ESTRO Technology Transfer Grant (TTG) Report

Low dose rate and high dose rate real-time prostate brachytherapy and advanced techniques in prostate external beam radiotherapy

Date of visit: *3-20 September, 2019*
Host Institute: *National Institute of Oncology, Budapest, Hungary*

Aims:

The primary objective of the visit to the National Institute of Oncology in Budapest, Hungary, was to familiarise myself with the technique of interstitial implants in brachytherapy (BT). In particular, US-based treatment planning procedures adopted in cervix BT (intracavitary and interstitial applications) and prostate cancer BT (interstitial applications) were investigated. The aim of the visit was to learn about these techniques with a view to the possible implementation of these treatment modalities at my place of work, the Sina Radiotherapy and Oncology Center in Tehran, Iran.

The recommendations of the relevant working groups of the Groupe Européen de Curiethérapie (GEC) and the European SocieTy for Radiotherapy and Oncology (GEC-ESTRO) on this topic are exhaustive; however, it was very important for me to gain a practical insight into the clinical workflow of one leading European institution. In particular, I had the opportunity to gain practical experience and get to the core of the following issues:

- Optimisation of US-imaging protocols and procedures in real-time treatment planning of the prostate (prostate cancer);
- Seed implant prostate brachytherapy with iodine-125
- Accurate applicator and needle reconstruction;
- Concepts of inverse planning and dose distribution optimisation;
- Recommended selection of dose volume parameters to evaluate accurately and report the dose to targets and organs at risk; and
- Pre-treatment quality assurance (QA) and in vivo dosimetry modalities.

During my visit to the National Institute of Oncology in Budapest, I also gained insight into several aspects of the physics of state-of-the-art delivery modalities and technologies used in prostate cancer radiotherapy. This was particularly useful regarding the highly hypofractionated regimens for prostate, liver, lung and brain cases with the Cyberknife™ machine.

The department

Details of the scientific content of the visit:

Real-time prostate brachytherapy enables the physician to deliver 20.5 Gy in one fraction for low-risk and selected intermediate-risk prostate cases as a monotherapy treatment, or two fractions with 10 Gy per fraction as a booster treatment after radiotherapy.

To be eligible for treatment, all patients must have undergone standard core biopsies or image-guided biopsies in order to confirm malignancy histologically. The pathology report should include the Gleason score, the percentage or proportion of each core that is involved by the tumour, and the presence or absence of perineural infiltration. Information on the spatial distribution of positive biopsies within the gland is also necessary to plan adequate dose coverage. A bone scan is suggested for Gleason scores of 4 + 3 and greater, also for patients with a level of prostate-specific antigen (PSA) > 20 ng/ml.

First, the patients are selected based on some pathological criteria that include the Gleason score, the PSA level and the stage of the cancer. The table below shows the eligibility and exclusion criteria for the receipt of curative high-dose-rate (HDR) brachytherapy (the table content has been modified from American Brachytherapy Society (ABS) and GEC-ESTRO guidelines):

Eligibility	Exclusion
Stage T1b – T3b Any Gleason scores Any PSA level	Absolute: 1. Preexisting rectal fistula 2. Medically unsuited for anaesthesia 3. No proof of malignancy Relative: 1. Transurethral resection of prostate within 3-6 months 2. International prostate symptom score > 20 3. Maximum urinary flow rate (Qmax) < 10 ml/s 4. Pubic arch interference

After each patient is assigned monotherapy or booster treatment according to their medical situation, the next step is the preparation and anaesthesia of the patient for implantation.

Epidural anaesthesia can be initiated and set up with continuous perfusion (using Naropin or Lidocaine) to be titrated for postoperative pain control. This method permits quick recovery after the treatment is finished. Spinal anaesthesia with long-lasting morphine also works well for patients with “23-hour” overnight hospital stays. In patients who need general anaesthesia, postoperative pain is managed with patient-controlled analgesia (PCA). General anaesthesia is preferred when the procedure is performed in a brachytherapy suite, using an intraoperative real-time dosimetry approach. The patient will not need to be moved for treatment and will be awakened after the treatment is finished and catheters are removed.

Once the patient is anaesthetised, he is placed in the lithotomy position. The perineum is palpated to determine the space available to insert the catheters (the area between the posterior edge of the pubic symphysis and the anus). After the patient is prepped and draped, the transrectal ultrasound (TRUS) probe is secured to a brachytherapy stand, which can be floor or table mounted (Figure 1). To obtain the best TRUS image of the prostate, the probe must be parallel to the posterior border of the prostate. The probe should apply light pressure to the anterior rectal wall to obtain an artifact-free image of the prostate without causing significant distortion of the prostate.

Figure 1: Floor-mounted TRUS probe.

The use of a water-filled balloon can enhance image resolution, creating better contact to the posterior portion of the prostate. Occasionally, air trapped between the probe and the rectum causes "ghosting" of the image. The air is released by inserting a straight urinary catheter into the air pocket. Adjustment of the pelvis angulation may be of some help to gain a clearer view of the organ and prevent pubic symphysis interference of the brachytherapy catheter insertion. The position of the patient and template is a critical step in the procedure. The urethra should be positioned superiorly and parallel to the TRUS probe.

Before starting the procedure, a Foley catheter is inserted into the bladder. This enables visualisation of the urethra by TRUS and helps to prevent accidental puncturing of the urethra during the implant. Then the physician starts to acquire an image of the prostate from base to apex by moving the probe continuously by hand. Then the TPS is used to reconstruct the sagittal view from axial slices. The physician contours the clinical target volume (CTV) (Figure 2) the urethra and the rectum. This is necessary for inverse planning.

The critical step of contouring is the production of the contours of the base and apex of the prostate. The following three methods are used to outline the apex of the prostate:

1. The position of the urethra relative to the centre of the prostate is followed. Because the urethra is positioned anteriorly immediately after its exit point from the urogenital diaphragm, the apex of the prostate is usually just superior to this point.
2. The sphincter muscles are more prominent just before they merge with the urogenital diaphragm. The apex of the prostate can be outlined by following the medial edge of the muscle from the rectum towards the pubic symphysis.
3. The marker seeds inserted during the procedure confirm the location of the apex. If the seed is located near a slice identified by one of the methods, this confirms the location of the apex.

The base of the prostate is difficult to see because of volume averaging and its complex shape. Both tenting and deflating the bladder can cause the bladder wall to appear thicker than it is. The following four methods are used to outline the base of the prostate:

1. The Foley catheter balloon or contrast media is used to mark the inside wall of the bladder.
2. Sixty millilitres of radiopaque contrast (2:58 ml of Visipaq:NaCl 0.9%) are injected into the bladder.
3. A marker seed is placed at the base.
4. The cystoscopy findings are used to evaluate the shape of the bladder neck.

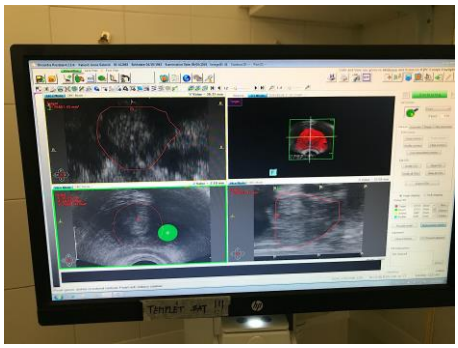

Figure 2 Contouring of CTV and organs at risk by physician.

After completion of the contouring process, the physicist employs the inverse planning process to find the optimal positioning of catheters or needles (Figure 3).

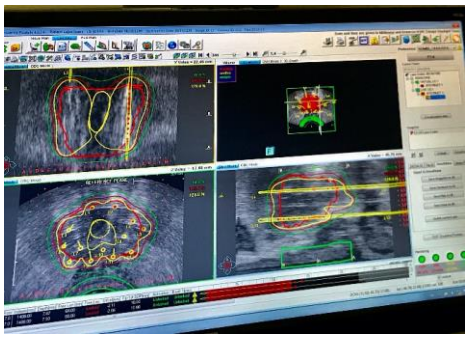

Figure 3 Use of inverse planning process to find the optimal positioning of catheters or needle.

After the physician finds the optimal needle position, the physician inserts each catheter transperineally either at the pre-marked entrance points, through preset template holes, or at the X and Y coordinates suggested by the inverse planning software. The two most anterior medial catheters are placed first, followed by the latero-posterior catheters. This enables monitoring for pubic arch interference and to correct the setup (i.e., to correct pelvis rotation) to avoid interference through the procedure. It also minimises the ultrasound shadow effects behind implanted needles. The two medial anterior catheters are more at risk of piercing the urethra and the bladder neck, so they must be guided with the greatest care under direct ultrasound image guidance. Use of the sagittal view enables visualisation of the tip of the catheters and correlates their positions with regard to the bladder wall. Using both sagittal and transverse views enables an adequate view of the catheter placement throughout the procedure. As more catheters are inserted, the locations of these catheters become less visible, so further adjustment is difficult.

The prostate might move due to the insertion of the needles, so the physician constantly checks the contours of the CTV and OARs to modify them if necessary.

Once the catheters are in the correct position, the guide template is sutured to the perineum. There are various ways that the guide templates fix the catheters. Some are friction based, other have patented locking devices. After a second look to ensure that all catheters are placed to the correct depth, the obturators are retracted and the needles are locked to the template guide.

The physicist then uses inverse planning to determine dwell positions and dwell times. Then the technician connects the transfer tubes to the correct needles (Figure 4).

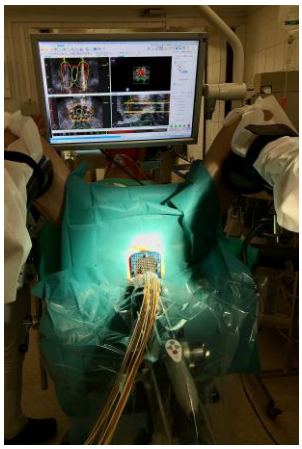

Figure 4: Connection of the transfer tubes to the correct needles

The dose constraints used during this procedure were:

Rectum: D2 cc ≤ 60%; D0.1 cc ≤ 80%.
Urethra: D10cc ≤ 115 %; D30cc ≤ 110 %.
CTV: V100 95%; V150 ≤ 50%; D90 110

Other parameters for reporting were:

Rectum: D0.01 cc, D1 cc, D10 and volume
Urethra: D0.01 cc, D0.1 cc and volume
CTV: V90, V200, D100, DHI, COIN and volume

To remove the implant, each catheter is slowly pulled to within 2cm of the skin, and then all catheters are removed at once. Once all the catheters are removed, pressure is applied to the implant site using gauze for a few minutes until the bleeding stops. Patients with epidural pain control in place do not generally need additional medication for pain control during removal. Gauze with topical antibiotic (bacitracin) is taped to the perineum until the patient is discharged.

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