeds). All migrated seeds were originally from the retromandibular region. No adverse dosimetric consequences were found in the target region. Pulmonary symptoms were not reported by any patient in this study.

CONCLUSIONS: In our patient set, migration of radioactive seeds with an initial radioactivity of 0.6−0.7 mCi to the chest following parotid brachytherapy was rare. Late migration of a single seed from the central target region did not affect the dosimetry significantly, and patients did not have severe short-term complications. This study proposed a novel technique to localize the anatomical origin of the migrated seeds during brachytherapy. Our evidence suggested that placement of seeds adjacent to blood vessels was associated with an increased likelihood of seed migration to the lungs.

Keywords: Brachytherapy; Seed migration; Parotid; 3D reconstruction

Introduction

Over the past decade, permanent radioactive seed implantation has been shown to be effective for the treatment of cancers of the prostate, breast, liver, parotid, and many other sites (1−4). The long-term persistence or stability of seeds implanted in the implant bed ensures a constant dosage delivery to target tissues and eradicates local disease. However, one of the risks associated with this approach is the migration of implanted seeds to the lungs through venous system, which occurs from 0.7% to 55% of seeds per patient and 0.19−0.98% per seed after prostate brachytherapy (5). Permanent I-125 seed implantation has been used in management of parotid gland malignant tumors with satisfactory local control rate and benefit in facial nerve preservation (6). But to our knowledge, seed migration to the lungs after parotid brachytherapy has not been reported in the literature.

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Alteration dosimetry on the target region and irradiation effects on the lung tissue are two potential problems arising from radioactive seed migration (7). Detecting the precise location and the number of the migrated seeds is critical for providing necessary feedback on personalized treatment planning and is important to ensure the sufficient dose coverage onto implanted region.

Therefore, this article reports the incidence of seed migration to the lungs after parotid brachytherapy and proposes a novel method to locate the migrated seeds from the target region.

Methods and materials

A total of 321 patients (186 males and 135 females) undergoing parotid cancer brachytherapy at the Peking University School and Hospital of Stomatology from January 2006 to December 2011 were retrospectively evaluated. Their ages ranged from 14 to 82 years (median 48 years; mean 46.3 years). Patients with a history of secondary surgery or trauma in a previously treated region were excluded. The study was approved by the Ethics Committee of the Peking University School and Hospital of Stomatology.

The procedure of brachytherapy

The brachytherapy treatment planning system (Beijing Astro Technology Ltd Co, Beijing, China) was used for I-125 seed implantation planning. The planning target volume was outlined to cover the lesion with a 5–10 mm margin. The planned dose (PD) was 120–160 Gy for patients without history of radiotherapy and 80–120 Gy for patients who had previously received radiotherapy. Dosages delivered to organs at risk were designed within acceptable limits of tolerance. In preplan, needles were implanted from different angles to avoid bone, major blood vessels, and important tissues (Fig. 1a). Based on the preplan, CT and/or a 3D-printed individual template were used to guide needle implanting and seed placement (Fig. 1b). All I-125 seeds were implanted as free seeds (0.8 mm wide and 4.5 mm long; Model 6711, Beijing Atom and High Technique Industries Inc, Beijing, China). The half-life of each seed was 59.6 days, and seed activity was 0.6–0.7 mCi. Postplan was performed immediately or 1 day after the implantation to verify seeds placement and dose distribution (Fig. 1c). The D90 (dose delivered to 90% of the target volume) ranged from 85.4 to 176.9 Gy with a median of 140.5 Gy, which was larger than PD in all patients. The V100 (the percentage of the target volume receiving at least 100% of the PD) of each patient ranged from 95.2% to 98.9% with a median of 97.6%. The V150 (the percentage of the target volume receiving at least 150% of the PD) of each patient was less than 50% (Fig. 1d).

Migration seed on chest radiographs

Routine head and neck CT scans and chest X-rays were taken following implantation for monitoring tumor

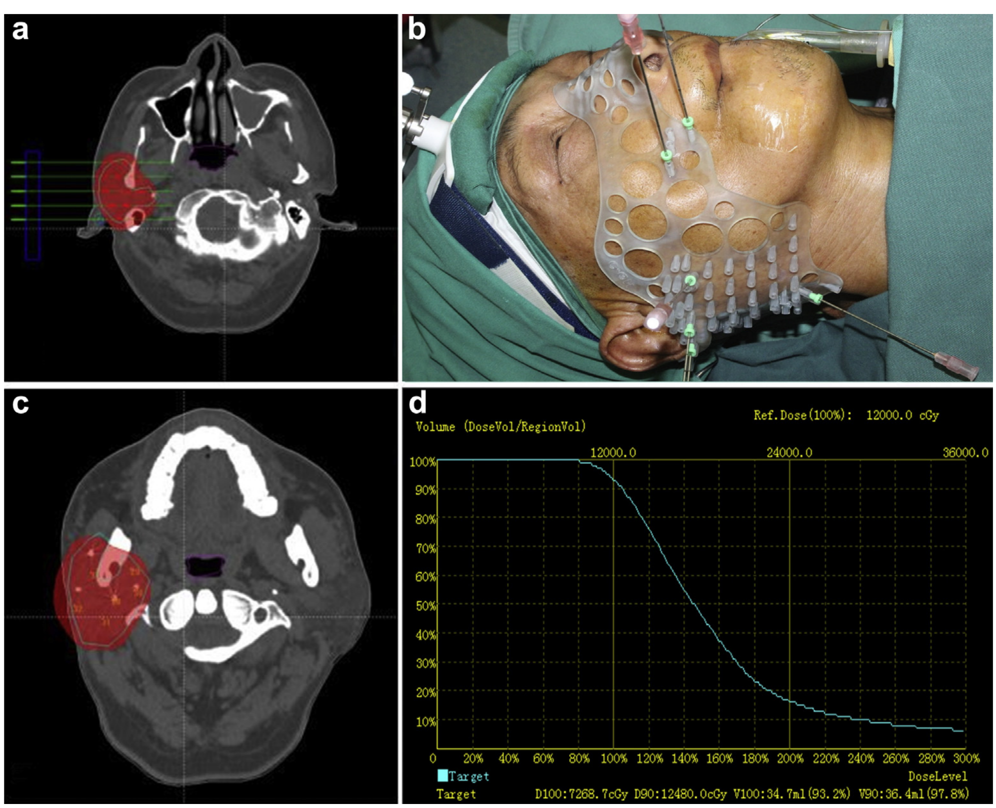

Fig. 1. The administration of iodine-125 seeds parotid brachytherapy. (a) The isodose curve in the implant plan from CT scan. (b) Hollow interstitial needles were inserted into the target region, and I-125 radioactive seeds were implanted permanently according to the preplan with customized template guidance. (c) The isodose curve after seed implantation from CT scan. (d) The dose-volume histograms of the planning target volume after seed implantation.

recurrence and metastasis. Chest X-rays were used for screening pulmonary seed migration (Fig. 2).

Migration seed detection technique

The Dicom format images (0.75-mm slice) of the archival CT scans were read directly in Mimics software (version 15.0, Materialise NV, Leuven, Belgium). Thresholding method was used to segment the maxillofacial bones and the implanted seeds, separately (Fig. 3). All segmented models could be rotated and visualized in 3D. After stored in STL file format, the segmented models were introduced into Geomagic Studio software (version 12.0, Geomagic Inc, Morrisville, NC, USA). Then, a rigid transformation (translation and rotation) of the maxillofacial bone over time were aligned together by the ‘‘best fit registration’’ function. The bones were considered as the stable anatomical structures in longitudinal CTs; and therefore, after aligning the bones, their corresponding seeds were transformed automatically into a uniformed coordinate system (8). The number and the location difference of the seeds over time could be compared and visualized. Patient 6 was used to demonstrate the workflow of the migrated seed detection technique (Fig. 4). The associated clinical factors for the occurrence and the number of seed migration were analyzed. Postimplantation dosimetry was reevaluated using the computerized treatment planning system. Adverse clinical sequelae from seed embolization to the lung were documented.

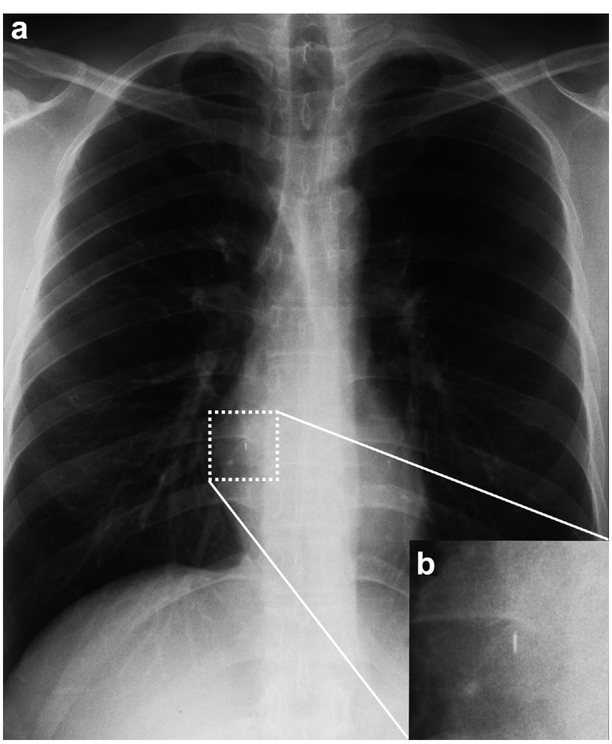

Fig. 2. (a) The presence of a metallic object in the right lower lobe of the lung with radiopaque markers of the same size as the implanted seeds in chest X-ray 6 months after parotid brachytherapy, which is better illustrated in a magnified view (b).

Results

A total of 15,218 seeds were implanted as free seeds in 321 patients (average 49.7 seeds per patient, range 22–155 seeds) during the study period. A total of 246 patients received postoperative adjuvant therapy, and 75 patients received a single therapy. All patients had one or more postimplant chest X-rays to be evaluated. Six pulmonary emboli of the seeds were identified in 6 patients (one per patient). The overall pulmonary embolization rate of patients was 1.87% (6/321) and 0.04% (6/15218) of seeds. Of the six migrated seeds, three had migrated to the right lobe of the lung and three to the left lobe. Clinical data for the implanted seed number, initial seed activity, migration time, location of seeds on the chest X-ray, and anatomical origin of the migrated seeds were summarized in Table 1. The migrated seed detection results revealed that each of the six migrated seeds were originally located in the retromandibular region and from the central region of the tumor bed. The median follow-up duration was 62 months (range 36–104 months), during which time none of the 6 patients showed evidence of local recurrence or distant metastasis. No significant adverse dosimetric consequences were noted in the target region, according to TPS D_{90} analysis. Subsequent chest X-rays confirmed a stable seating of the seeds within the lungs and without any delayed migration at a median follow-up of 62 months (range 36–104 months). Pulmonary symptoms such as pain, cough, or dispense were not reported by any patient in this study.

Discussion

Permanent I-125 seed implantation has been used over the past decade in management of parotid gland malignant tumors with an 88.7–100% 5-year local control rate, and the PD was 120–160 Gy for patients without history of radiotherapy and 80–120 Gy for patients who had previously received radiotherapy (4, 6). However, the radioactive free seeds may rotate within facial tissue and potentially embolize to distal organs through the vascular system. This potential risk could influence the dose distribution in the implanted region and harm the distal organ with radiation. In this study, six instances of postimplantation seed migration to the lung were reported among 321 consecutive patients undergoing parotid brachytherapy, and a novel technique was proposed to localize the anatomical origin of the migrated seeds.

The biggest challenge of visualizing implanted seeds on a traditional 2D image is overlapping, touching of seeds, and interference from the bone. Identifying each of the implanted seed manually is laborious, and detecting the migrated seeds is challenging. 3D-migrated seed detection

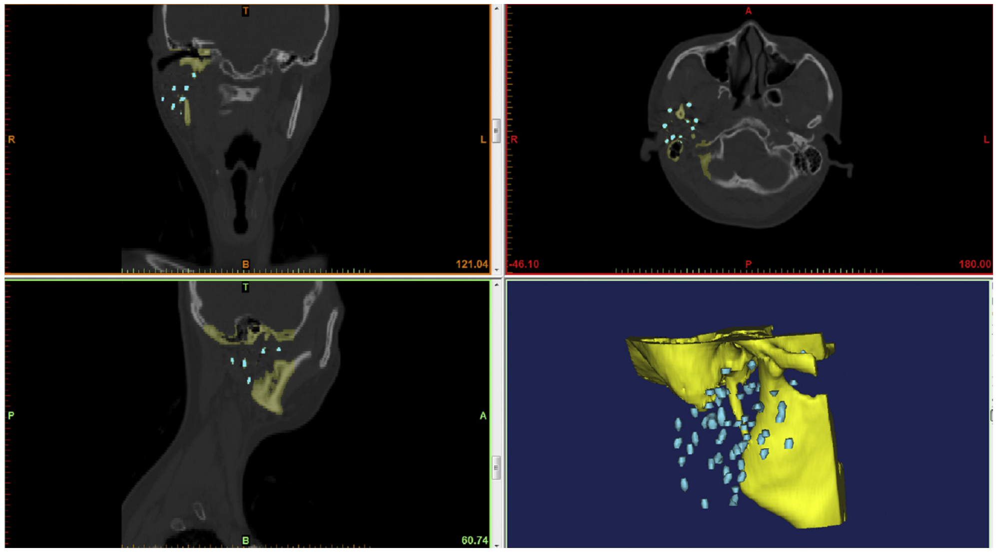

Fig. 3. Reconstruct the bone and the implanted seeds, separately from archival follow-up CT image.

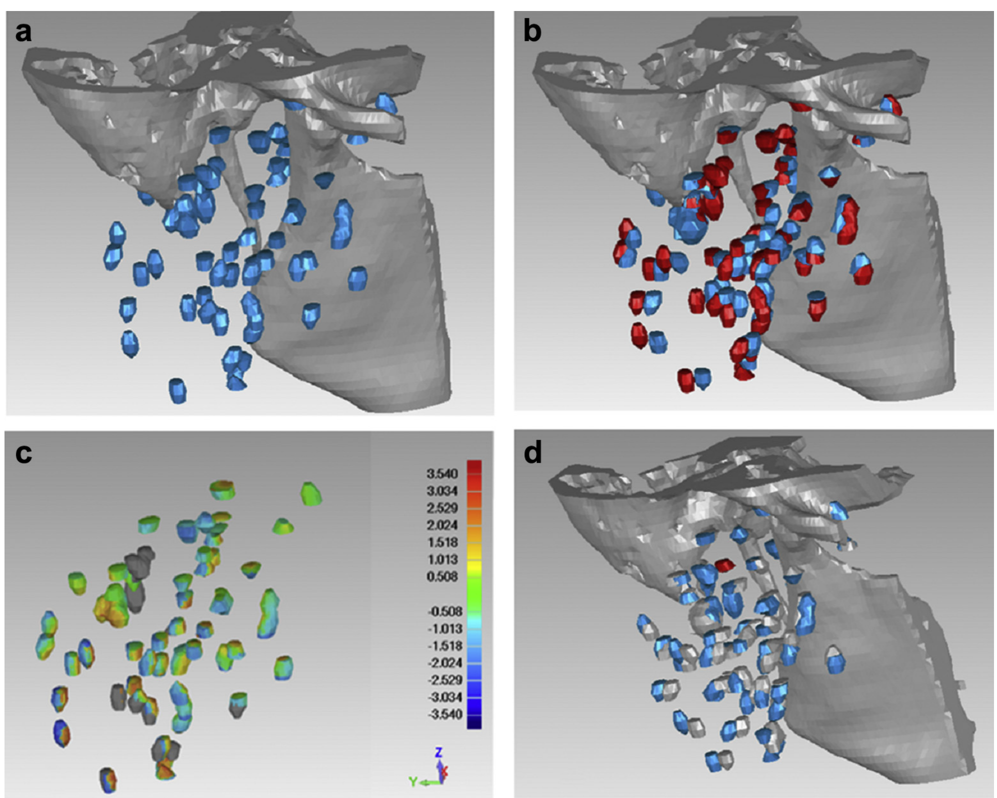

Fig. 4. Patient no. 6 is used to illustrate the workflow of the novel migrated seed detection method. 64 I-125 seeds were implanted in the parotid and peri-parotid region for the treatment of malignant myoepithelioma after surgical resection. Immediate postimplantation evaluation does not reveal any seed lost by comparing the number of the reconstructed seed with the number of the implanted seeds on intraoperative medical records (a). The maxillofacial bones over time are aligned together by the best fit registration, and their corresponding seeds are transformed automatically to a uniformed coordinate system as the same with the bones (b). The number and the location difference of the seeds over time could be compared and visualized (Fig. 3c). In this case, 63 metallic seeds remain in the parotid region. Color-code map is used to visualize displacement or missing seeds, therefore narrowing down the suspected migrated seed region (as shown in the gray, distance discrepancy > 4 mm) (c). The migrated seed is visualized 2-month postimplantation, highlighting in red in the lateral region of the styloid process and frontal region of the mastoid in (d). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Clinical characteristics of patients and seed migration in parotid brachytherapy

Patient no.	Age (y)	Gender	Postsurgical pathology	Seed number	PD (Gy)	Seed activity (mCi)	Embolization at the lung	Migration time[a] (m)	Original location
1	51	F	Adenoid cystic carcinoma	32	110	0.7	Right lower lobe	12–36	Posterior angle of the mandible
2	51	M	Squamous cell carcinoma	45	120	0.6	Left upper lobe	2–6	Inferior-posterior edge of the mandible
3	14	F	Mucoepidermoid carcinoma	42	120	0.7	Right upper lobe	2–6	Posterior angle of the mandible
4	79	M	Mucoepidermoid carcinoma	32	120	0.7	Left upper lobe	6–24	Posterior edge of the ramus
5	31	M	Adenoid cystic carcinoma	62	140	0.6	Left middle lobe	24–36	Posterior edge of the ramus
6	29	M	Malignant myoepithelioma	64	120	0.6	Right middle lobe	0–2	Lateral of the styloid process

M = male; F = female; PD = peripheral dose.
[a] Postimplantation months.

may, therefore, be a cost-effective and patient-friendly (no additional irradiation) method for monitoring seed loss and pinpointing the precise anatomical origin of the migrated seeds. If the migrated seeds could be more efficiently identified, brachytherapists could then search for possible factors associated with the seed migration and improve the brachytherapy quality control methods.

In this study, the incidence of pulmonary seed migration occurred in 1.87% of parotid brachytherapy patients and in 0.04% of seeds. This is relatively low compared with the incidence of seed migration in prostate brachytherapy (0.7–55%) (5, 9). Perhaps, because no hollow organs around face for seeds to fall into (in contrast to the hollow organs such as the rectum and the urethral canal in prostate brachytherapy). Although the mechanism of seed migration to the lungs is still unclear, the prevailing theory is that the seeds migrate through the venous system (10, 11, 12). Eshleman *et al.* concluded that seed migration after prostate brachytherapy was more likely when implantation was performed specifically with free seeds and in extraprostatic tissues, the region which was flanked by the periprostatic venous plexus (5). This explanation is plausible for the present study, as well. Our 3D-migrated seed detection method suggested that all six migrated seeds were originally from the retromandibular region, where large blood vessels passed through the stylomandibular tunnel or formed ventrally around the posterior edge of the ramus. Theoretically, seeds may "escape" through the retromandibular vein to the jugular veins, subclavian veins, inferior vena cava, right heart, and ultimately into pulmonary circulation. The seeds could lodge in the pulmonary system in long term since the diameter of the pulmonary end veins is similar to the seed diameter (13). Conversely, seed migration has not been observed in the superficial lobe of the parotid gland. This region is occupied by glandular tissue and the masseter muscle, where large lumens are absent. In addition, likely because the small vessels become irreversibly transformed to fibrous tissue due to radiation, the potential migration pathways are blocked. Therefore, it is conceivable that individualized arrangement of radioactive seeds along the blood vessels of the face may be useful in reducing the incidence of pulmonary seed emboli during parotid brachytherapy.

Consequences of seed migration include reduction of radiation dose at the tumor bed, and potential, albeit unknown, adverse effects on lung tissue (9). In our study, the premigration and postmigration dosimetry calculations (dose-volume histogram D_{90}) revealed the successful delivery of a satisfactory dosage (D90 > PD) to the parotid region in our 6 patients. This finding is consistent with that of other studies pertaining to the use of loose seeds, as all the six migrated seeds had been proved originally from the central area of the tumor bed, where the dosage coverage could be compensated for by neighboring seeds. In addition, the total number of seeds found in the lungs accounted for less than 1% of seeds implanted in the target area with relatively low initial radioactivity. Moreover, the time course for seed migration varied in our study, ranging from months to years. As the radioactive seeds decay over time (estimated three half-life durations in an exponential decay pattern), the seeds are expected to have relatively low residual activity or no emitting count. Therefore, the later the seed migrates, the less likely negative dosimetric consequences to the target region and to the distal lodging organ.

To date, no adverse clinical consequences have been reported for pulmonary embolization in our patients during a minimum of 3 years of follow-up. Miura *et al.* calculated doses of radiation to lung tissue with Monte Carlo simulation and noted that 21–28 keV of low energy emission I-125 source deposited in the lung would affect approximately 1 cc. of lung volume and would be unlikely to have any measurable effect on pulmonary function (14). However, it is conceivable in prostate brachytherapy that seeds could migrate or become entrapped in other organ systems and induce adverse effects such as acute myocardial infarction (15), pulmonitis (14), and potential radiation-induced cancer (11). Therefore, although no detrimental effects have been demonstrated to date in our patient set, efforts should be made to reduce the incidence of radioactive seed migration and prevent potential long-term complications.

Conclusions

Radioactive seed migration to the lung is a rare phenomenon after parotid brachytherapy. In this study, a novel migrated seed detection technique is proposed, and it is feasible for visualizing and localizing the anatomical origin of the lost seeds in the parotid and periparotid gland region. Single seed migration from the central implantation region does not affect the dosimetry of the target organ and does not lead to severe complications following short-term observation. However, placement of the seeds adjacent to blood vessels is associated with an increased likelihood of seed migration to the lungs. Although the embolized seeds have not yet been shown to cause any detectable effects, long-term follow-up of such patients is required.

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