Review Article

Expert consensus on computed tomography-assisted three-dimensional-printed coplanar template guidance for interstitial permanent radioactive ^{125}I seed implantation therapy

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ABSTRACT

Interstitial permanent radioactive seed implantation delivers a high local dose to tumors and sharply drops off at surrounding normal tissues. Radioactive seeds implanted via ultrasound or computed tomography (CT) guidance are minimally invasive and facilitate quick recovery. Transrectal ultrasound-guided ^{125}I seed implantation assisted by a transperineal plane template is standard for early-stage prostate carcinoma, with a highly consistent target volume dose distribution. The postplan dose evaluation is consistent with the preplan evaluation. Until now, there was no workflow for seed implantation elsewhere in the body, and it was difficult to effectively preplan for seed implantation because of patients' position changes, organ movement, and bone structure interference. Along with three-dimensional (3D) printing techniques and seed implantation planning systems for brachytherapy, coplanar and X Y axis coordinate templates were created, referred to as 3D-printed coplanar templates (3D-PCT). ^{125}I seed implantation under CT guidance with 3D-PCT assistance has been very successful in some carcinomas. Preplanning was very consistent with postplanning of the gross tumor volume. All needles are kept parallel for 3D-PCT, with no coplanar needle rearrangement. No standard workflow for 3D-PCT-assisted seed implantation exists at present. The consensus topics for CT-assisted guidance compared to 3D-PCT-assisted guidance for seed implantation are as follows: Indications for seed implantation, preplanning, definition of radiation doses and dosimetry evaluation, 3D-PCT workflow, radiation protection, and quality of staff. Despite current data supporting ^{125}I seed implantation for some solid carcinomas, there is a need for prospectively-randomized multicenter clinical trials to gather strong evidence for using ^{125}I seed implantation in other solid carcinomas.

KEY WORDS: ^{125}I seed, brachytherapy, computed tomography guidance, interstitial permanent implantation, three-dimensional printing coplanar template

INTRODUCTION

Interstitial permanent radioactive ^{125}I seed implantation brachytherapy has become an important salvage treatment modality for all kinds of recurrent solid carcinomas.[1-5] The American Cancer Society, the Urology Society, the Clinical Oncology Society, the Radiation Oncology Society, the Brachytherapy Society, and the NCCN guidelines recommend seed implantation as the modality of choice for early-stage prostate carcinoma treatment.[6-8] Seed implantation techniques for prostate carcinomas are well-established and quality assurance is controlled by transperineal ultrasound-guidance combined with planar template assistance to achieve a precise three-dimensional (3D) distribution of seeds in the prostate and ensuring seed implantation treatment is strictly followed up as per preplanning.

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In 2002, Chinese scholars introduced computed tomography (CT)-guided technology into the field of seed implantation for recurrent solid carcinomas in the head and neck, chest, abdomen, pelvis, and spinal cord, greatly improving the accuracy of seed implantation. The indications of seed implantation have been expanded and a series of clinical studies have been produced.[9-19] However, CT-guided puncturing for seed implantation is very complicated and time-consuming, and operators spend a very long time learning these skills. With patients' body movements and interference with organs at risk (OARs), it is difficult to completely follow the preplanning steps, and prescribed doses are not always appropriate in real-time operative conditions.[20] With the wide application of 3D-printing technology in medical science, a new digital guiding 3D-printing template for seed implantation has been developed and designed with digital information such as central X and Y axes and seed needles' path information with 5 mm between needle holes.[21] There are two kinds of digital templates according to their function: 3D-printing coplanar templates (3D-PCT) and 3D-printing noncoplanar templates (3D-PNCT). 3D-PCT is indicated when seed needles need to be kept in the same direction and parallel to each other. The optimal conformity of radiation doses of implanted seeds in most locations in the human body could be achieved by 3D-PCT guidance. A 3D-PNCT is used for noncoplanar needle distribution, where needles cannot be kept parallel, but with optimized conformity.[21] 3D-PCT is dependent on coordinated X and Y axes, with 0.5 mm of space between the needle holes, Arabic numbers on the X-axis, and English letters on the Y-axis. To visualize the X and Y axes

Table 1: Detailed requirements and workflow

Workflow	Operators
Preoperative condition assessments	
Medical history, physical examination, and diagnosis	
Imaging examination and evaluation of patient's KPS	
Routine laboratory tests, hematological, and biochemical examination	
Preoperative CT-simulated location	
Preoperative discussion: Evaluation of indications and risk of seed implantation	Radiation oncologist
Positioning preparation	Radiation oncologist, physicists, therapists
Posture training for patient: Supine, prone and lateral position	
Preoperative preparation: Skin and intestinal preparation, bladder emptying and catheter indwelling for pelvic carcinoma, OB suppository in the vagina for gynecological tumors	
Patient posture fixation: Head and neck fixed with face mesh and vacuum pad; chest, abdomen, pelvis, and spine setup with vacuum cushion	
Fixed frame installation	
CT simulation positioning	Therapists
Posture fixation choice: Easy-to-operate position, taking into account patient comfort and tolerance	
Skin surface marking: X and Y axis marks on skin surface for location of tumor by laser lines, upper and lower boundaries and central points marked, position of the bed-raising line, and the left and right laser lines on the vacuum pad	
4D-CT scan: 4D-CT scan for movement of organs	
Fixed needle: The center of X and Y axis coordinates as stable needle hole	
Preoperative planning	RRadiation oncologist, physicists
CT scans: Images transmitted to treatment planning system; image fusion and 3D reconstruction	
3D-PCT choice: Different sizes of template to ensure that the whole tumor is covered	
Delineation of target and OAR: Radiation oncologist and physicists delineate the target volume and OAR	
Principle-of-plan design: All needles kept parallel with 1-1.5 cm intervals	
3D printing	
3D-PCT-assisted CT-guided seed implantation	Radiation oncologist, physicists
Patient setup: Patient and CT are positioned before seed implantation	
Anesthesia: Local infiltration, tongue root block and general, intercostal nerve block anesthesia	
Installation frame and 3D-PCT reset: 3D-PCT and stable frame installed according to body surface's X, Y, and Z axis laser lines	
Stable needle insertion: Stable needle insertion into stabilization holes on the surface by 3D-PCT	
Seed needle insertion: All needles inserted into the preplanning depth on the target according to preplan	
Needle position verification: CT scan again to check needle-by-needle whether the position complies with the preplan. If the error is >2 mm, the needle position is adjusted until satisfactory. If the error is <1 mm, no optimization is necessary	
Seed implantation: Seeds implanted according to preplan	
Dose evaluation: CT scans taken again immediately after seed implantation	
Postoperative dose evaluation	Radiation oncologist, physicists
Postoperative CT scanning: Postoperative CT images transferred into planning system	
Delineation of target areas and OAR: To evaluate the dosimetric parameters of target and OAR	
Follow-up	

KPS=Karnofsky performance status, CT=Computed tomography, 4D-CT=Four-dimensional-CT, 3D=Three-dimensional, 3D-PCT=3D-printed coplanar templates, OAR=Organs at risk, OB=Ohne Binde

on CT scans, X-ray markers were set to the end of the X and Y axes.[21,22]

BASIC REQUIREMENTS OF COMPUTED TOMOGRAPHY-ASSISTED THREE-DIMENSIONAL-PRINTED COPLANAR TEMPLATES-GUIDED RADIOACTIVE SEED IMPLANTATION

Radioactive seed implantation brachytherapy is dependent on image guidance to precisely implant radioactive seeds into a tumor target according to preplanning. The distribution of the seeds in the target needs to be highly consistent with the preplan, and dose distribution conformity should meet requirements. Seed implantation is advantageous as it is minimally invasive, requires only one surgery, and each seed delivers a very small dose. At the same time, seed implantation brachytherapy is part of the field of external beam radiotherapy (EBRT). The basic principles of EBRT should apply to interstitial brachytherapy, including target determination, definitions of prescribed doses, and acceptable limits for OAR radiation doses, among others.[23,24]

Table 2: Characteristics of computed tomography-assisted three-dimensional-printed coplanar templates-guided seed implantation in different organs

Workflow	Fixed organ	Organ movement
Preoperative localization	Required	Required
Preoperative planning	Required	Required
4D-CT	Unrequired	Required
Real-time optimization	Unrequired	Required
Laser light	Required	Required
Stabilization	Required	Required
Fixed needle	Required	Required
Postoperative evaluation	Required	Required

CT=Computed tomography, 4D-CT=Four-dimensional-CT

Definitions for target and OARs: According to Report 83 of the International Commission on Radiation Units and Measurement, the definitions for the tumor target and OARs are: (1) gross tumor volume (GTV): lesion area with a certain shape visible by various imaging and clinical examinations; (2) clinical target volume (CTV): including GTV and subclinical targets and which may be invaded by tumors; (3) planning target volume: including CTV, patient organ movement during irradiation, routine positioning movement, target displacement during treatment, and target volume changes, resulting in an appropriate expansion of irradiation volume. Internal target volume is a concept of EBRT, which is seldom considered in seed implantation; and (4) OAR refers to the area covered by the irradiated and adjacent normal tissues or organs.

Target prescription doses and dosimetric evaluation parameters: (1) Prescribed doses are defined according to evidence-based medicine or clinical experience. However, there are no prospective dose-escalation studies on prescribed doses for seed implantation therapy except in prostate cancer. The American Brachytherapy Society recommends prescribed doses of 140–160 Gy for ^{125}I seed implantation for prostate cancer (with at least 90% of prostate volume [D90] affected by the prescribed dose) and 115 Gy combined with

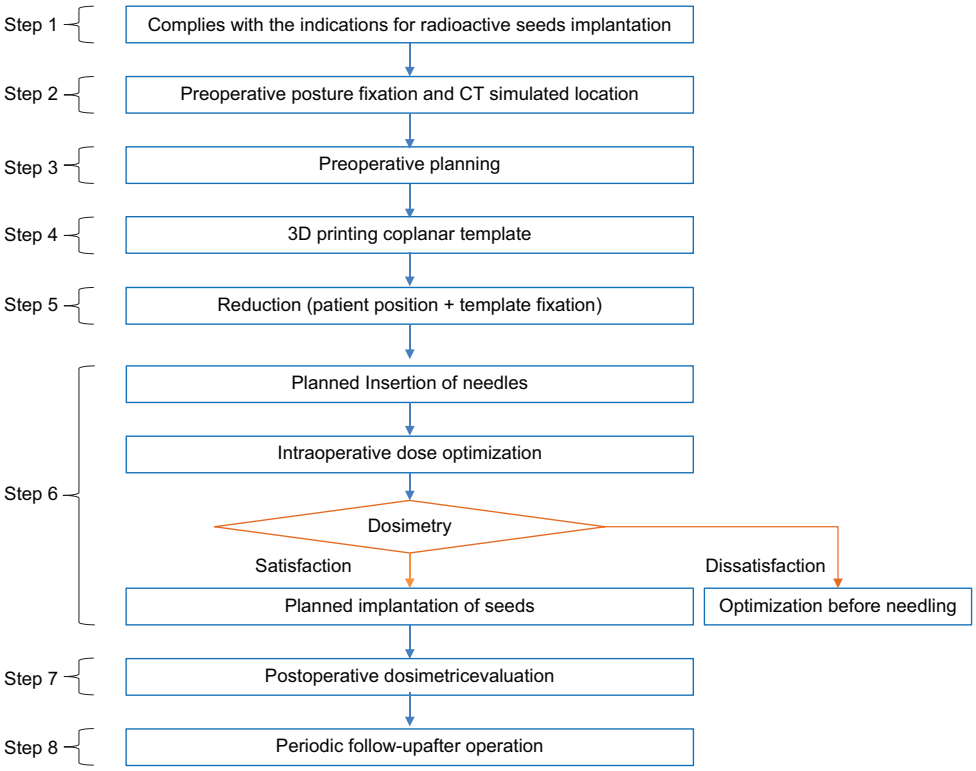

Figure 1: The circuit diagram of computed tomography-assisted three-dimensional-printed coplanar templates guidance for seed implantation

EBRT.[7] The prescription doses for tumors in other organs have been based on those for prostate cancer, which have been published both in China and abroad. For recurrent solid tumors, 110–160 Gy with an activity of 0.3–0.7 mCi (11.1–25.9 Mbq) is recommended. (2) Dosimetric evaluation parameters including target and OAR: D90, D100, V100 (i.e., the percent of the prostate receiving 100% of the prescribed dose), V150, V200, and so on. In addition, the Conformal Index, Homogeneity Index, and External Target Volume Index were usually used to evaluate the quality of the treatment plan;

Limitation for OAR dose: For brachytherapy by ^{125}I seed implantation, the relationship between the doses to OARs and adverse effects are still unclear, and further randomized prospective clinical trials are needed. At present, low-dose seed implantation brachytherapy dose parameters for OARs are referred to as high-dose afterloading. Dose parameters for OARs in prostate cancer are as follows: Rectum: D_{2cc} <100% prescription dose; $D_{0.1cc}$ <200 Gy. Urethra: D10 <150% prescription dose; D30 <130% prescription doses.[7]

^{125}I seed physical characteristics: Radioactive ^{125}I seeds are commonly used in the clinic, with a half-life of 60 days and delivering photon energy of 27 KeV. In recent years, loose seeds have been gradually replaced by stranded seeds because loose seeds tended to migrate in tissues.[24,25]

INDICATIONS AND CONTRAINDICATIONS OF COMPUTED TOMOGRAPHY-ASSISTED THREE-DIMENSIONAL-PRINTED COPLANAR TEMPLATES-GUIDED SEED IMPLANTATION

Indications for radioactive ^{125}I seed implantation include: (1) any recurrent carcinoma after surgery or EBRT; or refusal of surgery or EBRT, when the diameter of the tumor is <7 cm; (2) pathological diagnosis; (3) satisfactory needle puncture path design in preplan; (4) no tendency of bleeding or hypercoagulability; (5) generally acceptable condition of the body with KPS >70; (6) able to tolerate radioactive seed implantation; and (7) estimated survival time of >3 months.

Contraindications of radioactive seed implantation include: (1) severe bleeding tendency, with platelets $<50 \times 10^{10}$/L and coagulation dysfunction (prothrombin time >18 s, prothrombin activity <40%; anticoagulant therapy and/or antiplatelet coagulants should be discontinued for at least 1 week before seed implantation); (2) burst tumor; (3) severe diabetes mellitus; (4) no suitable puncture paths according to preplan; and (5) the estimated target dose could not meet the designed prescribed dose requirements.

The relative contraindications of radioactive seed implantation are: (1) extensive metastasis with a predicted survival of <3 months; (2) severe complications, infectious period, low immune function, and renal insufficiency; and (3) allergy to iodine contrast agents.

Recommendation for CT-assisted 3D-PCT-guided seed implantation; CT-assisted 3D-PCT-guided radioactive seed implantation is a new minimally-invasive form of brachytherapy, which is suitable for salvage treatment of recurrent and metastatic solid tumors. Standardized workflows of CT-assisted 3D-PCT-guided seed implantation include patient position fixation, CT-simulated positioning, preplanning design, 3D-PCT image production, stabilization by 3D-PCT, needle puncture for seed implantation, implantation of ^{125}I seeds, and postplan evaluation [Tables 1 and 2]. The key to successful seed implantation is strict quality assurance in all steps.[26,27]

WORKFLOW FOR COMPUTED TOMOGRAPHY-ASSISTED THREE-DIMENSIONAL-PRINTED COPLANAR TEMPLATES-GUIDED RADIOACTIVE SEED IMPLANTATION

The flowchart was shown in Figure 1.

RADIATION PROTECTION FROM ^{125}I SEED IMPLANTATION

The half-value layer of ^{125}I seeds is 0.025 mmPb, and its half-life is about 60 days. After 60 days, the energy of ^{125}I seeds decreases to half of its initial energy and 10% of its initial energy in 6 months, which is considered negligible after 1 year. Contact with children and pregnant women should be avoided within 2 months of seed implantation.[28-30] If long-term contact is required (more than a few hours), the patient should be kept at a distance of 1.5–2.0 cm or instructed to wear a lead neck, vest, and apron.

MANAGEMENT AND FACULTY TRAINING OF ^{125}I SEED IMPLANTATION THERAPY

At present, seed implantation brachytherapy in China is a restricted technology, which requires strict training to obtain a license. The relevant state administrative departments carry out supervision. In 2009, the Ministry of Health released the Technical Management Standards for Radioactive Seed Implantation Brachytherapy for the first time. In 2017, the National Health and Family Planning Commission released the Technical Management Standards for Radioactive Seed Implantation Brachytherapy (2017 edition), further amending and standardizing the institutional, personnel, and technical conditions and requirements for carrying out seed implantation. It was emphasized that physicians should receive systematic training for at least 3 months, participate in seed implantation therapy for at least 30 cases under the guidance of superior physicians, and participate in the entire management process of patients, including preoperative diagnosis, preoperative planning, implantation modality, postoperative dose verification, perioperative management, and follow-up. Only after passing the examination could they go on duty. Specific detailed requirements can be found on the official website of the National Health Commission.[30]

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Conflicts of interest
There are no conflicts of interest.

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