Original Article

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Fiducial Marker Practice in Prostate Radiotherapy in Turkey

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Abstract

Objective: During prostate radiotherapy (RT), localization strategies of the prostate gland are essential. Fiducial markers (FMs) are one of the various methods for prostate localization. FMs for prostate RT have been in use for several years. This study aimed to evaluate the current trends in FM practices used in the treatment of prostate cancer in Turkey.

Materials and Methods: An electronic survey containing 15 questions was developed on SurveyMonkey.net and sent to the email addresses of 600 radiation oncologists (ROs) via the Turkish Society for Radiation Oncology. Then, the data were collected and analyzed.

Results: A total of 33 ROs completed the survey. Upon analysis, results revealed that the mean FM experience duration was 6.6 years (range: 1-18 years). FM replacement was mainly done transrectally (90%) by urologists (67.7%). Antibiotic prophylaxis and anticoagulant cessation were often practiced. At least three gold FMs were inserted in most of the cases.

Conclusion: Many centers use FMs for prostate RT in Turkey. There are some differences in FM usage. Standardization of the practice could help to investigate and improve FM utilization in prostate RT.

Keywords: Fiducial marker, prostate cancer, radiotherapy, stereotactic

Introduction

Prostate cancer is the most common cancer in males (1). Radiotherapy (RT) is one of the main treatment options for prostate cancer. The effectiveness of RT depends on the delivery of a high dose of radiation to a tumor site while limiting the side effects of radiation on surrounding structures (2,3). Advances in technology have enabled the delivery of highly conformal radiation doses. However, it may be difficult to localize the prostate gland during irradiation because it is a moving organ (4). Fiducial markers (FMs), which are implanted within the prostate gland before RT, are one of the various methods employed to localize the prostate gland. FMs for prostate RT have been in use for several years in Turkey. A variety of FMs are available, and the insertion procedure of FMs can differ among clinics. This study aimed to evaluate the current trends in FM practices used in the treatment of prostate cancer in Turkey.

Materials and Methods

The Turkish Society for Radiation Oncology Urooncology Subgroup has approved this study. An electronic survey was developed on SurveyMonkey.net. The questionnaire contained 15 questions with a combination of yes/no, multiple-choice, and open-ended questions.

This questionnaire was sent to several radiation oncologists (ROs) in Turkey, who are members of the Turkish Society for Radiation Oncology. Each participant was contacted through email and invited to complete the survey. The survey was concluded on November 30, 2018.

Results

Completed questionnaires were received from 34 ROs. One of the responders who did not use FMs routinely in clinical practice was excluded from the study. Upon analysis of the data collected from the questionnaires, it was revealed that the mean FM experience duration was 6.6 years (range: 1-18 years).

Approximately 90% of the FMs were inserted transrectally, whereas 16.7% were inserted transperineally. Three responders stated that they use both methods. Approximately 73.3% of the responders administered antibiotics to patients before FM implantation. The duration of prophylaxis varied from 1 to 10

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days among specialists. Ciprofloxacin, as a single agent, was the most preferred antibiotic (87.5%). Almost half of the responders (45.8%) suggest a special diet to patients mostly a fiber-rich diet and avoid forming bloatedness.

The seventy-five percent of the responders asked patients to stop consuming aspirin, an NSAID, or anticoagulants 2-14 days before FM insertion. Poor agreement between practices was presented. Less than half (42.9%) of the responders administered anesthetics before FM insertion.

Most of the responders (77.3%) used gold markers of various shapes and sizes from different vendors. One of the responders used PEEK fiducials, whereas the other responders did not specify the FMs they utilized. Majority of the responders (64.3%) inserted three FMs, 28.6% inserted four seeds and 7.1% inserted five seeds. FM positioning was not consistent between responders. Approximately 35% of the responders prefer to insert at least one FM into the prostate base and another into the apex, whereas 27% of the responders prefer to insert one FM into the prostate base, one into the mid-gland, and one into the apex. The remaining responders did not specify the positioning of the FM.

Except for one, all ROs preferred to wait for 1-15 days between FM insertion and computed tomography (CT) planning. The most common waiting periods were 7 (55.1%) and 10 (20%) days. Different imaging methods were used. The most common methods are listed in Table 1.

Table 1. Characteristics of fiducial marker practice

Center responders working in	**(%)**
University hospital	24.2
State hospital	36.4
Private hospital	39.4
Primary responsible person for insertion	**(n)**
Urologists	22
Interventional radiologists	12
Radiation oncologist	2
Radiotherapy methods	**(%)**
IMRT	71
SBRT	58.1
IGRT	54.8
3D-conformal RT	3.2
Imaging methods	**(%)**
CBCT	63.3
MCVT	36.7
2D-kV imaging	33.3
2D-MV imaging	13.3
Cyberknife fiducial tracking system	43.3
Other	10

IMRT: Intensity-modulated radiation therapy, SBRT: Stereotactic body radiation therapy, IGRT: Image-guided radiation therapy, 3D: T-dimensional, CBCT: Cone-beam computer tomography, MVCT: Megavoltage computed tomography, 2D-kV: Two-dimensional kilovoltage, 2D-MV: Two-dimensional megavoltage

Discussion

In recent years, several developments have been recorded in prostate cancer RT. Advanced techniques, such as intensity-modulated RT, image-guided RT, and stereotactic body RT have been developed and different fractionation schedules, such as moderate or ultra-hypofractionation, require more precision than conventional treatments. Decreased margins are needed for lowering potential side effects of escalating doses for tumor control (2,3). Two-dimensional (2D) megavoltage or kilovoltage imaging uses pelvic bone structures to verify the position of the prostate gland. FMs allow superior verification of the prostate position relative to the bony anatomy, with 3D position corrections (4,5). Cone-beam CT (CBCT) offers three-dimensional (3D) imaging; however, prostate gland visualization remains a challenge, owing to inadequate soft-tissue contrast. In some treatment delivery systems, FMs provide intrafraction target motion information that is not obtained using CBCT. Also, internal organ motion causes daily variations in rectal and bladder filling. This makes it challenging to target the prostate accurately.

FMs have been used for almost two decades in Turkey. The absolute number of centers routinely inserting FMs for prostate RT is unknown. FM insertion is not covered under health insurance, being the main limitation for its use in Turkey.

FM insertion into the prostate gland is an invasive procedure. There are two main approaches: transrectal and transperineal. The transrectal approach is most widely used for FM placement, which is the same as the practice in Turkey. It requires the same equipment and setup used for prostate biopsies. Therefore, urologists are more familiar with this approach. In one study, Moman et al. (6) found that there were no differences between these two approaches in terms of toxicity and quality of life. Some series reported less than 1% toxicity with the transperineal approach (7,8).

The practice of administering antibiotics before implantation is nearly standard in Turkey; however, there is no standard regime in terms of the antibiotic type, dose, and duration. Fluoroquinolones are the most frequently used antibiotics before FM insertion just as before prostate biopsy (9). The use of prophylactic antibiotic therapy before transrectal procedures can cause increased rates of antibiotic-resistant infection (9). In their study, Moman et al. (6) reported no infection after transperineal FM implantation without routine prescription of prophylactic antibiotics.

In our series, most of the responders stopped anticoagulant treatment before the procedure; however, this may not be necessary. In a series by Iocolano et al. (10), a total of 57 patients on chronic anticoagulation therapy who did not stop the medication before FM insertion were observed. Neither rectal bleeding nor cardiac event was noted. Therefore, they suggested that the use of anticoagulant medication is not an absolute contraindication to FM insertion.

Transrectal prostate biopsy is generally performed under local anesthesia. In our study, although the FM insertion procedure was mostly performed transrectally (90%), the rate of anesthesia usage was less than half. A possible explanation for this may

be that the insertion procedure is less painful than biopsy. In a prospective study on pain score with transperineal FM insertion under local anesthetic, a total of 30 patients were evaluated (11). A visual analog scale from 0 to 10 was used to assess pain before, during, and after the procedure. It was revealed that transperineal ultrasound-guided gold seed implantation without conscious sedation is well-tolerated and associated with a low complication rate.

There is generally a time interval between implantation and CT planning for possible inflammation, edema, bleeding, and fiducial migration. Delouya et al. (12) reported less FM migration and a better match with delayed CT planning for a minimum of 3 days. Mostly, a delay of 7 or 10 days is preferred in Turkey practice. Linam et al. (13) reported no significant differences in table shifts between the same day and delayed CT simulation.

There is limited information on the ideal number of FMs and their location within the prostate gland. Three or four FMs are generally used in different studies. At least three FMs allow ROs to determine the prostate position in different imaging planes. Igdem et al. (14) suggested that implanting three FMs is safe and well-tolerated. Kudchadker et al. (15) reported that a single FM does not always reliably represent the position of the entire prostate and that three FMs were suitable. Theoretically, a fewer number of FMs may be associated with lower rates of implantation-related side effects.

There is no consensus on where to place the FMs. For optimal results, the markers should be implanted in a triangular configuration with a minimum distance of 1 cm between them (16). In many studies, at least one FM is inserted into the apex and another into the base for a correct prostate gland localization and laterally considering the urethra damage (14,16,17).

Study Limitations

The main limitation of the study was that the responders were ROs. They may not be aware of the insertion procedure, because the procedure is mainly performed by urologists and interventional radiologists.

Conclusion

FMs allow the localization of the prostate gland during treatment and are used in many centers by ROs for prostate RT in Turkey. However, the real numbers of the FMs used are not known. There are some differences in the FM insertion procedure and clinical usage. Standardization of FM practice could help investigate and improve the utilization of FM in prostate RT.

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Ethics

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Authorship Contributions

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