

**PREDICTORS FOR RECTAL AND INTESTINAL ACUTE  
TOXICITIES FROM 3D-CRT PROSTATE CANCER:  
RESULTS OF A PROSPECTIVE MULTICENTER STUDY**

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## **PURPOSE**

**TO INVESTIGATE IN PROSTATE CANCER PATIENTS TREATED  
WITH CONFORMAL RADIATION  
THE CORRELATION BETWEEN CLINICAL, TECHNICAL,  
DOSIMETRIC VARIABLES AND ACUTE RECTAL TOXICITY,  
USING RTOG/EORTC SCORING SYSTEM AND  
PATIENTS' ASSESSED 11 ITEM QUESTIONNAIRE**

## **METHODS AND MATERIALS 1.**

### **AIROPROS 0102 TRIAL: PRE-REQUISITES**

- ✓ **TOXICITY SCORING SCALES DISCUSSED AND ACCEPTED**
- ✓ **DEFINITION AND VALIDATION OF A SELF-ASSESSED QUESTIONNAIRE ON RECTAL TOXICITY**
- ✓ **CONSISTENCY IN RECTUM CONTOURING**
- ✓ **DOSIMETRIC CONSISTENCY IN DOSE AND DVH CALCULATION**

## METHODS AND MATERIALS 2.

✓ **RECTAL ACUTE TOXICITY EVALUATION SYSTEMS**

**A. MODIFIED\* RTOG/EORTC (GRADE 2-3)**

**B. PATIENT ASSESSED 11 ITEM QUESTIONNAIRE BASED ON SOMA LENT SCALE**

<b>STOOL FREQUENCY</b>	<b>2 ITEMS</b>
TENESMUS	2 ITEMS
SOILING	3 ITEMS
PAIN	1 ITEM
<b>BLEEDING</b>	<b>1 ITEM</b>
DRUG PRESCRIPTION	2 ITEMS

✓ **TIMING OF TOXICITY EVALUATION:**

**TIME 0: BEFORE TREATMENT**

**TIME 1: ONE MONTH AFTER TREATMENT COMPLETION**

## METHODS AND MATERIALS 3.

✧ **1132 PATIENTS ACCRUED** (JULY 2002 – MARCH 2004; 22 CENTRES)



✧ **1124/1132 (99.3%) available for RTOG/EORTC LGI toxicity**

**1116/1132 (98.6%) available for “stool frequency”**

**1060/1132 (93.6%) available for “rectal bleeding”**

# METHODS AND MATERIALS 4.

## PRE-TREATMENT AND TREATMENT CHARACTERISTICS

### CLINICAL

✓ HYPERTENSION	46.2 %
✓ ANDROGEN DEPRIVATION	74.2%
✓ HAEMORRHOIDS	21.1 %
✓ ANTICOAGULANTS	21.0 %
✓ HYPOGLICAEMIC DRUGS	8.4 %

### DOSIMETRIC

✓ PELVIC IRRADIATION	5.8 %
✓ DOSE TO THE PELVIS (mean)	46.8 Gy
✓ SEMINAL VESICLES IRRADIATION	81.1 %
✓ DOSE TO THE SEMINAL VESICLES (mean)	66.2 Gy
✓ DOSE TO THE PROSTATE (mean)	74.4 Gy
✓ MEAN DOSE TO THE RECTUM (mean)	50.1 Gy

# METHODS AND MATERIALS 5.

## STATISTICAL ANALYSIS

### ✓ VARIABLES EXAMINED

#### CLINICAL:

HYPERTENSION  
DIABETES  
ANDROGEN DEPRIVATION ( $\leq 3$  mos;  $> 3$  mos)  
HAEMORRHOIDS  
CONCOMITANT USE OF DRUGS

#### DOSIMETRIC:

TOTAL DOSE DELIVERED  
PELVIC IRRADIATION  
PROSTATE VOLUME  
MEAN AND MAXIMUM RECTAL DOSE  
(*RECTAL DVH CONSTRAINTS*)

### ✓ UNIVARIATE AND MULTIVARIATE LOGISTIC ANALYSES

# RESULTS

## END POINTS ANALYZED

- RTOG/EORTC LGI TOX (GRADE  $\geq 1$ )
- **RTOG/EORTC LGI TOX (GRADE  $\geq 2$ )**
- SEVERE DIARRHEA
- **INCREASED STOOL FREQUENCY**
- TENESMUS
- PAIN
- **MODERATE/SEVERE BLEEDING**
- SEVERE FECAL INCONTINENCE
- USE OF DRUGS

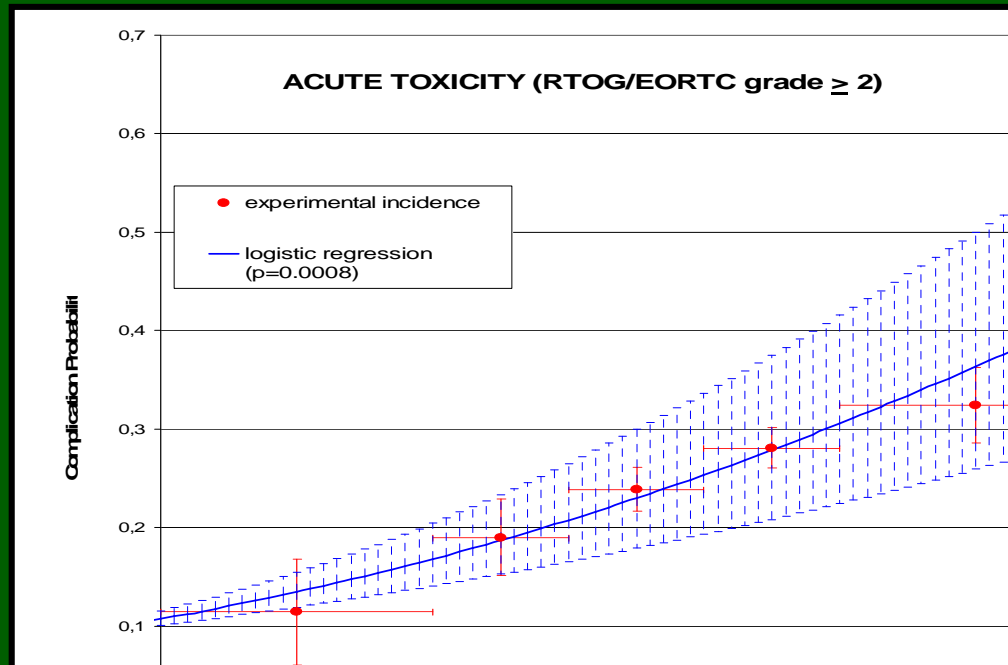
## RESULTS 1.

**RTOG/EORTC LGI grade  $\geq 2$**  ( 293/1124 events, 26% )

	univariate analysis			MVA	
	p value	Inc. % no	Inc. % yes	p value	OR
HAEMORRHOIDS	0,08	25,0	30,6	<b>0,02</b>	1,51
ANTICOAGULANTS	0,02	27,6	20,2	<b>0,02</b>	0,63
DIABETES	0,07	25,3	34,0	0,34	1,28
AD	0,06	31,9	24,4	<b>0,04</b>	0,65
PELVIC XRT	0,04	25,4	36,9	0,11	1,56
MEAN RECTAL DOSE *	0,02	22,0	29,9	<b>0,0004</b>	1,035

\*median stratified, median value = 51 Gy

**THE PREDICTING VALUE OF  
MEAN RECTAL DOSE**



## RESULTS 2.

### SOMA/LENT grade $\geq 2$ (QUESTIONNAIRES)

#### INCREASED STOOL FREQUENCY

(more than 4 bowel movements per day)

40/1116 events, 3.6%

	univariate analysis			MVA	
	p value	% no	% yes	p value	OR
AD > 3 months	0,002	6,8	2,3	0,002	0,32
Seminal vesicles irr.	0,02	0,9	4,2	0,07	6,46
Mean rectal dose*	0,06	2,5	4,7	0,47	1,02
V60				0,02	1,024

\*median stratified, median value=51 Gy

### RESULTS 3.

**SOMA/LENT grade  $\geq 2$  (QUESTIONNAIRES)**

#### **MODERATE/SEVERE RECTAL BLEEDING**

**(more than 2 times per week)**

*127/1060 events, 12.0%*

	Chi-squared test			MVA	
	p value	% no	% yes	p value	OR
Haemorrhoids	0.002	10.5	18.2	0.02	1.73
AD	0.08	16.2	10.8	0.17	0.67
Mean rectal dose				0.009	1.04

## CONCLUSION 1.

THE ANALYSIS OF **RTOG/EORTC GRADE 2-3 ACUTE LGI TOXICITY** SHOWS:

- ✓ MEAN RECTAL DOSE IS THE STRONGEST PREDICTOR FOR ACUTE RECTAL TOXICITY (2.8 % / Gy)
- ✓ HORMONAL THERAPY AND ANTICOAGULANTS ARE PROTECTIVE FACTORS FOR ACUTE RECTAL TOXICITY

## CONCLUSION 2.

THE ANALYSIS OF **SELF-REPORTED QUESTIONNAIRES** SHOWS:

- ✓ DOSIMETRIC PARAMETERS ARE HIGHLY PREDICTIVE FOR  
RECTAL BLEEDING (MEAN RECTAL DOSE)  
SEVERE STOOL FREQUENCY (V60)
- ✓ LARGER IRRADIATED VOLUMES ARE CORRELATED TO  
SEVERE STOOL FREQUENCY  
TENESMUS

## CONCLUSION 2.

(SELF-REPORTED QUESTIONNAIRES cont'd)

- ✓ HAEMORRHOIDS ARE ASSOCIATED WITH A HIGHER INCIDENCE OF  
RECTAL BLEEDING  
TENESMUS
- ✓ HYPOGLYCAEMIC AND ANTIHYPERTENSIVE DRUGS ARE HIGHLY ASSOCIATED  
WITH DIARRHEA (ANTIHYPERTENSIVES: PROTECTIVE)
- ✓ HORMONAL THERAPY IS PROTECTIVE FOR  
SEVERE STOOL FREQUENCY  
RECTAL BLEEDING  
TENESMUS