Master of Science Thesis

Evaluation of automatic treatment planning using iterative method, for permanent seed implantation of the prostate

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Abstract

Purpose: The aim of this study was to investigate if the inverse planning available in the dedicated planning program VariSeed 7.1, can generate plans of equal quality to plans generated through manual planning.

Materials and Methods: In this study the dedicated permanent seed implantation planning system VariSeed 7.1. (Varian, Paolo Alto California) was used for inverse planning, using a dose-volumehistogram based optimization algorithm. Seven patients with different prostate sizes and shapes were randomly selected amongst those patients that had already gone through the implantation. For each of these patients six sets of dose volumetric requirements with different weight factors and placement restrictions were investigated. The tests were organized so to shift priority from good prostate dose coverage at the first tests to sparing the organs at risk. Decreasing the dose to the organs at risk was achieved by increasing the weight factors to the organs at risk or prohibiting seed placement close to them. The dose-volumetric criteria for a good dose plan are as follows: Prostate V100 > 96%, Prostate V150 < 65%, Urethra D30 < 150% and finally V69 < 3 cm^3 for the rectum. The algorithm was confined to use Rigid Absorbable Permanent Implant Device (RAPID) strands with no loose seeds; the algorithm was also restricted from placing seeds in the middle of the prostate. The calculation time and number of needles allowed was set high so that these conditions did not affect the planning results negatively, they where set to 200 seconds and 40 needles respectively.

Results: The results from the tests show that the algorithm generates acceptable dose coverage for large prostates when priority is put mainly upon achieving acceptable dose coverage of the target and little priority is put on the organs at risk. The target dose coverage decreases with decreasing prostate size. Acceptable dose coverage of the target was achieved for all prostate sizes when an extra 3 mm placement area around the prostate was added. The rectum and the urethra both received acceptable doses throughout all the tests. However, the dose received by the urethra was lower when using the manual planning method. The seed geometry produced by the optimization algorithm was very randomized and clustered. The clustering of the seeds generated few large high dose volumes, compared to several small high dose volumes generated with the manual planning. The treatment margins around the target were also too thin for the automatic planes.

Conclusion: From a dose-volumetric point of view the inverse planning method can generate plans with acceptable dose coverage for both the target and the organs at risk. However in the presented study, the urethra received a lower dose using the plans generated manually with the peripheral loading method, than with the automatic optimized plans. Shifting dose coverage priority to minimize the urethra dose means compromising target dose coverage. The seed geometry put forward by the algorithm is randomized and clustered compared to the manual peripheral loading. Thus the algorithm generates large high dose volumes compared to the manual peripheral loading were several smaller high dose volumes are created.

1. Introduction

Prostate cancer is the most common form of male cancer. It stood for about a 35.3% of all cancer incidences in Sweden 2003 which becomes 9035 cases [1].

There are several treatment modalities for the prostate cancer, hormone therapy, radical prostatectomy (surgical removal of the prostate), external beam radiotherapy and brachytherapy. The word brachy is Greek and means near, and having a short distance from the radioactive source to the prostate is just what is strived after in brachytherapy. This is achieved with a method where radioactive sources are placed within the prostate, so they can radiate the cancer cells from within the prostate.

In brachytherapy a high dose can be given to the target without giving too much dose to the surrounding healthy tissue, due to the high dose gradients. It is an old idea to place radioactive sources in the prostate. Originally it was performed by hand in open surgery, where the surgeon placed the sources by hand with only the touch of his hand to verify the placements of the seeds. This frequently led to areas of significant underdosage or overdosage [2]. Recently the technology has advanced so far that one can do more accurate dose plans, using dose calculating software combined with transrectal ultrasound imaging.

There are mainly two forms for brachytherapy of the prostate: High Dose Rate, temporary implant brachytherapy, HDR, and Low Dose Rate, permanent implant brachytherapy, LDR. The differences between the two methods are that with HDR-needles, in which a highdoserate source is inserted, are placed within the prostate. This source can be stopped at different locations for an adjustable length of time, and afterwards the source is removed. LDR brachytherapy involves placing several small sources, seeds, throughout the prostate. Depending on the size of the organ and the activity of the seeds 40-90 seeds are used; radionuclide ^{125}I or ^{103}P. These sources are left there permanently so they can irradiate the cancer cells under a longer time period. The more tested of the two methods is the implantation of permanent seeds.

This work will apply to the permanent implantation of ^{125}I seeds, fixed in a Rigid Absorbable Permanent Implant Device (Rapid) strand. The work contains an evaluation of the inverse optimization algorithm associated with the Varian produced dedicated treatment planning software VariSeed 7.1. (Varian, Paolo Alto California). The dose calculation formalism for permanent seed implantation and theory regarding inverse optimization processes will be presented in this work. This work will also present a brief introduction to the treatment planning process and seed implantation. Inverse planning with optimization algorithms are mathematical processes where the treatment planning software automatically calculates seed configurations for implantation. The optimization process utilizes user defined weighted dose volumetric requirements and restrictions on the target volume and the organs at risk to optimize the treatment plan.

If the treatment plans generated by the inverse optimization algorithm used in VariSeed 7.1. are of equal or greater quality to those generated manually the planning time could be minimized. Reduction of planning time is most beneficial in intra operative planning, where a reduction in planning time would result in reduced sedation time for the patient and reduced time needed in the operation room.

1.2 ^{125}I Seed implantation

1.2.1 Volume studies and treatment planning

When performing an implantation a preoperative volume study can initially be performed. The volume study is used to make a pre-operative plan, to get a good assessment of the number of seeds needed for the implantation. The first step in a preoperative volume study is to position the patient like he would be during the real implantation. Then a transrectal ultrasound (TRUS) probe is inserted into the patient. With this probe a series of transversal pictures of the prostate is taken with a separation of 5 mm, beginning with the base plane. The pictures are saved on the treatment planning computer. Afterwards the physician contours the anatomy on the picture series, which defines the structures in the program. There are three organs that have to be contoured: the prostate (target volume), the urethra and the rectum (the organs at risk). The pubic arch is also contoured in order to avoid it when the needles are inserted. The coordinate system of the needle insertion template is superimposed in the planning program. This template is placed upon the TRUS so the physician has a positioning coordinate system outside the patient correlated with the coordinates in the planning program and the internal structures in the patient.

Once the organs are contoured, the physicist can begin to generate a plan for the patient. The treatment planer can place seeds in the planning program at the predefined template coordinates. There are three main approaches when planning the placement of the seeds uniform loading, peripheral loading and the modified peripheral loading method. In the modified peripheral loading method the treatment planner places the seeds in the periphery of the prostate and some complimentary seeds in the middle portion of the prostate. When placing the seeds with this method the dose to the urethra can be minimized, and central hotspots can be avoided.

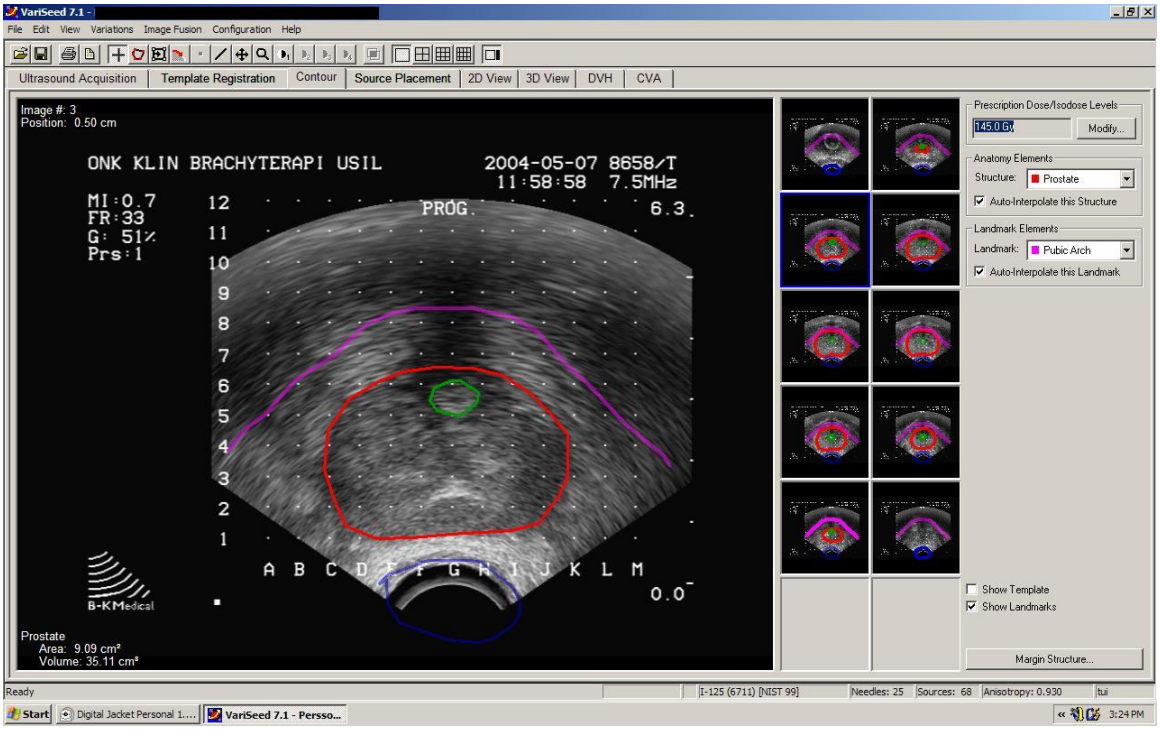


Fig 1.1: *Screen dump from contouring the prostate, rectum, urethra and pubic arch using VariSeed 7.1.*

The intraoperative planning is performed much in the same way as in the preoperative planning; the difference is that the medical physicist has to create the dose plan in the operation room with the patient sedated. When imaging the prostate with the TRUS, the probe is placed parallel to the urethra with the urethra in the middle column of the template, so it can be more easily avoided by the needles. The probe must be placed so that it does not deform the prostate. Finally the probe is placed so that the dorsal edge of the prostate coincides with the bottom row of the template. There are several advantages with the intraoperative planning method compared with the preoperative planning, first the reconstruction of the patients position does not have to be as exact, the prostate size can change from the time of the volume study (it can grow with time or it can shrink from hormone therapy) and finally the anesthesia may also relax the pelvic musculature thus changing the prostate shape [3]. However, when performing the intraoperative plan the physicist has to do all the calculations in the operating room, this in turn can increase sedation time for the patient and time needed in the operating room.

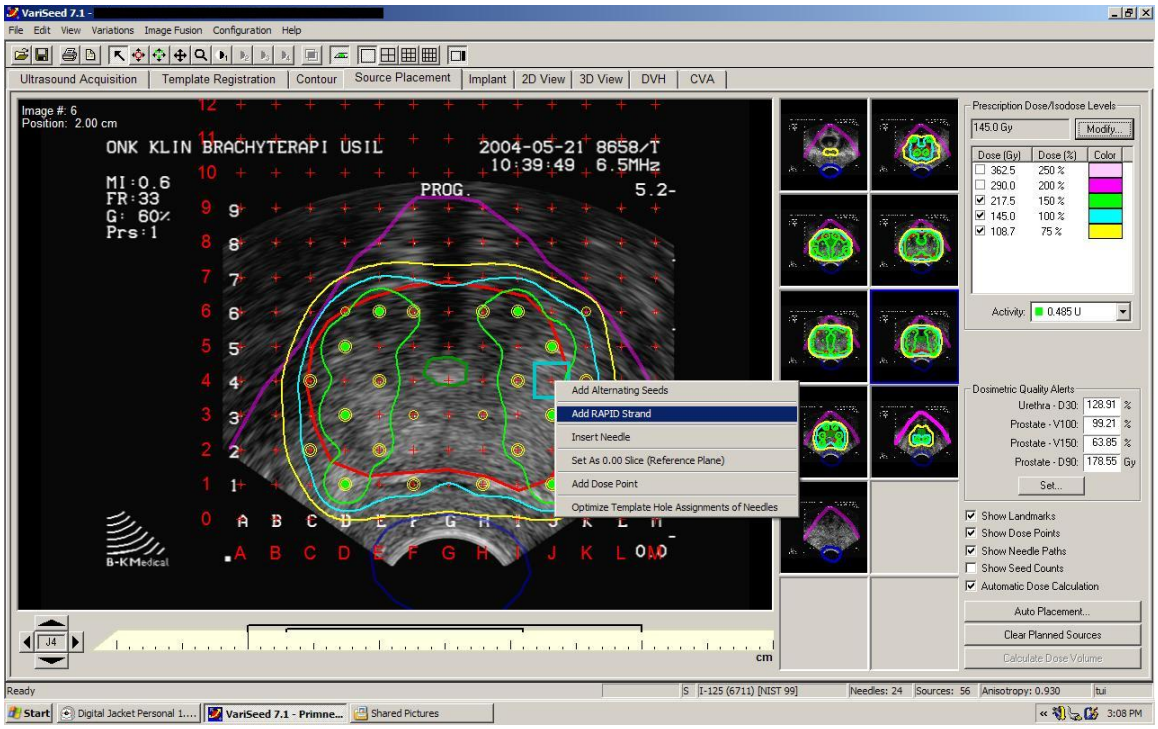


Fig 1.2: *Screen dump from planning the placement of Rapid strands using VariSeed7.1.*

1.2.2 Template guided needle insertion

When loading the needles the tip is filled with bone wax (or molten Anusol suppositories) so that the seeds will stay in the needle, this plug will be approximately 3 mm long. Then the rapid strands are cut according to the loading plan in groups of 2, 3, 4 or 5 sometimes single seeds can be used, but it is avoided (one rapid strand contain 10 seeds). When the needles are loaded they are placed in a shielded cooled box, this cooled box has the same coordinates as the template. The reason for cooling down the needles is that when the needles are placed in the prostate the wax starts to melt. If the wax melts body fluids can travel up in the needle and make the rapid strands swollen. In that case the seeds will be jammed in the needle.

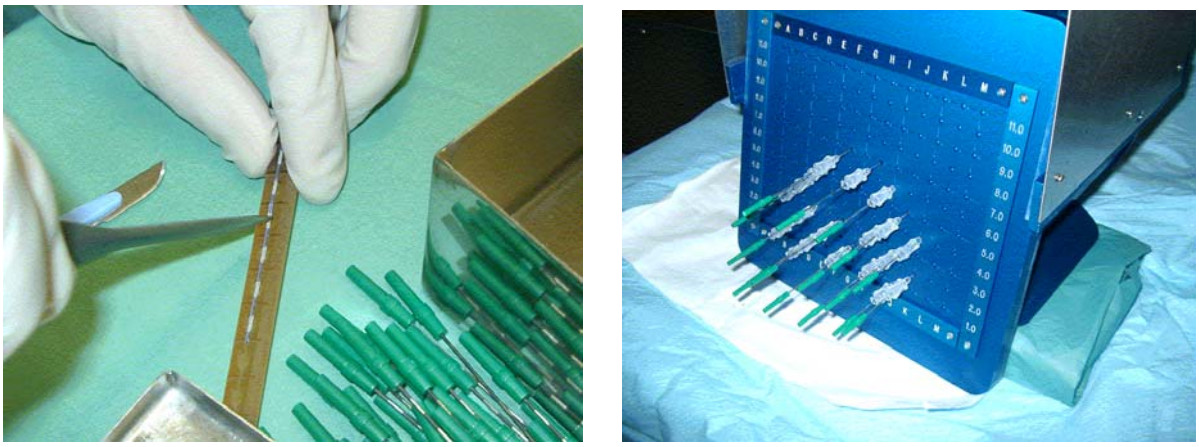


Fig 1.3: *Cutting of the RAPID strands to be placed in the insertion needles (left). Positioning the needles in the cooled shielded box at the corresponding template coordinates (right).*

The physician uses various types of equipments to establish the needle position when implanting the seeds. First, the physician uses the TRUS used during the planning, there he can se if the needle is in the same location in the prostate as on the template (the needle can bend off its track). The physician can feel his way through as well, the resistance for the needle insertion is greater in the prostate. At this moment the physician can also try to dislocate the needle a little bit from its template coordinates. This would be advantageous if it would improve the dose coverage to have a seed in-between two template coordinates. A third way to verify the seed location is by use of X-ray fluoroscopic equipment. With these pictures it is easier to see how far into the prostate the seeds have come relative the base plane of the prostate.

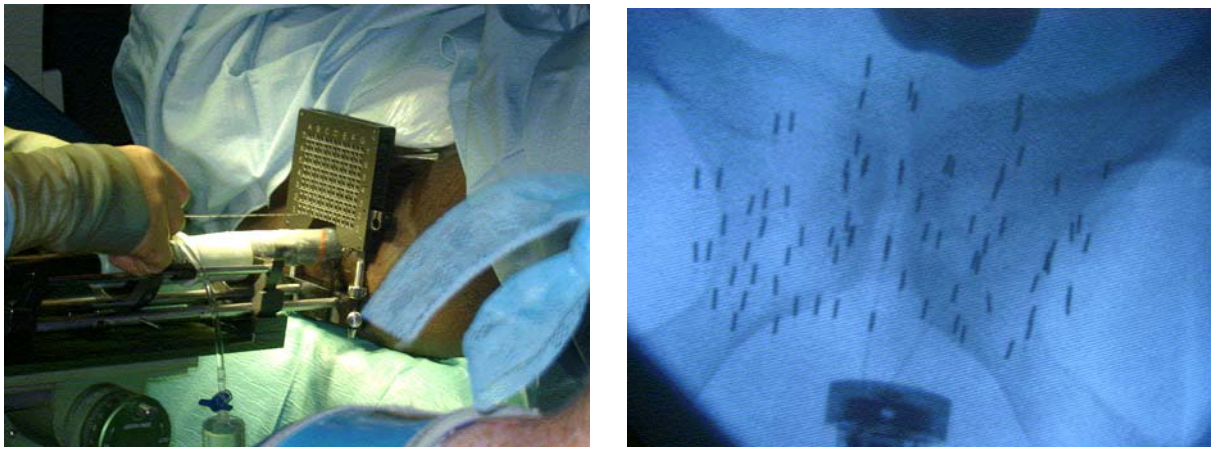


Fig 1.4: *Needle insertion into prostate using needle guiding template (left). Verification picture for seed positions in prostate, using X-ray fluoroscopic picture (right).*

Uncertainties in seed positioning during implantation include, needle dislocation, prostate deformation and swelling. The problem of needle dislocation occurs when the insertion needle bends slightly inadvertently from its template coordinates in the prostate. When inserting the needles in the prostate, the prostate gets deformed. When the seeds have been placed, the needle is retracted and the prostate returns to its original shape, thus moving the seeds a little bit. The movement of the prostate is minimized by the use of stabilization needles however they can not keep the prostate completely fixated. The prostate can also swell during the implantation thus the seeds placed at the end of the implantation may be dislocated when the swelling subsides.

During the insertion of the seeds the physicist updates the doseplan interactively for the actual positions of the seeds. When performing the interactive planning the physicist uses the dose calculating program which is connected to the TRUS. The ultrasound image appears in the program with all the planned seeds. Thus when the actual seeds appear in the picture, the physicist corrects the location of the original planed seeds to the actual location. With this tool one can see if there appears any “cold spots” i.e. areas with insufficient dose coverage appears due to seed dislocation. As this is performed during the implantation, complimentary seeds may also be inserted to cover these “cold spots”.

1.2.3 Post implant dosimetry

Several centers perform a CT and/or MRI-based dosimetric study at 4-6 weeks following therapy in order to verify the quality of the implant performed [4, 5]. The actual positions of the seeds are determined, and the dose to the prostate and organs at risk are calculated. At our department at Universitets sjukhuset i Lund (Usil) the verification of the quality of the implant starts immediately after the implantation with verification images, where a new series of transverse TRUS images with the seeds in the prostate without any needles is taken. Then the ultrasound probe is removed and an X-ray picture is taken of the prostate.

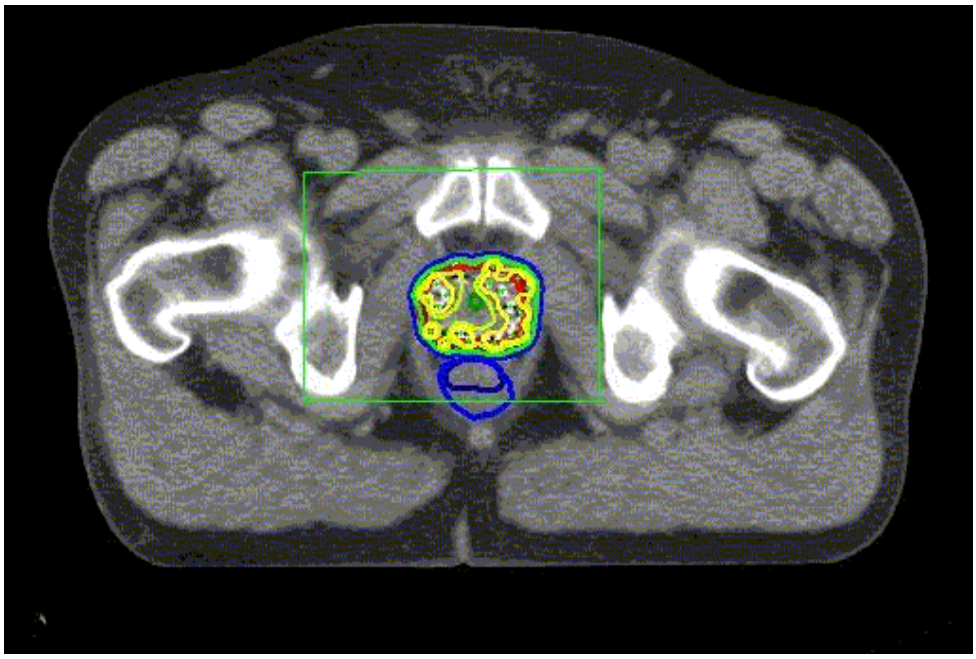


Fig 1.5: *Screen dump of CT scan from post dosimetry using Vari Seed 7.1.*

2. Materials and Methods

2.1 Dose Calculations

2.1.1 Sources

For implantation at our department the Rigid Absorbable Permanent Implant Device (RAPID) strand was used. These consist of a series of ten ^{125}I seeds (Amersham Health model 6711) connected at a fixed spacing of 10 mm by an absorbable suture. The advantage of having the seeds fixed in a strand is that it decreases the seed migration and increases the precision of the seed spacing.

^{125}I is produced by nuclear reactors. ^{125}I decays via electron capture with five different photon energies according to table 3.1 [6].

Table 2.1: *Number of emitted photons and energies per ^{125}I disintegration.*

Photon energy [keV]	Photons per disintegration
27.202	0.406
27.472	0.757
30.98	0.202
31.71	0.0439
35.492	0.0668

The weighted mean energy is 28.37 keV, with 1.476 emitted photons per disintegration.

The seed is constructed so that the ^{125}I is deposited upon the surface of a silver rod encapsulated by a titanium capsule, according to fig 2.1. The silver rod also acts as a radiographic marker which emits characteristic x-rays from photoelectric interaction with the photons emitted by the ^{125}I, the energies of these photons are 22.1 keV (0.15 photons per disintegration) and 25.5 keV (0.04 photons per disintegration). Low energy electrons are also emitted but these are all absorbed in the titanium capsule.

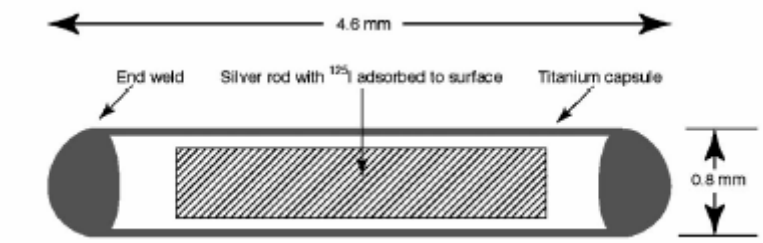


Fig 2.1: *Cross section of Amersham Health Seed model 6711, [5].*

The half value layer in lead for the photons emitted by these ^{125}I seeds is 0.025 mm, and radiation protection of personnel is not such a big problem for these low energy photons. The self absorption of the radiation is approximately 37.5 %, and the apparent activity is approximately 1.6 times the contained activity. The half life of ^{125}I is 59.4 days, thus 90 % of the dose is delivered within 197 days.

2.1.2 Dose calculation formalism

Generally the dose calculation formalism for permanent radioactive seed implantation is based on the AAPM TG-43 report [6], which gives detailed instructions on how to calculate the dose distribution around the seeds.

In the AAPM TG-43 there are two types of dose calculation formalisms, the 2D (cylindrically symmetric line source) and the 1D (point source) formalisms. The form used in this work is the 2D formalism.

The general equation describes the dose rate, $\dot{D}(r,\theta)$, at different distances, r, from the center of the source, and at different angels θ between the source longitudinal axis and the point of interest:

$$\dot{D}(r,\theta) = S_K \cdot \Lambda \cdot \frac{G_L(r,\theta)}{G_L(r_0,\theta_0)} \cdot g_L(r) \cdot F(r,\theta)$$

Here, r_0 denotes the reference distance, which is specified to 1 cm. The reference angle θ_0 defines the source transverse plane i.e. 90° or π/2. The reference point for the source is denoted $P(r_0,\theta_0)$.

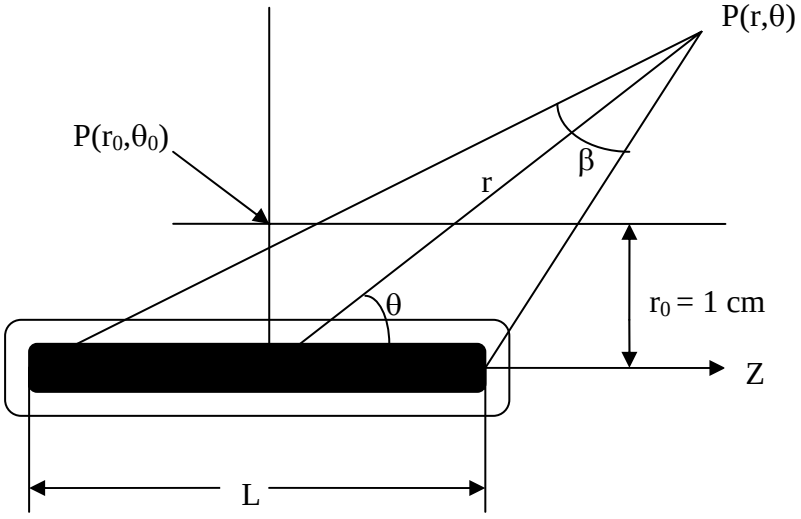


Fig 2.2: *Coordinate system used for seed dosimetry calculations*

The other quantities of the equation are **the air-kerma strength**, S_K, the **dose constant**, Λ, **the geometry function**, $G_L(r,\theta)$, **the radial dose function** for a line source, $g_L(r)$, and the **anisotropy function**, $F(r,\theta)$.

The **air-kerma strength**, S_K, has unit of μGym^{2}h^{-1} and is denoted by the symbol U, 1 U = 1μGym^{2}h^{-1}. The air-kerma strength is the product of **the air-kerma rate,** $\dot{K}_\delta(d)$, in vacuum at distance d and the distance d squared. The reference air kerma rate is the air kerma in air at a distance of one meter corrected for air attenuation and scattering [μGy/h] [7].

$$S_K = \dot{K}_\delta(d) \cdot d^2$$

The distance *d* is the distance between the center of the source and the point of air kerma rate specification, which should be located on the transverse plane of the source. The low-energy cutoff, δ, exclude those photons with too low energy to make any significant dose contribution at a distance of more than 0.1 cm in tissue (typically below 5 keV).

The **dose rate constant**, Λ, in water is defined as the dose rate at the reference position divided by S_K.

$$\Lambda = \frac{\dot{D}(r_0, \theta_0)}{S_K}$$

The dose rate constant depends both on the radionuclide and source model, its also influenced by the internal design of the source and the experimental methodology used to determine the dose rate at the reference point. Through Monte Carlo calculations and measurements of the dose rate constant the AAPM TG-43 came to a consensus that for the Amersham 6711 seed, ${}_{con}\Lambda = 0.965$ [cGy*h^{-1}*U^{-1}]. This value was averaged over a series of simulations and measurements.

The **geometry function**, $G_L(r,\theta)$, has the purpose to work as a correction for the effective inverse square law, with which dose rates can be estimated through interpolation from tabulated discrete points. If the source had been a point source the correction would just simply have been the inverse square of the distance from the source. For a line source the geometric function is.

$$G_L(r,\theta) = \begin{cases} \dfrac{\beta}{Lr\sin\theta} & if \quad \theta \neq 0^\circ \\ \left(r^2 - L^2/4\right)^{-1} & if \quad \theta = 0^\circ \end{cases}$$

Where β is the angle in radians between the two hypothetical lines from the ends of the line source to the calculation point, $P(r,\theta)$, L is the length of the source, as the seeds used in the present work are the Amersham Health model 6711 which contain a right cylindrical active volume. These seeds have a length of 4.6 mm and a diameter of 0.8 mm.

The **radial dose function**, $g_L(r)$, accounts for dose falloff on the transverse plane due to of the attenuation and scattering of the photons in tissue. The radial dose function is defined as follows:

$$g_L(r) = \frac{\dot{D}(r,\theta_0)}{\dot{D}(r_0,\theta_0)} \frac{G_L(r_0,\theta_0)}{G_L(r,\theta_0)}$$

Where $g_L(r_0) = 1$. The values for g_L were determined through both experiments and Monte Carlo simulations. The consensus values derived by AAPM TG-43 for the line source approximation of the Amersham health seed model 6711 are reproduced in table 2.2

Table 2.2: *Values for the radial dose function, $g_L(r)$, at different distances for Amersham 6711 line source with length L=3.0 mm.*

r [cm]	$g_L(r)$	r [cm]	$g_L(r)$
0.10	1.055	3.00	0.632
0.15	1.078	4.00	0.496
0.25	1.082	5.00	0.364
0.50	1.071	6.00	0.270
0.75	1.042	7.00	0.199
1.00	1.000	8.00	0.148
1.50	0.908	9.00	0.109
2.00	0.814	10.00	0.0803

The **anisotropy function**, *F(r,θ)*, describes the dose variations as function off polar angle relative to the transverse plane, and is defined as follows.

$$F(r,\theta) = \frac{\dot{D}(r,\theta)}{\dot{D}(r,\theta_0)} \frac{G_L(r,\theta_0)}{G_L(r,\theta)}$$

F(r,θ) becomes equal to unity at the transverse plane i.e. $\theta = \theta_0 = \pi/2$. The function usually has its maximum on the transverse plane. The function decreases of the transverse plane both when r decreases, as θ approaches 0° or 180°, as encapsulation thickness increases and as photon energy decreases. In AAPM TG-43 derived values for this function for different distances and angles from the source are presented. The results were derived through Monte Carlo simulations, and they are presented in table 2.3.

Table 2.3: *Values for the anisotropy function, F(r,θ), for different polar angels,θ , and distances, r, from source center, for Amersham model 6711 .*

Polar angle	r [cm]					
θ (degrees)	0.5	1	2	3	4	5
0	0.333	0.370	0.442	0.488	0.520	0.550
5	0.400	0.429	0.497	0.535	0.561	0.587
10	0.519	0.537	0.580	0.609	0.630	0.645
20	0.716	0.705	0.727	0.743	0.752	0.760
30	0.846	0.834	0.842	0.846	0.848	0.852
40	0.926	0.925	0.926	0.926	0.928	0.928
50	0.972	0.972	0.970	0.969	0.969	0.969
60	0.991	0.991	0.987	0.987	0.987	0.987
70	0.996	0.996	0.996	0.995	0.995	0.995
80	1.000	1.000	1.000	0.999	0.999	0.999
$\phi_{an}(r)$	0.973	0.944	0.941	0.942	0.943	0.944

2.2 Inverse planning

2.2.1 Dose volume histogram based optimization algorithm

Inverse planning is a method where the planning computer automatically calculates the positions for the seeds in the prostate, so to achieve acceptable dose coverage. The inverse planning can either place seeds based on a geometric loading method or on dose volumetric requirements. VariSeed7.1 is equipped with a dose volumetric based optimization algorithm [8].

Generally, the dose volume histogram based optimization algorithm uses an objective function, to describe how well a plan complies with the dose distributions requirements defined by the user for both the target and critical structures. An example of this objective function is as follows [9].

$$\Im = \sum_i c_i \left\{ \sum_j w_{ij} \left(d_{ij} - D_i \right)^2 + \sum_k u_{i,k} \left(d_i \left(V_{i,k} \right) - D_{i,V_k} \right)^2 \right\}$$

For the i:th structure, D_i represents the prescribed target dose or the tolerance dose for the organs at risk. The dose calculated for voxel *j* in structure *i* is denoted d_{ij}, and w_{ij} is the assigned weight to that voxel. In the structure i, $d_i(V_{i,k})$ is the k:th calculated dose volume point, and $D_{i,Vk}$ is the prescribed dose volume point for the same structure. $u_{i,k}$ is the weight term assigned to that dose volume point. And finally c_i is the overall importance term for the structure.

The first term in the objective function is only dependent upon the calculated dose and the prescribed dose. It is a measure of the difference in prescribed dose and calculated dose for a given seed configuration. If the prescribed dose and the calculated dose are equal the contribution to the objective function will be zero. If voxel *i* is to close to a seed, the contribution to the objective function will be unreasonably high, so the weight term $w_{i,j}$ can be assigned different values relative to seed positions so to create a short distance cutoff. Inside this cutoff region the weight factors are set to zero.

The second term of the objective function represents the dose volume constraints for the target and critical structures. This term adds to the objective function if a certain percentage of the target or critical structure exceeds the prescribed dose volume. Here $u_{i,k}$ is the relative importance factor which can be set to zero if the constraint is satisfied.

If the number of needles allowed is limited an additional factor can be added to the objective function, adding a penalty if the number of needles allowed is passed. In this factor N is the number of needles used and N_{max} the number of needles allowed.

$$w_n \left(N - N_{\max} \right)$$
$$w_n = 0 \;\; if \;\; N \le N_{\max}$$

In VariSeed7.1 the user can define dose rules and placement rules. The user can require that a certain percentage of the organ volumes (either target or organ at risk) should receive a dose higher or lower than either a defined dose or a percentage of the prescribed dose. In the placement restriction the user can define how large exclusion area he wants around the organs at risk, and how large inclusion area around the prostate he wants. The user can also define the number of needles allowed, the allowed calculation time and the minimum number of seeds in a needle.

2.2.2 Optimization of the objective function

The smaller the value of the objective function the better the dose distribution complies with the dose volume constraints defined. In order to optimize the plan the objective function is minimized by the planning system. The seeds placed by the algorithm can only be located at the coordinates defined by the template. When the algorithm places the RAPID strands, the seeds in the needle are located at a fixed distance of 10 mm, but the strands can be shifted 5 mm depending upon the insertion depth. There are also only one strand per needle, thus there cannot be placed two seeds in the base and two seeds in the apex of the prostate in the same needle (at the same template coordinates), which can be done manually.

In the iterative method, a seed configuration is initially randomly created, doses and volumes are calculated as well as the objective function. Then the program will change the position of a randomly selected seed to a new neighboring location. The doses, volumes, and objective function are recalculated. If the value of the objective function is reduced the new configuration is accepted, and if it is increased the new configuration is rejected. The algorithm continues in this manner until the objective function has reached a minimum. The problem with this method is that the optimization process can get trapped in a local minimum. A local minimum means that a configuration has been obtained where if a seed is moved the objective function will increase, but if several seeds where to be changed the objective function may decrease. There is also a larger risk for the objective function to be trapped in one of these minimum if there is a restriction upon the number of needles [9].

2.3 Equipment

For this study the VariSeed 7.1. treatment planning system was used to calculate the doses to the target and the organs at risk. The program is equipped with an inverse optimization algorithm, which can automatically generate plans for seed implantation. This program was installed on a computer with Intel Pentium processor 1.60 GHz.

The planning program uses the transverse prostate images from the TRUS for the planning. The slices used are spaced by 5 mm separation. A grid of sampling points for dose calculation is defined using the transverse ultrasound images in a coordinate system attached to the guiding template. Needles are only allowed at the template coordinates. Seed positions are determined in the planning program, which calculates the dose distribution by summing up all the dose contributions from the planned seeds using the dose distributions calculated through the formalism described above [8].

2.4 Test subjects

The patients used in this study were selected out of those patients that had already gone through the implantation, so that the inversely planned source placements could be compared with the manually planned ones. As these patients had already gone through the implantation, the target definitions had already been made. Seven patients with different prostate shapes and volumes were selected randomly. The most relevant parameter for this study were the volumes of the patients prostates, this is presented in table 2.4.

Table 2.4: *The prostate volumes for the seven patients randomly selected for this study.*

# Patient	Prostate Volume[cm^3]
1	34.1
2	29.6
3	43.4
4	27.6
5	14.4
6	17.0
7	27.8

2.5 Methods

The test started with defining several requirements for the optimization process. They were constraints on the placements of the seeds, dose volume requirements and weight factors on the dose volume requirements. It was decided to use five different sets of requirements. The results from the five tests were analyzed, to see how good dose coverage the optimization algorithm provided.

Initial requirements for the optimization algorithm

- ≥2 seeds in every needle, because RAPID strands were used and loose seeds were to be avoided.
- Maximum calculation time was put to a fairly long time (200s) to make sure that the iteration process should be able to generate the best plan.
- Up to 40 needles was allowed to make sure that the dose distribution should not be compromised by the number of needles used.
- The program was restricted from putting any needles in the middle column of the template, to avoid insertion of needles near the urethra.

The first test aimed at giving the prostate the desired dose with low priority to the organs at risk (the urethra and the rectum). Then the rest would put more emphasis on the risk organs, test 2 and 3 by excluding placement areas around the urethra and rectum. Test 4 and 5 does this by shifting the dose volumetric weight factors so to increase the priority for sparing the organs at risk.

Three dose volume requirements were defined. First the dose to 30% of the urethra volume is to be below 150% of the prescribed absorbed dose (Rx), at least 96% of the prostate volume is to receive 100% Rx, and the prostate volume receiving 150% Rx is to be lower than 65%. The dose volumetric requirements and weight factors are presented in Table 2.5. The reason for defining two identical dose volumetric requirements in table 2.5 is that the planning program only allows weight factors up to the value of ten, thus by defining two identical requirements the user can double the importance of that requirement.

Table 2.5: *Placement and dose volume restrictions for the five tests ("Rx" is the prescribed dose to the PTV, 145 Gy).*

Placement restrictions:	Test 1	Test 2	Test 3	Test 4	Test 5
Include area mm, outside prostate	1	1	1	1	1
Exclude area mm around urethra	2	3	4	2	2
Exclude area mm around rectum	2	3	4	2	2
Dosevolume restrictions:					
Prostate V100 > 96%; Weight	10	10	10	10	10
Prostate V100 > 96%; Weight	10	10	10	10	-
Urethra D30 < 150% Rx; Weight	1	1	1	2	5
Prostate V150 < 65%; Weight	1	1	1	3	5

When analyzing the results from the first test series it became obvious that there would be a need to expand the test series to get better dose coverage for smaller prostates. There would also be a need to distribute the sources in a better way.

To test if these problems could be solved a second test series was initiated. It was carried out in the same manner as the previous one, but in an attempt to get a better dose coverage for smaller prostates a larger area around the prostate was also included for seed placements. A manual element was also included in this test. When the seeds are placed automatically with a large area included around the prostate, it is possible that the strands are not anchored in the prostate. However the strands positions in the planning program can be changed so that they pass through the prostate, thus are anchored.

Table 2.6: *Placement and dose volume restrictions for the extra tests.*

Placement restrictions:	Test 6
Include area mm, outside prostate	4
Exclude area mm around urethra	2
Exclude area mm around rectum	2
Dose volume restrictions:	
Prostate V100 > 96%; Weight	10
Prostate V100 > 96%; Weight	10
Urethra D30 < 150% Rx; Weight	1
Prostate V150 < 65%; Weight	1

2.6 Plan evaluation

When evaluating a dose plan the dose volume histograms are very important, they describe how large a part of the organ receives different doses. The visual inspection of the dose distribution is also very important. One strives to have a 3 mm treatment margin around the prostate. The three dose volumetric requirements used during the tests were used during the evaluation together with two additional criteria. These additional criteria where that at least 90% of the prostate volume should receive a dose of more than 145 Gy and finally 3 cm^3 of the rectum should receive a dose lower than 69% Rx.

When evaluating the optimized plans the dose volume values mentioned above where noted for the generated plans, for each of the six tests. They where then compared to the dose volumes from the manually planed ones.

The number of seeds and needles used was noted for each of the optimized plans, these where then compared with the number of seeds and needles used in the manual plans.

Finally the optimized plans where also compared to the manual plans from a seed geometric point of view, i.e. how the optimization algorithm places the seeds relative to the manual peripheral loading.

When evaluating the optimized plans it was discovered that the algorithm in some cases tended to place the seeds into groups on one side of the prostate leaving the other side almost vacant of seeds. In some cases the algorithm placed most of the seeds in the odd or in the even planes.

The dose volume histograms were examined in greater detail to see if the clustering of seeds would yield a larger high dose volume, and if so the problem could maybe be solved by implementing a new high dose volume restriction. The volume difference between the optimized plans and the manual plans were calculated at high doses and normalized to the prostate volume.

3. Results and discussion

3.1 Plan evaluation

When analyzing the results from all the generated plans it was found that the prostate volume receiving at least 150% of the prescribed dose rarely passed 65%. The rectum always passed its dose requirements, and the difference in dose to the rectum for the manual plan and the optimized ones was minor. Hence, these values where excluded from the presentation.

3.2 Dose volumetric results

The results from the first set of tests are presented in table 3.1 to 3.5, where the plans have been ordered by prostate size. The results from test 6 are presented in table 3.6 and 3.7. The values presented with bold numbers are the ones that did not pass the dose volume requirements. The values in the column ProstV100, is the percentage of the prostate volume that receive at least 100% of the prescribed dose, and ProstD90 is the dose that 90% of the prostate volume receives. The "difference from manually" is defined as V100optimized [%] - V100manuall [%], and D90optimized – D90manually [Gy], respectively.

Table 3.1: *Prostate doses and differences from the manual plans, resulting from test 1.*

#Patient	Vol[cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually
3	43.4	96.7	-1.2	165.8	-9.1
1	34.1	97.0	-1.2	169.6	-3.3
7	29.8	96.4	-1.8	166.4	-9.5
2	29.6	96.4	0.9	169.4	5.3
4	27.6	**93.9**	-5.3	159.1	-23.2
6	17.0	**83.8**	-13.8	**130.4**	-43.5
5	14.4	**73.8**	-24.2	**112.3**	-55.8

Table 3.2: *Prostate doses and differences from the manual plans, resulting from test 2.*

#Patient	Vol[cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually
3	43.4	96.5	-1.4	164.6	-10.3
1	34.1	96.9	-1.3	171.5	-1.3
7	29.8	**95.8**	-2.4	163.3	-12.6
2	29.6	**87.9**	-7.6	**141.3**	-22.9
4	27.6	**90.6**	-8.6	147.2	-35.1
6	17.0	**64.1**	-33.6	**85.6**	-88.3
5	14.4	**57.6**	-40.4	**98.2**	-69.9

Table 3.3: *Prostate doses and differences from the manual plans, resulting from test 3.*

#Patient	Vol[cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually
3	43.4	96.1	-1.9	170.0	-4.8
1	34.1	97.0	-1.2	170.3	-2.6
7	29.8	**95.6**	-2.6	165.9	-9.9
2	29.6	**80.5**	-15.0	117.7	-46.5
4	27.6	**81.1**	-18.6	**119.7**	-62.6
6	17.0	**53.9**	-43.7	**73.8**	-100.0
5	14.4	**54.2**	-43.7	**93.2**	-74.9

Table 3.4: *Prostate doses and differences from the manual plans, resulting from test 4.*

#Patient	Vol [cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually
3	43.4	96.7	-1.3	165.0	-9.9
1	34.1	97.0	-1.2	170.7	-2.2
7	29.8	96.7	-1.5	167.3	-8.5
2	29.6	**95.2**	-0.3	161.4	-2.8
4	27.6	**92.7**	-6.5	153.4	-29.0
6	17.0	**84.9**	-12.7	**132.6**	-41.2
5	14.4	**78.6**	-19.4	**118.6**	-49.5

Table 3.5: *Prostate doses and differences from the manual plans, resulting from test 5.*

#Patient	Vol[cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually
3	43.4	**93.5**	-4.4	153.7	-21.2
1	34.1	**93.2**	-5.0	153.7	-19.2
7	29.8	**91.8**	-6.4	148.9	-26.9
2	29.6	**92.6**	-2.9	152.6	-11.6
4	27.6	**89.8**	-9.5	**144.5**	-37.9
6	17.0	**87.0**	-10.7	**137.7**	-36.2
5	14.4	**74.8**	-23.1	**114.4**	-53.7

The results shown in table 3.1-3.5 show that the best dose coverage for the target is achieved when little priority is placed upon the organs at risk. The organs at risk receive acceptable doses even when low priority is put on them. It is also clearly seen that the target dose coverage is reduced significantly for smaller prostates. The set of requirements that generate the best results is test 1, but the problem with decreasing dose coverage in smaller prostates must be remedied.

When the organs at risk are spared through seed placement restriction, the prostate volume in the vicinity of the urethra receives insufficient dose coverage. If the exclusion area becomes too large the apex of the prostate can become vacant of seeds, thus creating a cold spot. This effect is amplified in smaller prostates, as this exclusion area encompasses a larger portion of the total target volume in smaller prostates.

The reason that the smaller prostates do not receive the prescribed dose is that the algorithm is restricted to not place any seeds outside the prostate. When a plan is manually constructed one can place a RAPID strand so that it is anchored to the prostate and the end seeds are outside the prostate but these still irradiate the prostate. But the algorithm cannot place the seeds like this as it would reject the end seeds as being outside the included area.

Table 3.6: *Prostate doses and differences from the manual plans, resulting from test 6.*

#Patient	Vol[cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually
7	29.8	98.4	0.2	166.0	-9.8
2	29.6	98.5	3.0	168.9	4.7
4	27.6	97.9	-1.3	166.3	-16.1
6	17.0	97.9	0.3	169.4	-4.4
5	14.4	98.5	0.6	174.9	6.8

This last set (test6) of dose volume weight factors and placing restrictions managed to generate plans that passed all the dose volumetric requirements. As expected it placed RAPID strands so they were anchored in the prostate with the end seeds right outside the prostate. But it also placed strands that were not anchored in the prostate.

Table 3.7: *Prostate doses and differences from the manual plans, resulting from test 6 (with manual correction)*

#Patient	Vol[cc]	ProstV100[%]	Diff from manually	ProstD90[Gy]	Diff from manually	Comments
7	29.8	98.2	0.0	173.2	-2.6	Manually adjusted
2	29.6	98.3	2.8	178.6	14.4	
4	27.6	98.4	-0.9	169.4	-13.0	
6	17.0	97.6	-0.0	171.3	-2.5	Manually adjusted
5	14.4	98.7	0.8	175.9	7.8	

After manually correcting the plans so that all the strands were anchored in the prostate the plans still meet the dose volumetric requirements table 3.7. Some of the plans needed a little bit more adjustment than the others so the prostate would not receive too high dose, when the seeds where moved to be anchored in the prostate.

It was found that 30% of the urethra rarely got a dose higher than 150% of the prescribed dose. However there was still a significant difference in dose to the urethra through the optimized plans and the manual ones. The urethra doses from test 1, test6, and test6 with manual correction are presented in table 3.8 - 3.10 (only the results from these tests are presented because the other test sequences did not give acceptable dose coverage of the prostate).

Table 3.8: *Urethra doses and differences from the manual plans, resulting from test 1*

#Patient	Vol[cc]	UretD30[%]	Diff from manually
3	43.44	142.51	22.94
1	34.11	140.22	15.20
7	29.82	141.14	13.08
2	29.63	**151.97**	33.04
4	27.56	133.40	-0.54
6	16.95	117.93	-19.04
5	14.42	115.62	-4.25

As can be seen in table 3.8 there is a significantly higher dose to the urethra in the optimized plans, except for patient 4, 6 and 5 but this is due to the overall low dose coverage for small prostates in test1.

Table 3.9: *Urethra doses and differences from the manual plans, resulting from test 6*

#Patient	Vol[cc]	UretD30[%]	Diff from manually
7	29.82	139.82	11.76
2	29.63	134.56	15.63
4	27.56	129.98	-3.96
6	16.95	137.88	0.91
5	14.42	148.75	28.88

Table 3.10: *Urethra doses and differences from the manual plans, resulting from test 6 (with manual correction)*

#Patient	Vol[cc]	UretD30[%]	Diff from manually
7	29.82	137.87	9.81
2	29.63	137.01	18.08
4	27.56	131.50	-2.44
6	16.95	140.45	3.48
5	14.42	140.76	20.89

The urethra would still receive a significantly higher dose if the optimized plans would have been used compared to the manual plans. The reason for the lower urethra dose to patient 4 for the optimized plan compared to the manual plan was due to the high dose coverage in the manual plan.

3.3 Needles and seeds comparison

The number of needles and the number of seeds used in all the plans where compared with the numbers used in the manual plans

Table 3.11: *Number of needles and seeds used in the manual plans*

# Patient	Nr of needles	Nr of seeds	Nr of single seeds
3	28	80	6
1	23	70	2
7	19	57	0
2	25	68	1
4	28	62	2
6	18	49	0
5	21	41	5

Table 3.12: *Number of needles and seeds used in plans generated in test 1.*

# Patient	Nr of needles	Diff from manually	Nr of seeds	Diff from manually
3	22	-6	71	-9
1	19	-4	61	-9
7	20	1	52	-5
2	19	-6	61	-7
4	23	-5	55	-7
6	14	-4	35	-14
5	13	-8	29	-12

Table 3.13: *Number of needles and seeds used in plans generated in test 6.*

# Patient	Nr of needles	Diff from manually	Nr of seeds	Diff from manually
7	19	0	55	-2
2	24	-1	68	0
4	24	-4	58	-4
6	18	0	48	-1
5	19	-2	45	4

Table 3.14: *Number of needles and seeds used in plans generated in test 6manuall adjusted.*

# Patient	Nr of needles	Diff from manually	Nr of seeds	Diff from manually
7	19	0	57	0
2	23	-2	67	-1
4	24	-4	58	-4
6	17	-1	46	-3
5	18	-3	44	3

As can be seen most of the optimized plans used fewer seeds. This can be correlated to the insufficient dose coverage particularly in tests 2-5, and the smaller dose margin in tests 1 and 6. Although there where a 1 mm and a 4 mm seed placement area included around the target in test 1 and test 6 respectively, the optimization algorithm does not take into account the 3 mm 145 Gy isodose margin used in manual planning.

3.4 Dose margins and irregular seed placements

The plans generated by the algorithm in test 1 lacked sufficient dose coverage for smaller prostates. When the algorithm was not allowed to place seeds more than 1 mm outside the prostate the algorithm could not place seeds in the far edge of the prostate. As the algorithm was not allowed to place loose seeds, it could not place seeds in thin areas of the prostate as the seeds are fixed at a distance of 10 mm (fig 3.1). However in manual planning the peripheral strands are anchored in the prostate with the end seeds usually just outside the prostate. These seeds still irradiate the peripheral parts of the prostate and contribute to the dose coverage. When the algorithm was permitted to place seeds 4 mm outside the prostate the seeds could be placed in the thin areas of the prostate.

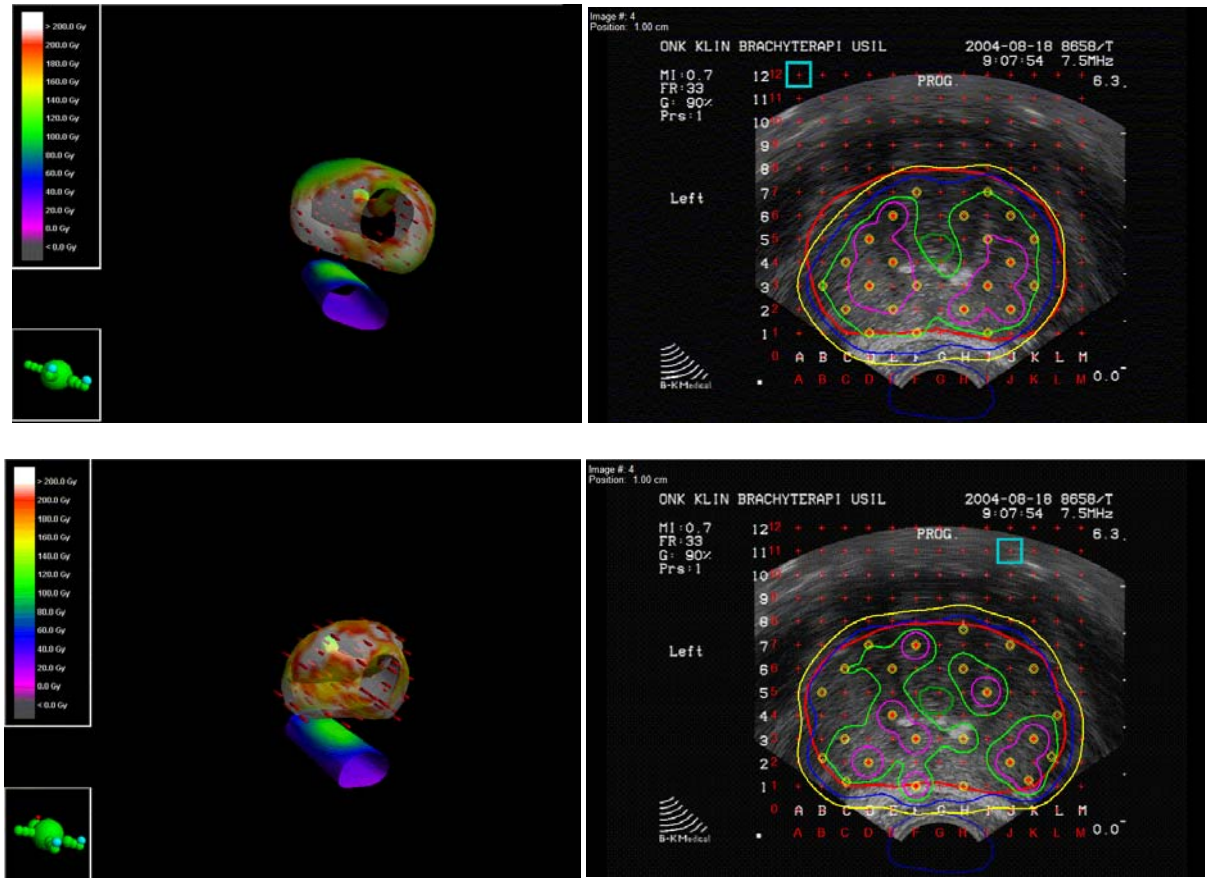
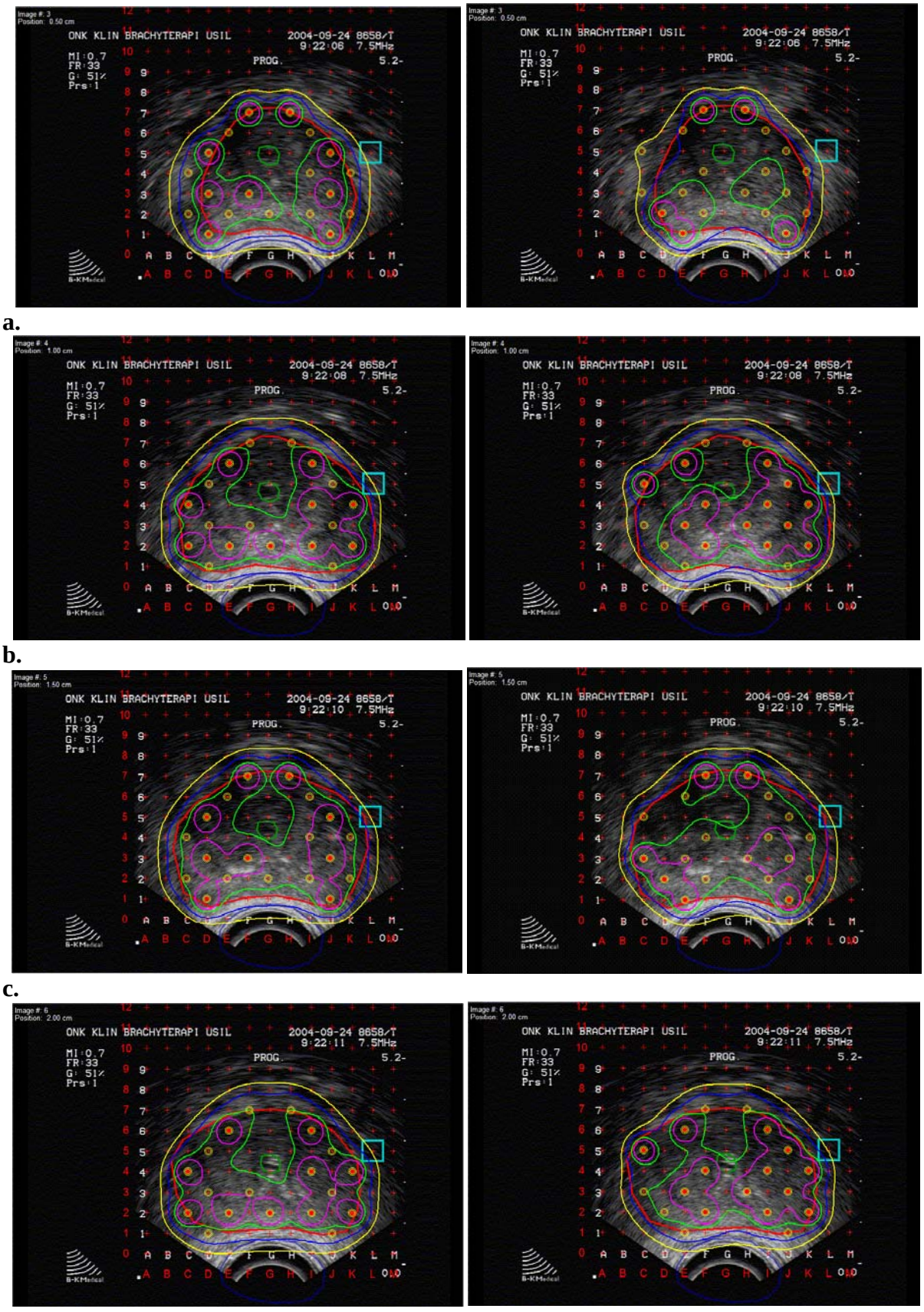


Fig 3.1: *Patient 4, seed configuration for test 1 in top pictures, test 6 bottom pictures.*



a.

b.

c.

d.

Fig 3.2: *Manual (left) and inverse (right) placement geometry for Patient 7 test 1 in the 5 mm (a.), 10 mm (b.), 15 mm (c.) and 20 mm (d.) planes from the base plane. Isodose levels 100%, 150% and 200% of the prescribed absorbed dose are shown above.*

In fig 3.2 the difference between the manual plans and the optimized plans in seed geometry can be observed for patient 7 in test 1. When observing the manual plan it is clear that the modified peripheral loading method has been used. The seeds have been placed in the periphery of the prostate in a very symmetrical pattern, with only a few seeds in the central area to fill up the dose coverage. Whereas the geometry generated by the algorithm is much more random and clustered. Most noticeable is the fact that the algorithm has clustered most of the seeds into the even planes (10, 20 mm planes), without any seeds shifted 5 mm to the odd planes. It is also seen that the algorithm tend to place the seeds clustered on one side of the prostate. This clustering of the seeds generates larger high dose areas than for the manual plans.

When observing fig 3.1 and 3.2 it is seen that the dose margins are a bit thin for the optimized plans, even when the dose margins are increased in 3.2 by increasing the seed placement area. The problem is that the algorithm does not account for the dose margin it only considers the contoured organs, thus if the dose margin should be considered in the calculations the prostate should be contoured with a three millimeter margin.

3.5 High dose DVH comparison

The difference in prostate volumes from the optimized plans and the manual plans receiving the absorbed doses of 100, 125, 150, 175, 200, 225, 250, 275 and 300 Gy, normalized to the total prostate volume is plotted in the diagrams 3.3 and 3.4 (volume for optimized plan – volume from manual plan). The comparisons from test 2-5 are not included because these plans did not meet the absorbed dose volumetric requirements and is thus uninteresting for further analysis.

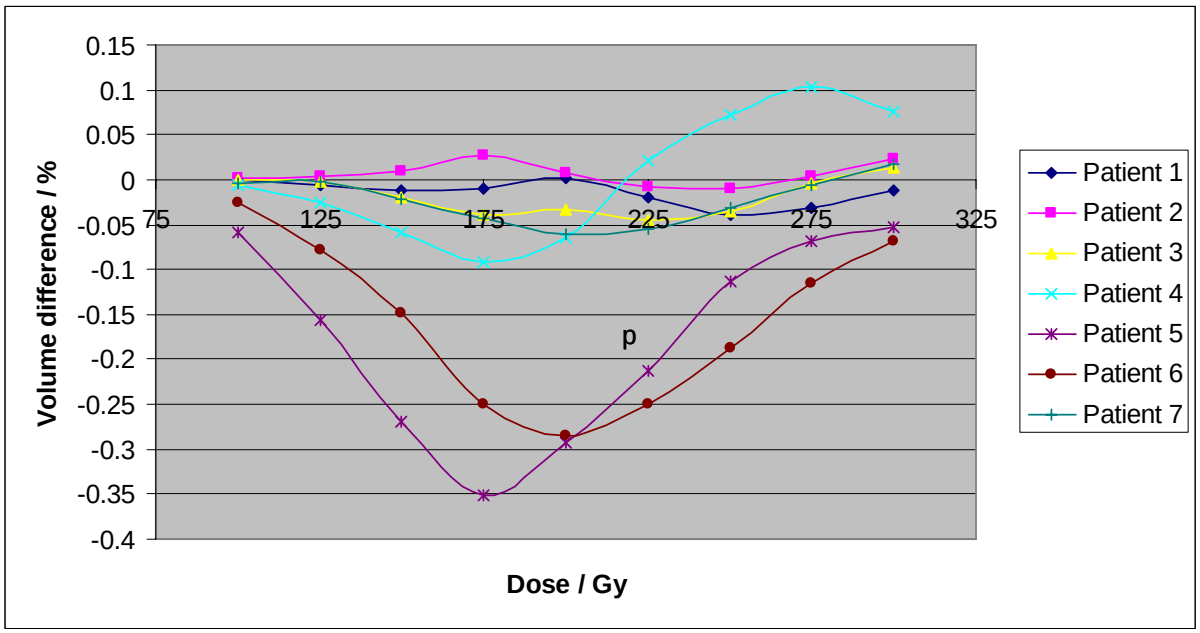


Fig 3.3: *Difference in prostate volumes receiving respective absorbed dose levels from optimized plan and manual plan normalized to respective prostate volume, in test 1.*

It is seen in Fig 3.3 that the volumes receiving higher absorbed doses are larger in the manual plans. The reason for this is that there was a larger 100% dose margin in the manual plans, which gives higher absorbed doses in the peripheral of the prostate. The drops in

patient 5 (14.42 cm^3) and 6 (16.95 cm^3) are due to that these small prostates had worst dose coverage in test1

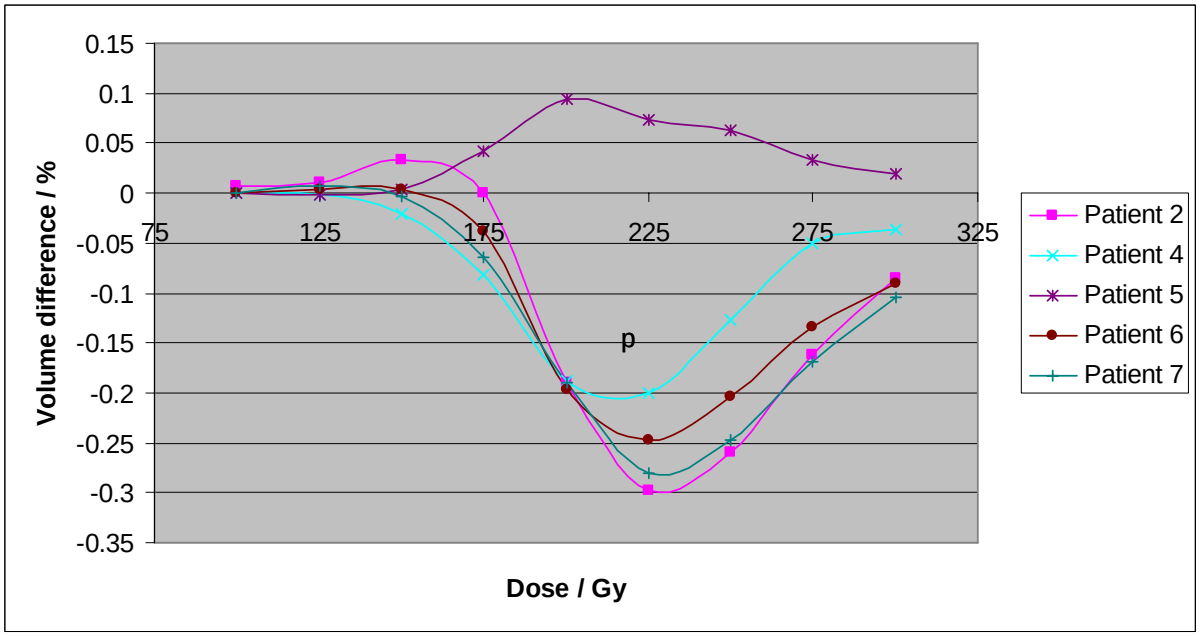


Fig 3.4: *Difference in prostate volumes receiving respective absorbed dose levels from optimized plan and manual plan normalized to respective prostate volume, in test 6.*

It is seen in the figures above that the volumes receiving high absorbed doses is lower in the optimized plans than in the manual ones, however the difference is very small. In fig 3.4 the small drop around 225 Gy with most of the patients is correlated to the number of seeds used. From table 3.14 it is seen that in test 6 more seeds where used in the manual plan except for with patient 5. So the drop in Fig 3.4 is due to those extra seeds, which where placed just outside the prostate. These seeds contribute with absorbed dose in the periphery of the prostate, but the higher dose contributions are given to a volume at a short distance from the seeds which then are located outside the prostate.

Hence the differences are as small as seen above, that a new dose volumetric requirement imposed upon the inverse planning algorithm will not make any difference.

4. Conclusions

From a dose volumetric point of view the inversed planned seed configurations presents acceptable dose coverage for both the target and the organs at risk. However the urethra would receives a smaller dose using the planes generated manually with the peripheral loading method, than with the automatic optimized plans. Shifting dose coverage priority to minimize the urethra dose means compromising target dose coverage.

The seed geometry put forth by the inverse planning method is very randomized and clustered compared to the peripheral loading method used manually. Thus the algorithm generates few but large high dose volumes compared to several small volumes in the manual method. These large high dose volumes can not be used to encompass known tumor sites inside the prostate, because the requirements defined by the user do not have a determinable effect upon these volumes locations.

The visual inspection of the optimized plans showed that the optimized plans had insufficient dose margins. The user can neither here increase isodose margins near known tumor sites.

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