Dosimetric verification of dose optimisation algorithm during endovascular brachytherapy of the peripheral vessels

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ABSTRACT

AIM: Dosimetric verification of the dose optimisation model used in endovascular brachytherapy, evaluation of the optimised dose distributions using elaborated indices.

BACKGROUND: The equipment used for standard radiotherapy is used in vascular brachytherapy for prevention of restenosis after angioplasty.

MATERIAL AND METHOD: A paraffin-wax phantom, thermoluminescent detectors and MD-55 Gafchromic® films were used for dose measurements. The edge dose index (EDI), central dose index (CDI) and treatment length index (TLI) were introduced to compare dose distributions calculated and measured.

RESULTS: Obtained values ($p>0.05$) show no statistically significant differences between calculated doses and measured doses. EDI values showed improvement in dose homogeneity on the edges of the application after optimisation. After optimisation CDI values from 0.9% to 1.6% for calculated and from -1.8% to 3.1% for measured showed improvement in dose homogeneity in the central part of the application. Observed values of TLI from 3% to 21% for calculated doses and from 7% to 24% for doses measured by Gafchromic® films showed increase of RIL for optimised treatment plans.

CONCLUSIONS: 1/ The designed phantom allowed repeatable dosimetric verification of dose distributions in endovascular brachytherapy. 2/ Measurements with thermoluminescent detectors and Gafchromic films proved the accuracy of the calculation algorithm in endovascular brachytherapy conditions. 3/ Elaborated indices were found to be a useful tool in describing dose homogeneity. They allowed the process of optimisation to be controlled and thus an increase in dose homogeneity by 30% at the edges and by 7% in the middle of the treated volume to be achieved.

KEY WORDS: endovascular brachytherapy, Gafchromic® films, dose optimisation

BACKGROUND

Treatment methods of atherosclerotic disease of peripheral vessels were limited to vascular bypass surgery until 1977, when Gruentzig introduced percutaneous transluminal angioplasty (PTA) to medical practice [1, 2, 3]. However, a significant fraction of patients after PTA developed symptoms of recurrent vessel narrowing due to the process of restenosis. During PTA treatment the stenotic part of the artery undergoes high pressure of 14 to 18 atmospheres, which involves several biological processes inside smooth muscle cells which lead to accelerated proliferation of cells in the treated part of the vessel. The paradigm elaborated for standard radiotherapy was introduced as the start of vascular brachytherapy for the prevention of restenosis after angioplasty procedures [4]. Intravascular brachytherapy prevents inward remodelling and induces an increase in lumen area but partially prevents healing of the disrupted vessel surface [5, 6, 7, 8]. Standard brachytherapy equipment is used (microSelectron HDR with 370 GBq Ir -192 source). Intervention length (IL) defined by the angioplasty length of PTA should be covered with a homogeneous

dose of 12 to 20 Gy with additional margin of 10 mm for the most distal and proximal part of the injured vessel wall.

Multiple clinical trials have shown that endovascular brachytherapy has reduced the risk of restenosis from 30–60% to 5–15%, if the irradiation is planned to meet individual needs and is delivered accurately. However, using irradiation for treatment inside the vessel requires dose verification, which is much more difficult than in other brachytherapy techniques because in vivo dose checks are almost impossible [9, 10, 11, 12, 13, 14].

AIM OF THE STUDY

The aim of the study was dosimetric verification of the dose optimisation model used in endovascular brachytherapy and evaluation of the optimised dose distributions using elaborated indices.

MATERIAL AND METHOD

The set-up of irradiated volume required definition of certain parameters presented below in Figures 1 and 2. The reference isodose length (RIL) was defined as vessel length at the reference depth (RD) covered by 90% isodose. The properties of dose distribution in such a set-up require that intervention length (IL) be shorter than RIL by about 10 mm. RIL describes dose distribution and depends on the isotope properties, reference depth (RD) and the source configuration described by active source length (ASL) [14, 15].

Intervention length (IL) is defined by the length of the vessel wall between the most distal and proximal parts of all inflated balloons used during the PTA procedure. Reference lumen diameter (RLD) is the lumen diameter measured from media to media after angioplasty procedure. Active source length (ASL) is defined as the distance between the centre of the first and the last stepping source position. Reference depth (RD) is defined as RLD/2 plus additional margin (r) of usually 2 mm into the vessel wall [16, 17, 18, 19, 20].

Phantom description

The authors designed and constructed the paraffin-wax phantom shown in Figure 3 and used it for the dose measurements. For 0.15 to 0.85 weight fractions of the phantom components the physical density of the phantom material is 0.93 g/cm^3 (according to NIST).

Fig. 1. Dose planning parameters in endovascular brachytherapy. IL (interventional length); ASL (active source length); RIL (reference isodose length)

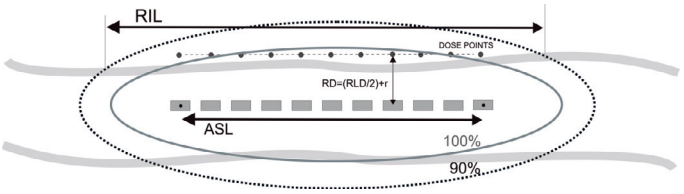

Fig. 2. Definition of RIL based on dose distribution along the axis of the source arrangement [6, 12]

The exchangeable layers made it possible to place thermoluminescent detectors or films in a stable and reproducible way at chosen distances of RD= 5, 7 and 10 mm (from catheter axis to detector).

Dose measurements and statistical evaluation of the results

Thermoluminescent detectors LiF 100 with TLD 3500 reader and MD-55 Gafchromic® dosimetry media were used as dosimeters [21]. Calibration of the LiF detectors and MD-55 films were performed using a Co-60 beam in reference conditions. Films were digitised using Microtek® ScanMaker 900i. The treatment plans for 15 cases were prepared for active source length ASL=25, 50, 75, 100 and 125 mm, respectively. The dose at dose points was assumed for 10 Gy at the distances RD=5, 7 and 10 mm from the axis of the catheter. Each set of calculations and measurements was carried out for the non-optimised and then for the optimised treatment plan. TLD detectors were placed inside the phantom in the places corresponding to positions of defined reference points. Gafchromic® films were placed between the layers of the designed phantom at

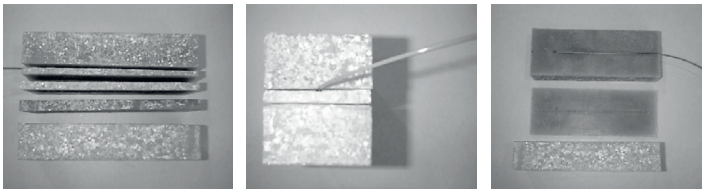

Fig. 3. The paraffin wax phantom with three exchangeable layers providing set-up of reference depths of 5, 7 and 10 mm from the axis of a standard 6F catheter

distances from the axis of the catheter equal to the chosen reference depths (RD). Measurements were performed three times and mean values of the doses at the dose points were compared.

For the statistical evaluation of the obtained results (calculated doses vs. measured doses)

Wilcoxon matched pair test for dependent samples at α=0.05 was used. Next the calculated and measured doses were divided into two groups for every treatment plan. The first group contained doses calculated and measured in the central part of the application, and the second group contained doses calculated and measured at the edges of the application. Comparisons (edge vs. central part) were performed for unoptimised and optimised treatment plans respectively. Mann-Whitney U test for independent samples was used at α=0.05.

Verification of the optimisation algorithm

For the treatment plan without optimisation, dwell times were equal for all source positions. Doses on the edge part of the treatment volume were lower than the prescribed reference dose, while in the central part of the application doses were higher than those prescribed. After optimisation of the treatment, dwell times were different for particular active source positions. Three indices, the edge dose index (EDI), central dose index (CDI) and treatment length index (TLI), were defined and introduced to describe and compare dose distributions calculated and measured and the impact of the optimisation on doses. EDI is the difference between doses before and after the optimisation as a percentage of the dose after optimisation at the reference point at the edge of the applicator. So it describes the dose increase near the edge due to the applied optimisation procedure. The central dose index, CDI (CDI_c – calculated, CDI_m-measured), respectively describes the difference between the dose prescribed and calculated or measured at the reference point located in the middle of the active length. TLI describes the percentage increase of the length of the RIL (reference isodose length) after the optimisation procedure.

Clinically, the first two indices, EDI and CDI, show the changes in dose homogeneity around the applicator, while TLI detects changes in treatment volume.

All indices were determined for calculated and measured doses, and marked by lower case $_c$ or $_m$, respectively, as presented in equations 1–3.

$$EDI_c = \frac{D_{c(o)} - D_{c(uo)}}{D_{c(o)}} 100\%$$

$$EDI_c = \frac{D_{m(o)} - D_{m(uo)}}{D_{m(o)}} 100\%$$

where: $_{c(uo)}$, $D_{m(uo)}$ D are calculated and measured doses for non-optimised treatment plan, $D_{c(o)}$, $D_{m(o)}$ calculated and measured doses for optimised treatment plan, respectively.

$$CDI_m = \frac{CD_m - D_{REF}}{CD_m} 100\%$$

$$CDI_c = \frac{CD_c - D_{REF}}{CD_c} 100\%$$

where: CD_c – dose in the central part of the application calculated, C_m – dose in the central part of the application measured by TLD, D_{REF} – reference dose (10 Gy).

$$TLI_c = \frac{RIL_{c(o)} - RIL_{c(uo)}}{RIL_{c(o)}} 100\%$$

$$TLI_m = \frac{RIL_{m(o)} - RIL_{m(uo)}}{RIL_{m(o)}} 100\%$$

where: $RIL_{c(uo)}$ – calculated RIL for unoptimised treatment plan, $RIL_{c(o)}$ – calculated RIL

for optimised treatment plan, $RIL_{m(uo)}$ – measured RIL for unoptimised treatment plan, $RIL_{m(o)}$ – measured RIL for optimised treatment plan.

RESULTS

The designed phantom allowed conditions of endovascular brachytherapy to be reconstructed and dose distributions calculated by the treatment planning system to be verified. The plot of calculated and measured doses at the conditions chosen as an example (depth of 5 mm, ASL of 100 mm) is presented in Figure 4. The left part of the figure represents doses for the non-optimised treatment plan and the right part for the optimised plan.

The results of the statistical analysis of the doses in dose points calculated by Plato 14.3 versus those measured with TLD dosimeters and Gafchromic® films are shown in Table 1.

The comparisons were done for unoptimised and optimised treatment plans for ASL= 25, 50, 75, 100 and 125 mm and RD = 5, 7, and 10 mm, respectively. Wilcoxon test was used.

Obtained values ($p>0.05$) for most treatment plans show no statistically significant differences between calculated doses and doses measured by TLD dosimeters and Gafchromic® films. The same results were obtained for unoptimised and optimised treatment plans.

Results of the comparison between doses from the edges and central part of the application for ASL= 25, 50, 75, 100 and 125 mm and RD = 5, 7, and 10 mm are shown in Table 2. Doses calculated and measured with TLD and Gafchromic® films were taken into account for optimised and unoptimised treatment plans, respectively. Mann-Whitney U test at $\alpha=0.05$ was used.

Obtained p values show that only for unoptimised treatment plans did statistically significant differences occur – between the doses (in dose points), lying in the middle and at the edges of the active length. This result shows inhomogeneity in dose distributions before the optimisation procedure was applied. Similar results were obtained for doses calculated and those measured with thermoluminescent detectors and Gafchromic® films. After the optimisation procedure p values showed no statistically significant differences between doses (at dose points) lying at the edges and in the middle of the active length, for both calculations and measurements.

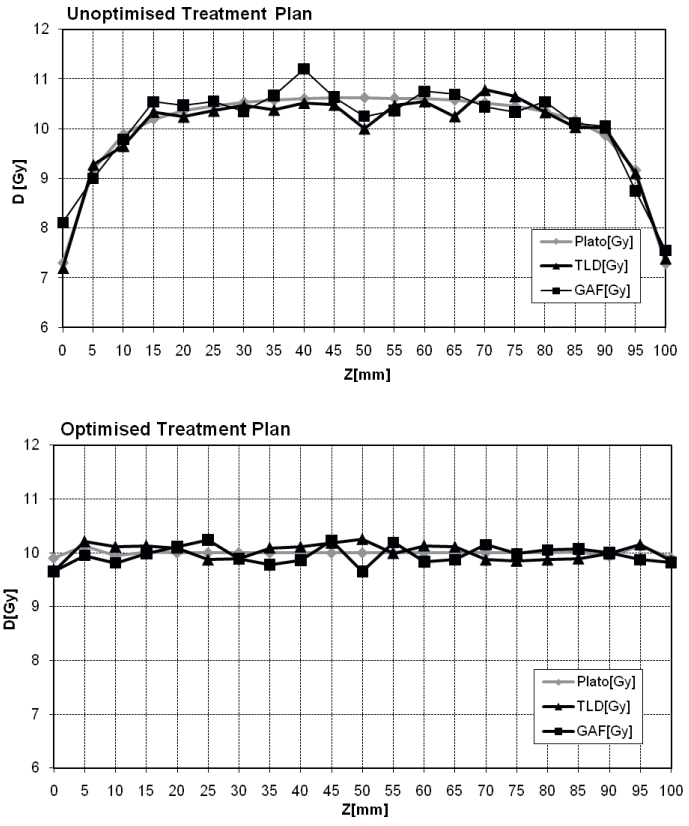

Fig. 4. Calculated and measured doses for ASL = 100 mm and RD = 5mm. Gray line with squares – doses calculated by Plato; black line with triangles – doses measured by TLD dosimeters; Black line with squares – doses measured by Gafchromic films

In Table 3 the edge dose index (EDI) is shown for doses calculated (Plato) and measured, for ASL= 25, 50, 75 100 and 125 mm.

For ASL = 25, 50, 75, 100 and 125 mm and chosen reference depths of 5, 7 and 10 mm corresponding values of CDI are listed in Table 4 and the percentage difference between doses calculated/measured and reference dose (10 Gy) prescribed in the central part of the application is shown. Values obtained for treatment plans with optimisation are presented with a grey background.

CDI values for the unoptimised treatment plan show that in the central part of the treatment length, doses were higher by 3% to 10% than prescribed, for calculated and measured values. After optimisation CDI values from 0.9% to 1.6% for calculated and from -1.8% to

Table 1. Calculated vs. measured dose distributions for unoptimised and optimised treatment plans, Wilcoxon Test at $\alpha=0.05$

		(Wilcoxon)p			
		Unoptimised		Optimised	
ASL [mm]	RD [mm]	Plato vs. TLD	Plato vs. GAF	Plato vs. TLD	Plato vs. GAF
25	5	0.917	0.600	0.059	0.249
	7	0.600	0.249	0.345	0.116
	10	0.093	0.249	0.917	0.138
50	5	0.374	0.182	0.450	0.398
	7	0.859	0.230	0.689	0.213
	10	0.965	0.859	0.155	0.010
75	5	0.100	0.289	0.569	0.453
	7	0.379	0.164	1.000	0.423
	10	0.148	0.103	0.103	0.569
100	5	0.192	0.476	0.754	0.237
	7	0.281	0.781	0.076	0.099
	10	0.313	0.385	0.566	0.313
125	5	0.424	0.162	0.110	0.148
	7	0.182	0.121	0.073	0.431
	10	0.732	0.233	0.431	0.118

Table 2. Doses from the edges vs. doses from central part of the application for treatment plans before and after optimisation U Mann-Whitney Test at $\alpha=0.05$

		(U Mann-Whitney) p					
		Unoptimised			Optimised		
ASL [mm]	RD [mm]	Plato	TLD	GAF	Plato	TLD	GAF
25	5	0.064	0.064	0.064	1.000	1.000	0.240
	7	0.057	0.064	0.355	1.000	0.165	0.348
	10	0.057	0.064	0.064	1.000	1.000	0.165
50	5	0.006	0.006	0.028	0.352	0.100	0.463
	7	0.006	0.018	0.006	0.853	0.715	0.410
	10	0.006	0.028	0.011	0.357	0.584	0.715
75	5	0.001	0.002	0.024	0.395	0.462	0.345
	7	0.001	0.001	0.001	0.089	0.092	0.247
	10	0.002	0.002	0.005	0.671	0.430	0.318
100	5	0.002	0.041	0.025	1.000	0.222	0.522
	7	0.002	0.047	0.003	1.000	0.035	0.370
	10	0.002	0.054	0.004	0.561	0.848	0.142
125	5	0.001	0.074	0.052	0.651	0.156	0.141
	7	0.001	0.010	0.046	0.643	0.208	0.246
	10	0.001	0.002	0.001	1.000	0.344	0.916

Table 3. The edge dose index for calculated and measured doses at chosen reference depths (RD) of 5, 7 and 10 mm for ASL = 25, 50 ,75, 100 and 125 mm

	RD=5 mm			RD=7 mm			RD=10 mm		
ASL [mm]	EDI_C	EDI_mTLD	EDI_mGAF	EDI_C	EDI_mTLD	EDI_mGAF	EDI_C	EDI_mTLD	EDI_mGAF
25	15.6	11.4	19.6	14.2	15.1	18.3	10.0	10.8	18.5
50	21.9	23.5	28.3	22.1	23.2	33.3	19.6	22.3	28.1
75	24.7	25.2	34.6	25.5	27.5	38.0	24.0	29.0	34.2
100	26.3	28.9	16.0	27.6	28.0	40.3	26.6	25.3	18.2
125	27.3	29.0	35.8	28.8	30.2	39.7	28.3	29.2	39.0

Table 4. Central dose index values for unoptimised and optimised (grey background) treatment plans for ASL= 25, 50, 75, 100 and 125 mm

	RD=5 mm			RD=7 mm			RD=10 mm		
ASL [mm]	CDI_C	CDI_mTLD	CDI_mGAF	CDI_C	CDI_mTLD	CDI_mGAF	CDI_C	CDI_mTLD	CDI_mGAF
25	10.1	8.3	8.8	11.1	7.8	3.4	11.1	9.0	10.2
	-0.4	-0.9	1.6	-0.4	-0.9	1.6	-1.0	-1.8	1.2
50	7.7	8.9	5.3	9.1	8.4	8.2	10.2	7.7	11.9
	0.0	0.3	0.4	-0.1	0.3	0.6	-0.3	0.8	3.1
75	6.2	6.3	5.6	7.6	7.4	8.4	9.0	8.2	8.7
	0.0	0.6	1.3	0.1	1.4	1.6	-0.1	-0.1	1.2
100	5.6	3.6	6.1	7.1	6.6	7.3	8.7	7.6	7.5
	0.0	1.2	-0.9	0.0	0.7	0.1	0.1	-0.4	0.0
125	5.0	5.4	4.5	6.3	7.1	5.2	7.9	8.2	8.3
	0.0	-0.6	0.6	0.0	1.7	1.7	0.0	1.0	2.0

Table 6. Treatment length index values – percentage increase of RIL after optimisation of the treatment plans for ASL= 25, 50, 75, 100 and 125 mm

TLIC[%]					
RD [mm]	ASL=25 mm	ASL=50 mm	ASL=75 mm	ASL=100 mm	ASL=125 mm
5	18.5	9.1	8.9	7.6	3.1
7	20.7	13.2	13.8	9.3	6.0
10	18.5	16.7	12.3	8.9	5.5
TLImGAF[%]					
RD[mm]	ASL=25 mm	ASL=50 mm	ASL=75 mm	ASL=100 mm	ASL=125 mm
5	21.5	11.8	11.2	9.6	6.5
7	22.0	14.8	15.9	11.5	8.7
10	24.0	20.7	10.3	13.0	6.3

3.1% for measured doses were observed. CDI values showed improvement in dose homogeneity in the central part of the application after optimisation.

In Table 5 values of the treatment length index (TLI) are shown as a percentage increase of reference isodose length after optimisation of the treatment plans, for ASL= 25, 50, 75, 100, 125 mm and chosen RD values of 5, 7 and 10 mm. TLI values shown in this table are based on calculations from the treatment planning system (TLI_C) and dose values obtained from measurements with Gafchromic® films (TLImGAF).

Observed values of TLI from 3% to 21% for calculated doses and from 7% to 24% for doses measured by Gafchromic® films showed increase of RIL for optimised treatment plans. After optimisation of the dwell times vessel lengths covered by the reference isodose were higher by 5 mm to 14 mm without increase of ASL.

DISCUSSION

Calculated and measured doses at dose points were compared using the Wilcoxon matched pair test for dependent samples at alpha value = 0.05. For dose values calculated and measured, and ASL= 25, 50, 75, 100 and 125 mm, obtained p values for treatment plans without optimisation and for optimised plans show no statistically significant differences between calculated doses and doses measured by TLD dosimeters and those obtained from Gafchromic® films (Table 1).

Calculated and measured doses for every ASL were divided into three groups containing an equal number of points – two groups from the edges of the application and one group from the central part. Points from the edges were used to form one group containing points for both ends, and compared with doses from points from the central part of the application. Doses from the edges were compared to doses from the central part of the application using Mann-Whitney U test for independent samples at alpha value = 0.05. Obtained p values presented in Table 2 show that only for unoptimised treatment plans were there statistically significant differences between doses at the centre and at the edges of the applications for calculated doses and for measured doses (TLD and Gafchromic® films).

Edge dose index was previously defined as percentage increase of the doses at the edges of the application after optimisation of the treatment plan. Values of EDI (Table 3) showed in general 10 to 40% increase of the dose at the edges of the application for the optimised treatment plan for doses calculated and measured with TLD and Gafchromic films. For the unoptimised treatment plan doses at the dose points located at the central part of the application are in general higher by 5 to 12% for calculated and measured doses than the prescribed doses to the reference dose points. This is shown by higher values of CDI for the unoptimised treatment plan (Table 4). After optimisation of the treatment plan lower central dose index values (Table 5) showed that the doses differ by not more than 1 to 2.8% from the prescribed reference dose (10 Gy) at the centre of the application for both calculated and measured values.

Treatment length index values presented in Table 5 show the percentage increase of the length of RIL after optimisation of the treatment plan. RIL length values based on calculations and measurements are higher in general by 9 to 24% when the treatment plan is optimised. Increase of RIL after treatment plan optimisation showed that increasing ASL is not necessary for particular PTL. After optimisation of the treatment plan, it is possible to avoid underdosage at the edges of the treatment length. For the central part of the application, the dose is closer to the prescribed reference value. Dose distribution is more homogeneous and this is advantageous from a clinical point of view. The probability of a "geographical miss" is lower for the optimised treatment plan.

CONCLUSIONS

1. The designed and constructed phantom allowed for reliable and repeatable dosimetric verification of dose distributions in endovascular brachytherapy.

2. Measurements with thermoluminescent detectors and Gafchromic® films proved the accuracy of the calculation algorithm in endovascular brachytherapy conditions.

3. Elaborated indices were found to be a useful tool in describing dose homogeneity around

the applicator in endovascular brachytherapy. They allowed the process of optimisation to be controlled and thus an increase in dose homogeneity by 30% at the edges and by 7% in the middle of the treated volume to be achieved.

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