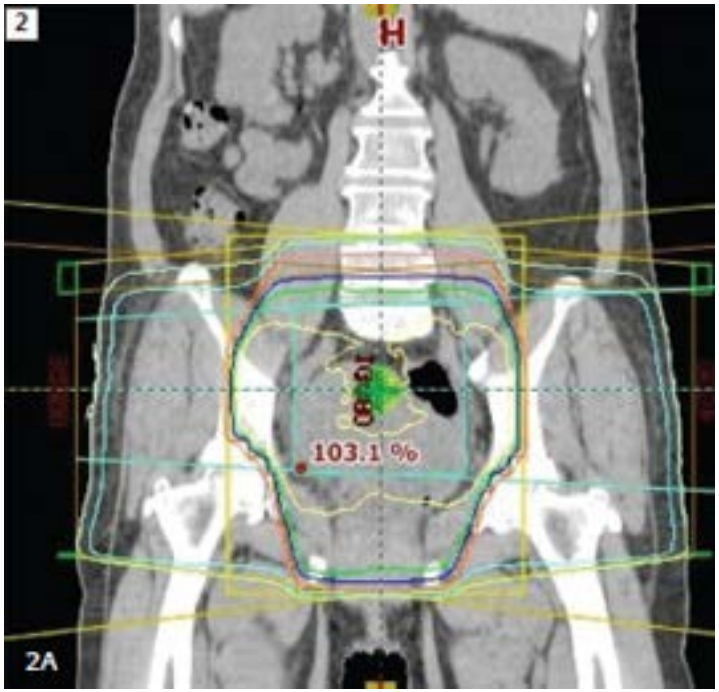
Dose Constraints for Target volume and OARs

Petch Alisanant,MD.
King Chulalongkorn Memorial Hospital
Bangkok, Thailand

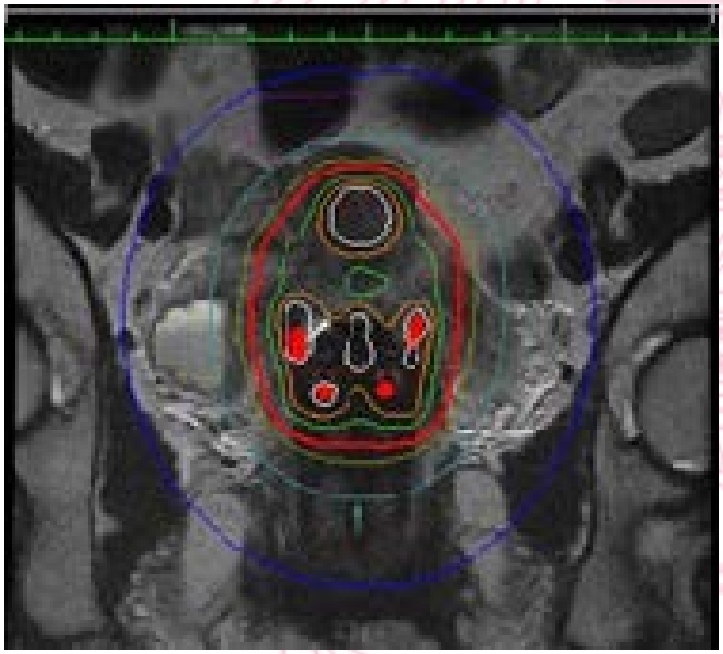
Planning aim to dose prescription

Planning aim dose
- Set of dose and dose/volume constraints for a treatment

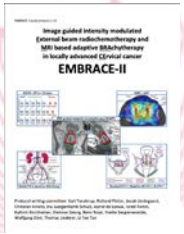
Prescribed dose
-Finally accepted treatment plan (which is assumed to be delivered to an individual patient)







EMBRACE II dose constraints



Target	D90 CTV_{HR} $EQD2_{10}$	D98 CTV_{HR} $EQD2_{10}$	D98 GTV_{res} $EQD2_{10}$	D98 CTV_{IR} $EQD2_{10}$	Point A $EQD2_{10}$
Planning Aims	> 90 Gy < 95 Gy	> 75 Gy	>95 Gy	> 60 Gy	> 65 Gy
Limits for Prescribed Dose	> 85 Gy	-	>90 Gy	-	-
OAR	Bladder D_{2cm^3} $EQD2_3$	Rectum D_{2cm^3} $EQD2_3$	Recto-vaginal point $EQD2_3$	Sigmoid D_{2cm^3} $EQD2_3$	Bowel D_{2cm^3} $EQD2_3$
Planning Aims	< 80 Gy	< 65 Gy	< 65 Gy	< 70 Gy*	< 70 Gy*
Limits for Prescribed Dose	< 90 Gy	< 75 Gy	< 75 Gy	< 75 Gy*	< 75 Gy*

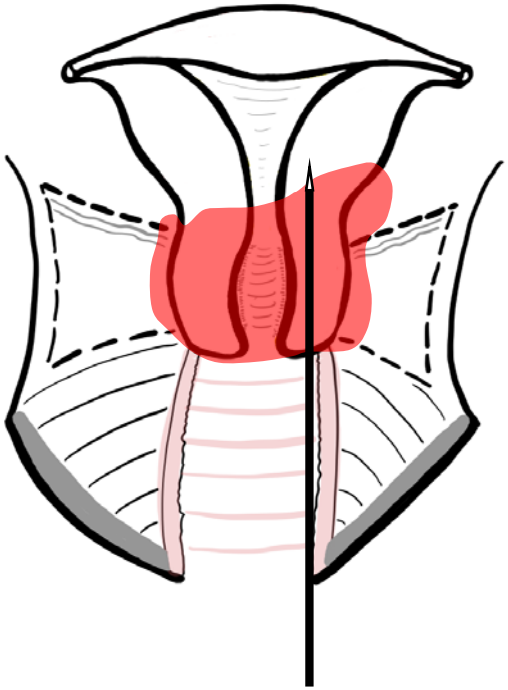
* for the sigmoid/bowel structures these dose constraints are valid in case of non-mobile bowel loops resulting in the situation that the most exposed volume is located at a similar part of the organ

Dose Constraints



1. Target volume → good local control , overall survival

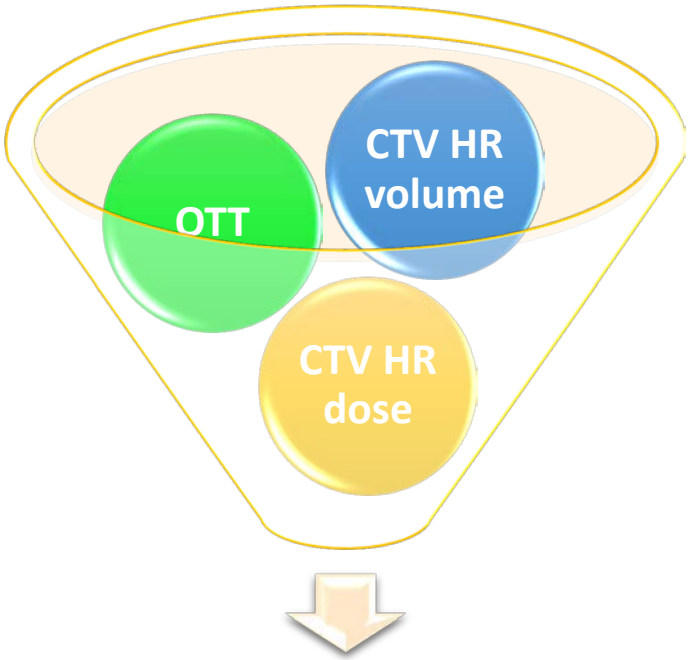
2. Organ at risks → reduce long term toxicity
    - Bladder
    - Rectum
    - Bowel
    - Vagina



Target volume

Effect of tumor dose, volume and overall treatment time on local control after radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer

Kari Tanderup [a,*], Lars Ulrik Fokdal [a], Alina Sturdza [b], Christine Haie-Meder [c], Renaud Mazeron [c], Erik van Limbergen [d], Ina Jürgenliemk-Schulz [e], Primoz Petric [f,g], Peter Hoskin [h], Wolfgang Dörr [b], Søren M. Bentzen [i], Christian Kirisits [b], Jacob Christian Lindegaard [a], Richard Pötter [b]



retroEMBRACE data n=488

Volume	3-year Local control
CTV_{HR} ≤ 20 cc Limited size	> 94 %
CTV_{HR} ≤ 30 cc Intermediate size	> 93%
CTV_{HR} ≤ 70 cc Large size	> 86%

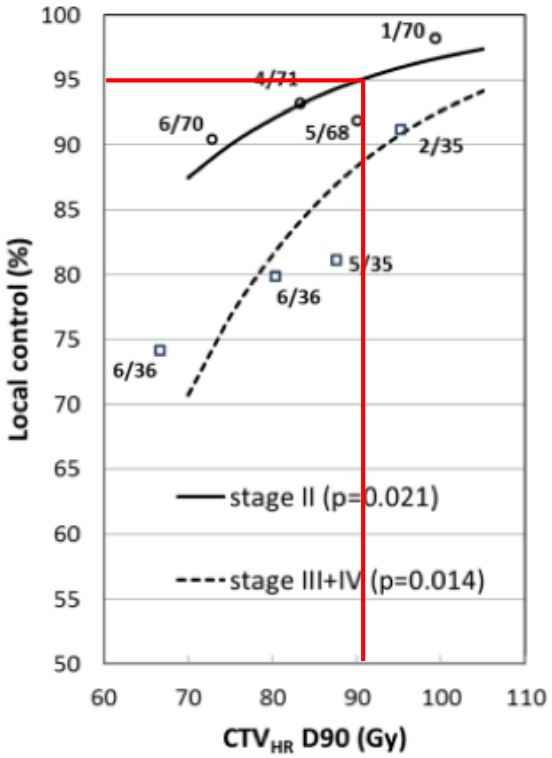
Rx : ≥85Gy EQD2 in 7 weeks

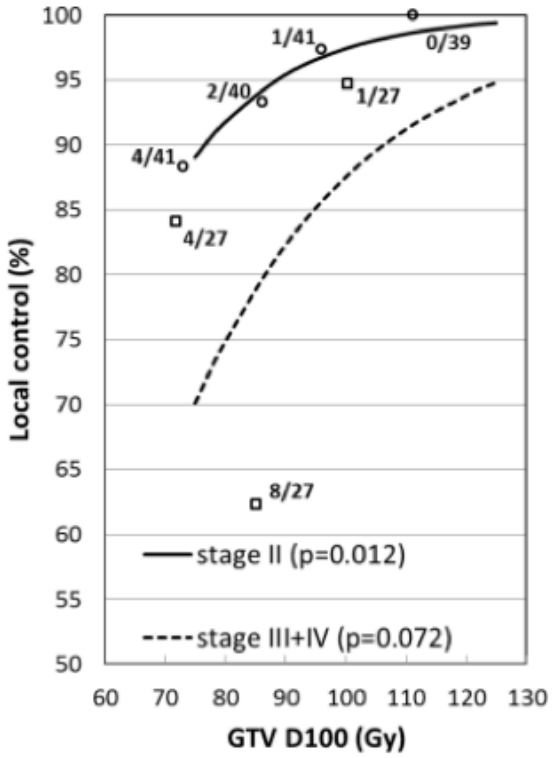
CTV_{IR} D98 ⩾60Gy and GTV_{res} D98 ⩾95Gy → similar LC+

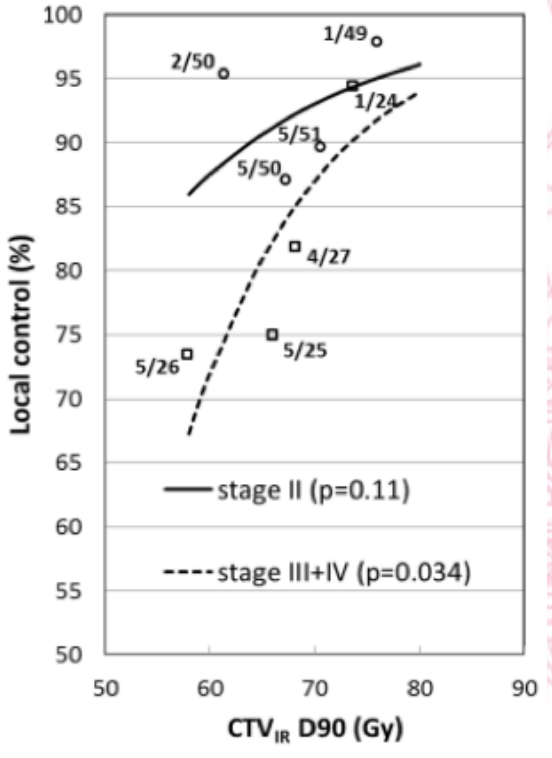
⇧ CTV_{HR} volume by 10 cm^3 → ⇧ 5 Gy for ≈ LC

Tanderup K, Radiother Oncol 2016 Sep 30;120(3):441-6

Dose response in stage II and stage III for adaptive CTV-THR, GTV-Tres and CTV-TIR.



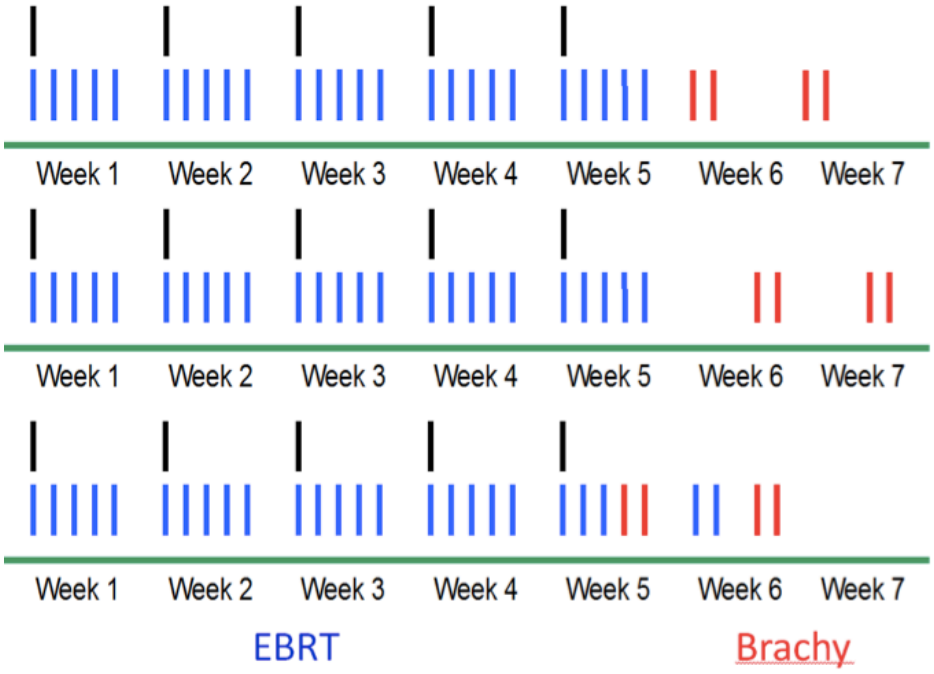




Tanderup K, Radiother Oncol 2016 Sep 30;120(3):441-6.

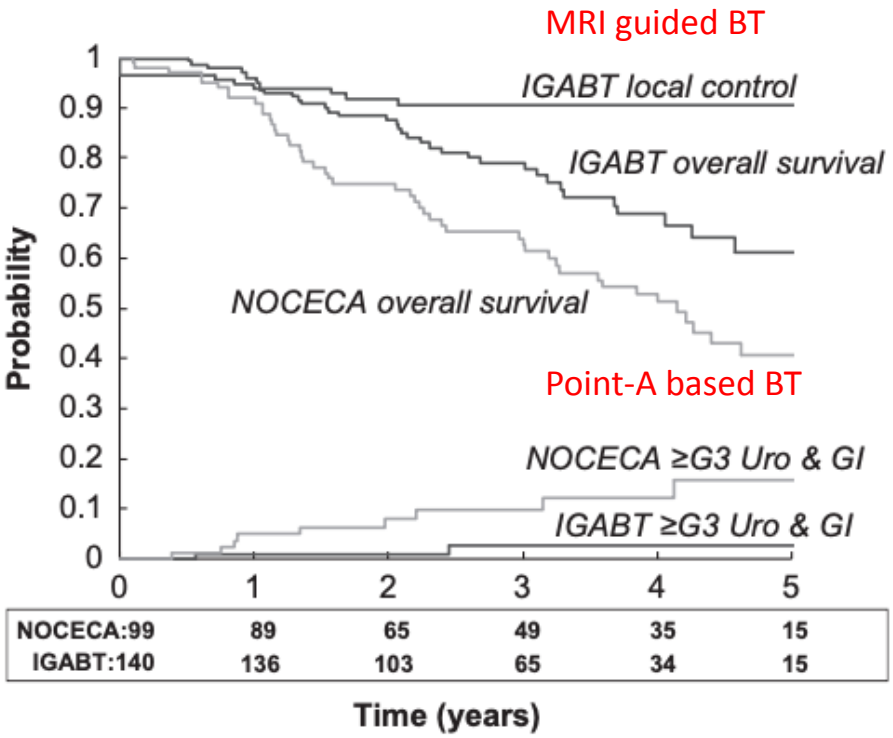
Overall treatment time (OTT)

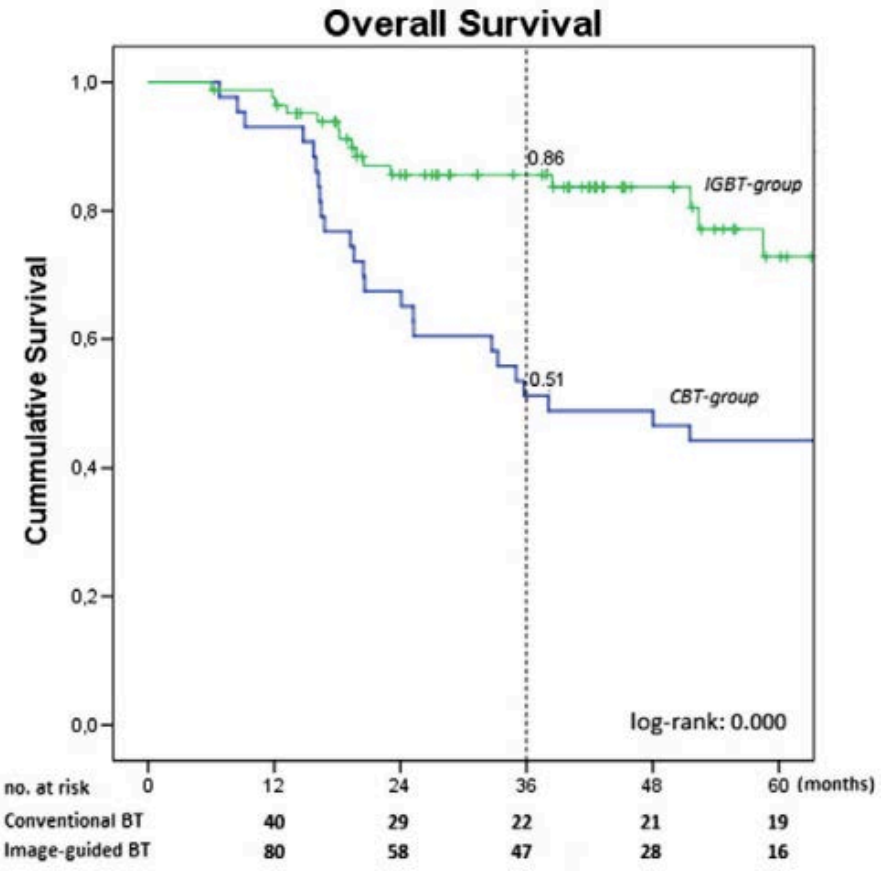
- OTT defined from the first external beam fraction to the final external beam or brachytherapy fraction dose is delivered
- Should less than 50 days
- ⇧ OTT by one week → ⇧ CTV_{HR} dose by 5 Gy for compensation



Tanderup K, Radiother Oncol 2016 Sep 30;120(3):441-6

⇧ Local control → improved survival





Aarhus Experience

Leiden Experience

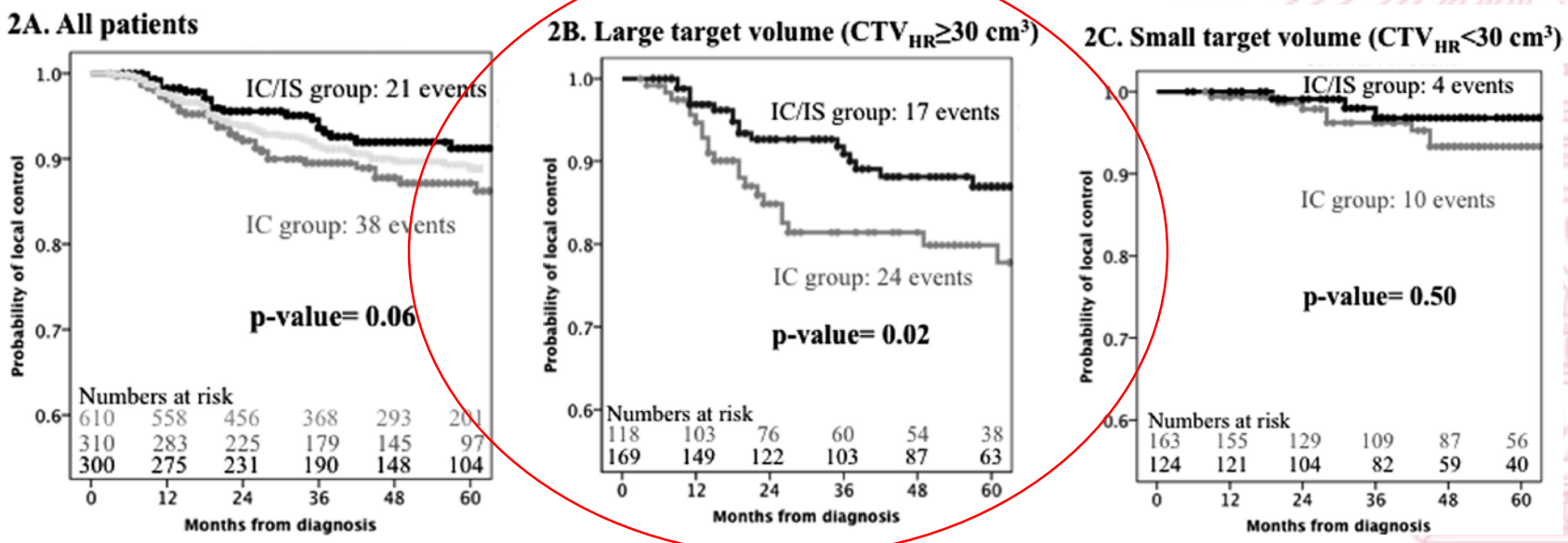
Linedegaard,Acta Oncol. 2013 Oct;52(7):1510-9.

Rijkmans EC, Gynecol Oncol. 2014 Nov;135(2):231-8.

Retro EMBRACE : IC vs IC+IS

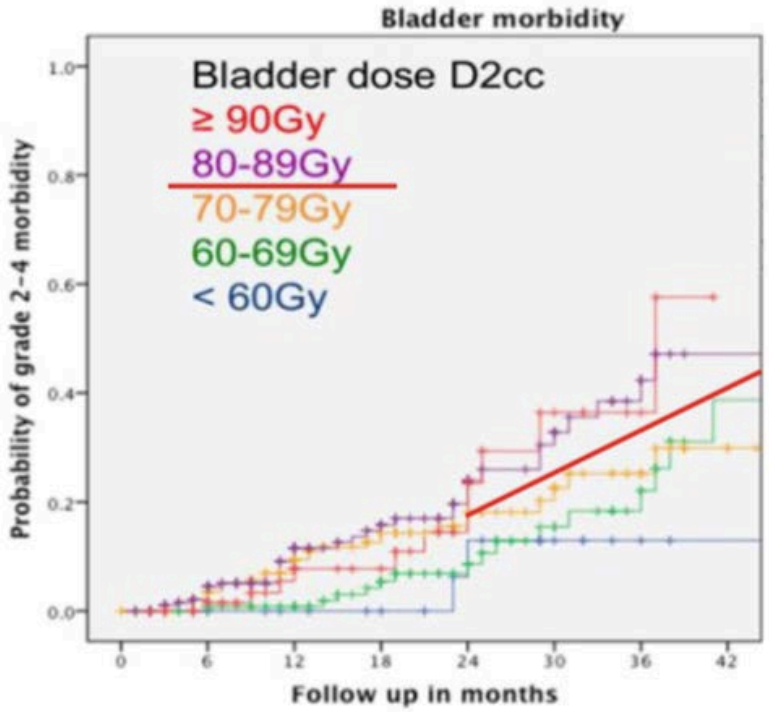
- n = 610 (IC/IS Group = 300 , IC Group = 310)

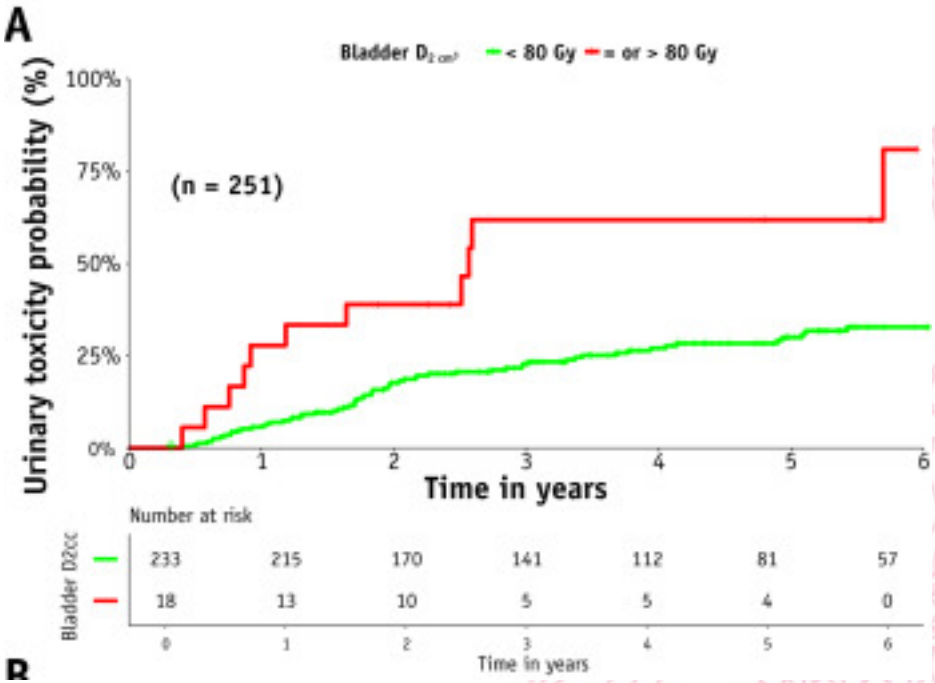
Local Control



Fokdal L, et al. Radiother Oncol 2016;120:434-40.

Bladder toxicity





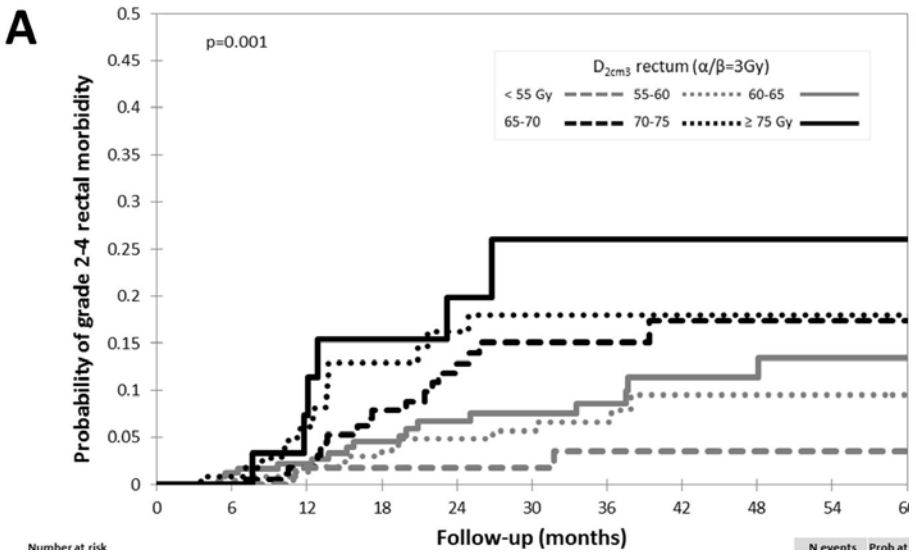
Bladder D_{2cm^3} > 80 Gy → ⇧ ≥ Gr2 morbidity

Bladder D_{2cm^3} ≤ 80 Gy EQD2 → < 15% severe urinary complications

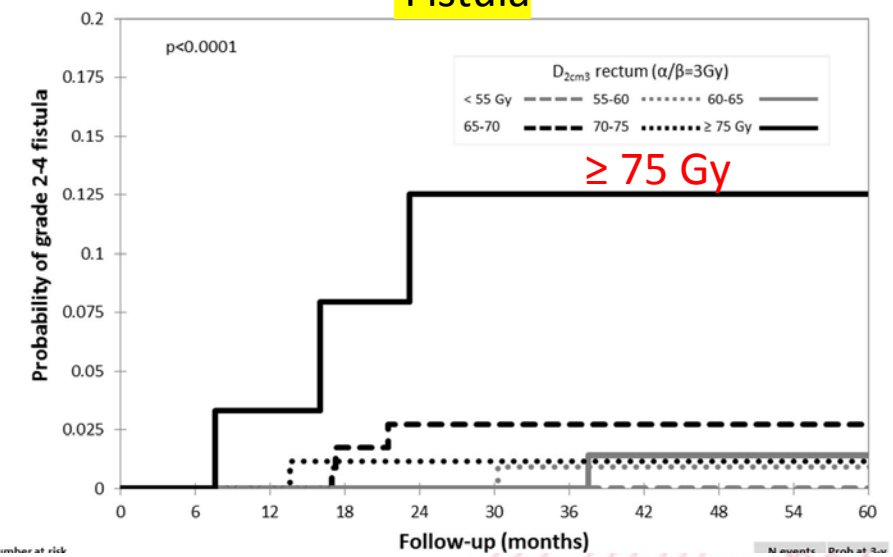
EMBRACE study

Manea E, Int J Radiat Oncol Biol Phys. 2018 Jun 1;101(2):411-420.

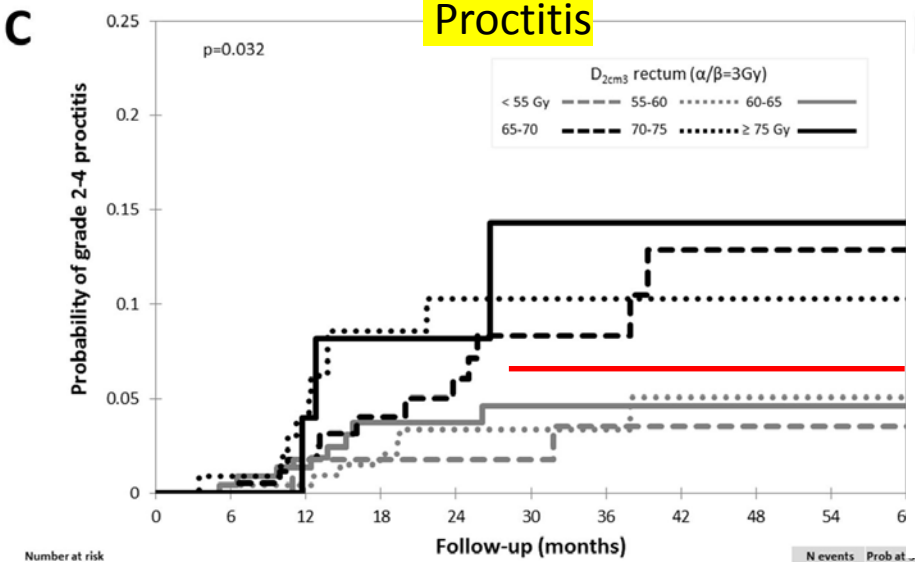
Rectal toxicity



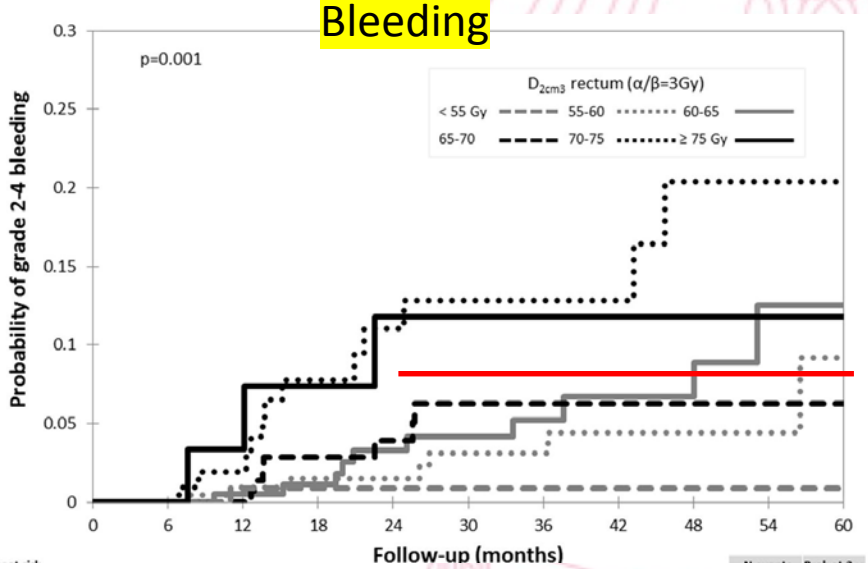
Fistula



Proctitis

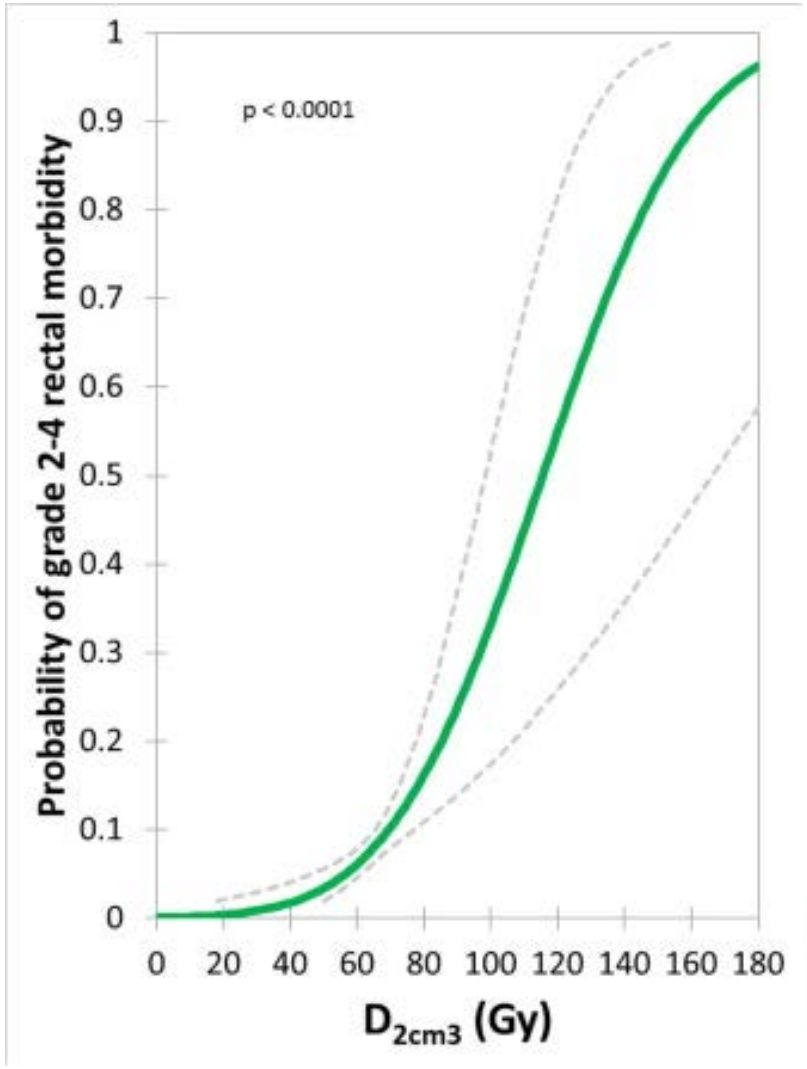


Bleeding



Mazeron R, Radiother Oncol. 2016 Sep;120(3):412-419.

Rectal toxicity

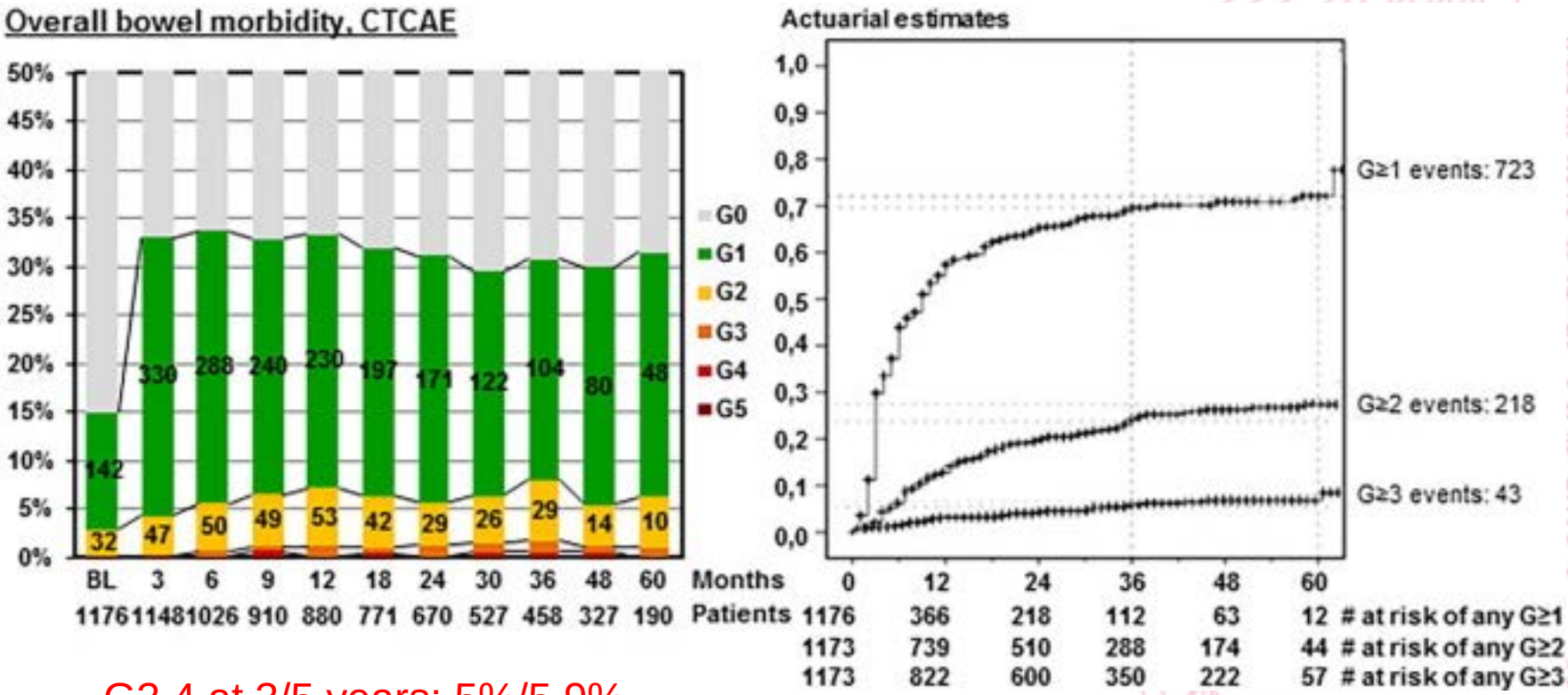


Mazeron R, Radiother Oncol. 2016 Sep;120(3):412-419.

EMBRACE

Bowel morbidity following radiochemotherapy and image-guided adaptive brachytherapy for cervical cancer: Physician- and patient reported outcome from the EMBRACE study

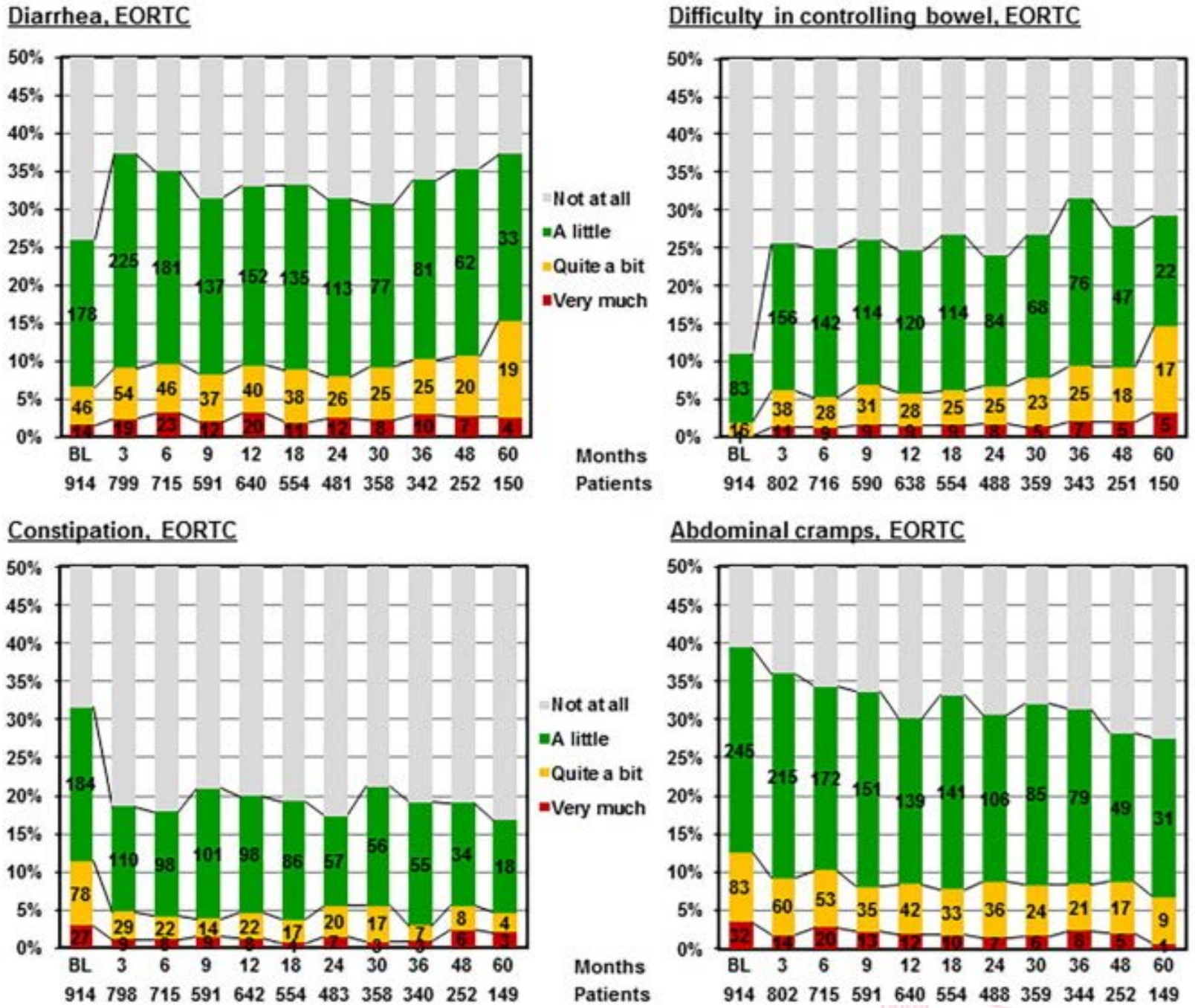
Nina Boje Kibsgaard Jensen [a,*], Richard Pötter [b], Kathrin Kirchheiner [b], Lars Fokdal [a], Jacob Christian Lindegaard [a], Christian Kirisits [b], Renaud Mazeron [c], Umesh Mahantshetty [d], Ina Maria Jürgenliemk-Schulz [e], Barbara Segedin [f], Peter Hoskin [g], Kari Tanderup [a], EMBRACE Collaborative Group [1]



G3,4 at 3/5 years: 5%/5.9%

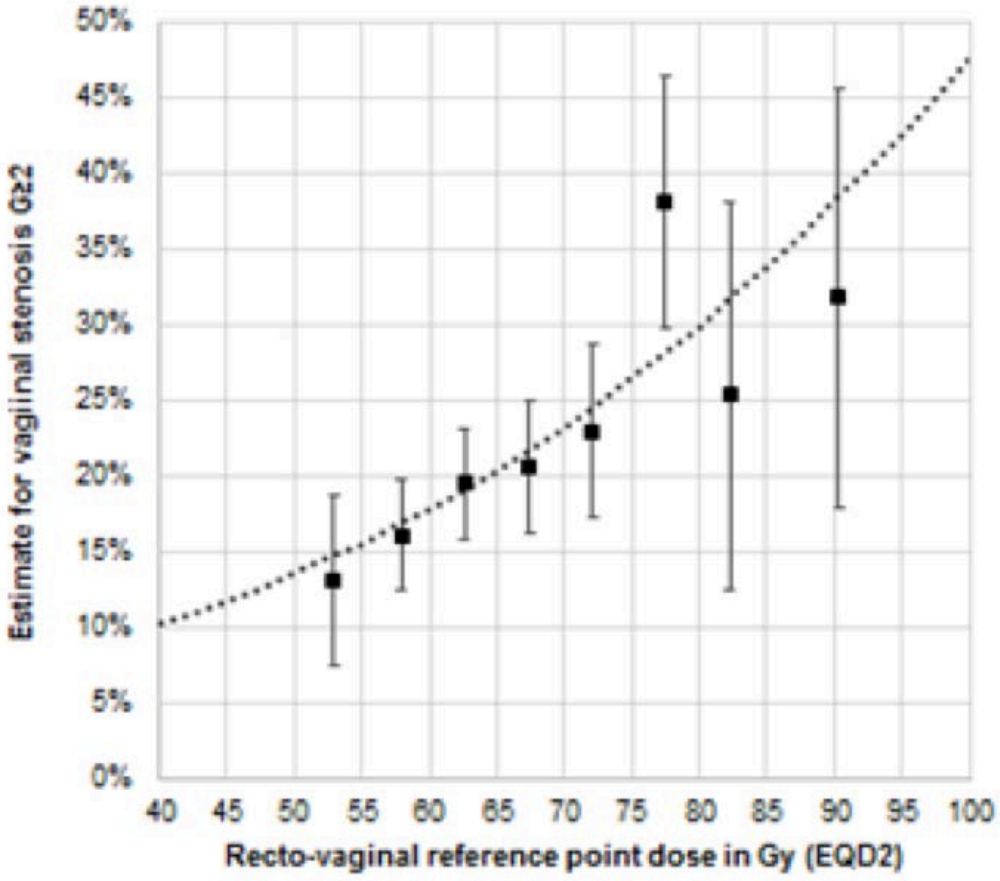
Jensen NBK, Radiother Oncol. 2018 Jun;127(3):431-439.

PRO



Jensen NBK, Radiother Oncol. 2018 Jun;127(3):431-439.

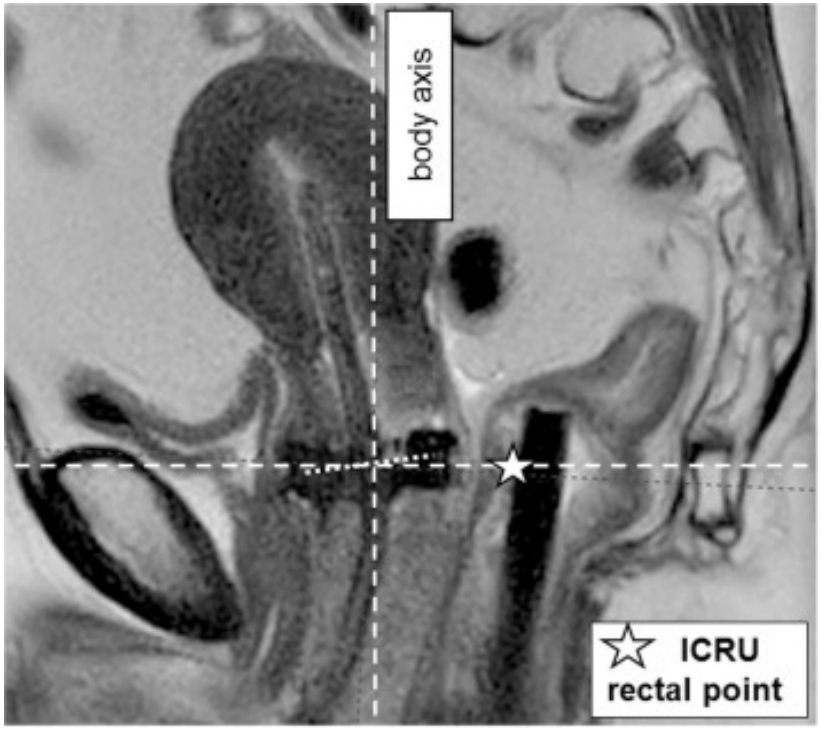
Vagina



At a dose level of 65Gy the incidence of vaginal stenosis was 20% and this increased to 27% at a dose of 75Gy

K. Kirchheiner et al./Radiotherapy and Oncology 118 (2016) 160–166.

Vagina

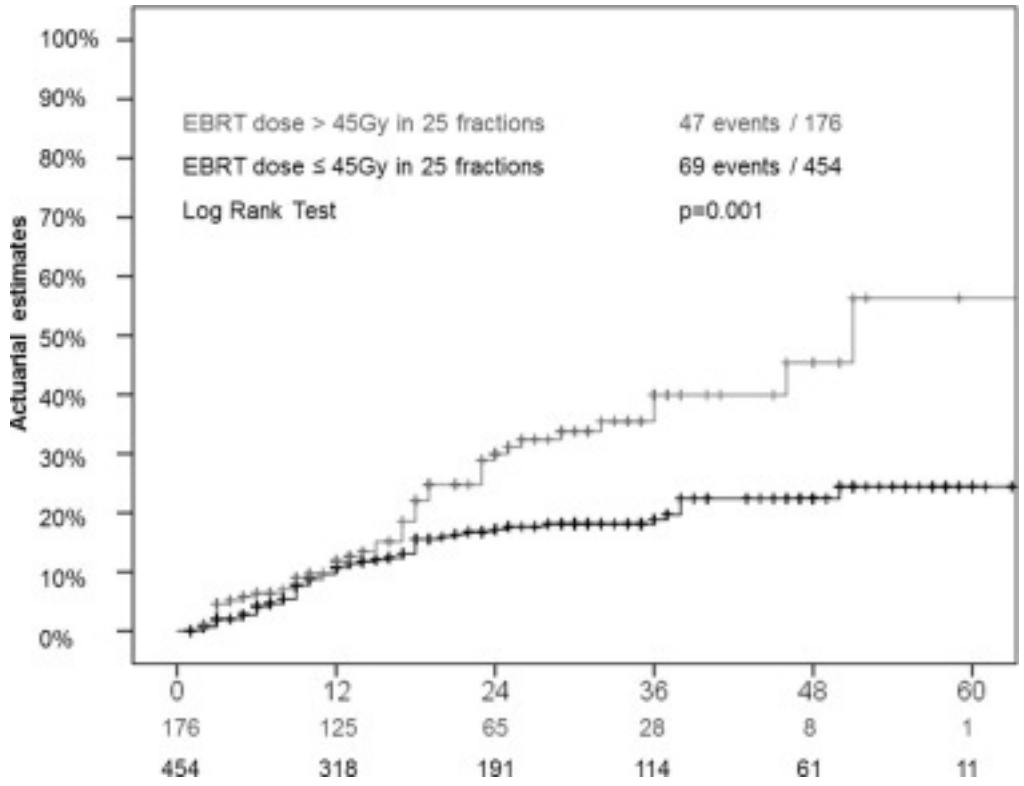


Vaginal stenosis

- Recto-vaginal point dose
- EBRT dose > 45 Gy/25Fx
- Tumor extension in the vagina

K. Kirchheiner et al./Radiotherapy and Oncology 118 (2016) 160–166.

Vagina

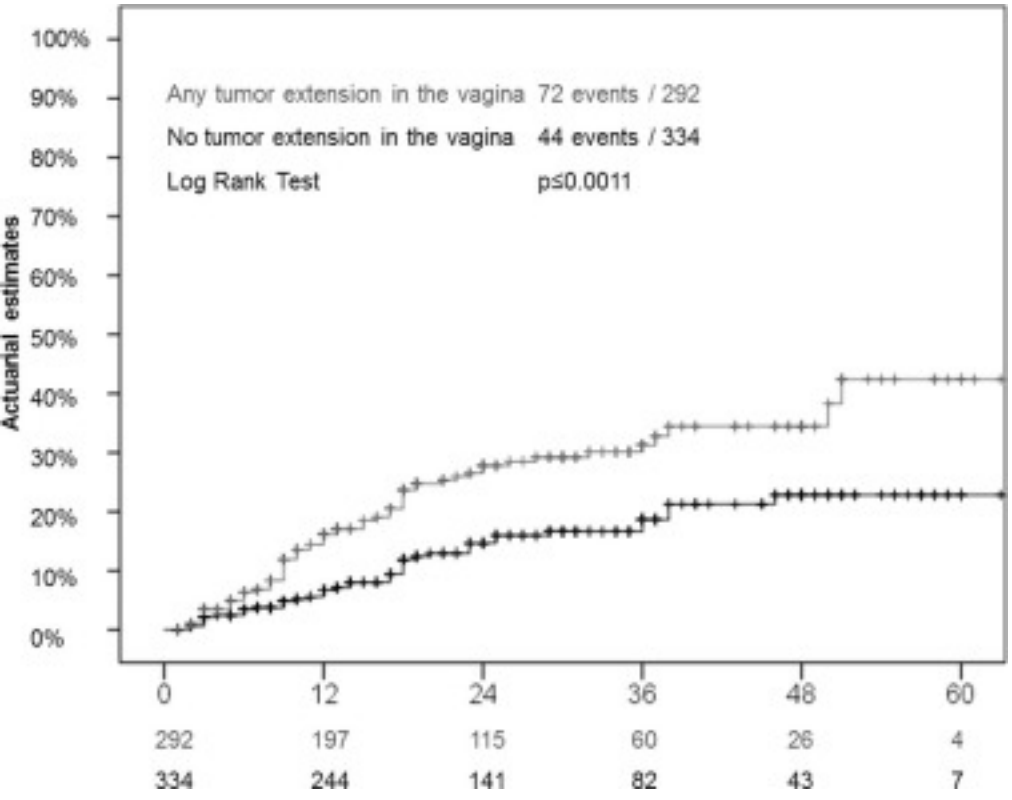


Vaginal stenosis

- Recto-vaginal point dose
- EBRT dose > 45 Gy/25Fx
- Tumor extension in the vagina

K. Kirchheiner et al./Radiotherapy and Oncology 118 (2016) 160–166.

Vagina



Vaginal stenosis

- Tumor extension in the vagina

K. Kirchheiner et al./Radiotherapy and Oncology 118 (2016) 160–166.

Planning aim and dose prescription EMBRACE II protocol

Target	D90 CTV_{HR} $EQD2_{10}$	D98 CTV_{HR} $EQD2_{10}$	D98 GTV_{res} $EQD2_{10}$	D98 CTV_{IR} $EQD2_{10}$	Point A $EQD2_{10}$
Planning Aims	> 90 Gy < 95 Gy	> 75 Gy	>95 Gy	> 60 Gy	> 65 Gy
Limits for Prescribed Dose	> 85 Gy	-	>90 Gy	-	-

CTVHR > 85 Gy		> 90 Gy - <95 Gy
EMBRACE II treatment schedule		
EBRT 45 Gy / 25 Fx $EQD2_{10}$ = 44.2 Gy	Brachy 7 Gy x 4 Fx $EQD2_{10}$ = 39.7 Gy	**$EQD2_{10}$ = 83.9 Gy**
KCMH treatment schedule		
EBRT 50.4 Gy / 28 Fx $EQD2_{10}$ = 49.6 Gy	**Brachy 8 Gy x 3Fx $EQD2_{10}$ = 36 Gy**	**$EQD2_{10}$ = 85.6 Gy**

Example

EMBRACE II protocol : EBRT 45 Gy in 25 Fx + Brachytherapy 7 Gy x 4 Fx

		1st Brachy	2nd Brachy	3rd Brachy	4th Brachy	Total dose EBRT+BT	Aim
		Gy	Gy	Gy	Gy	$EQD2_{10}$	
GTV	D_{98}	10.1	10.1	10.7	10.7	115	>95
CTV_{HR}	D_{98}	6.5	6.5	6.7	6.7	80.8	>75
	D_{90}	7.9	7.9	8.1	8.1	92.3	>90
CTV_{IR}	D_{98}	3.6	3.6	3.8	3.8	61.2	>60

	Too low	Acceptable	Good
GTV D_{98}	0 - 7.8	7.8 - 8.4	> 8.4
CTV_{HR} D_{98}	0 - 5.9		> 5.9
CTV_{HR} D_{90}	0 – 7.2	7.2 – 7.8	7.8 – 8.4
CTV_{IR} D_{98}	0 – 3.6		> 3.6

Planning aim and dose prescription EMBRACE II protocol

OAR	Bladder D_{2cm^3} $EQD2_3$	Rectum D_{2cm^3} $EQD2_3$	Recto-vaginal point $EQD2_3$	Sigmoid D_{2cm^3} $EQD2_3$	Bowel D_{2cm^3} $EQD2_3$
Planning Aims	< 80 Gy	< 65 Gy	< 65 Gy	< 70 Gy*	< 70 Gy*
Limits for Prescribed Dose	< 90 Gy	< 75 Gy	< 75 Gy	< 75 Gy*	< 75 Gy*

EBRT 45 Gy / 25 Fx
$EQD2_3$ = 43.2 Gy

	Good	Acceptable	Too much
Bladder D_{2cm^3}	0 - 5.4	5.4 – 6.2	> 6.2
Rectum D_{2cm^3}	0 – 3.9	3.9 – 4.9	> 4.9
Sigmoid D_{2cm^3}	0 – 4.9		> 4.9
Sigmoid D_{2cm^3}	0 – 4.9		> 4.9


Q&A