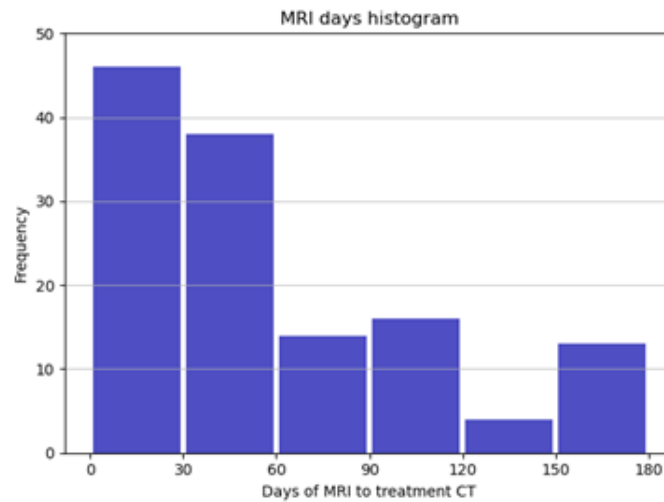


# Supplementary material

## 1 Analysis of the impact of the time of the mpMRI acquisition prior to the treatment and other factors

Regarding the time between MRI and begin of the treatment, we are presenting the histogram of MRI acquisition in days:



In addition, we run a cox regression analysis with a cut-off of 1 month between MRI and begin of EBRT, along with other covariates such as ADT, Radiation technique (IMRT, 3D-CRT), PSAGroups (1: <10ng/ml, 2: 10-20 ng/ml, 3: >20 ng/ml), Risikogruppe (0 for low, 1 for intermediate and 2 for high risk), GleasonScore (1 for  $\leq 7$ , 2 for 7 and 3 for  $\geq 8$ ). The results of Cox regression indicated no higher risk for the patients who had MRI before 1 month to the ones who had MRI after 1 month, as well as for each covariate.

```

Call:
coxph(formula = Surv(TimeToEvent, BiochemischesRezidiv) ~ ADT +
      mri_after_30_days + Technik + PSAGroups + Risikogruppe +
      GleasonScore, data = dfmri)

      n= 129, number of events= 26

              coef exp(coef)  se(coef)      z Pr(>|z|)
ADT          -0.003649  0.996358  0.502031 -0.007  0.99420
mri_after_30_days -0.250034  0.778774  0.433322 -0.577  0.56393
Technik       0.937987  2.554833  0.543629  1.725  0.08445 .
PSAGroups     0.260298  1.297316  0.285321  0.912  0.36161
Risikogruppe  0.026648  1.027006  0.542422  0.049  0.96082
GleasonScore  1.089223  2.971963  0.399910  2.724  0.00646 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

              exp(coef) exp(-coef) lower .95 upper .95
ADT              0.9964      1.0037   0.3725   2.665
mri_after_30_days  0.7788      1.2841   0.3331   1.821
Technik          2.5548      0.3914   0.8803   7.415
PSAGroups        1.2973      0.7708   0.7416   2.269
Risikogruppe     1.0270      0.9737   0.3547   2.974
GleasonScore     2.9720      0.3365   1.3572   6.508

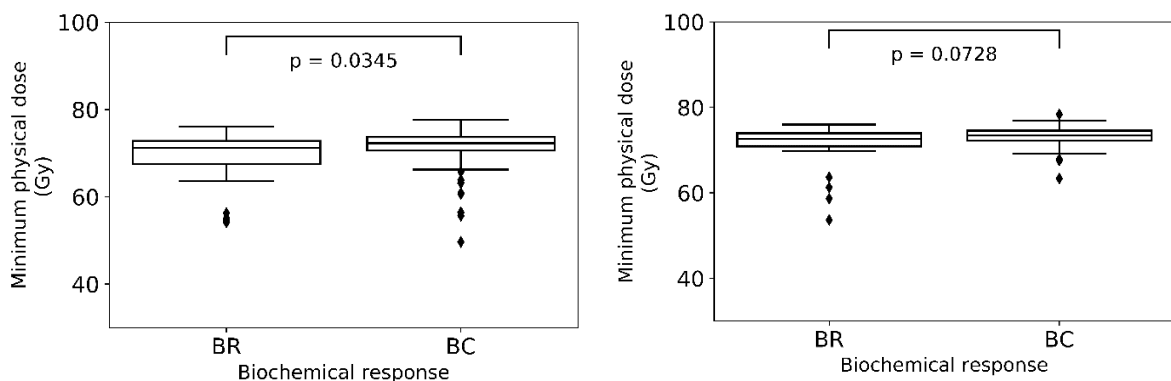
Concordance= 0.726 (se = 0.059 )
Likelihood ratio test= 14.48 on 6 df,  p=0.02
Wald test              = 13.67 on 6 df,  p=0.03
Score (logrank) test = 14.21 on 6 df,  p=0.03

```

## 2 Comparison of dose values in prostate gland and GTV

We compared the minimum physical dose for mpMRI-GTV and prostate gland for the biochemical control (BC), defined by BRFs, and biochemical relapse (BR) groups. For the BC group the median of the minimum dose in the prostate gland was 72.3 Gy (range 49.7 Gy – 77.7 Gy) whereas in the mpMRI-GTV it was 73.5 Gy (range 63.4 Gy – 78.4 Gy). For the BR group the median of the minimum dose was 71.3 Gy (range 54.2 Gy – 76.1 Gy) and 72.7 Gy (range 53.7 Gy – 76.0 Gy) for the prostate gland and mpMRI-GTV respectively.

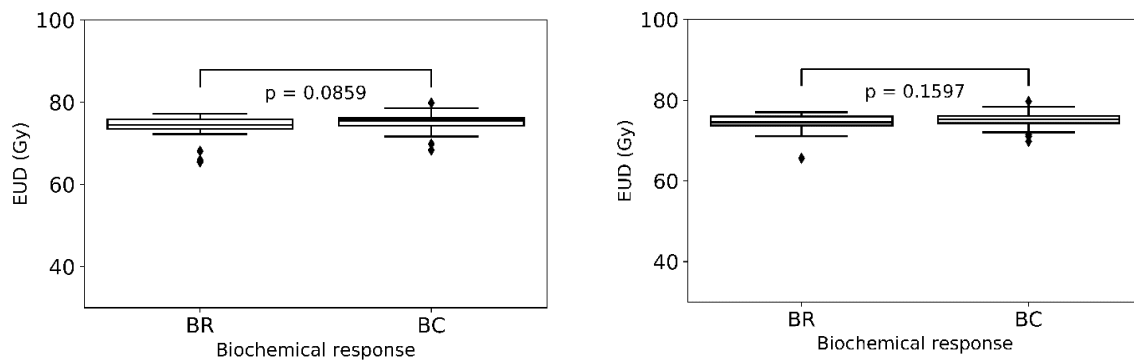
As illustrated in Fig. 1, the minimum physical dose between the two groups is significantly different for prostate gland ( $p = 0.0345$ ) but not for mpMRI-GTV ( $p = 0.0728$ ).



**Figure 1:** Boxplots for the minimum physical dose for prostate gland (left,  $p = 0.0345$ ) and mpMRI-GTV (right,  $p = 0.0728$ ) for the biochemical control (BC) and biochemical relapse (BR) groups.

Regarding EUD and BC group the median value for the prostate gland was 75.5 Gy (range 68.3 Gy – 79.8 Gy) whereas for the mpMRI-GTV it was 75.3 Gy (range 69.8 Gy – 79.7 Gy). For the BR group the median EUD was 74.5 Gy (range 65.5 Gy – 77.2 Gy) and 74.5 Gy (range 65.6 Gy – 77.0 Gy) for the prostate gland and mpMRI-GTV respectively.

Figure 2 illustrates the results of the comparison of equivalent uniform dose for prostate gland and mpMRI-GTV. No significant differences between the two groups and for both target types were showed: for prostate gland  $p = 0.0859$  and for mpMRI-GTV  $p = 0.1597$ .



**Figure 2:** Boxplots for the EUD for prostate gland (left) and mpMRI-GTV (right) for the biochemical relapse (BR) and biochemical control (BC) groups.

### 3 Dose-Volume parameters for prostate gland and mpMRI-GTV

**Table 1:** Dose-Volume parameters for prostate gland and mpMRI-GTV for biochemical relapse (BR) group and biochemical control (BC) group. The Wilcoxon test for comparing the two groups is used with significance level  $\alpha=0.05$ . (\*) indicates a marginal significant difference, (\*\*) indicates a strong significant difference

	mpMRI-GTV			Prostate gland		
	Mean (SD)		Wilcoxon p-value	Mean (SD)		Wilcoxon p-value
	BC	BR		BC	BR	
Dmin [Gy]	73.12 (2.08)	70.89 (5.35)	0.07	<b>71.2(4.19)</b>	<b>68.55(6.34)</b>	<b>0.03(**)</b>
Dmax [Gy]	76.83 (1.71)	75.97 (2.76)	0.22	77.91(1.84)	77.03(2.52)	0.12
Dmean [Gy]	75.16 (1.50)	74.26 (2.78)	0.17	75.21(1.53)	74.19(2.62)	0.10
D98% [Gy]	73.85 (1.81)	72.18 (4.39)	0.20	77.33(2.31)	71.21(4.96)	0.10
D50% [Gy]	75.18 (1.49)	74.34 (2.78)	0.23	75.25(1.49)	74.30(2.50)	0.12
D2% [Gy]	76.35 (1.62)	75.53 (2.68)	0.28	76.79(1.59)	76.04(2.25)	0.13
D70% [Gy]	74.83 (1.49)	73.98 (2.82)	0.22	74.80(1.55)	73.67(2.94)	0.13
D80% [Gy]	74.63 (1.49)	73.75 (2.85)	0.24	74.52(1.60)	73.31(3.22)	0.16
D65% [Gy]	74.92 (1.49)	74.08 (2.80)	0.24	74.92(1.53)	73.82(2.83)	0.12
D60% [Gy]	75.01 (1.49)	74.17 (2.79)	0.23	75.03(1.52)	73.98(2.72)	0.11
D35% [Gy]	75.33 (1.50)	74.59 (2.76)	0.20	75.57(1.48)	74.75(2.31)	0.14
D30% [Gy]	75.53 (1.51)	74.67 (2.74)	0.21	75.69(1.48)	74.89(2.28)	0.14
D15% [Gy]	75.83 (1.56)	74.99 (2.68)	0.22	76.08(1.50)	75.33(2.23)	0.12
D25% [Gy]	75.62 (1.53)	74.77 (2.68)	0.22	75.80(1.49)	75.03(2.26)	0.13
D3% [Gy]	76.27 (1.61)	75.45 (2.68)	0.28	76.67(1.57)	75.95(2.25)	0.13
D1cc [Gy]	62.40 (28.38)	63.33 (26.89)	0.89	76.78(1.58)	76.04(2.24)	0.12
D0.1cc [Gy]	76.20 (1.63)	75.43 (2.76)	0.32	77.27(1.67)	76.49(2.31)	0.12

## 4 Dose-Volume parameters for prostate gland and mpMRI-GTV for biochemical response at 5 years

### 4.1 Gleason score: any

	mpMRI-GTV			Prostate gland		
	Mean (SD)			Mean (SD)		
	BC	BR	Wilcoxon p-value	BC	BR	Wilcoxon p-value
Dmin [Gy]	72.60 (3.16)	71.75 (3.97)	0.48	70.89 (4.29)	69.19 (5.37)	0.23
Dmax [Gy]	76.68 (1.95)	76.23 (2.71)	0.59	77.79 (1.86)	76.99 (2.86)	0.34
Dmean [Gy]	74.98 (1.83)	74.52 (2.46)	0.52	75.08 (1.65)	74.23 (2.71)	0.28
D98% [Gy]	73.50 (2.61)	72.75 (3.32)	0.55	73.02 (2.74)	71.39 (4.72)	0.27
D50% [Gy]	75.00 (1.83)	74.61 (2.45)	0.61	75.13 (1.61)	74.35 (2.59)	0.35
D2% [Gy]	76.20 (1.86)	75.73 (2.59)	0.59	76.70 (1.63)	76.00 (2.54)	0.36
D70% [Gy]	74.64 (1.85)	74.23 (2.43)	0.59	74.67 (1.68)	73.69 (2.99)	0.32
D80% [Gy]	74.44 (1.86)	73.98 (2.42)	0.61	74.38 (1.76)	73.33 (3.22)	0.35
D65% [Gy]	74.74 (1.84)	74.34 (2.43)	0.63	74.79 (1.65)	73.85 (2.89)	0.30
D60% [Gy]	74.82 (1.83)	74.44 (2.44)	0.61	74.91 (1.64)	74.02 (2.79)	0.30
D35% [Gy]	75.27 (1.82)	74.85 (2.48)	0.56	75.45 (1.59)	74.83 (2.44)	0.41
D30% [Gy]	75.36 (1.82)	74.92 (2.49)	0.54	75.57 (1.59)	74.97 (2.43)	0.43
D15% [Gy]	75.67 (1.83)	75.20 (2.52)	0.52	75.97 (1.58)	75.38 (2.46)	0.42
D25% [Gy]	75.45 (1.82)	75.00 (2.50)	0.55	75.69 (1.58)	75.10 (2.43)	0.44
D3% [Gy]	76.12 (1.85)	75.65 (2.57)	0.57	76.58 (1.62)	75.91 (2.53)	0.35
D1cc [Gy]	61.86 (28.67)	63.23 (27.17)	0.97	76.67 (1.63)	76.00 (2.52)	0.35
D0.1cc [Gy]	76.04 (1.89)	75.66 (2.61)	0.66	77.18 (1.71)	76.43 (2.61)	0.32
D98% EQD2 (*)	72.71 (4.3)	71.23 (4.86)	0.34	71.97 (4.38)	69.27 (6.78)	0.21
gEUD2Gy (*, **)	74.79 (3.41)	73.71 (3.95)	0.27	74.86 (3.17)	72.80 (5.10)	0.12

\*for fixed  $\alpha/\beta=1.6\text{Gy}$ , \*\* for  $a=-10$

### 4.2 Gleason score: <8

	mpMRI-GTV			Prostate gland		
	Mean (SD)			Mean (SD)		
	BC	BR	Wilcoxon p-value	BC	BR	Wilcoxon p-value
Dmin [Gy]	72.78 (2.50)	70.53 (5.00)	0.23	71.09 (3.72)	68.75 (5.49)	0.19
Dmax [Gy]	76.83 (1.93)	75.15 (2.97)	0.06	77.97 (1.79)	76.12 (3.28)	0.08
Dmean [Gy]	75.06 (1.81)	73.71 (2.99)	0.13	75.19 (1.56)	73.47 (3.32)	0.15
D98% [Gy]	73.68 (2.14)	71.70 (4.16)	0.22	73.25 (2.18)	70.71 (5.74)	0.25
D50% [Gy]	75.07 (1.82)	73.82 (2.99)	0.16	75.23 (1.55)	73.65 (3.13)	0.16
D2% [Gy]	76.32 (1.84)	74.72 (2.95)	0.06	76.83 (1.57)	75.27 (3.06)	0.10
D70% [Gy]	74.72 (1.84)	73.51 (3.00)	0.21	74.75 (1.62)	72.86 (3.67)	0.16
D80% [Gy]	74.51 (1.86)	73.27 (3.00)	0.21	74.46 (1.70)	72.45 (4.00)	0.18
D65% [Gy]	74.81 (1.83)	73.60 (3.00)	0.21	74.88 (1.59)	73.05 (3.53)	0.16
D60% [Gy]	74.90 (1.82)	73.69 (2.99)	0.18	75.00 (1.58)	73.24 (3.39)	0.15
D35% [Gy]	75.35 (1.81)	74.01 (2.99)	0.12	75.56 (1.53)	74.21 (2.95)	0.20
D30% [Gy]	75.44 (1.81)	74.08 (2.99)	0.11	75.68 (1.52)	74.35 (2.95)	0.20
D15% [Gy]	75.76 (1.82)	74.31 (2.98)	0.10	76.10 (1.51)	74.73 (2.99)	0.19
D25% [Gy]	75.54 (1.81)	74.15 (2.99)	0.12	75.18 (1.52)	74.48 (2.96)	0.20
D3% [Gy]	76.23 (1.83)	74.66 (2.95)	0.06	76.72 (1.55)	75.20 (3.05)	0.12
D1cc [Gy]	61.59 (28.96)	66.79 (22.26)	0.74	76.82 (1.56)	75.29 (3.02)	0.10
D0.1cc [Gy]	76.15 (1.88)	74.70 (3.00)	0.11	77.34 (1.65)	75.64 (3.08)	0.07

D98% EQD2 (*)	72.77 (3.50)	69.96 (5.97)	0.19	72.12 (3.49)	68.60 (8.03)	0.30
gEUD2Gy (*, **)	74.78 (3.07)	72.71 (4.47)	0.12	74.88 (2.78)	71.82 (6.03)	0.18

\*for fixed  $\alpha/\beta=1.6\text{Gy}$ , \*\* for  $a=-10$

### 4.3 Gleason score: $\geq 8$

	mpMRI-GTV			Prostate gland		
	Mean (SD)			Mean (SD)		
	BC	BR	Wilcoxon p-value	BC	BR	Wilcoxon p-value
Dmin [Gy]	71.56 (5.54)	73.11 (1.41)	0.84	69.78 (6.59)	69.68 (5.18)	0.84
Dmax [Gy]	75.84 (1.84)	77.44 (1.72)	0.08	76.76 (1.88)	77.95 (1.87)	0.29
Dmean [Gy]	74.47 (1.85)	75.43 (1.13)	0.32	74.42 (1.98)	75.08 (1.38)	0.65
D98% [Gy]	72.45 (4.28)	73.93 (1.21)	0.56	71.67 (4.63)	72.15 (3.07)	1.00
D50% [Gy]	74.55 (1.82)	75.48 (1.14)	0.26	74.54 (1.84)	75.13 (1.46)	0.51
D2% [Gy]	75.51 (1.85)	76.86 (1.44)	0.14	75.88 (1.74)	76.80 (1.42)	0.32
D70% [Gy]	74.22 (1.84)	75.04 (1.11)	0.39	74.15 (1.91)	74.61 (1.52)	0.56
D80% [Gy]	74.04 (1.84)	74.77 (1.10)	0.36	73.89 (1.99)	74.31 (1.53)	0.60
D65% [Gy]	74.31 (1.84)	75.16 (1.12)	0.32	74.26 (1.89)	74.74 (1.51)	0.56
D60% [Gy]	74.39 (1.83)	75.27 (1.13)	0.29	74.36 (1.87)	74.88 (1.49)	0.56
D35% [Gy]	74.79 (1.81)	75.78 (1.20)	0.19	74.81 (1.81)	75.52 (1.39)	0.43
D30% [Gy]	74.88 (1.81)	75.87 (1.22)	0.23	74.90 (1.79)	75.66 (1.37)	0.43
D15% [Gy]	75.15 (1.83)	76.19 (1.28)	0.23	75.22 (1.75)	76.11 (1.33)	0.36
D25% [Gy]	74.96 (1.81)	75.96 (1.24)	0.26	74.99 (1.78)	75.80 (1.36)	0.43
D3% [Gy]	75.46 (1.85)	76.75 (1.40)	0.16	75.78 (1.73)	76.70 (1.40)	0.32
D1cc [Gy]	63.51 (26.81)	59.28 (31.28)	0.69	75.82 (1.73)	76.79 (1.44)	0.29
D0.1cc [Gy]	75.44 (1.88)	76.72 (1.48)	0.19	76.25 (1.79)	77.30 (1.54)	0.19
D98% EQD2 (*)	72.34 (7.41)	72.64 (2.54)	0.65	71.10 (7.67)	70.02 (4.91)	0.43
gEUD2Gy (*, **)	74.82 (4.87)	74.83 (2.57)	0.90	74.73 (4.80)	73.89 (3.07)	0.65

\*for fixed  $\alpha/\beta=1.6\text{Gy}$ , \*\* for  $a=-10$

## 5 TCP fitting results with fixed $\alpha/\beta=1.6\text{Gy}$ for mixed follow-up and 5 years

### 5.1 Model fitting results

Target type	$D_{50}$ (Gy) [95%CI]	$\gamma$ [95%CI]	$\alpha/\beta$ (Gy)	LL	Follow-up time	Patients number	Events number	Gleason score
prostate gland	67.13 [65.0, 69.2]	4.0 [2.7, 5.4]	1.6	60.02	Mixed time	129	26	any
mpMRI-GTV	67.10 [64.86, 69.20]	3.8 [2.6, 5.3]	1.6	61.18	Mixed time	129	26	any
prostate gland	65.41 [62.76, 67.8]	4.4 [3.1, 6.1]	1.6	36.03	Mixed time	103	14	< 8
mpMRI-GTV	65.96 [63.46, 68.22]	4.7 [3.2, 6.6]	1.6	36.77	Mixed time	103	14	< 8
prostate gland	63.9 [60.8, 67.0]	2.9 [1.9, 4.1]	1.6	48.08	5 years	108	19	any
mpMRI-GTV	56.3 [51.6, 61.1]	1.3 [0.9, 1.9]	1.6	49.55	5 years	108	19	any
prostate gland	62.96 [59.54, 66.12]	3.6 [2.4, 5.1]	1.6	28.29	5 years	86	10	< 8
mpMRI-GTV	59.18 [54.78, 63.32]	2.4 [1.6, 3.5]	1.6	29.68	5 years	86	10	< 8

### 5.2 EQD2 values for 90% and 95% TCP for prostate gland and mpMRI-GTV

Target type	EQD2 for TCP=90% (min, max)	EQD2 for TCP=95% (min, max)	$\alpha/\beta$ (Gy)	Follow-up time	Gleason score
prostate gland	78.6 (73.1, 86.7)	83.1 (76.3, 93.4)	1.3	Mixed time	any
mpMRI-GTV	78.4 (73.5, 85.6)	82.4 (76.3, 91.5)	2.9	Mixed time	any
prostate gland	78.4 (73.2, 86.2)	82.7 (76.3, 92.6)	1.6	Mixed time	any
mpMRI-GTV	77.3 (72.1, 84.5)	81.2 (74.9, 90.4)	1.6	Mixed time	any
prostate gland	75.5 (69.8, 82.3)	79.3 (72.5, 87.9)	1.6	Mixed time	< 8
mpMRI-GTV	75.5 (70.0, 82.4)	79.1 (72.5, 87.8)	1.6	Mixed time	< 8
prostate gland	78.5 (70.8, 89.9)	84.1 (74.6, 98.6)	1.6	5 years	any
mpMRI-GTV	83.5 (69.3, 101.9)	93.9 (76.1, 117.5)	1.6	5 years	any
prostate gland	74.7 (67.5, 84.1)	79.2 (70.5, 91.0)	1.6	5 years	< 8
mpMRI-GTV	75.4	81.6	1.6	5 years	< 8

	(65.3, 88.6)	(69.3, 98.3)			
--	--------------	--------------	--	--	--

## 6 Results for logistic regression model including Gleason

### 6.1 Mixed follow-up time for $\alpha/\beta=1.3\text{Gy}$ for prostate gland and $\alpha/\beta=2.9\text{Gy}$ for mpMRI-GTV

```
Call:
glm(formula = relapsed ~ dose_ptv + volume_gtv + gscorelevel,
     family = "binomial", data = datacombi)
```

```
Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.9729  -0.5619  -0.4461  -0.2626   2.5708
```

```
Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)  9.43944    4.59452   2.054  0.03993 *
dose_ptv     -0.19255    0.06243  -3.084  0.00204 **
volume_gtv   0.11523    0.05674   2.031  0.04226 *
gscorelevel  1.36321    0.45084   3.024  0.00250 **
```

```
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

(Dispersion parameter for binomial family taken to be 1)

```
Null deviance: 129.66 on 128 degrees of freedom
Residual deviance: 103.80 on 125 degrees of freedom
AIC: 111.8
```

### 6.2 Mixed follow-up time for $\alpha/\beta=1.6\text{Gy}$

```
> step.model <- mylogitAll %>% stepAIC(trace = FALSE, direction = "both")
> summary(step.model)
```

```
Call:
glm(formula = relapsed ~ dose_ptv + volume_gtv + gscorelevel,
     family = "binomial", data = datacombi)
```

```
Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.9705  -0.5649  -0.4454  -0.2641   2.5734
```

```
Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept) 10.05218    4.79468   2.097  0.03604 *
dose_ptv     -0.20068    0.06517  -3.079  0.00207 **
volume_gtv   0.11493    0.05665   2.029  0.04247 *
gscorelevel  1.36445    0.45061   3.028  0.00246 **
```

```
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

(Dispersion parameter for binomial family taken to be 1)

```
Null deviance: 129.66 on 128 degrees of freedom
Residual deviance: 103.86 on 125 degrees of freedom
AIC: 111.86
```

### 6.3 At 5 Years for $\alpha/\beta=1.6\text{Gy}$

```
> step.model <- mylogitAll %>% stepAIC(trace = FALSE, direction = "both")
> summary(step.model)
```

```
Call:
glm(formula = relapsed ~ dose_gtv + dose_ptv + volume_gtv + gscorelevel,
     family = "binomial", data = datacombi)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-1.7887	-0.5614	-0.4468	-0.3107	2.4065

Coefficients:

	Estimate	Std. Error	z value	Pr(> z )
(Intercept)	4.85930	5.79152	0.839	0.4014
dose_gtv	0.34981	0.24061	1.454	0.1460
dose_ptv	-0.47206	0.25420	-1.857	0.0633 .
volume_gtv	0.09080	0.05143	1.765	0.0775 .
gscorelevel	1.00875	0.48779	2.068	0.0386 *

---

Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 100.474 on 107 degrees of freedom  
Residual deviance: 83.759 on 103 degrees of freedom  
AIC: 93.759