DOSIMETRIC OPTIONS AND POSSIBILITIES OF PROSTATE LDR BRACHYTHERAPY WITH PERMANENT I-125 IMPLANTS

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Introduction

LDR prostate brachytherapy with permanent I-125 implants as monotherapy is the well-established option of treatment for low and intermediate risk prostate cancer. Few moments are very important in patient selection and application of this treatment:

• Accurate staging of prostate cancer including physical, clinical, laboratory examinations, and the modern diagnostic methods – US, MRT, CT.
• Visualization of the target and organs at risk, precise contouring and real time planning.
• Treatment efficiency dependence on the dose, and dosimetric options and possibilities, adaptive brachytherapy.
• Significance of different types of implants for the quality of implant and post implant dosimetry.
Prostate cancer diagnosis and radiological imaging

- PSA test, digital rectal examination (DRE), prostate biopsy morphology and radiological imaging techniques.
- DRE cannot accurately determine tumor site in respect of the prostate capsule (T), and pelvic lymph l / m condition (N).
- In case of tumor invasion through the prostate capsule, tumors are classified as high risk and prostate brachytherapy with permanent I-125 implants is completely inappropriate method in these cases.
- Modern radiological investigations allow the detection of prostate tumor location and the application of adaptive radiation therapy (dose escalation to the gross tumor volume).
Visualization of the target and organs at risk

• Modern LDR prostate brachytherapy is based on **transperineal implantation** (implantation of the needle applicators through the perineum), guided by **transperineal ultrasound**.

• Brachytherapy planning methods can be planning before the procedure - **preplanning** or planning during the procedure - **real time planning**.

• **Real-time** scheduling technique is **far superior**, because the correction of the contours during the implantation procedure is necessary to ensure the **quality of the implant**.
Visualization of the target and organs at risk

• Prostate **volume** determines the **quantity and activity** of I-125 implants required for the patient.
• Implant activity ranging from **0.3 to 0.5 mCi**.
• In LDR prostate brachytherapy with permanent I-125 implants the patient's prostate **should not exceed 60 cm³**.
• Before ordering implants, and before the procedure, it is recommended to **accurately measure the prostate volume using US**.
• In addition, it is appropriate to assess changes in prostate **tumor site with MRI and US**.
• These data gives the opportunity to **escalate the dose**, to the suspected neoplastic lesions - **adaptive brachytherapy**.
Visualization of the target and organs at risk, patient positioning

- Patient position and US applicator is in rectum
- We can see prostate in sagittal and transverse planes
Visualization of the target and organs at risk, contouring

- Calibration of coordinate system between US and integrated planing system (accuracy less than 1 mm)
- Contouring of the prostate and critical structures (urethra, rectum wall) - 5 mm step.
Visualization of the target and organs at risk, implantation

- Real time intraoperative planning
- Placement of the peripheral needles and loose seeds with MICK aplicator
- Recontouring and recalculation of plan
- Placement of internal needles and seeds
Visualization of the target and organs at risk, implanted seeds

- Sagittal US view of implanted seeds in the prostate
- 3D view of dose distribution and dose distribution in the planning system
Treatment efficiency dependence on the dose, and dosimetric options and possibilities

• According to ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer, dose distribution in the target (prostate) must be homogeneous.
  • $D_p 90$ (dose covering 90% of prostate volume) - 145 Gy.
  • $V_p 100$ (prostate volume, which receives a 100% of prescribed dose) - 95 – 100%.
  • $D_u 30$ (dose which receives 30 per cent. of urethra) ≤ 200 Gy.
  • $V_R 100$ (rectal volume, which receives a 100% of prescribed dose) ≤ 0.5 cm$^3$.
• These are the main parameters of the prostate brachytherapy with permanent I-125 implants which describes the quality of implantation.
Dose parameters of intraoperative dosimetry

- Dose prescription to the delineated target volume – 145 Gy
- Urethra – D 30 should not be over 200 Gy
- Rectum V 100 should not be over 0.5 cc
- Dose coverage of target volume should be over 95%

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<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Dose to delineated target volume</td>
<td>145 Gy</td>
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<tr>
<td>Urethra D 30</td>
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**Dose Information**

**Prostate:**
- Total Volume: 28.09 cc
- V200: 8.29 cc [29.48%]
- V150: 18.74 cc [68.72%]
- V100: 27.23 cc [98.94%]
- D90: 175.99 Gy [121.37%]

**Urethra:**
- Total Volume: 1.03 cc
- D30: 202.91 Gy [139.94%]

**Rectum:**
- Total Volume: 7.36 cc
- V100: 0.04 cc [6.84%]
Treatment efficiency dependence on the dose, and dosimetric options and possibilities

Studies, which investigates efficiency of brachytherapy depending on the dose ($D_{p\ 90}$):

• Stock R.G. et al. (Mount Sinai research group) were among the first in 1998 published 4 years results of biochemical relapse-free survival (BRFS). In this study, found that **BRFS when $D_{p\ 90}<140$ Gy is 68% and when the $D_{p\ 90}>140$ – 92%**. This study also found that increasing the dose resulted in better results in poor and moderate-risk prostate cancer patients and patients with good forecasts had little effect.

• In 2007 Muont Sinai group of researchers published a multicenter study. In this study, patients were divided according to the dose $D_{p\ 90}$: <140 Gy, 140-200 Gy and more than 200 Gy.

• This study showed that **brachytherapy dose escalation had benefit for all patients, even if the patient belongs to the good prognosis group.**
Treatment efficiency dependence on the dose, and dosimetric options and possibilities

- The review from Alfredo Polo et al. accentuates the significance of dose escalation using modern radiological investigations for radiotherapy planning:

- “Dose painting was the term coined by Ling et al., in their review of image-guided radiotherapy. The idea was to visualize significant tumor subvolumes and to paint some additional dose onto that volume. Permanent seed implantation is an ideal scenario for dose painting using functional imaging. Future developments using functional ultrasound (power doppler imaging, elastography) could bring functional imaging into the operating room”
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- In 2010 in VUOI clinical study was initialized: “Adaptive prostate cancer treatment with I-125 implants, safety and efficacy study”.
- Adaptive therapy treatment is an opportunity to increase (escalate) dose, to the suspected neoplastic lesions, visualized with radiological methods.
- Adaptive RT is often used in EBRT techniques (IMRT, IGRT) using individualized adaptive dosimetry planning. There is little evidence about adaptive dose escalation in prostate BT using I-125 implants. Dose escalation in visualized tumor should improve the effectiveness of the brachytherapy, as well as it is in external beam radiation therapy.
- Adaptive prostate BT with I-125 implants is not a standard method of treatment, but this is technically feasible and could have future perspectives. This study is in initial phase now, and we should wait primary results for some time.
Significance of different types of implantation methods for the quality of implantation

- **Two main methods** of radioactive I-125 implants are available: Implantation of **loose prostate seeds**.
- Implantation of implants, which are connected to each other – **stranded sources**. Stranded sources have an equal distance between each other.

Implantation with **loose seeds allows great flexibility** in selection of source position in the prostate so we can achieve **good dose distribution**, which means **quality implant**.

However, **migration of loose sources are more often** (0,7-55 per cent) in comparison with **stranded seeds**.

**Majority of literature sources shows better clinical outcome after brachytherapy with loose seeds in comparison with seed strands.**
Post-implant dosimetry

The **most necessary** procedure after seed implantation is post-implant dosimetry.

- Usually performed **4 weeks after implantation** (when prostate edema is gone and implants are entrenched in the prostate).
- Post-implant dosimetry is made on the basis of CT or MRI data. **Dose distributions seem to differ from the planned ones** due to errors in needle localisation, errors in seed delivery, prostate deformation between needle insertion and retraction, individual edema resolution dynamics, seed migration.
- Usually, **decline of dose coverage** (Dp 90, Vp100) between intraoperative planning and post implant dosimetry is observed. Series of articles from reliable literature sources declares that **decline of dose coverage** between intraoperative planning and post implant dosimetry was **significantly larger for the stranded seed implants**.
Post-implant dosimetry

Fusion and delineation of intraoperative US and post implant CT (4-6 weeks procedure) – post-implant dosimetry
Post-implant dosimetry

Comparison between intraoperative and post-implant dosimetry

We observe increasing of $D_p 90$ for prostate and decreasing of $V_p 100$ for rectum in post-implant dosimetry.
The advantages of loose seeds (better clinical outcome and lower decline of dose coverage between intraoperative planning and post implant dosimetry) and stranded seeds (less migration) could be used by applying new implantation method, that is developing over recent years.

This method is based on seed connection with different intervals (1 cm, 0.5 cm, seed to seed). In this case, loose seeds is linked with special different interval connectors. Linking is done with special link machines.

For now there is a single study, which shows the advantage in implant quality of linked loose seeds over loose seeds. This is a novel methodic which could have a good future perspectives. However, it should pass the test of time to prove its advantage over loose seeds.
Discussion and conclusions

In this article we tried to overview, what could we do to improve prostate brachytherapy with permanent I-125 implants? In conclusion we must highlight some messages, what could this article could give:

• **We should explore all modern radiological techniques** in order to accurately determine the risk group of prostate cancer patient and **to choose the most appropriate treatment option**.

• **We should keep searching the optimal dosimetric options** in permanent prostate brachytherapy with I-125 implants.

• **Adaptive brachytherapy** with permanent I-125 implants, **could be one of the dose escalation methods**. However, we must wait for first results of this technique.
Discussion and conclusions

• **Post implant dosimetry** shows us most objective irradiation doses, therefore it is necessary after each implantation.

• **Loose seeds implantation technique** have an advantage over stranded seeds.

• **Implantation technique with seeds connected with spacers having different lengths** is a progressive and novel method but it should pass the test of time to prove its advantage over loose seeds.
THANK YOU !!!