

The prognostic value of ypN category for
rectal cancer depends on the type of
preoperative radiotherapy:
Report of a randomised trial

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RANDOMIZATION

5 x 5 Gy
immediate surgery
(TME) VS

conventionally fractionated
chemoradiation (50.4 Gy +
5-Fu, LV), 4-6 weeks
interval to surgery (TME)



Entry criteria

- Low-lying tumours, but no sphincter infiltration
- cT3 and resectable cT4

Material

316 patients from 19 hospitals

4 pts were excluded (did not fulfill the entry criteria)

312 patients were analysed

Follow-up

Median: 4 years

Range: 2.5 – 5.5 years

Postoperative pathology

	5 x 5 Gy	Chemoradiation	
T3-4	59%	41%	p<.001
N-positive	48%	33%	p=.02
Complete response	1%	16%	p<.001
Surgical margin + (R1)	14%	5%	p=.005

Results

No difference in incidence of local and distant recurrence, survival and sphincter preservation.

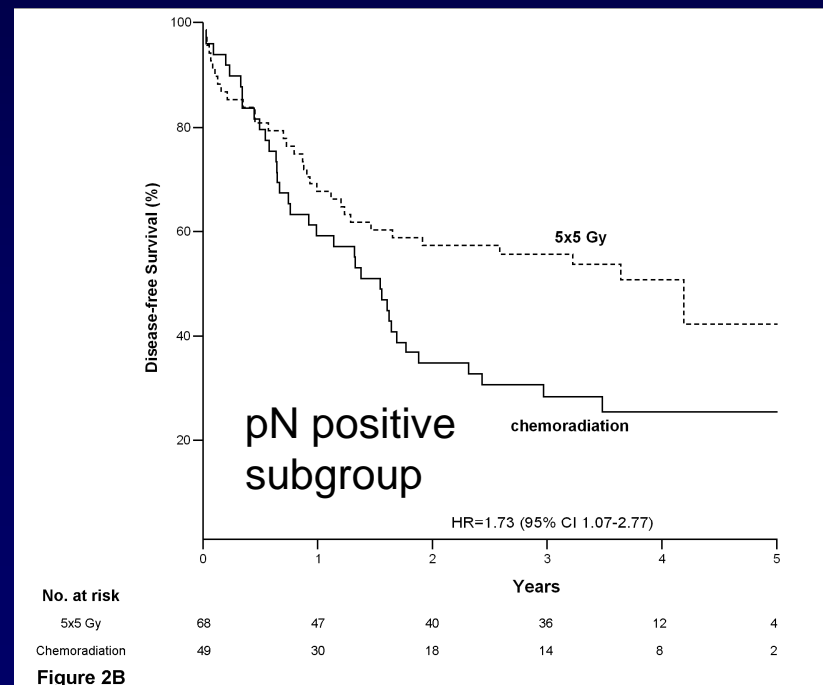
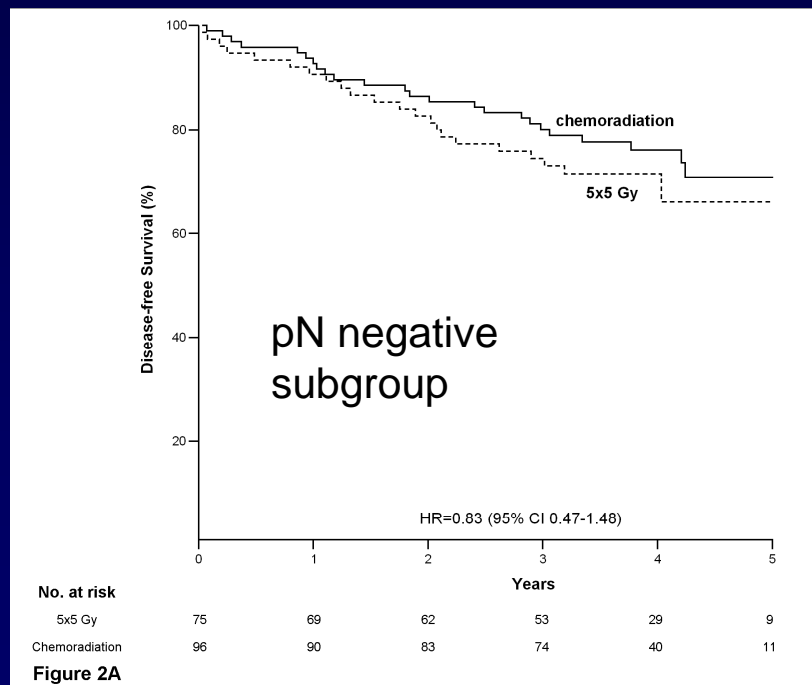
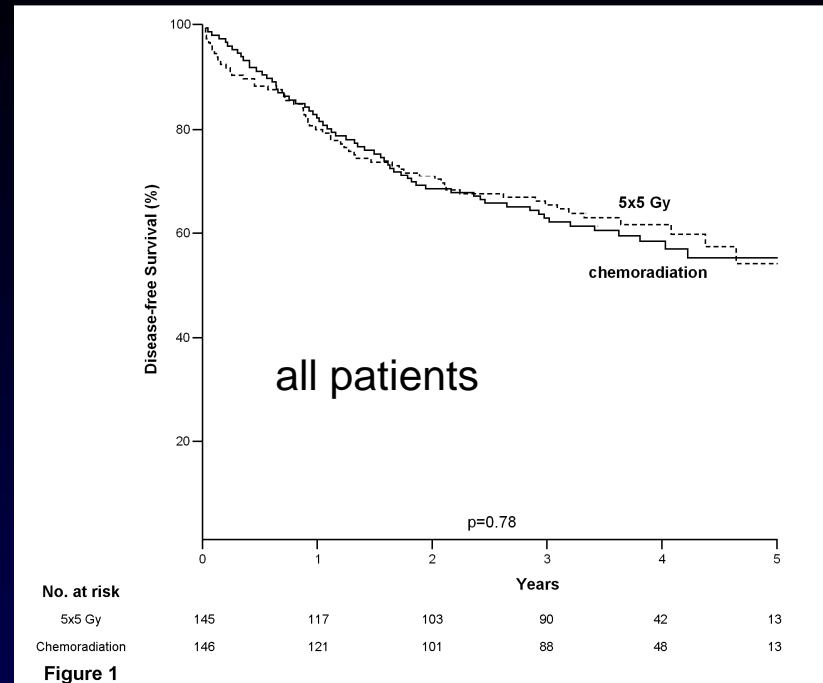
Bujko, Br J Surg 2006; 93: 1215

Suggestion: the prognostic value of pathologic findings is related to the type of preoperative radiotherapy.

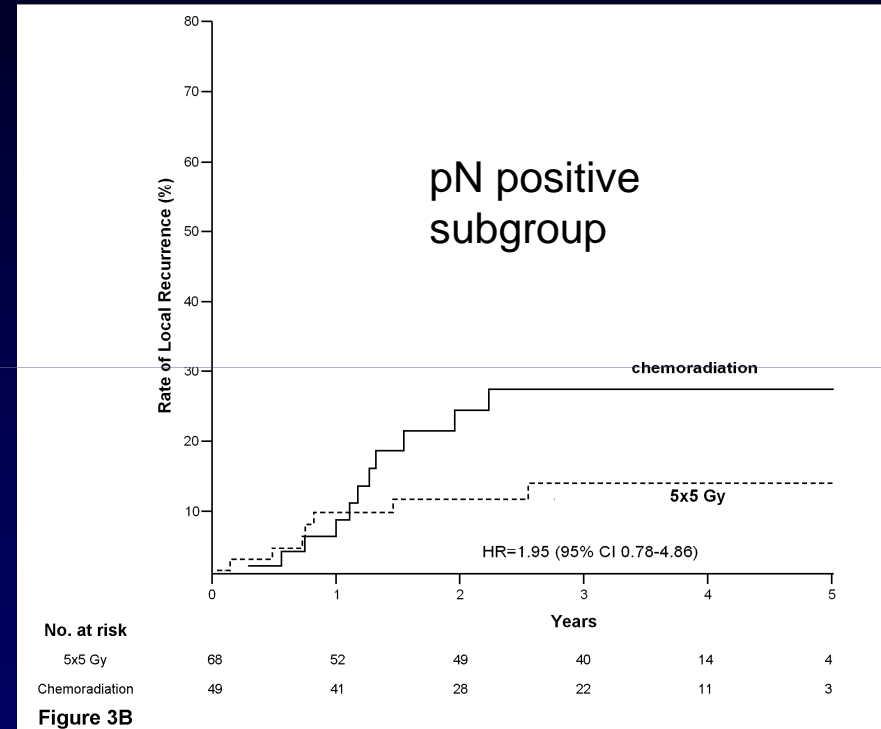
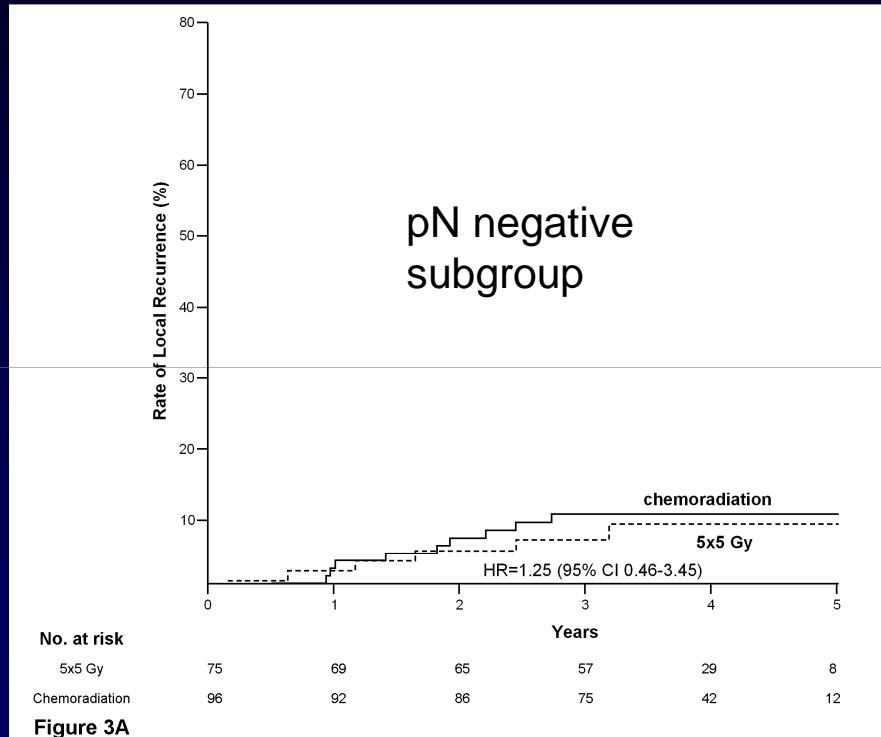
Cox's multivariate analysis of prognostic factors for disease-free survival (DFS)

- ypT- category
 - ypN – category
 - R0 vs. R1 surgery
 - Radiotherapy assignment
1. Only N-status was associated significantly with DFS, $p < .001$; HR=3.1
 2. Interaction between the N-status and treatment assignment for DFS; $p = .016$

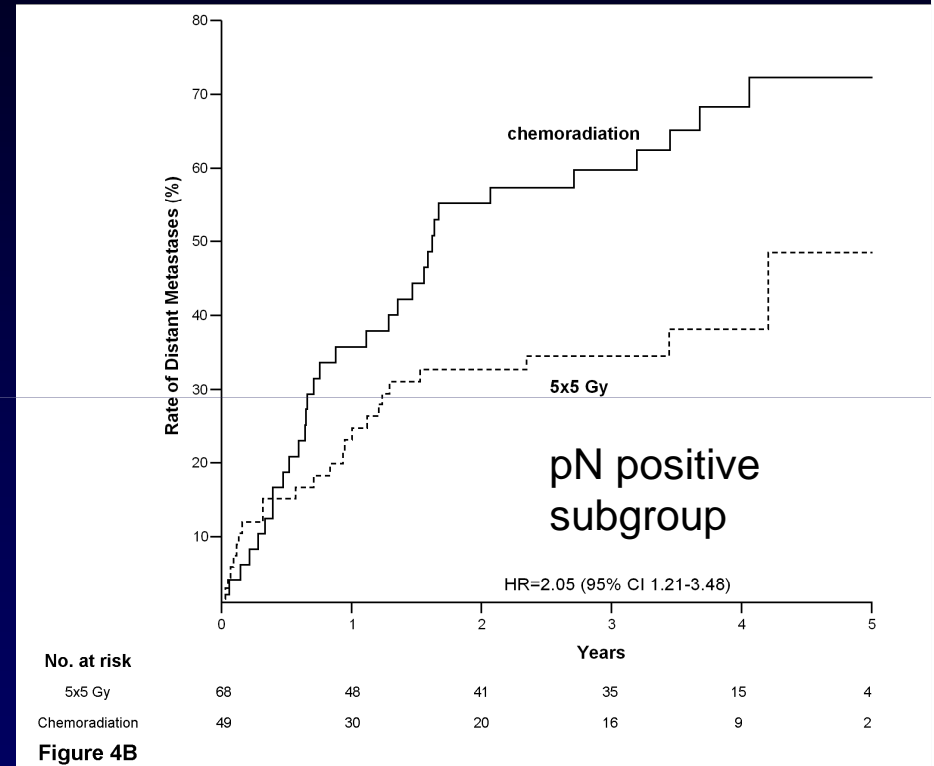
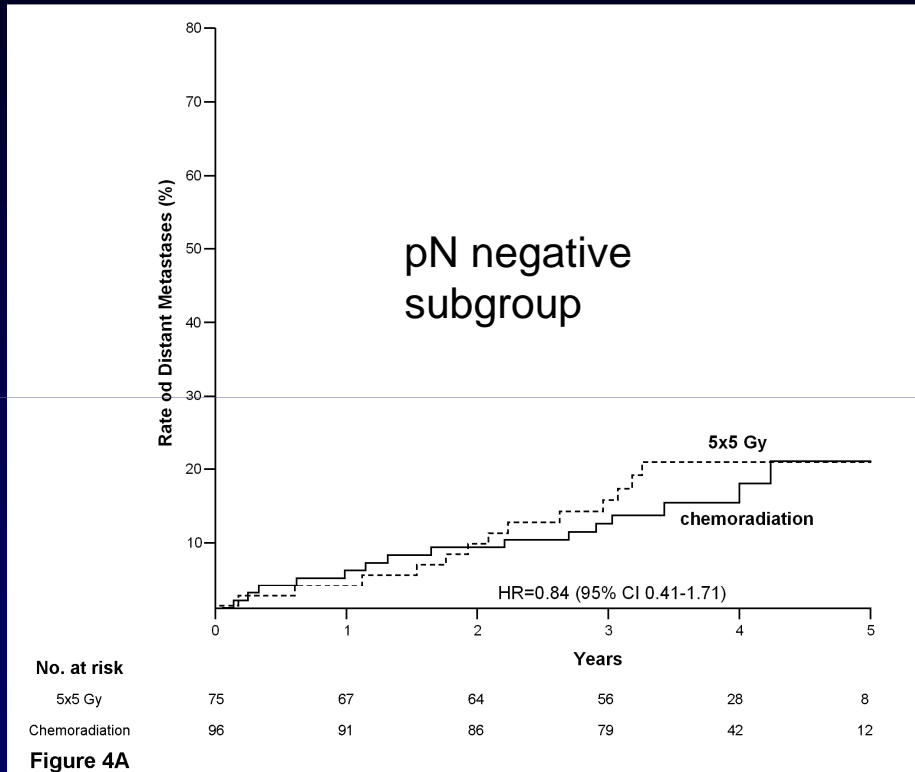
Disease-free survival



Incidence of local recurrence



Incidence of distant metastases



Conclusions

- For patients with positive nodal disease detected after preoperative radiotherapy the risk of local and distant recurrence was twice as high in the chemoradiation arm as compared to the short-course arm.
- Intensification of postoperative systemic treatment should be considered for patients with positive nodal disease after chemoradiation.

Observations which help to explain our findings

- Shortly after irradiation (5 x 5 Gy arm) nonviable cancer cells may look morphologically intact.

Suit, Arch Pathol 1964; 78: 648

- A long interval between radiotherapy and surgery (chemoradiation arm) allows for nonviable cancer cells to undergo necrosis.

Francois, J Clin Oncol, 1999; 17: 2396

Explanation cntd.

The stage migration in the chemoradiation arm

Before chemoradiation: Radiosensitive

N-positive disease



After chemoradiation: N-negative group

Explanation cntd.

before treatment

Assumption: due to randomization, the distribution of patients with both radiosensitive or radioresistant nodal disease was well balanced in the two groups.

after preoperative radiotherapy

5 x 5 Gy: radiosensitive + radioresistant N+

Chemoradiation: radioresistant N+

Hypothesis

Radioresistance of rectal cancer is associated with a high potential for developing distant metastases.

Dutch TME trial: patients with local recurrence

Distant metastases

5 x 5 Gy + TME (N=23)	74%
TME alone (N=73)	40%
	p = .004

van den Brink, J Clin Oncol, 2004; 22: 3958

Thank you for your attention