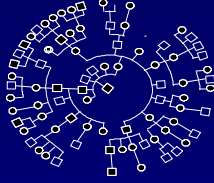


# Clinical Aspects of Rectal Cancer in Lynch Syndrome

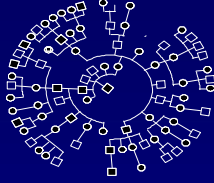
Andrea de Jong, Kirsi Pylvänäinen, Rutger van Bommel,  
Marjo van Puijenbroek, Hans Morreau, Jukka-Pekka Mecklin,  
Hans Vasen

The Netherlands Foundation for the Detection of Hereditary  
Tumours



Incidence rectal cancer in suspected  
HNPPC: 20-30%

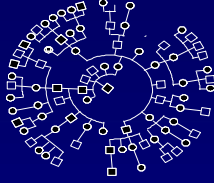
(Lee JS, et al. Am J Surg 2001, Moslein G, et al. Langenbecks Arch  
Chir Suppl Kongressbd 1998.)



MSI in sporadic rectal cancer is less frequent compared to colon cancer.

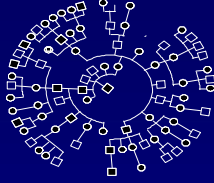
(Lothe RA et al. Cancer Res 1993, Nilbert M et al. Eur J Cancer 1999, Aaltonen La et al. N Engl J Med 1998.)

The exact diagnostic value of MSI-analysis of rectal cancer needs to be elucidated.

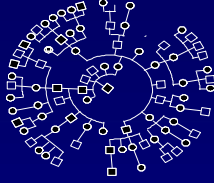


- Radiotherapy is the principal adjuvant therapy for rectal cancers.
- Mouse models: MMR-deficient cell show a higher radiation sensitivity.  

Fritzell JA et al. Cancer Res 1997;  
Seo Y et al. Clin Cancer Res 2004
- CRC in Lynch syndrome has a better outcome.



1. To evaluate the prevalence of rectal cancer (RC) in HNPCC families
2. To evaluate the proportion of RC in HNPCC showing MSI
3. To evaluate the occurrence of side-effects HNPCC-RC to radiotherapy
4. To evaluate the survival of patients with RC in HNPCC



- Dutch HNPCC Registry

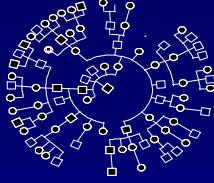
153 mutation families



- Finnish HNPCC Registry

111 mutation families

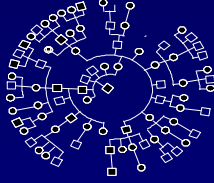




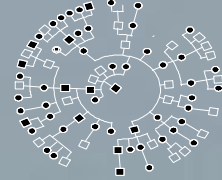
Rectal cancers mutation carriers:

date of birth, date of diagnosis, date and cause of death, stage of carcinoma, radiotherapy

MSI: International 5-marker set

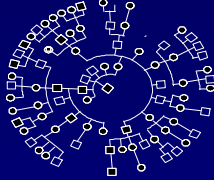


Survival curve: Kaplan and Meier  
End point: death due to RC.



# Results

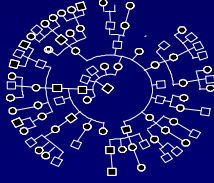




## Prevalence Rectal Cancer

	Dutch Registry	Finnish Registry
Nu. of families	153	111
Nu. of family members	1221	727
Total nu. of subjects with CRC (%)	444 (36.4%)	250 (34.4%)
Number of subjects with RC	47	42
Number of subjects with RC as primary tumor (%)	37 (8.3%)	30 (12.0%)
Average age first CRC	42.8	44.6
(range)	(16.5 – 85.7)	(20.0 – 75.0)
Average age first RC	42.3	44.2
(range)	(16.8 - 66.9)	(27.6 – 73.9)

Nu, number; CRC, colorectal cancer; RC, rectal cancer

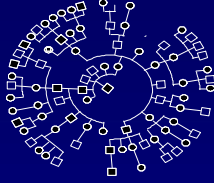


# MSI Results

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16 rectal cancers were tested for MSI

MSI-H	13	(81.2%)
MSS	3	(18.8%)
		(2 <i>hMLH1</i> , 1 <i>hMSH6</i> )

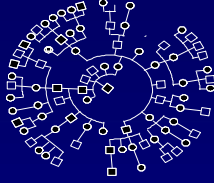


14 subjects received radiotherapy

Minor side effects: 5 (diarrhea, erythema)

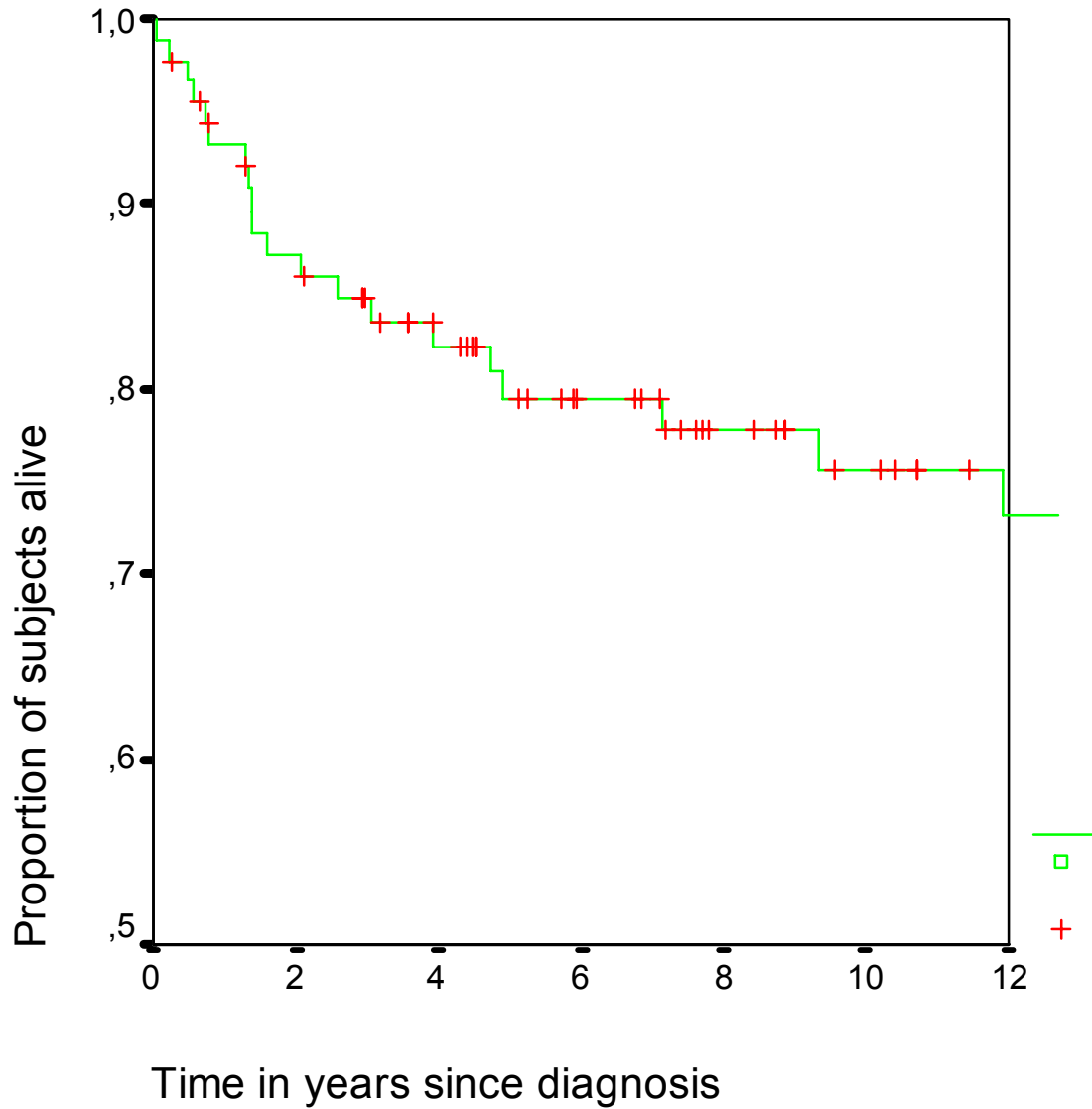
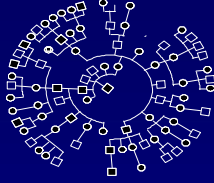
Major side effects: 0

# Stage rectal cancers

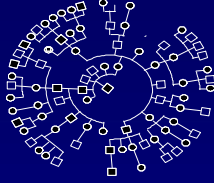


Stage	Number	
Local cancers	66	(74.2%)
Local metastases	10	(11.2%)
Distant metastases	4	(4.5%)
Unknown	9	(10.1%)
Total	89	

# Survival (I)



# 5 years - survival RC

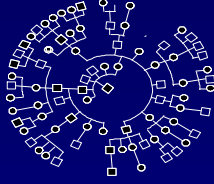


	HNPCC	General population
All	78.9%	62.2%*
Local Carcinomas	88.1%	81.7%**

\* Kerr J . Et al. Ann Oncol. 2005

\*\* O'Connell JB et al Dis Colon Rectum. 2004

# Conclusions



Rectal cancer is a frequent carcinoma in HNPCC

MSI is present in a large proportion of rectal cancers in HNPCC mutation carriers

MMR deficiency seems not of influence on the occurrence of side-effects due to radiotherapy

Survival appears to be better compared to the general population