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PERMANENT ^{125}I PROSTATE IMPLANTS : IMPORTANT DOSIMETRICAL CLINICAL PARAMETERS (A CASE STUDY)

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Abstract. The study report the results of 45 prostate cancer (T1 and T2 stages) treated during the last trimester of 2009 by using ^{125}I implants, with special reference to the dosimetric parameters in pre-planning and during online planning evaluation. To reach the treatment dose of target volume of 145 Gy, an average number of 46,9 radioactive seeds loaded in 10 to 30 needles were used. Consequently, the corresponding numerical values of eight dosimetric clinic parameters, *i.e* D_{90}, V_{100}, V_{200} for prostate volume, V_{150}, D_{10}, D_{30} for the prostate urethra and D_2, D_1 for rectal mucosa and rectum are presented and discussed with respect to different protocols currently used in clinical practice. At the same time, both conformal and homogeneity indexes showed were used to illustrate at which degree the implant geometry is influenced by the prostate tumours.

Key words: Prostate cancer, ^{125}I permanent implant, Dosimetric parameters, Quality control.

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1. INTRODUCTION

Prostate cancer is a disease of ageing men with an unknown aetiology and whose incidence rises up to 30 to 40 % in men over 80 years [1]. One of the best treatment consists of permanently implanting minute radioactive sources in prostate, ^{125}I due to its relatively short half-life of around 59 days as well to the low gamma

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ray energy of 35 keV emitted by the daughter ^{125}Tc represents an ideal radionuclide for prostate treatment [2]. Beginning with the first implant performed in 1983 [3], different medical institution have elaborated various protocols and guidelines for a good practice of this method. At present time, the advances in the ultrasound technology and development of new screening methods based on evidence of the prostate specific antigen (PSA) in sanguine serum allow an early diagnosis of prostate cancer. Based on pre-planning, post-planning and biochemical evaluation results, these recommendations described the applicable and evaluation criteria of ^{125}I implants in prostates cancer treatments.

In Romania, this type of treatment was use for the first time in 2006 at the Oncology Institute in Bucharest and later in Fundeni Clinical Institute in Bucharest and Parhon Clinical Hospital in Iasi [4].

By taking into account the accumulated expertise at the Oncology Institute,in this study we presented preliminary data of clinical dosimetry parameters of preplanning treatment of prostates cancer by using the ^{125}I implants.

2. MATERIALS AND METHODS

To be more representative in patients selection, we have used both European ESTRO/EAU/EORTC [5, 6] and American ABS [7, 8] recommendations regarding the including as well as the excluding criteria for ^{125}I implant treatments. Consequently, as including criteria we have considered: i.- confirmation of the prostates adenoma diagnosis in T1 - T2 stadium, ii. - PSA factor less than 10 ng/ml, iii. - Gleason score less than 7, and iv. - no transurethral resection of the prostate (TURP) performed in the last 6 months. The exclusion criteria were: i. - metastasis or locally advanced cancer, ii. - a prostate volume less than 70 cm^3, iii. - contraindication for generally anaesthesia, and iv. - recent TURP procedure performed [5, 9, 10].

According to these criteria, for our study we have selected a group of 45 patients aged between 49 and 75 years and treated with permanent ^{125}I implants for a period of three month, *i.e.* between October and December 2009. In the case of patients whose PSA was up to 20 ng/ml the ^{125}I brachytherapy alone was applied.

The Gleason score values of investigated patients varied from 6 to 7. The patients with Gleason score equal to 7 was deeply investigated because at this score there is an approximately 50% probability of biochemical relapse within five years [5].

For all prostate implants we have used the Prostate Seeds Implant Dosimetry (PSID) treatment planning produced by IBt Bebig [11]. Consequently, all reported values in this paper were calculated by means of this treatment planing.

As a rule, the target volume was defined in accordance with the ICRU Report

58 [12]. The working protocol was performed in conformity with the RTOG 98-05 [10] guideline while the dosimetric prerequisites conditions were based upon the American Association of Physicists in Medicine (AAPM) TG 40 [13], TG 64 [14] and TG 43 [15, 16] reports.

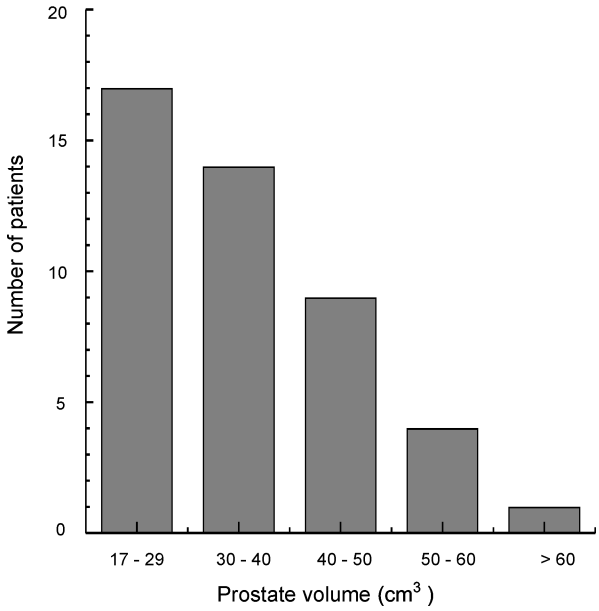

Fig. 1 – Distribution of the prostate volume vs. number of patients.

On average, each patient received 46,9 radioactive source by using 10 to 30 needles so that to reach at the Planing Target Volume (PTV) a dose of 145 Gy, [1, 5, 16], which, according to the new TG43 guidelines, represents the minimum peripheral dose to the margin of the target volume specified. At the same time, the dose in the centre of the volume which always is higher, should be kept up to 150 % or less than the prescribed one [1]. In these conditions, the total activity implanted had an average value of 1184,2 MBq with a minimum of 780,0 MBq and a maximum one of 1700,6 MBq [4] in direct correlation with prostate volume and anatomical structure of the patients.

3. RESULTS AND DISCUSSION

The prostate surrounds the urethra from bladder base to its apex, near the external sphincter. The prostate volumes of the investigated patients varied between 17,3 and 68,2 cm^3 with an average value of 35,2 cm^3 [17] while normal volume is estimated to be between 20 to 30 cm^3 [1] (Fig. 1). Consequently, only 17 patients have

a prostate volume in normal limits, while for the other 28 patients the prostate was higher than the average, but only 14 of them have confirmed the prostate adenoma.

Table 1.

The values of the main prostate clinical dosimetric parameters together with the recommended values by [5, 6, 8, 10, 15, 16]. (CTV- clinical target volume)

Parameter	Value			
	Min	Max	Average	Recomended
D_{min} (Gy)	91.0	157.0	130.1	no data
D_{90} (Gy)	166.3	218.6	188.1	D_{90} >145 Gy
V_{100} (%)	96.1	100.0	99.3	V_{100} >95 % of CTV
V_{150} (%)	58.0	95.4	73.7	V_{150} <50 % of CTV
V_{200} (%)	22.3	75.4	38.0	as low as possible

As a rule, the implantation method is indicated for the prostate volume less than 60 cm^3 since larger volumes are associated with a higher risk of side effects [10]. In the last case, before brachytherapy, a three month hormonal treatment for downsizing prostate volume with about 30% was applied [18].

For a correct and comprehensive evaluation of the doses delivered to patients, we have used in this study the following parameters [19]: D_{90} - minimum dose received by 90% of prostate volume, V_{100} - percent of prostate volume receiving 100% of prescribed radiation dose, V_{150} and V_{200} - percent of prostate volume receiving 150% and 200% of prescribed radiation dose whose numerical values are reproduced in Table 1.

According to these data, we have found that D_{90}, in the day of implant, has an average value of 188.1 Gy, in perfect perfectly concordance with the ref. [20] which recommends a value greater than 180 Gy. A good score we have also noticed in the case of V_{100} which,according to [21] should be at least 95%, and, in our case was systematically greater then 91.0 %, with an average value of 99,3 %. In the case of V_{150} parameter, we have systemically noticed values higher then recommended 50%. The V_{200} - the High Dose volume varied between 22.3 and 75.4 % with an average value of 38 %, fact explainable by the patient anatomy and the placement of prostate under the pubic arch, who limited the incidence angle of needle insertions.

Excepting the V_{150}, the numerical values of all the other parameters were in good concordance with recommended values as well as with those reported in literature [5, 6].

In the case of prostate brachitherapy, a correct estimation of dosimetric parameters for neighbouring organs at risk,*i.e.* prostate urethra and rectum is of maximum importance. For this reason, we have calculated the numerical values of the following parameters: D_{10} - dose that covers 10 of the prostatic urethra volume, D_{30} - dose that covers 30 % of the prostatic urethra volume, D_1 - dose that covers 1 % of the

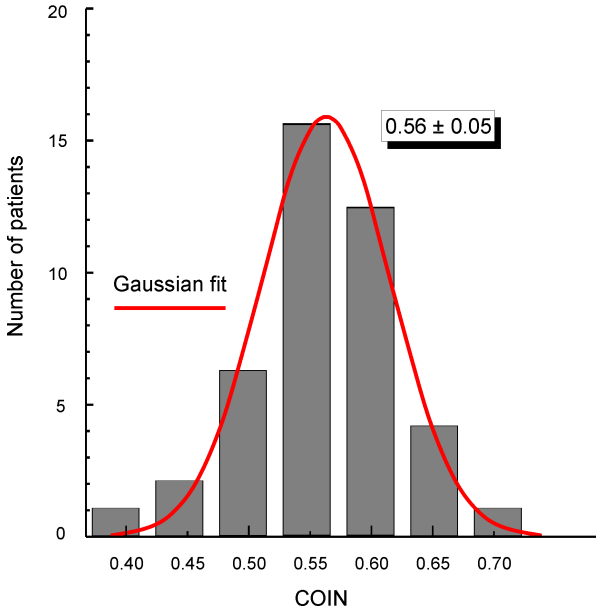

Fig. 2 – The experimental (columns) and computed (continuous line) distribution function of the conformal index-COIN.

mucosis of rectum volume, D_2 - dose that covers 2 % of the rectum volume and D_{max}- the maximum dose received by prostatic urethra and whose numerical values are illustrated in Table 2.

As the maximum dose of the prostate volume is not clearly established, for clinical cases there are generally accepted a global dose less than 360 Gy for all length of prostate urethra. Additionally, for the security reason D_{10} must be allowed up to 150 % (maximum D_{10} >217 Gy). In 13 case, we have found an average value of 211.1 Gy with a maximum value of 246.2 Gy, determining a light obstruction of urethra, resolved by installation of a Foley balloon.

The average values of V_{150} for the prostate urethra was around 10,1 %. Regarding this value, it should be mentioned that due to an asymmetric positioning of the urethra with respect to the prostate middle axis, the V_{150} of urethra and prostate could not be correlated.

For the prostate urethra, D_{30}, the secondary dosimetric parameter, was found to be less than 130 % of the prescription dose of 145 Gy for 55 % of patients but no greater than 200 Gy in the case of the other ones.

For rectum, the primary dosimetric parameter D_2 was smaller then 145 Gy with an average value of 131,9 Gy. The maximal value, 180,3 Gy is linked to the patients morphology and to the superficial preparation ahead the implant operation. The D_{max}, the secondary dosimetric parameter for rectum would desired to be less

Table 2.

The values of the main clinical dosimetric parameters at the organs at risk with respect to recommended values by [5, 6, 10].

Organ	Value			
Parameter	Min	Max	Average	Recommended
Urethra				–
Volume (cm^3)	1.3	37.2	3.5	
D_{10} (Gy)	181.6	264.2	211.1	217.0
D_{30} (Gy)	167.1	254.9	199.6	190.0
V_{150} (%)	0.0	73.6	10.1	15.0
Rectum mucosis				
Volume (cm^3)	0.5	3.7	1.7	
D_1 (Gy)	34.4	167.1	109.2	145.0
Rectum				
Volume (cm^3)	5.1	16.5	8.8	
D_2 (Gy)	51.1	180.3	131.9	145.0

than 200 Gy. It is recommended in common with the other published guidelines that the dose to a very small limited volume (0.1 cm^2) is more appropriate for dose calculation clinical relevance than a maximal dose value [6].

The overall quality of implants were estimated by means of two indexes: conformal and respective homogeneity ones.

The conformal index (COIN), which describes the normal tissue irradiation with respect to target coverage, is defined in the equation 1.

$$\text{COIN} = c_1 c_2, \tag{1}$$

where c_1 represents the PTV fraction which receives the reference dose D_{ref} of 145 Gy and illustrate how accurately the PTV is covered by reference dose (in the ideal situation,c_1 is equal to 1); c_2 represents the ratio between the reference tumor volume V_{ref} and the PTV and illustrates also at which extent the health tissue outside tumor is covered by the reference dose D_{ref}. (Ideally, the c_2 should be equal to 1 [19]).

By analysing the distribution function of COIN index, reproduced in Fig. 2 it results that, in spite of a relative reduced number of patients, the function is very well described by a Gaussian distribution, with a maximum of 0.56 and a half-width of 0.05, as a result of uncertainties in source placement in the prostate.

The next index we have used to characterize the quality of brachytherapy treatment was the homogeneity index HI which illustrate the fraction of target tumor which receives a dose between 100 % and 150 % of the reference dose, in concordance with the eq.:

$$\text{HI} = \frac{V_{100} - V_{150}}{V_{100}} \tag{2}$$

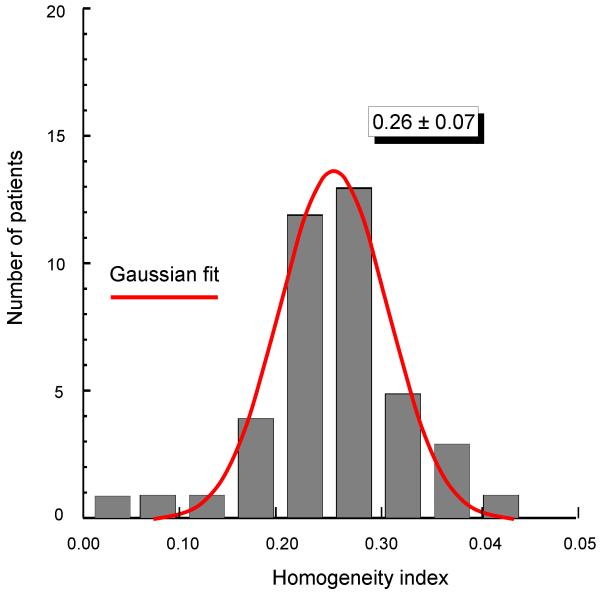

Fig. 3 – The experimental (columns) and computed (continuous line) distribution function of homogeneity index.

As in the previous case, the homogeneity index HI shows also a Gaussian distribution, with a maximum of 0.26 and a half-width of 0.07, explained by the peculiarities of implant geometry, implanted sources being distributed mainly at prostate periphery as well as by the prostate deformation induced by tumours (see Fig. 3).

4. CONCLUSION

The treatment planing of 45 patients with T1 and T2 prostate cancer by permanent ^{125}I implants were analysed and discussed with respect to eight dosimetric clinic parameters, *i.e* D_{90}, V_{100}, V_{200} for prostate volume, V_{150}, D_{10}, D_{30} for the prostate urethra and D_2, D_1 for rectal mucosa and rectum. These parameters were chosen as they offer improvements of quality radioactive source implant and evaluation protocols.

By using a the Prostate Seeds Implant Dosimetry treatment planning it was possible to calculate the numerical values of above mentioned parameters and to compare them with recommended values by ESTRO / EAU / EORTC protocol, currently used in clinical practice. Excepting the D_{30}, all other parameters calculated by us were in good concordance with the ESTRO / EAU / EORTC protocol.

Another two parameters, conformal (COIN) and homogeneity (HI) indexes showed, in spite of reduced number of patients, well defined Gaussian distribution,

whose maximum as well as half-width values show at which degree the implant geometry is influenced by the prostate deformation induced by tumours.

LIST OF ABBREVIATIONS

GEC - Groupe Europen de Curiethrapie
ESTRO -European Society for Therapeutic Radiology and Oncology
EAU -European Association of Urology
EORTC -European Organisation for Research and Treatment of Cancer
ABS - American Brachytherapy Society
ICRU - International Commission on Radiation Units and Measurements
RTOG -Radiation Therapy Oncology Group

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