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Short informative title

A Multimodal, Image-Guided, Surgical Robot-Assisted, Interstitial Brachytherapy for the Treatment of Head and Neck Tumors – A Preliminary Study

Short running title

Robot-Assisted Brachytherapy in head & neck

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A New Multimodal, Image-Guided, Robot-assisted, Interstitial Brachytherapy for the Treatment of Head and Neck Tumors – A Preliminary Study

Running head: Surgical robot-assisted, interstitial brachytherapy for head and neck tumor

Objective:

Interstitial brachytherapy (BT) is becoming an accepted treatment option for head and neck cancer patients for whom surgery poses high risks. Multimodal, image-guided, robotic surgery has the potential to allow precise seed implantation into tumors. Our aim was to introduce a new multimodal, image-guided surgical robot during the performance of interstitial BT for the treatment of tumors in the head and neck regions.

Methods:

Clinical data for 3 patients were analyzed, retrospectively; patients had received ^{125}I seed implantations from July 2019 to October 2019. Multimodal, image-guided, robotic surgery was performed in all patients. Postoperative CT data were imported to software to evaluate the accuracy of the seed position and the operation times.

Results:

The mean placement error of the ^{125}I seed was 1.9± 0.74 mm. The mean operation time is 47 min.

Conclusion:

The experimental results showed that the Remebot has promise for use during BT for the head and neck.

Introduction:

The oral and maxillofacial regions are heavily populated with many surgically and anatomically important structures including large nerves and vessels. Malignant tumors in this region may cause facial deformations and affect oral function. Thus, maxillofacial surgeons aim to identify minimally invasive and effective treatment methods. Interstitial BT is a form of intensive local irradiation that facilitates the effective protection of surrounding structures and the preservation of organ functions, resulting in a favorable therapeutic ratio[1]. In recent years, researchers have increasingly reported good results of interstitial BT during the treatment of malignant tumors in the head and neck[2]. Interstitial BT can be used alone, as an adjuvant after surgery, or as a local boost, in combination with external beam radiation therapy (EBRT).[3] ^{125}I seeds emit continuous, low doses of γ-rays, enhancing the accumulated dose of the target volume. Because the energy emitted by γ-

rays rapidly decays with increasing distances, the radioactive seed must be implanted adjacent to the tumor. The complexity of the skull base anatomyincreases the difficulty of performing BT in this region. Several researchers have attempted to perform computed tomography (CT)-guided, permanent, radioactive seed implantation, which could guarantee the precision of the implantation and decrease the exposure of surgeons to radioactivity.[4-6] In this study, we intend to implement a multimodal, image-guided surgical robot to perform interstitial BT in the head and neck region. The surgical robot could combine CT and magnetic resonance (MRI) images to identify lesions more accurately. Combined with a stereoscopic tracking camera, it could be used to guide surgeons during ^{125}I seed implantation. These developments have facilitated the successful treatment of local tumor masses, with reduced side effects compared with wide-field EBRT,[7] and can reduce the radicality of surgical resections to preserve normal function.[8-10] Currently, there are few studies which reported about the use of robot system in interstitial BT for malignant tumors in the head and neck regions. This study introduces a novel method for the accurate implantation of ^{125}I seeds in the head and neck region.

Materials and Methods:

Patients:

3 patients, aged between 49 and 75 years old, mean 59, received permanent implantations of ^{125}I seeds from July 2019 to October 2019, (Table 1) for recurrent and locally advanced malignant tumors of the head and neck. The tumor sites included the maxillary sinus, soft and hard palates and the base of the tongue. A prescription dose (peripheral matching dose) of 120 to 160 Gy was delivered to tumors, without prior radiotherapy. All surgeries were guided by the Remebot surgical robot (Beijing Baihui

Weikang Technology Co., Ltd; Beijing, China), and the study was approved by the Institutional Review Board First Medical Center of PLA General Hospital (reference number S2018-281-02).

Table 1 Patient characteristic

Methods:

Preoperative planning:

Prior to the surgery, all patients underwent MRI for preoperative planning. The images were transferred to a computerized treatment-planning system (TPS, Panther, Prowess Inc., USA). The radiation oncologist outlined the planned target volume (PTV) on each transverse image. A radiation dose of 120-160Gy was prescribed for the PTV, and calculated using the computerized TPS. Before the surgery, on the same day, fiducial markers containing ceramic balls were applied to each patient's head, and a preoperative volumetric CT scan was performed. The CT and MRI images were imported to the Remebot dedicated software and merged. Then 3D objects of interest, such as jaws and tumors, were segmented. The target points and trajectories were planned, on different views and 3D objects. Fiducial points were automatically marked in the CT images as centers can be automatically calculated from a series of high-contrast circular zones, thanks to the density and isotropy of the balls.

Intraoperative phase:

After general anesthesia, patients were placed in the supine position, and their heads were fixed using a Mayfield (Cicel, USA) 3-pin holder. The mobile trolley of Remebot surgical robot was wheeled in place within 700 mm away from the patient's head, stabilized by four electric actuators, and secured to the head holder using a support mechanism, to enhance the rigid immobilization between the robotic arm and the patient's head. Then, the optical tracking camera was placed above the patient's head, using a flexible pendant structure. The registration was performed using the following steps: 1) the registration between the camera space and the robotic arm space, by correlating two sets of points in either space from manually orienting the Robot-Marker (a unique visible target pattern detected and pinpointed in the camera images, engraved on the end-effector) through four positions surrounding the patient's head; 2) registration between the image space and the camera space, by collecting the centers of spherical pits after removing the balls as fiducial points to be paired with these marked in the image space, using a pointer with an unique Probe-Marker and a spherical tip; and 3) the final verification of the registration accuracy, as computed by the software, and the correspondence by other relevant landmarks. During the operative phase, the robotic arm moved to the selected target point and was oriented to the trajectory. The movement could be controlled by the surgeon, using 3 available modes (point-to-point, axial, and free). (Figure 1)

Postoperative analysis:

After implanting all seeds, a CT scan was performed to verify whether the seeds were in the expected positions within 24h postoperatively. The CT images were imported into the TPS, and the radio-oncologist outlined the tumor target and identified all of the seeds in the CT images. The ^{125}I seeds were identified on the CT images, using a combination of manual selection and an automated redundancy check feature that is available on the Panther TPS (Prowess Inc., USA). Location errors were compared with the preoperative plan to evaluate accuracy.

Figure 1 Postoperative isodose curves

Results:

The mean placement error for the ^{125}I seed was 1.9± 0.74 mm. The mean operation time is 47 min.

Discussion:

BT is a form of intensive, local irradiation. Considerable experience has been accumulated using low-dose BT for the treatment of carcinomas of the lip, tongue, floor of the mouth, oral mucosa, base of the tongue, tonsil, soft palate, and nasopharynx.[11-12] In carefully selected cases, postoperative BT alone can offer the similar or better 5-year local control rates as EBRT, at around 90%, but with less morbidity.[13] Given the proximity of many critical organs and tissues in the head and neck region, such as bones, sinuses, eyes and major vessels, implantation is often more difficult and dangerous in this region than in other regions of the body. [14] In this study, a multimodal, image-guided, surgical robot—Remebot was developed for interstitial BT to increase the precision of seed implantation. We propose the use of multimodal, image-guided, robotic assistance for BT in the head and neck region, while most studies related to robot-assisted radioactive seed implantation have described thoracoabdominal and prostate cancers. [4,5,15]

Our previous phantom experiments demonstrated that the mean deviation of the seed position was 0.82 mm. According to our study result, the mean placement error of the ^{125}I seed was 1.9±0.74 mm. For robot-assisted lung BT, the accuracy of 2 mm is clinically acceptable compared with manual procedures in expert clinical opinion.[6] The mean operation time is 47 min, including equipment placement, registration and implantation. Comparing to manual implantation, head fixation by 3-pin holder and registration between the image space and the camera space are required. We found that it did not increase too much operation time. So far, CT navigation and 3D printing template are two main methods to improve the accuracy of seed-placement. However, a very few reports have been reported with respect to the evaluation of accuracy of brachytherapy guidance in the head and neck region.[16-18] Among them, Huang et al. reported that 25 patients with head and neck tumors were implanted with ^{125}I radioactive seeds under the guidance of the 3D-printed individual template. The mean entrance point distance deviation for all 619 needles was 1.18 ± 0.81 mm, varying from 0.857 ± 0.545 to 1.930 ± 0.843 mm at different sites, and the mean time to insert one needle was 7.5 s. In another study published by Zhang et al., they evaluated the effect of computer-assisted techniques in the interstitial BT of the deep regions of the head and neck. The mean deviation of 5.2 mm and the average procedure time was 120.2 minutes for each patient including approximately 30 minutes for preparation time of the digital workflow and the mean needle implantation time was 41.7 minutes. Furthermore, Zhu et al.[19] developed a robotic assisted system for fully automated brachytherapy seed placement into skull base, and achieved 0.57 ± 0.21 mm and 1.41 ± 0.38 mm positioning accuracy in phantom and cadaver specimen, respectively. As far as we know, there has no literatures regarding clinical application of image-guided robotic brachytherapy. Compared to the 3D printing templates, robot-assisted system allows us prepare several more surgical plans for alterations in the volume and the shape of tumor or organ between the time of the preplan and the needle implantation. Moreover, we no longer need to produce surgical templates. In that case, we could reduce the preoperative economic and time cost.

As it is the first attempt for Remebot in ^{125}I seed implantation in head and neck region. There still has too much place for improvement. As the patient's head was stabilized by the skull clamp, the surgeon could not move the patient's head during the operation, which may not be convenient if the surgeon desires to change the angle of the patient's head and represents a major disadvantage of head clamp use. We plan to modify the head clamp by adding a special optical marker, which will allow the Remebot surgical robot to update the position of data acquired by the optical tracking system in real time. The problems posed by the line of sight between the camera and conventional infrared markers represent another non-negligible drawback during optical navigation. However, the Remebot surgical robot integrates an available third-generation stereoscopic optical tracking camera, [20,21] which has been used during the surgical navigation of rigid tissues, such as during neurosurgical and orthopedic surgeries,[22] maxillary orthognathic surgery, and laparoscopic surgery. Compared with second-generation optical trackers, the most commonly used optical systems, which emit infrared light and apply retro-reflective markers, this camera is fully passive and uses available visible light illumination to detect and track objects of interest, much like humans do, by triangulating 3D poses between two video cameras with overlapping projections. Multi-camera configurations could be used to eliminate line-of-sight interruptions or expand the field of measurement.[23-25] Registration error is another inevitable problem, which can be caused by image distortions, scalp deformations, needle deflection, and human error. In our study, we were able to control the registration error within 1 mm, which is acceptable for this surgery.

We found that seed migration occurred in one patient, who was diagnosed with carcinoma of the soft palate and the tongue ventrum, which may be caused by tongue movements during postoperative talking and chewing. Thus, we suggest that patients should receive postoperative CT scans within 24 hours after seed implantation. Tumors in the tongue or floor of mouth require to be punctured through a wide-open mouth. Once the patient's opened his mouth, the position of the mandible may be different from that while taking CT scan, which could lead to navigation error for Remebot. We attempted to apply two markers on the mandible and the puncture needle, to allow the position of the mandible to be identified in real-time and verified by the needle, even if the position of mandible shifted intraoperatively.

Conclusion:

In conclusion, a multimodal, image-guided, surgical robot has great potential application in the interstitial BT of head and neck carcinoma, which could achieve accurate radioactive seed implantation and reduce the side effects. However, larger sample sizes and comparative studies that examine this system relative to conventional methods remain necessary to verify its advantages.

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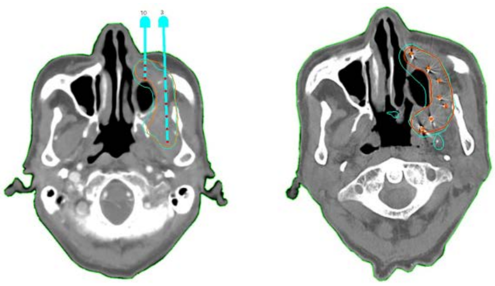

Figure 1 Pre- and post- operative isodose curves

Figure 2 Surgeon performed the seed implantation with the guidance of Remebot robotic system

Table 1 Patient characteristic

NO.	Sex	Age	Diagnosis	Oral and maxillofacial site	History of treatment
1	M	54	Moderate-high squamous cell carcinoma	Left soft palate, the base of tongue	Surgery*
2	F	49	Adenoid cystic carcinoma	Left maxillary sinus	Surgery
3	M	75	Mucoepidermoid carcinoma	Left buccal mucosa	Surgery

***** Because of the severe adverse reaction, this patient rejects external beam radiation therapy.