

新药时代放疗在淋巴瘤 治疗中的地位

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北京大学肿瘤医院放疗科简介

- ✓ 团队（110人）：医生28人、物理师16人、技术员40人、护士26人
- ✓ 博导2人、硕导5人、正高6人、副高12人、中级23人
- ✓ 专业亚组：头颈、胸组、腹组和乳腺妇瘤组
- ✓ 2009年引起国内第一台Rapid-Arc加速器（VMAT）
- ✓ 2011年引起国内第一台TrueBeam加速器（速光刀）
- ✓ 2012年引起国内第一台高场强MRI定位机
- ✓ 2016年引起国内首批Edge加速器（速锋刀）

放疗科设备概况



Edge



Truebeam



iX



600CD



MR



PET/CT



CT



Acuity

2017年底投入使用的新技术



EDGE：集大成的SBRT治疗平台



目 录



- 放疗在DLBCL治疗中的作用
- 放疗在PMBCL治疗中的作用
- 放疗在FL治疗中的作用
- 放疗在MALT治疗中的作用
- 放疗在NKTCL治疗中的作用
- 放疗技术进步、剂量降低
- 放疗远期不良反应
- 典型病例实战

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- 典型病例实战



- 放疗在早期DLBCL治疗中的作用
 - 前美罗华时代早期DLBC的治疗
 - 美罗华时代早期DLBCL 的治疗
- 放疗在骨受侵DLBCL治疗中的作用
- 放疗在复发难治DLBCL治疗中的作用

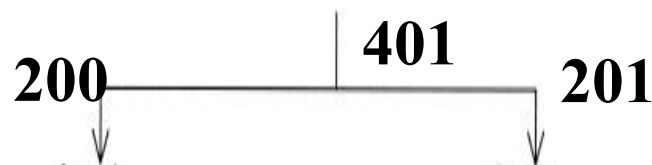
前美罗华时代早期DLBCL 研究

SWOG8736



入组标准：I、IE(可伴有肿块)

II、IIE(无肿块)
RANDOMIZE



3×CHOP+RT

8×CHOP

中位随访时间：4.4年

TABLE 1. CLINICAL CHARACTERISTICS OF 401 PATIENTS TREATED WITH EIGHT CYCLES OF CHOP OR THREE CYCLES OF CHOP PLUS RADIOTHERAPY.

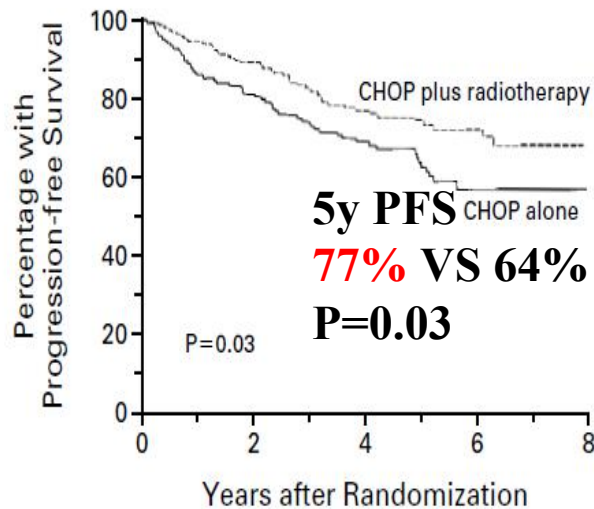
CLINICAL VARIABLE	8 CYCLES OF CHOP (N=201)	3 CYCLES OF CHOP PLUS RADIOTHERAPY (N=200)
	number (percent)	
Age		
≤60 yr	103 (51)	101 (50)
>60 yr	98 (49)	99 (50)
Stage		
I	135 (67)	136 (68)
II	66 (33)	64 (32)
Serum lactate dehydrogenase		
Normal	159 (79)	159 (80)
Increased	42 (21)	41 (20)
Performance status		
0 or 1	193 (96)	194 (97)
2	8 (4)	6 (3)
No. of risk factors*		
0 or 1	142 (71)	147 (74)
2	44 (22)	38 (19)
3	14 (7)	14 (7)
4	1 (<1)	1 (<1)

*Adverse risk factors were defined as an age >60 years, stage II disease, increased serum lactate dehydrogenase, and a performance status of 2.

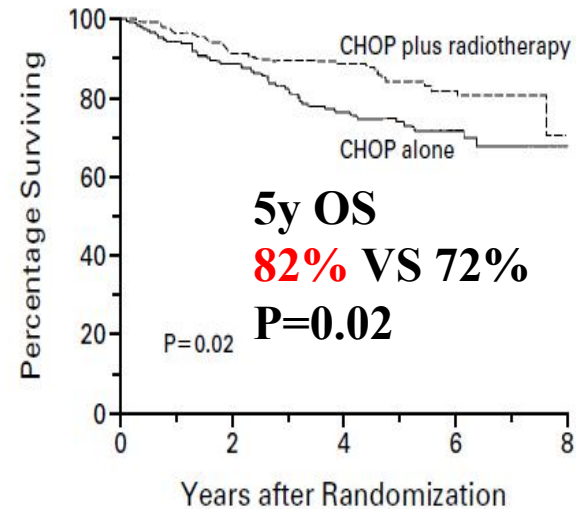
Miller TP, et al. NEJM, 339:21, 1998

前美罗华时代早期DLBCL 研究

SWOG8736



CHOP plus radiotherapy 200 178 119 70 17



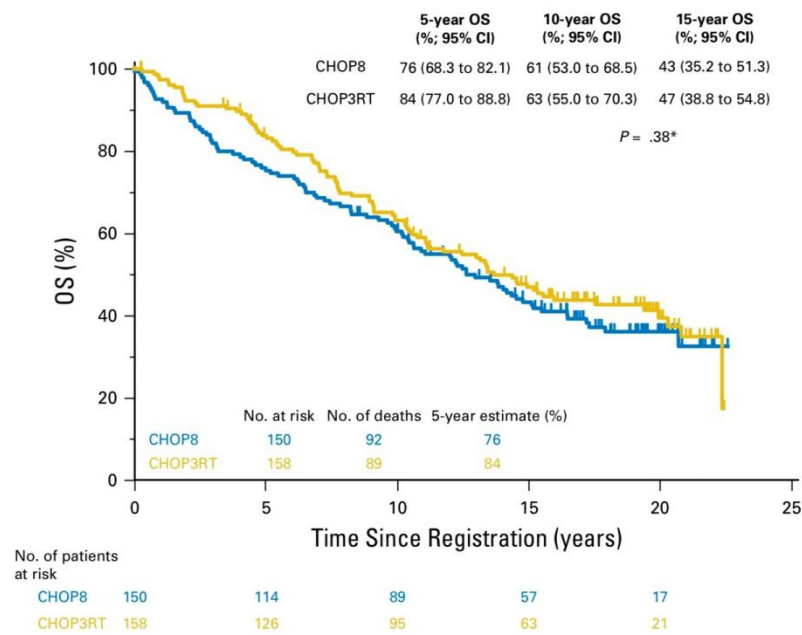
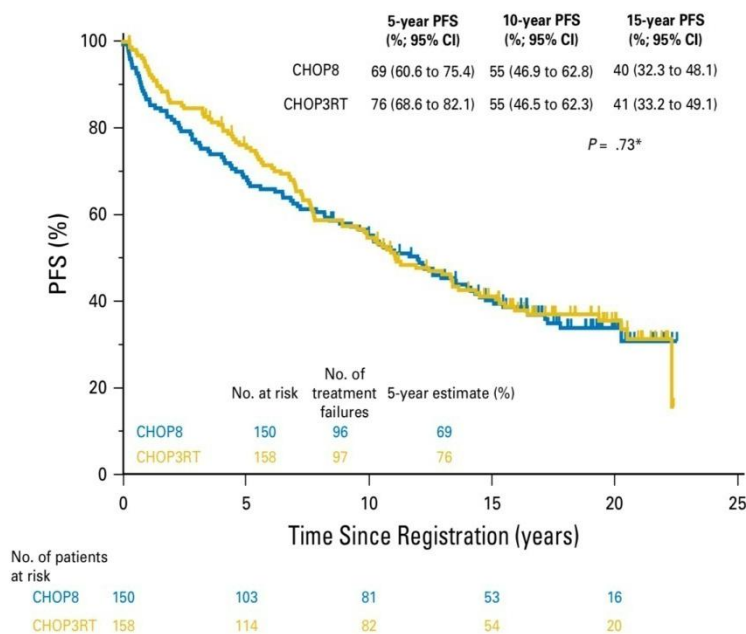
CHOP plus radiotherapy 200 185 128 75 17

前美罗华时代: **3×CHOP+RT** 优于 **8×CHOP**
早期中高度侵袭性NHL标准治疗方案

Miller TP, et al. NEJM, 339:21, 1998

前美罗华时代早期DLBCL 研究

SWOG8736长期随访结果



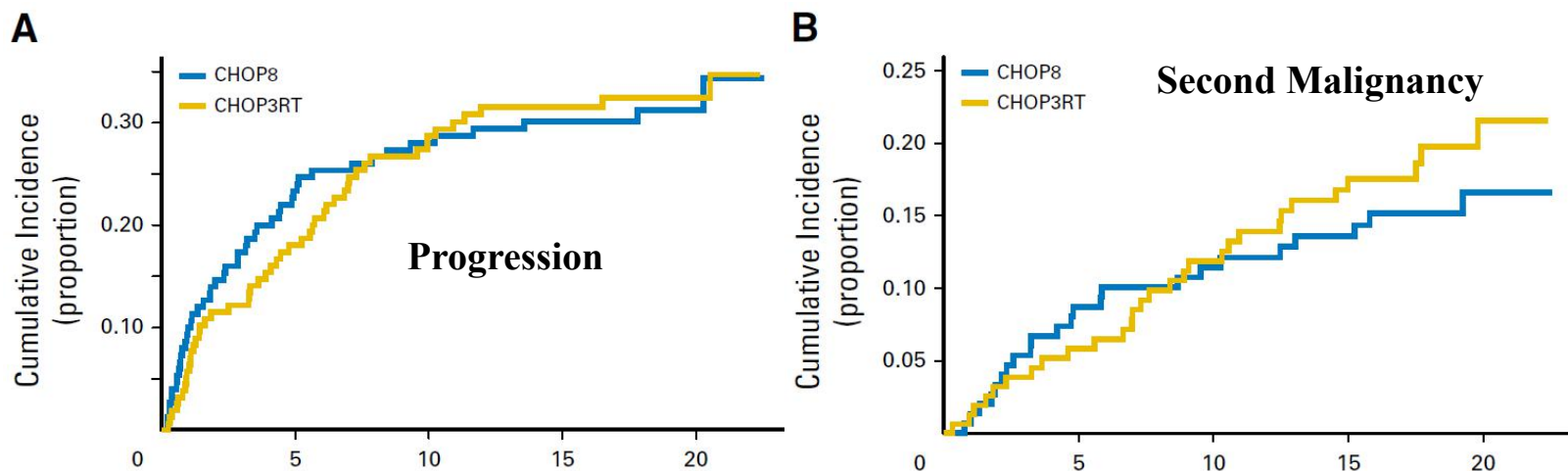
中位随访时间：17.7年

3×CHOP+RT与8×CHOP疗效相似

Stephens DM. JCO, 34:2997, 2016

综合治疗和单纯化疗比较

SWOG 8736: 死亡原因



死亡原因分析显示，放疗未显著增加第二原发性肿瘤

Stephens DM, et al. JCO, 2016;34:2997

前美罗华时代早期DLBCL 研究

ECOG 1484



入组标准:

I期（伴有纵膈/腹膜后LN受侵
或大肿块）、IE、II、IIE

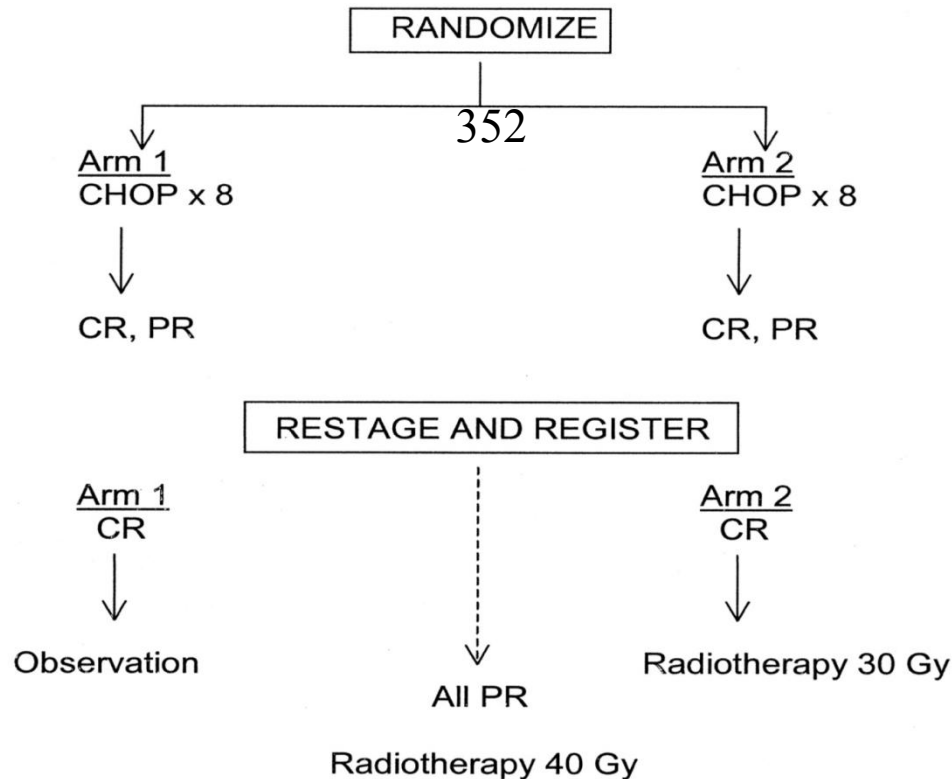


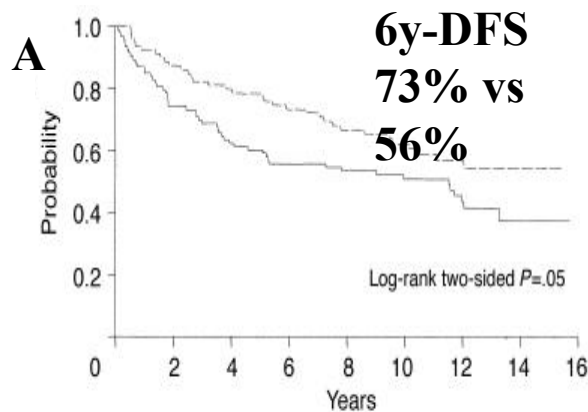
Table 1. Patient Characteristics

Characteristic	No. of Patients	%
Age, years		
Median	59	
Range	19-84	
Performance status		
0-1	325	92
2-3	27	8
Stage		
I	49	14
IE	62	18
II	137	39
IIE	104	29
Extranodal disease	166	47
Systemic symptoms		
No	267	76
Yes	85	24
No. of sites		
< 3	286	81
≥ 3	66	19
Largest tumor size, cm		
< 10	244	69
≥ 10	108	31
Mediastinal lymph nodes	68	19
Histologic subtype		
Large cell	287	82
Mixed	39	11
Small cleaved	26	7

Horning SJ. JCO, 22:3032, 2004

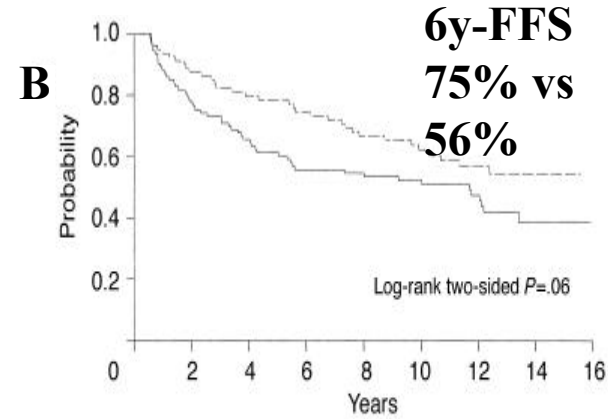
前美罗华时代早期DLBCL 研究

ECOG 1484 - 8×CHOP后CR



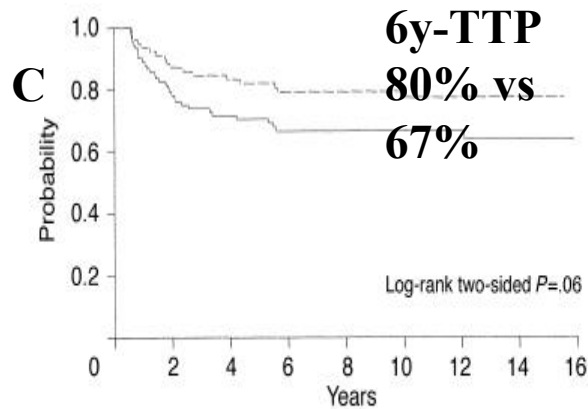
Group	Time Interval							
	0-2	2-4	4-6	6-8	8-10	10-12	12-14	14-16
Obs	24/93	11/69	6/58	2/50	2/45	4/36	2/22	0/8
LD XRT	10/79	6/69	5/62	5/57	3/49	3/36	1/23	0/10

(# events/# at risk)



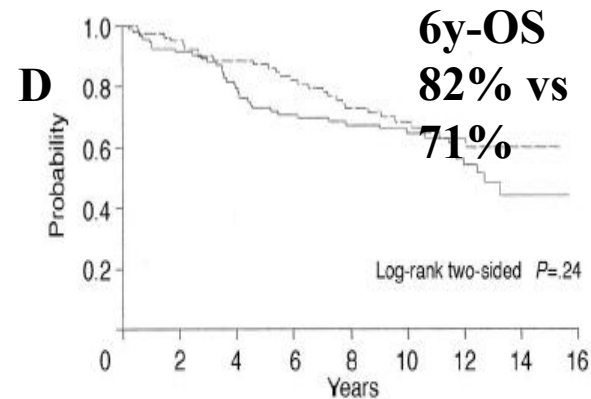
Group	Time Interval							
	0-2	2-4	4-6	6-8	8-10	10-12	12-14	14-16
Obs	21/93	11/72	9/61	1/50	2/46	3/38	4/27	0/8
LD XRT	10/79	6/69	4/63	6/58	3/50	3/40	1/26	0/10

(# events/# at risk)



Group	Time Interval							
	0-2	2-4	4-6	6-8	8-10	10-12	12-14	14-16
Obs	20/93	6/72	4/61	0/50	0/46	0/38	1/27	0/8
LD XRT	10/79	3/69	3/63	0/58	1/50	0/38	0/24	0/10

(# events/# at risk)



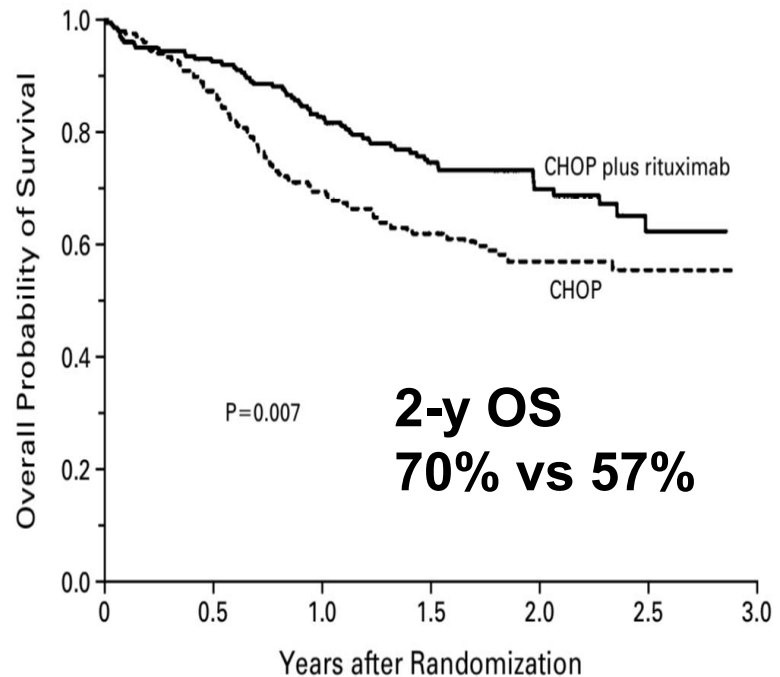
Group	Time Interval							
	0-2	2-4	4-6	6-8	8-10	10-12	12-14	14-16
Obs	8/93	11/85	8/73	3/63	2/56	6/46	3/27	0/9
LD XRT	4/79	5/75	5/68	7/63	3/53	3/39	1/24	0/10

(# events/# at risk)

美罗华时代DLBCL 研究



入组标准：
60-80岁，
未治疗DLBCL，
II, III, IV
期，
ECOG0-2分。



No. AT RISK						
CHOP plus rituximab	202	187	167	118	64	21
CHOP	197	171	136	96	58	16

Coiffier B, et al. N Engl J Med. 2002 Jan 24;346(4):235-42.

美罗华时代DLBCL 研究

MInt试验



入组标准:

18 - 60岁

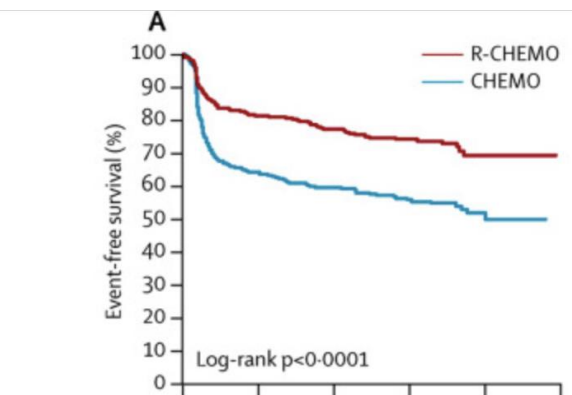
DLBCL CD20(+)

II - IV期 (aa IPI

0分)

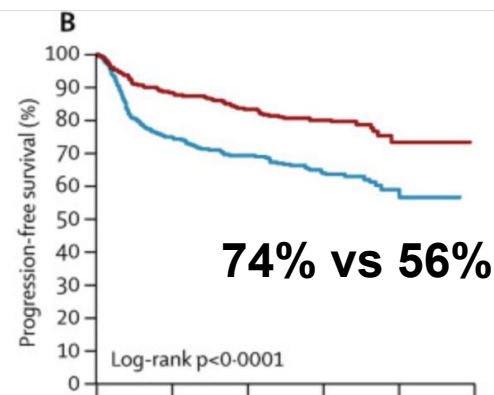
I 期(大肿块)

ECOG 0-3分



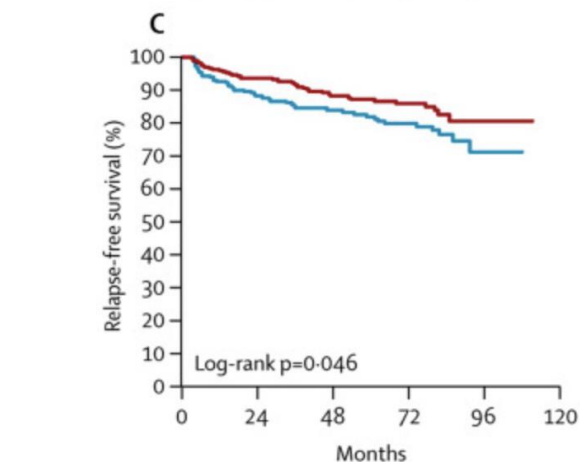
Number at risk

	CHEMO	410	233	163	117	25	0
	R-CHEMO	413	305	214	150	30	0



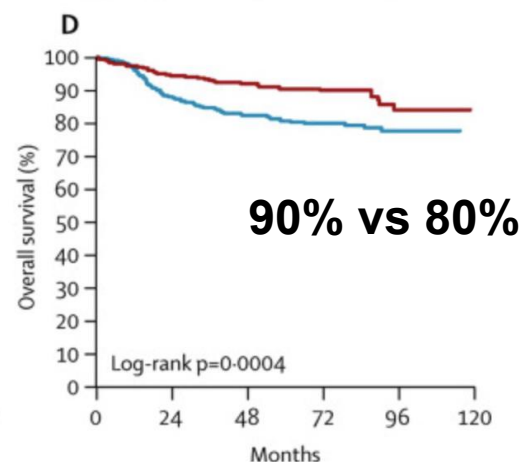
Number at risk

	CHEMO	410	264	183	132	26	0
	R-CHEMO	413	326	227	161	30	0



Number at risk

	CHEMO	239	186	133	93	8	0
	R-CHEMO	305	258	171	118	13	0



Number at risk

	CHEMO	410	323	226	175	40	0
	R-CHEMO	413	365	259	190	41	0

美罗华时代放疗在早期DLBCL 作用

SWOG 0014



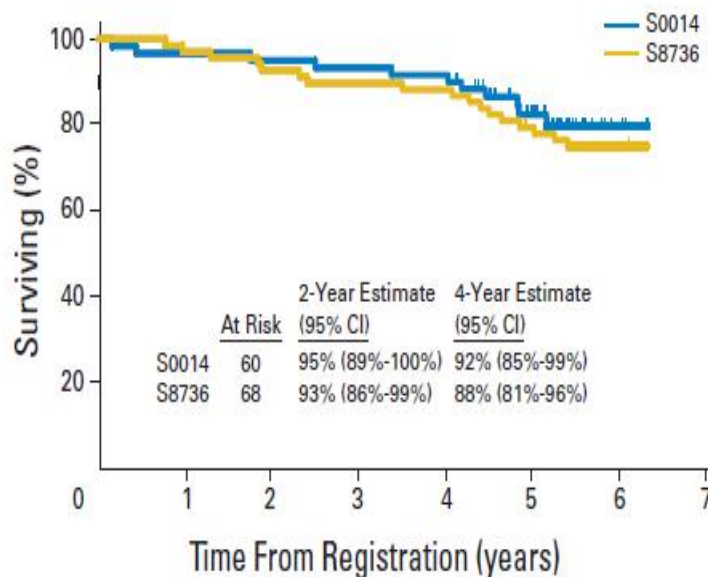
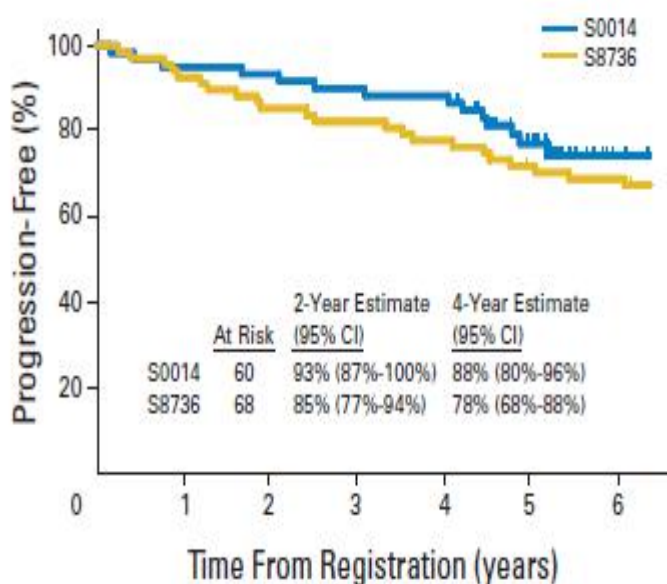
入组标准：I期伴预后不良因素（年龄
>60岁，LDH增高，WHO评分 $\geq$ 2分）、
II期非大肿块
入组情况：非随机
R-CHOP+RT（60例，SWOG0014）
vs CHOP+RT（68例，SWOG8736）
中位随访时间：5.3年

Table 1. Sixty Eligible Patients Receiving R-CHOP(3) Plus IFRT (from S0014) Compared With 68 Eligible Patients Receiving CHOP(3) plus IFRT (from S8736), Matched for Limited Disease, Aggressive B-Cell Histologies, and Presence of at Least One Stage-Modified IPI Risk Factor

Clinical Variable	S0014: R-CHOP + IFRT (n = 60)		S8736: CHOP + IFRT (n = 68)	
	No.	%	No.	%
Age, years				
Median	69		66	
Range	26-85		35-85	
≥ 60	44	73	52	76
Male sex	27	45	40	59
Bulky disease (stage I)	3	5	0	0
“B” symptoms	14	23	14	21
Histology				
DLBCL	56	93	60	88
Burkitt-like	3	5	7	10
High-grade B	1	2	1	1
LDH > ULN	13	22	17	25
Stage II (nonbulky)	26	43	32	47
WHO performance status				
0	42	70	51	75
1	17	28	15	22
2	1	2	2	3
Stage-modified IPI risk				
1	42	70	40	59
2	12	20	21	31
3	6	10	7	10

美罗华时代放疗在早期DLBCL作用

SWOG 0014

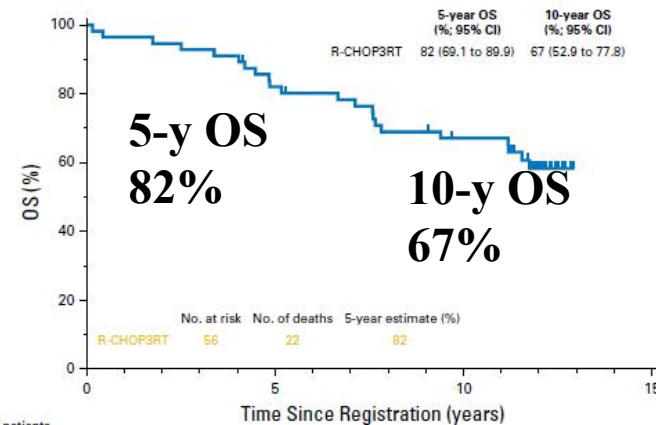
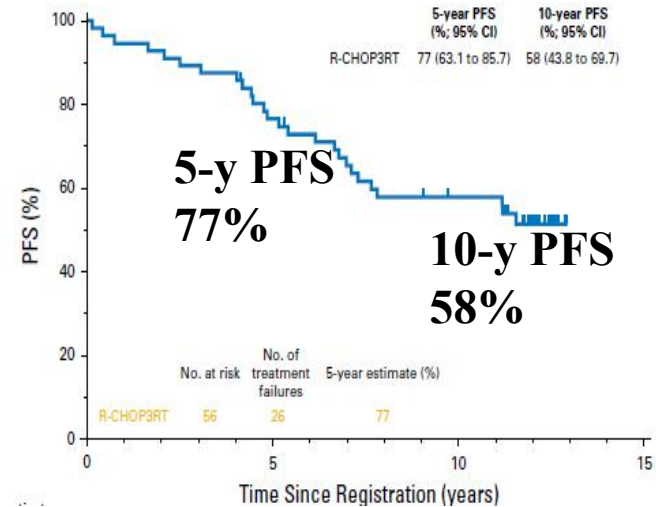
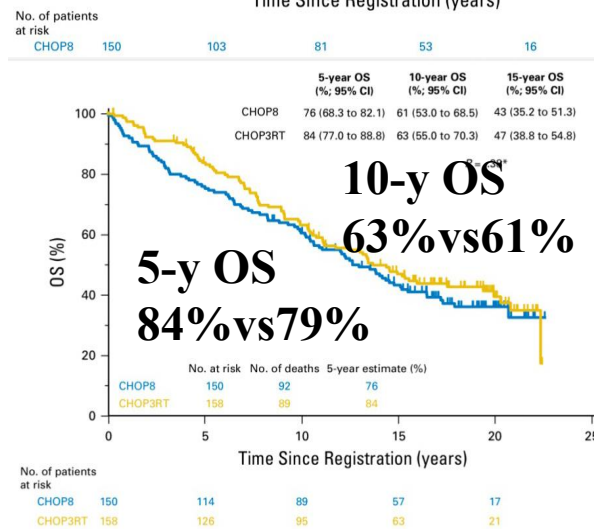
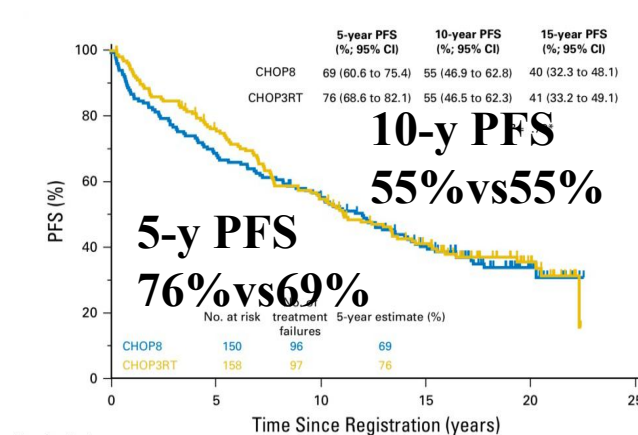


早期预后不良因素DLBCL, **R-CHOP+RT** 优于 CHOP+RT

Persky, et al, JCO, 26:2258-2263, 2008

美罗华时代放疗在早期DLBCL 作用

SWOG 8736 & 0014 长期结果



Persky, et al, JCO, 26:2258-2263, 2008.
Stephens DM. JCO, 34:2997, 2016.

R-CHOP CR后DLBCL放疗的作用

M. D. Anderson



➤ 例数:2001-1至2007-12, 469例DLBCL

➤ Ann Arbor分期:I期94例(20.0%)

II期96例(20.5%)

III期77例(16.4%)

IV期202例(43.1%)

➤ 所有患者都有PET检查

➤ 84%的患者接受R-CHOP

R-CHOP CR后DLBCL放疗的作用



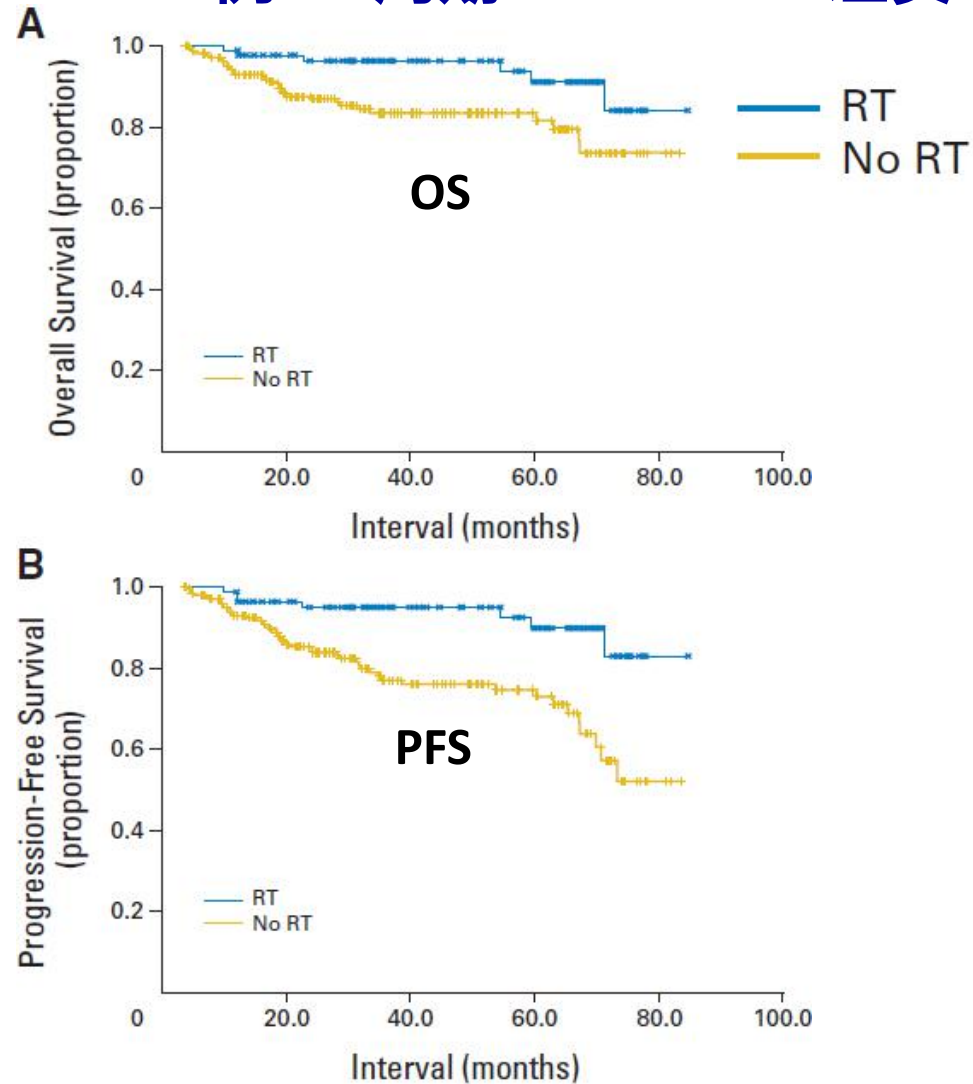
		放疗	未放疗	P 值
I-II期	5y-OS	92%	73%	0.0007
	5y-PFS	82%	68%	0.0003
III-IV期	5y-OS	89%	66 %	0.008
	5y-PFS	76%	55%	0.003

Phan J, et al. J Clin Oncol 28:4170-4176, 2010

R-CHOP CR后DLBCL放疗的作用



--291例6-8周期R-CHOP PET证实CR



Phan J, et al. J Clin Oncol 28:4170-4176, 2010

放疗在R-CHOP年代的作用



RICOVER-60

分组比较

RICOVER-60: 8XR-CHOP14 ◆306例中117例

放疗: 大肿块或结外受侵部位 大肿块(≥ 7.5 cm) 接受放疗

修正方案: 6 X R-CHOP-14 ◆164例
不做放疗(RICOVER-noRT)

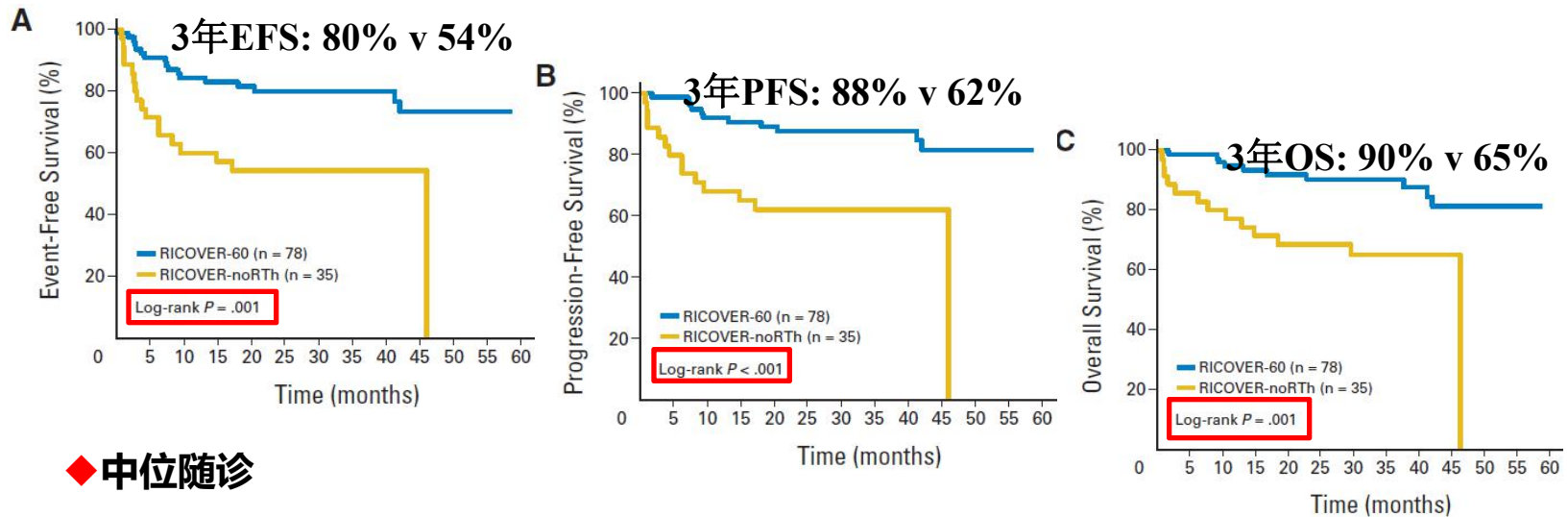
Held, et al, JCO, 32:1112-8, 2014

放疗在R-CHOP年代的作用



RICOVER-60 NoRT: 大肿块治疗

按照实际治疗分析



◆ 中位随诊

RICOVER-60: 34个月

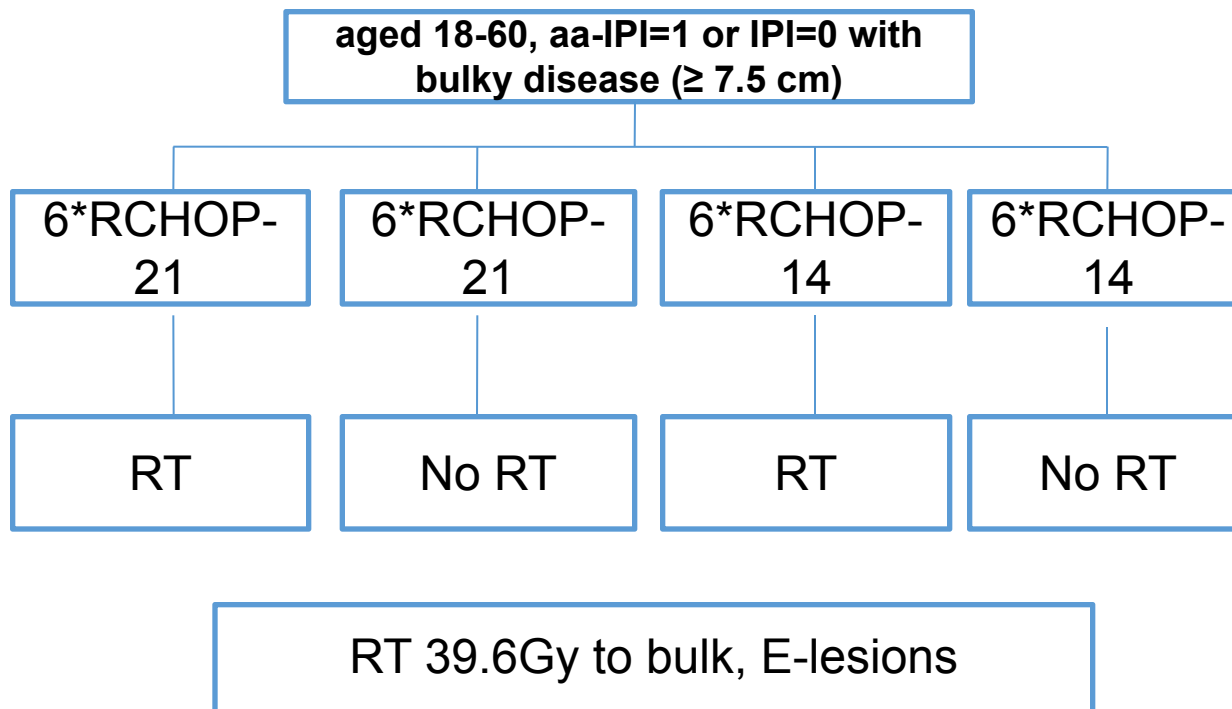
RICOVER-noRT: 39个月

Held, et al, JCO, 32:1112-8, 2014

放疗在R-CHOP年代的作用



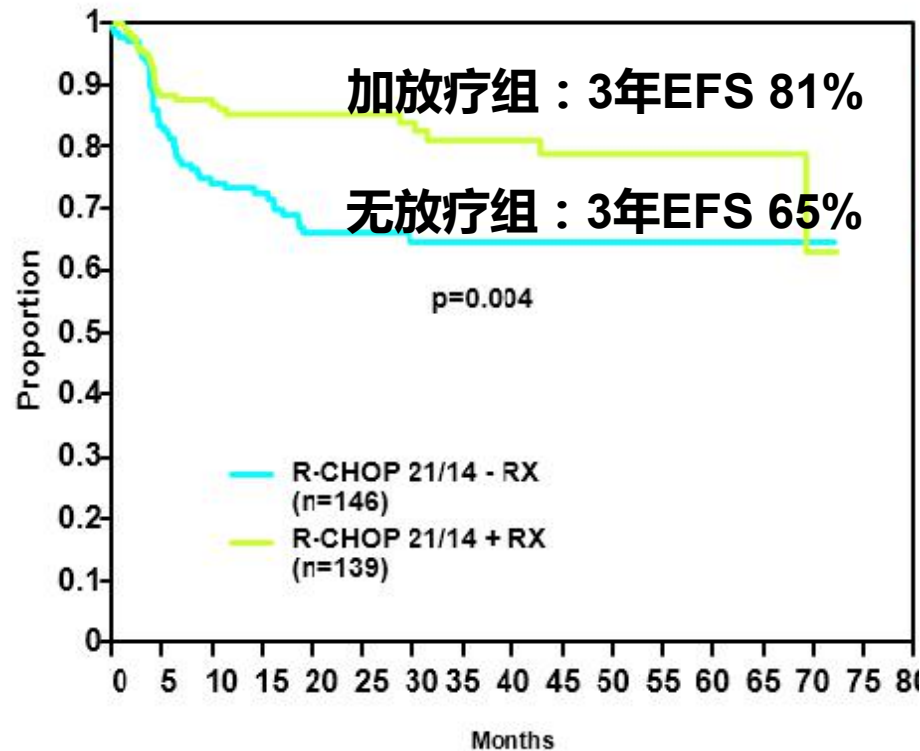
UNFOLDER (German High-Grade Non-Hodgkin's Lymphoma Study Group)



放疗在R-CHOP年代的作用



UNFOLDER



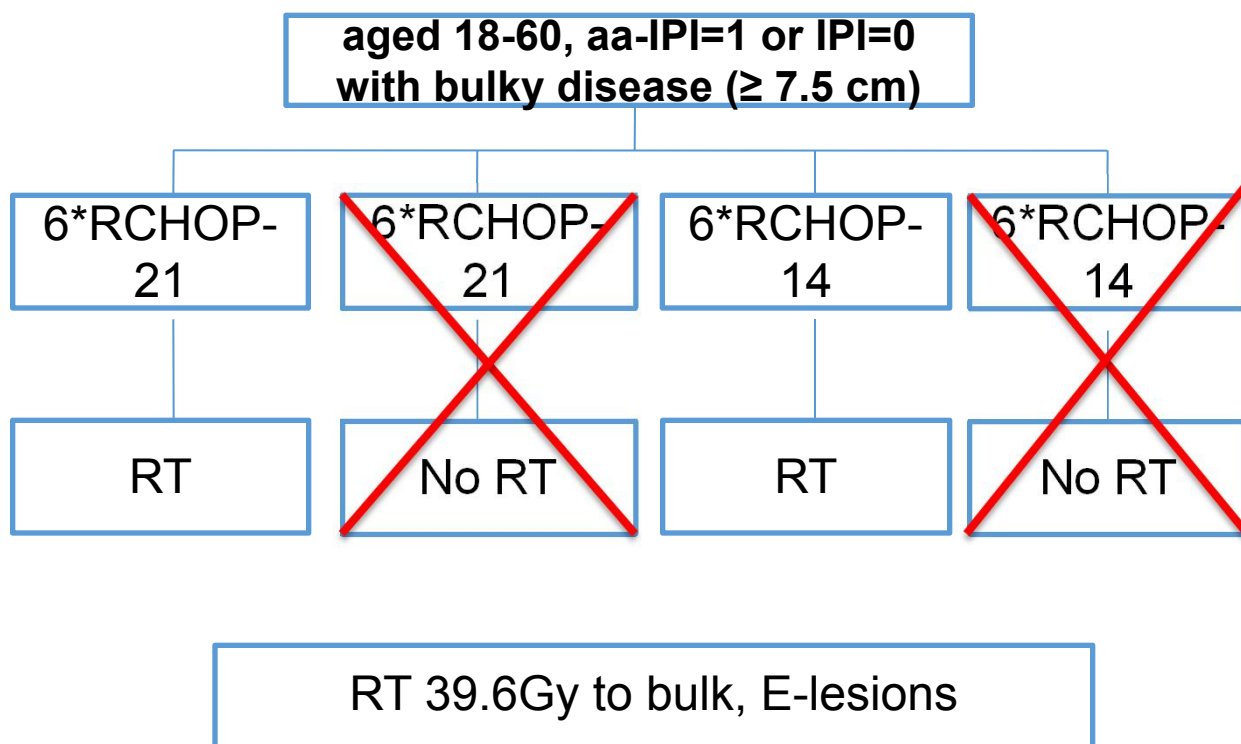
Median time of
observation:
30 months

Courtesy Dr. Held

放疗在R-CHOP年代的作用



UNFOLDER



美罗华时代放疗在早期DLBCL 作用

NCDB 结果



入组标准:

I、II期DLBCL

1998-2012, NCDB,

共59255名患者

目的: 影响治疗和预后的因素

中位随访时间: 5年

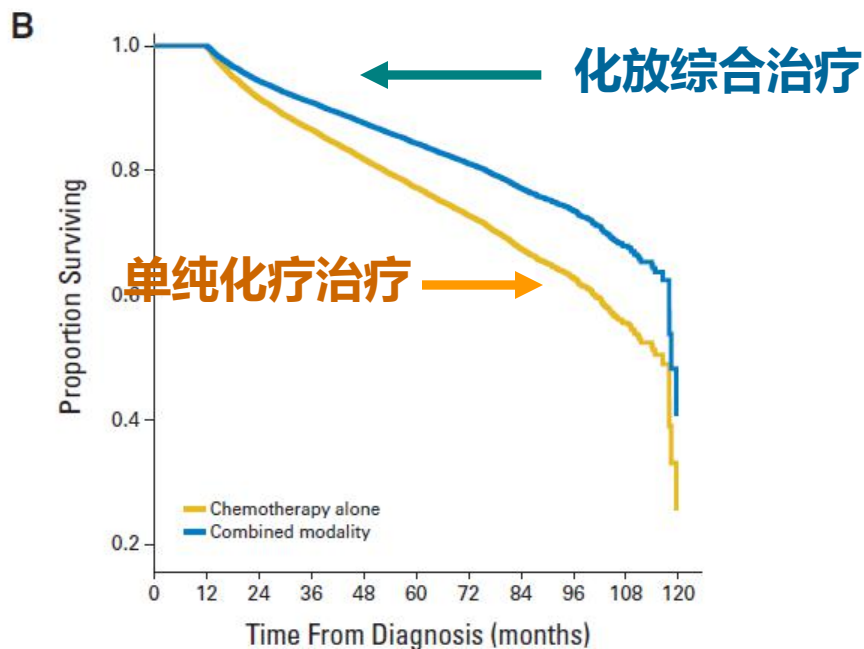
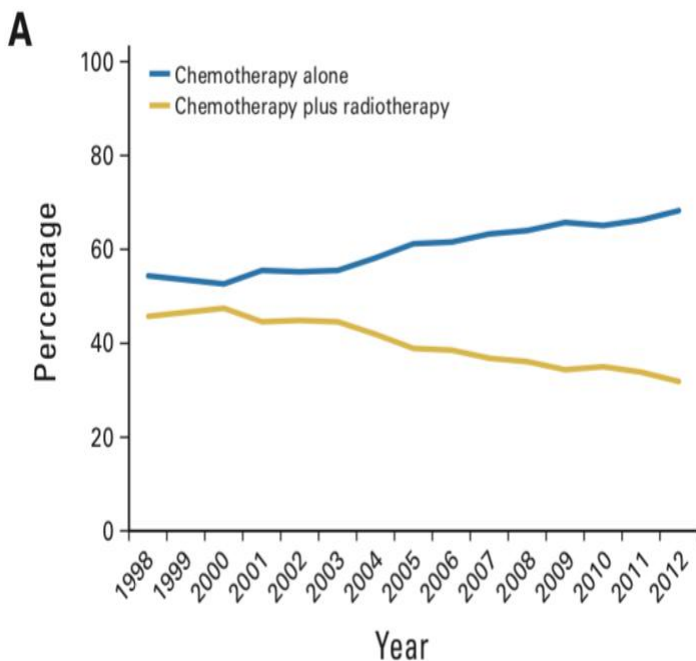
Table 1. Patient Demographics and Clinical Characteristics at Baseline (N = 59,255)

Characteristic	No. (%)
Sex	
Male	31,349 (53)
Female	27,906 (47)
Race	
White	52,655 (89)
African American	3,692 (6)
Other	2,295 (4)
Unrecorded	613 (1)
Age distribution, years	
≤ 60	24,681 (42)
> 60	34,574 (58)
Stage	
I	32,000 (54)
II	27,255 (46)
B symptoms	
Absent	26,959 (46)
Present	7,747 (13)
Unrecorded	24,549 (41)
Extranodal disease	
Absent	34,391 (58)
Present	24,864 (42)
Distance to treatment facility, miles	
≤ 30	47,664 (80)
> 30	10,155 (17)
Unrecorded	1,436 (2)
Year of diagnosis	
1998-2002	16,869 (29)
2003-2007	19,521 (33)
2008-2012	22,865 (39)

Vargo JA. JCO, 33:3710, 2015

放疗在早期DLBCL 的作用

NCDB结果



治疗方案	例数	5年OS(%)	10年OS(%)
R-CHOP/CHOP+ RT	24771	82	64
R-CHOP/CHOP alone	19810	75	55

早期DLBCL 的治疗

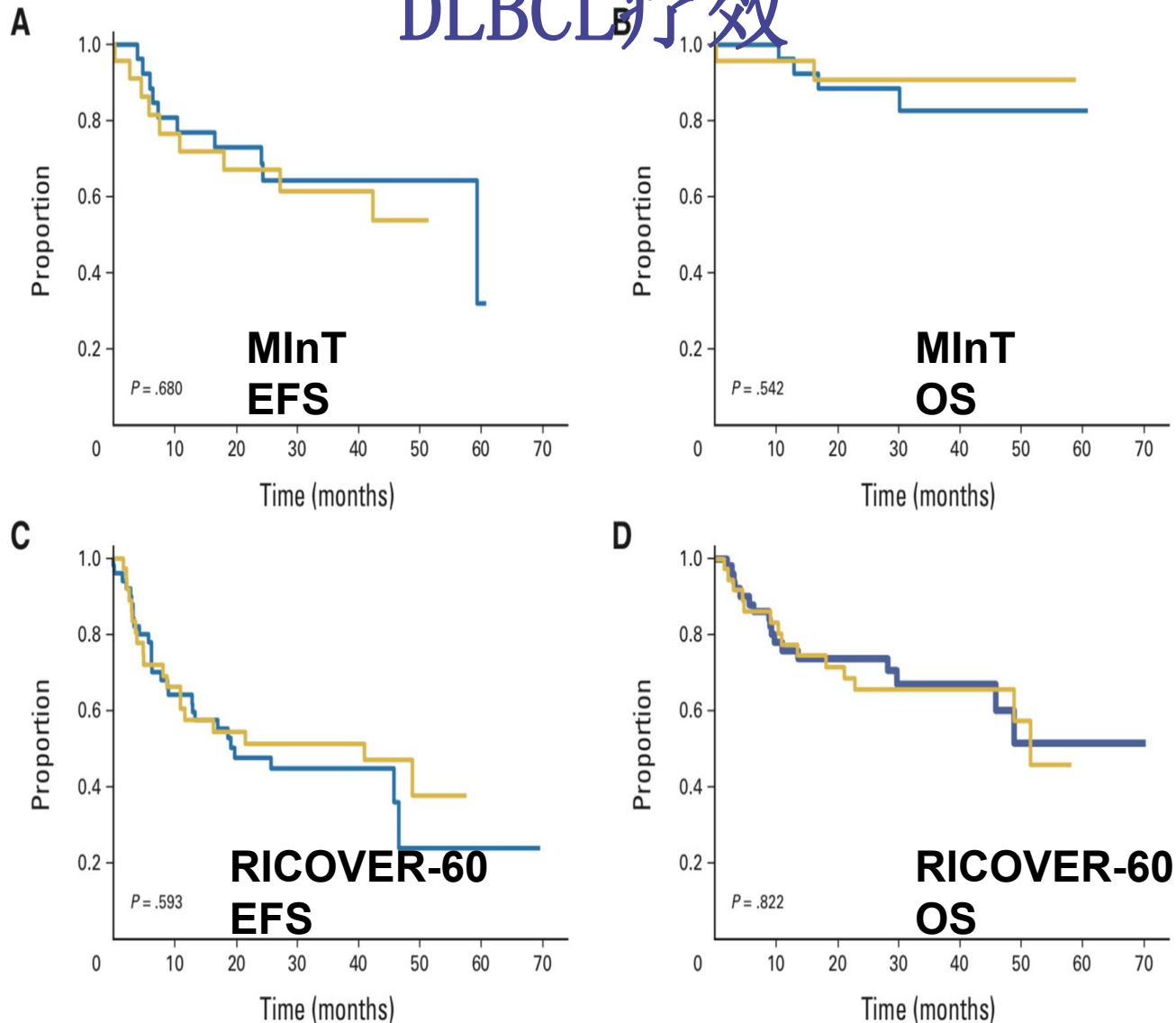


R-CHOP方案化疗+INRT/ISRT



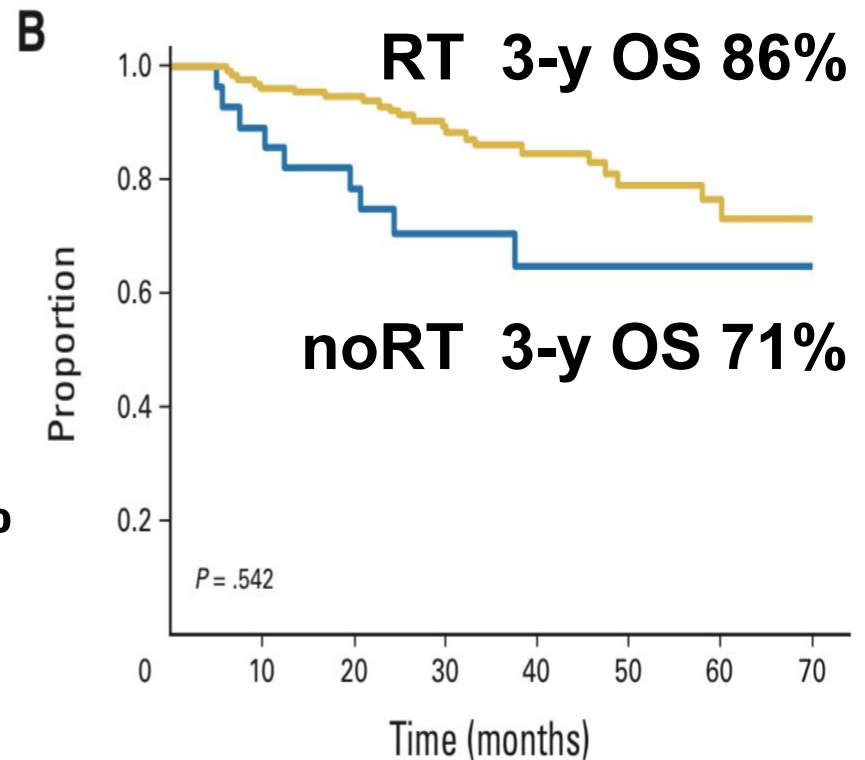
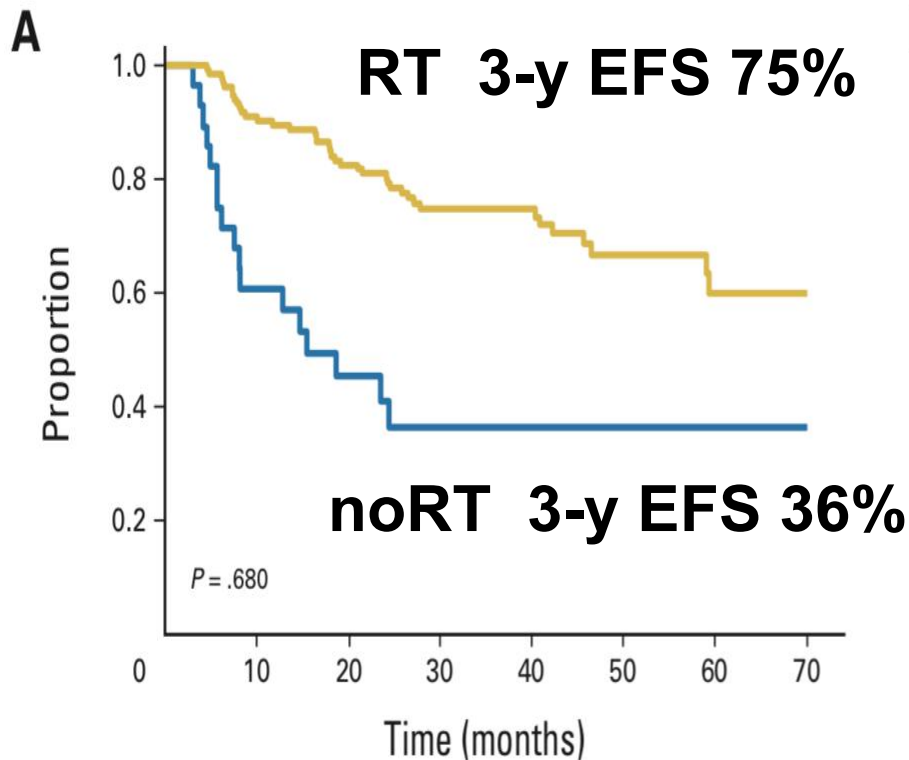
- 放疗在早期DLBCL治疗中的作用
 - 前美罗华时代早期DLBC的治疗
 - 美罗华时代早期DLBCL 的治疗
- 放疗在骨受侵DLBCL治疗中的作用

美罗华未提高骨受侵 DLBCL疗效



Held G, et al. J Clin Oncol. 2013 Nov 10;31(32):4115-22.

放疗在骨受侵DLBCL作用



Held G, et al. J Clin Oncol. 2013 Nov 10;31(32):4115-22.

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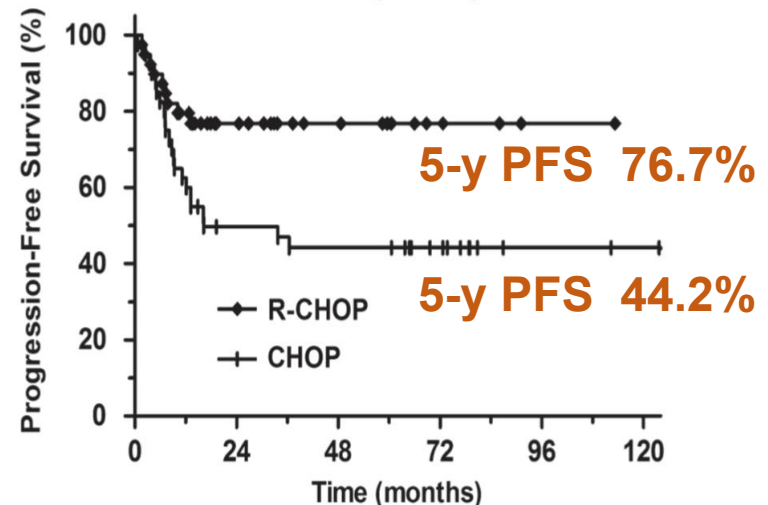
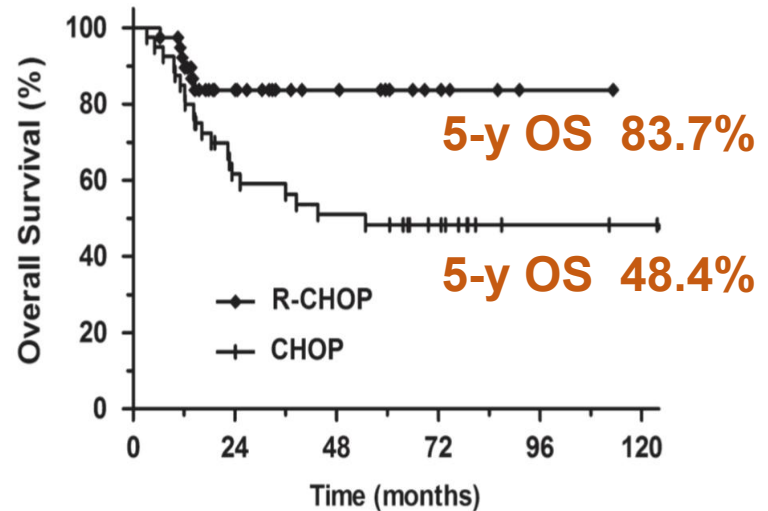
- 放疗在DLBCL治疗中的作用
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美罗华在PMBCL治疗中作用



Table II. Comparison of clinical characteristics between patients who received rituximab and those who did not.

Clinical characteristic	Rituximab (n = 39)	No rituximab (n = 40)	p-Value
	No (%)	No (%)	
Female	24 (61.5)	24 (60.0)	0.889
Age (<35 years)	25 (64.1)	30 (75.0)	0.292
B symptoms	18 (46.2)	11 (27.5)	0.085
Bulky disease	26 (66.7)	28 (70.0)	0.750
Local invasion	28 (71.7)	31 (77.5)	0.560
Elevated LDH levels	28 (71.7)	29 (72.5)	0.944
ECOG score			0.721
0-1	16 (41.0)	18 (45.0)	0.962
≥2	23 (59.0)	22 (55.0)	
Stage			0.428
I-II	33 (84.6)	34 (85.0)	
III-IV	6 (15.4)	6 (15.0)	0.210
aaIPI			
0-1	17 (43.6)	21 (52.5)	
2-3	22 (56.4)	19 (47.5)	
Radiotherapy	32 (82.1)	28 (70.0)	



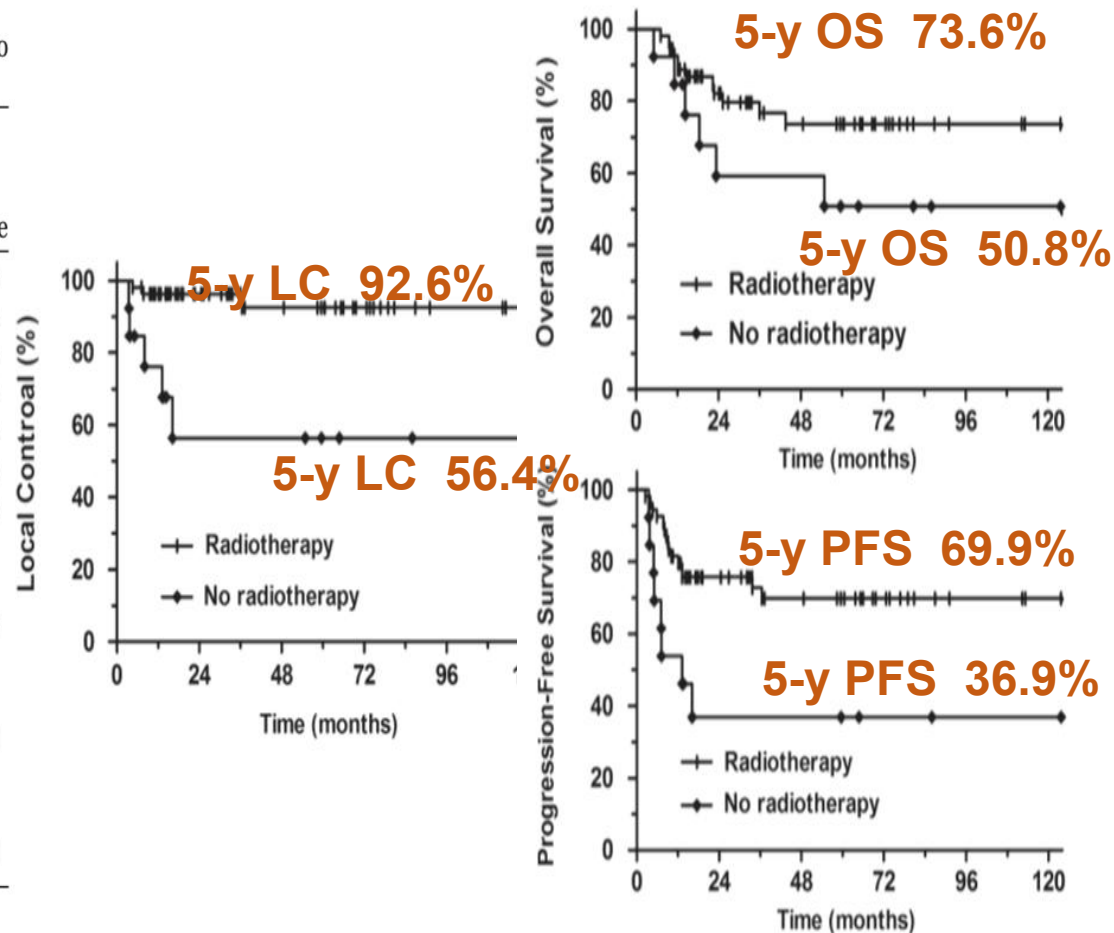
Xu LM, et al. Leuk Lymphoma. 2013;54(8):1684-90.

放疗在PMBCL治疗中作用



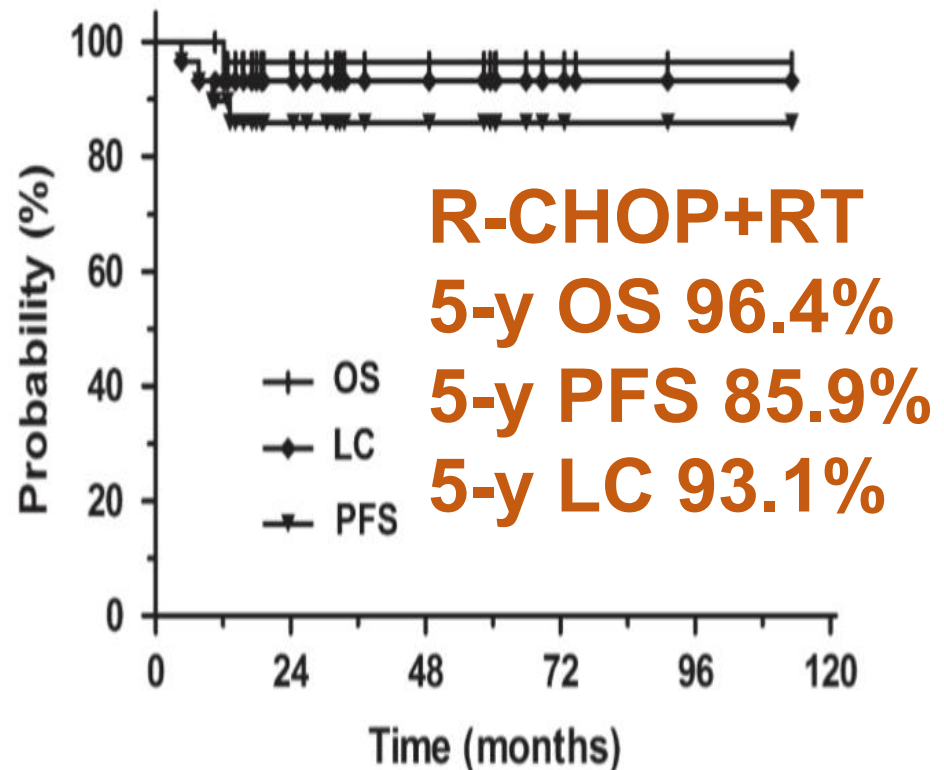
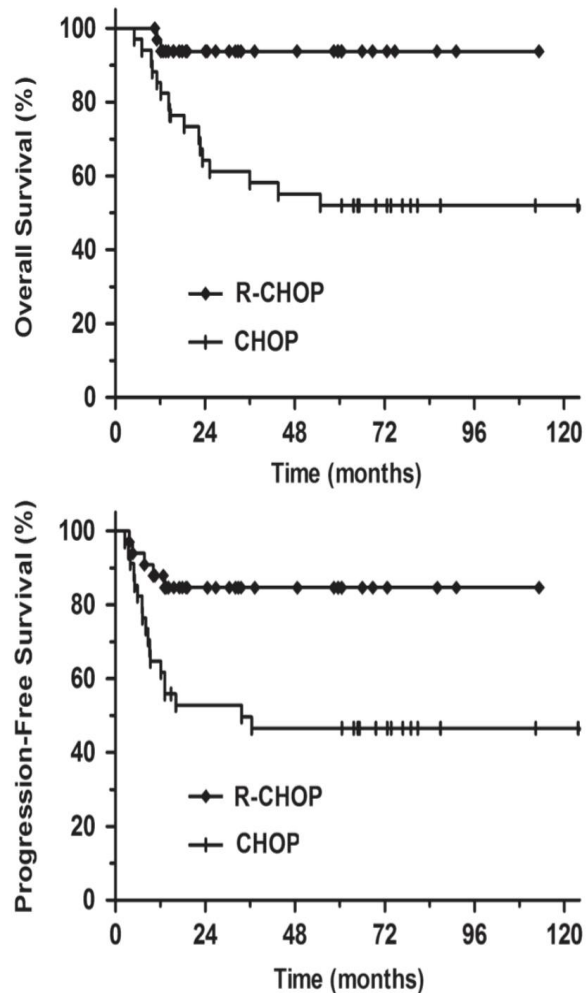
Table III. Comparison of clinical characteristics between patients who received radiotherapy and those who did not.

Clinical characteristic	Radiotherapy (n = 60)	No radiotherapy (n = 19)	p-value
	No (%)	No (%)	
Female	40 (66.7)	8 (42.1)	0.056
Age (< 35 years)	39 (65.0)	16 (84.2)	0.113
B symptoms	19 (31.7)	10 (52.6)	0.098
Bulky disease	39 (65.0)	15 (78.9)	0.255
Local invasion	43 (71.7)	16 (84.2)	0.273
Elevated LDH levels	40 (66.7)	17 (89.5)	0.053
ECOG score			0.133
0-1	23 (38.3)	11 (57.9)	0.022
≥ 2	37 (61.7)	8 (42.1)	
Stage			0.650
I-II	54 (90.0)	13 (68.4)	
III-IV	6 (10.0)	6 (31.6)	
aaIPI			0.210
0-1	28 (46.7)	10 (52.6)	
2-3	32 (53.3)	9 (47.4)	
Rituximab	32 (53.3)	7 (36.8)	



Xu LM, et al. Leuk Lymphoma. 2013;54(8):1684-90.

美罗华/放疗在早期PMBCL治疗中作用



Xu LM, et al. Leuk Lymphoma. 2013;54(8):1684-90.

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- 典型病例实战

早期FL的治疗



2004 - 2007年

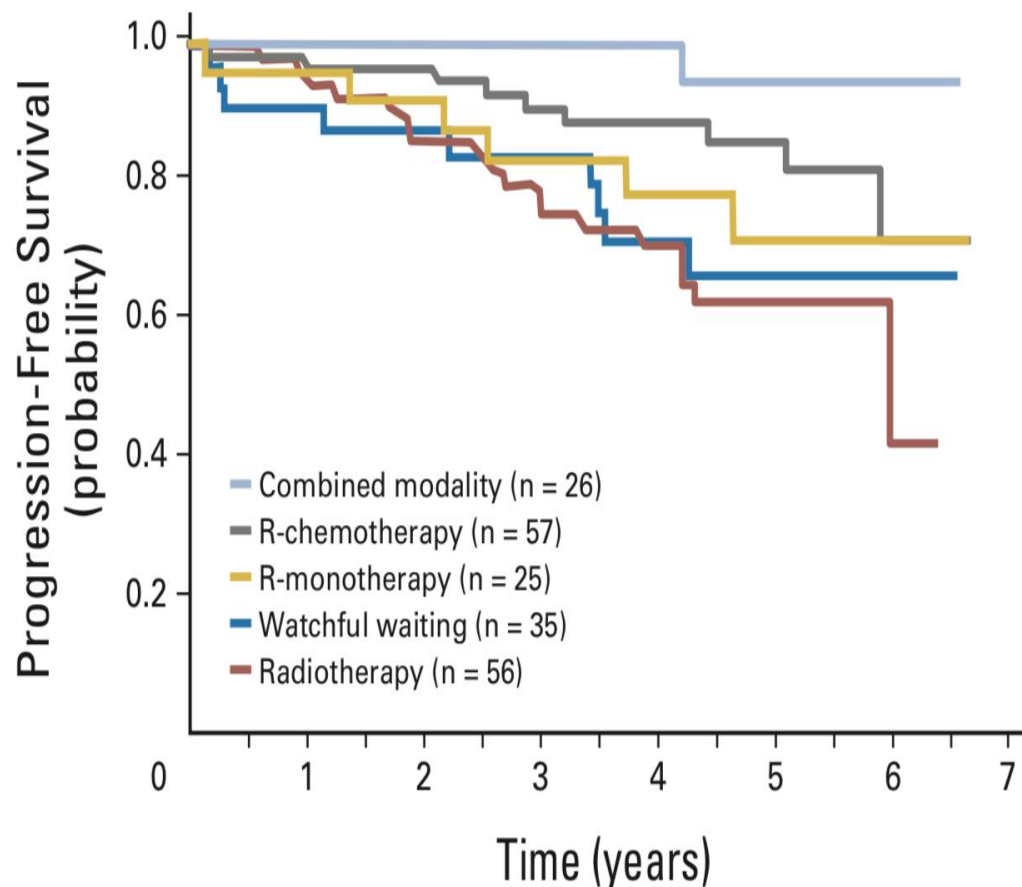
美国

471例 I期FL

206例严格分期

265例非严格分期

放疗患者不足1/3

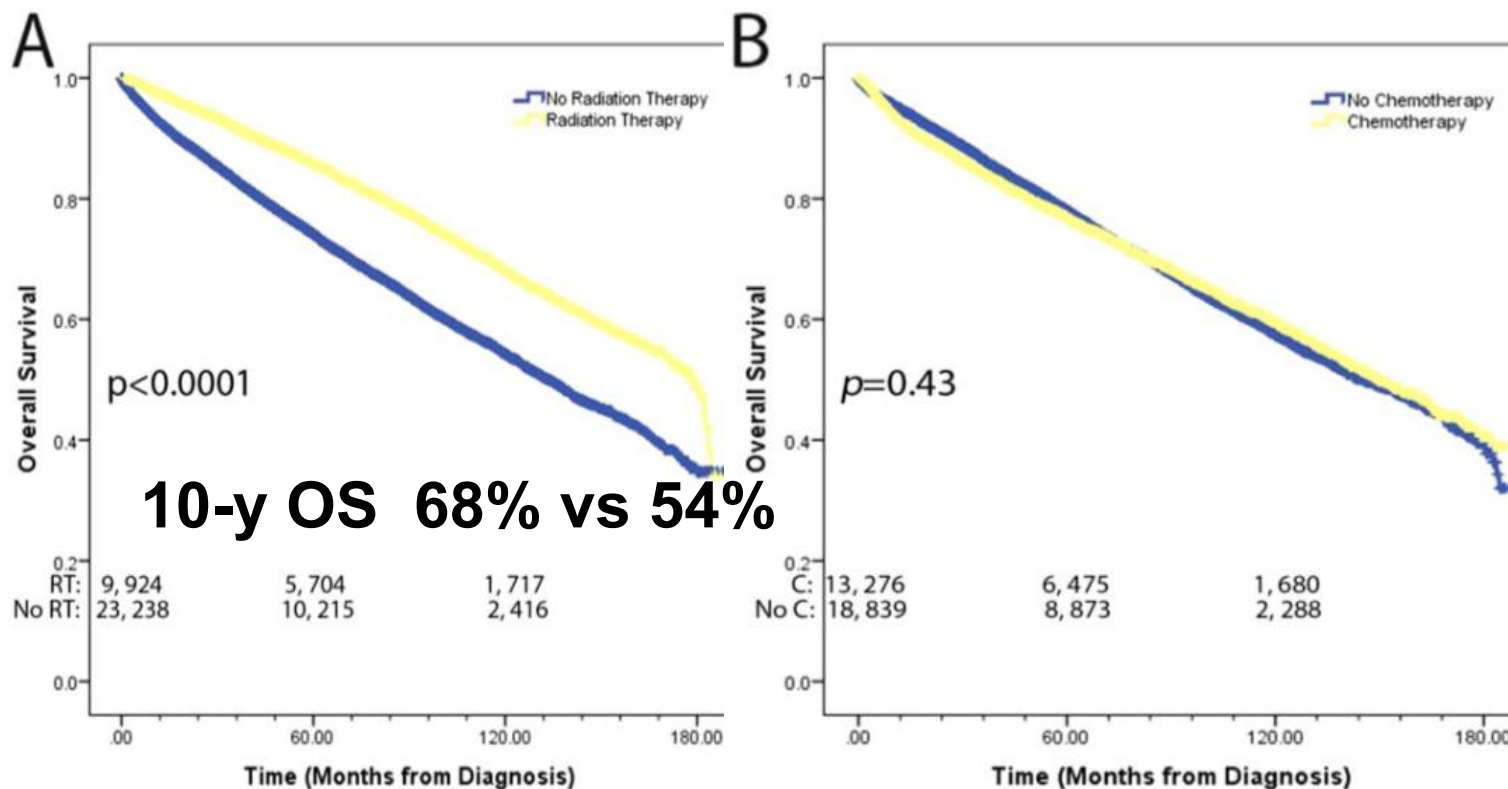


Friedberg JW, et al. J Clin Oncol.2012,30:3368-75.

放疗在早期FL治疗中作用



- NCDB数据库 1998-2012年 I-II级I-II期FL >18岁
- 35961例 30%首程放疗



Vargo JA, et al. Cancer. 2015 Sep 15;121(18):3325-34.

早期I-II级滤泡淋巴瘤放疗疗效

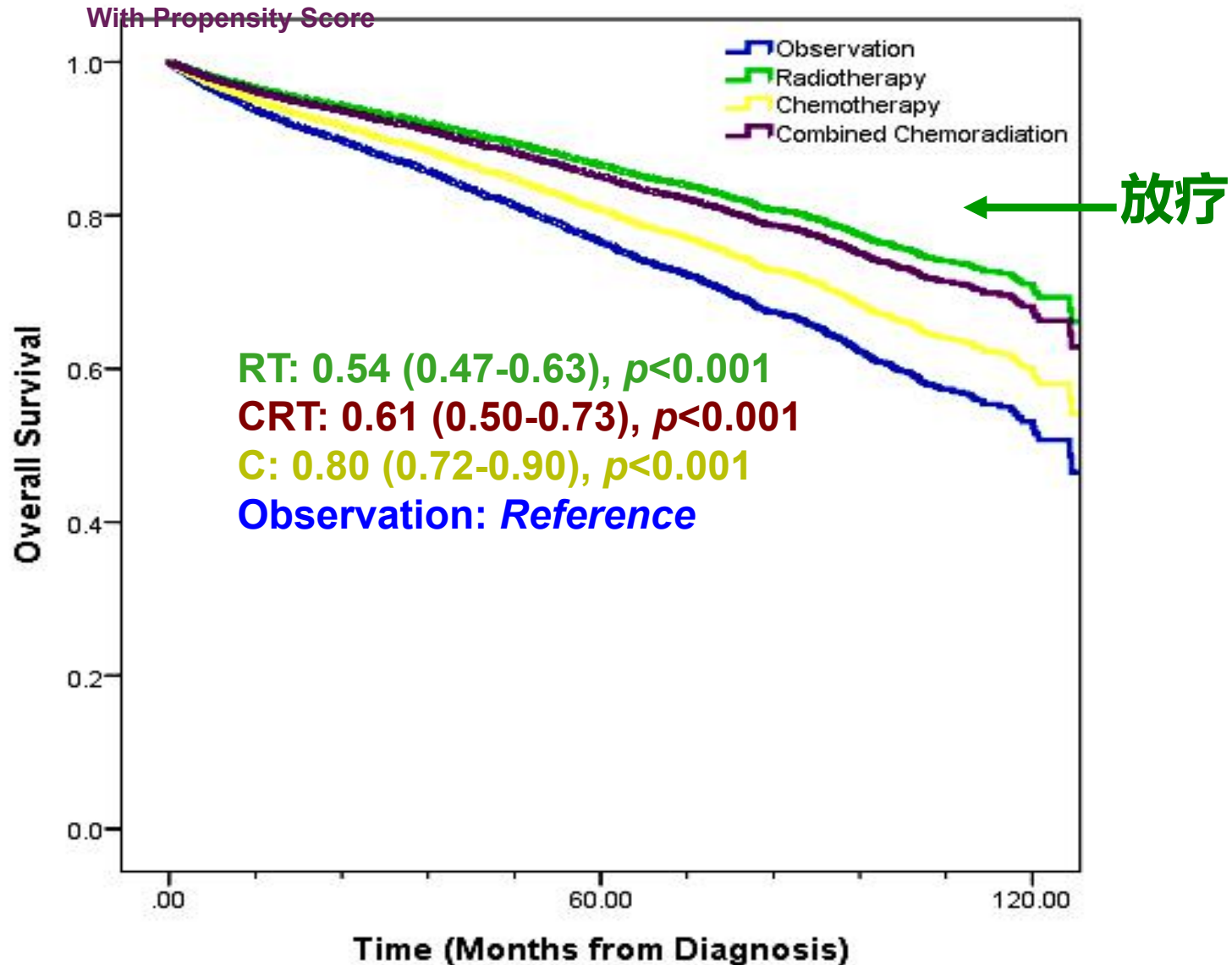
作者	年份	病例数	随访期 (年)	OS (10年)	PFS
Voss	2001	228		62	82
Wilder	2001	80	19	65	57
Neumann	2003	116	4	51	48
Petersen	2004	460	12.5	62	41
Guadagnolo	2006	79	19	74	47

局部控制率: 95%

OS=总生存率

早期低度恶性滤泡淋巴瘤

(2016 ASTRO John Austin Vargo)



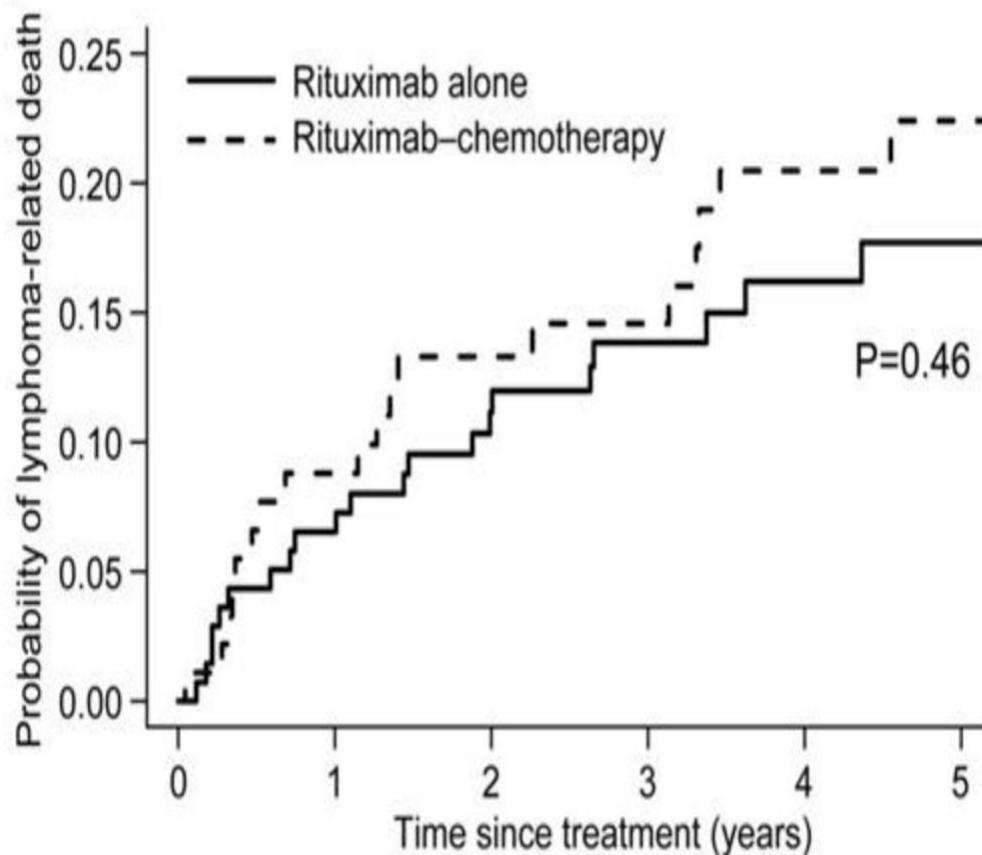
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胃MALT淋巴瘤美罗华治疗

- SEER数据库 1997-2007年 美罗华 vs 美罗华+化疗
- 5年淋巴瘤相关死亡 17.7% vs 22.4%

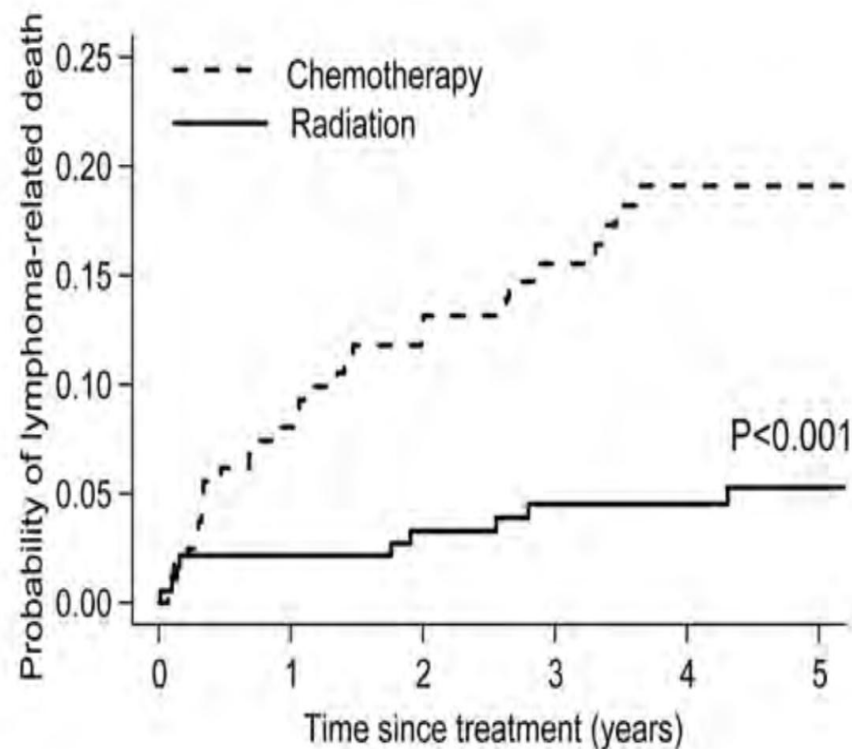


I期胃MALT淋巴瘤放疗优于化疗



SEER数据库 1997-2007年
347例IE期
185例放疗（7%初始联合化疗）
162例化疗（25%初始联合放疗）

放疗vs化疗 倾向配比评分



	放疗	化疗	P
5-y淋巴瘤相关死亡	5.3%	19.1%	0.001
5-y其他原因死亡	25.7%	24.8%	0.58

Olszewski AJ, et al. Ann Oncol. 2013, 24(5):1352-9.

早期胃MALT淋巴瘤放疗的疗效 (部分包括其他部位)



作者	年份	病例数	随访期(m)	CR	OS	EFS	PFS
Wirth et al.	2013	102	95	96%	70% (10y)		88% (10y)
Kim et al.	2013	64	39	100%	94%		
Zullo et al.(review)	2010	112		97.3%			
Gobbi et al.	2009	24	67	100%			
Yamashita et al.	2008	41	40	100%	96.7%		90.6
Tsang RW et al.	2003	103	61	98%	98%	77%	98%
Park et al.	2002	6		100%		100%	
Yahalom et al.	2002	51		96%	83%		

CR=完全缓解 OS=总生存率

早期粘膜相关淋巴组织淋巴瘤 (ASTRO)



作者	例数	放疗剂量	CR率 (%)	生存率 (%)	放疗并发症
Dabaja 等 (前瞻性)	104 (全部)	30–36 Gy	100	100 (10Y DSS) 100 (10Y OS)	干眼症: (5/26) 返酸: (2/39) 口干症: (2/6), 均1度
Miyazawa 等	45 (眼眶)	30–36 Gy	100	100 (5Y CSS) 94.5 (5Y OS)	白内障 结膜: 20% 其他: 70%
Lee 等	47 (眼眶和非胃)	中位30.6 Gy (29例放疗)	100 (放疗)	5Y PFS: 82% (放疗) vs 34% (非放疗); p =0.003	
Tatekawa 等	55 (眼眶)	中位30 Gy	100	89 (5Y PFS) 100 (5Y OS)	干眼症: 2/55 白内障: 25/55
Harada等	86 (眼眶)	中位30 Gy		100 (10Y DSS) 93.5 (10Y OS)	白内障 (单眼计) 无铅挡: 36/65 铅挡: 12/39 P=0.037
Ohga等	92 (眼眶)	中位30 Gy	100	81.5 (5Y PFS) 100 (5Y OS)	白内障: 35.6% 干眼症: 15.1% (≥2级)

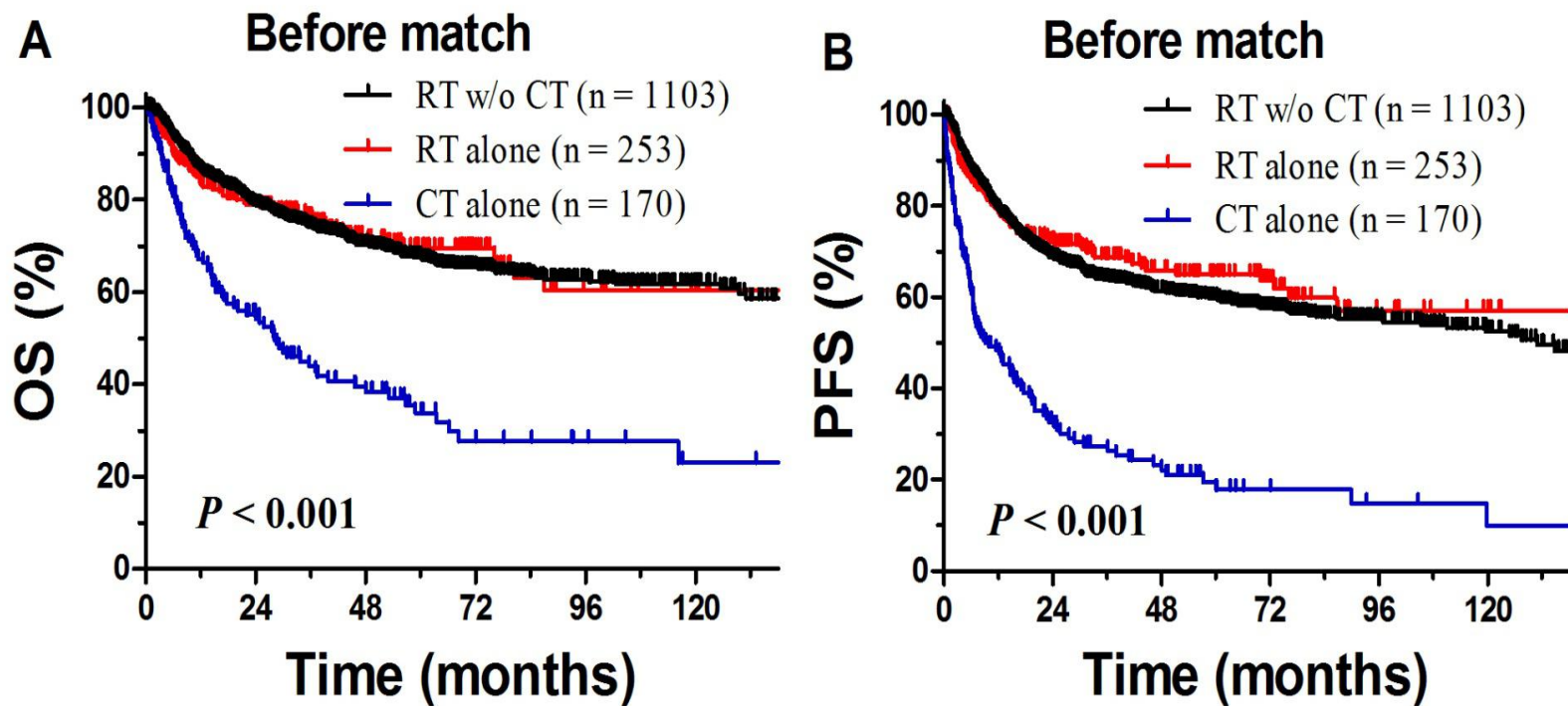
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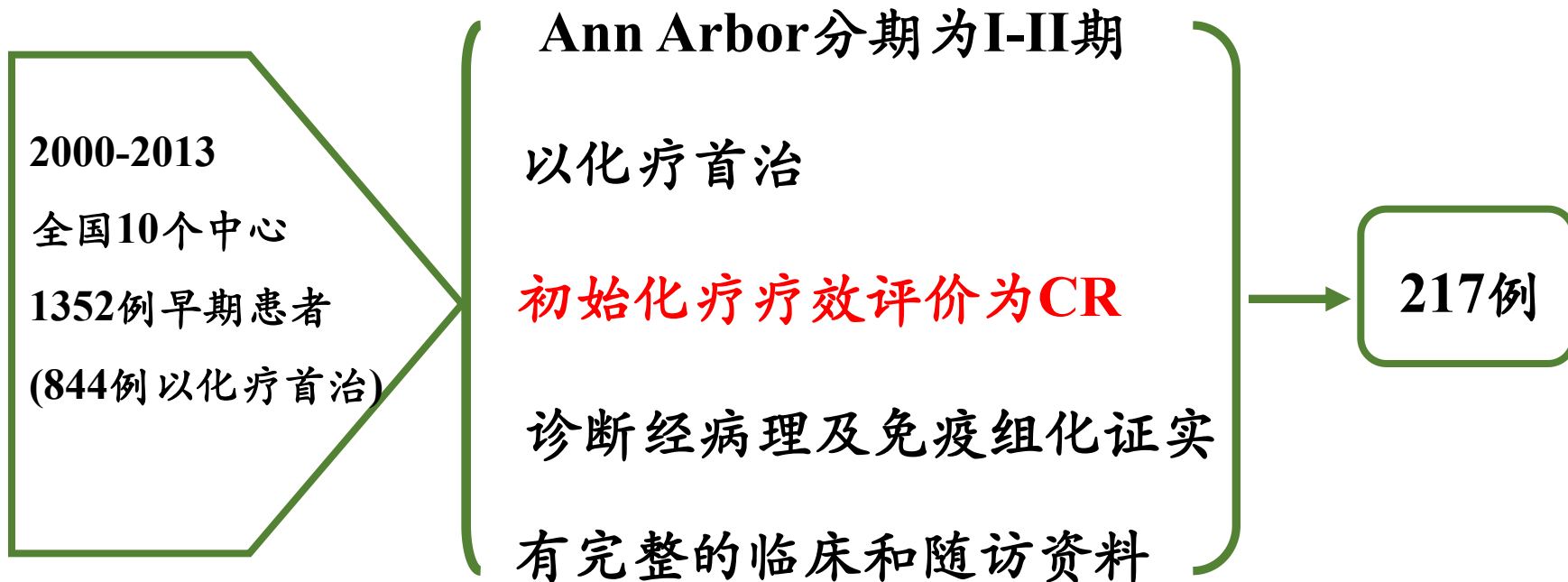
早期NK/TCL放疗为主优于单纯化疗

--10个中心1273例患者结果

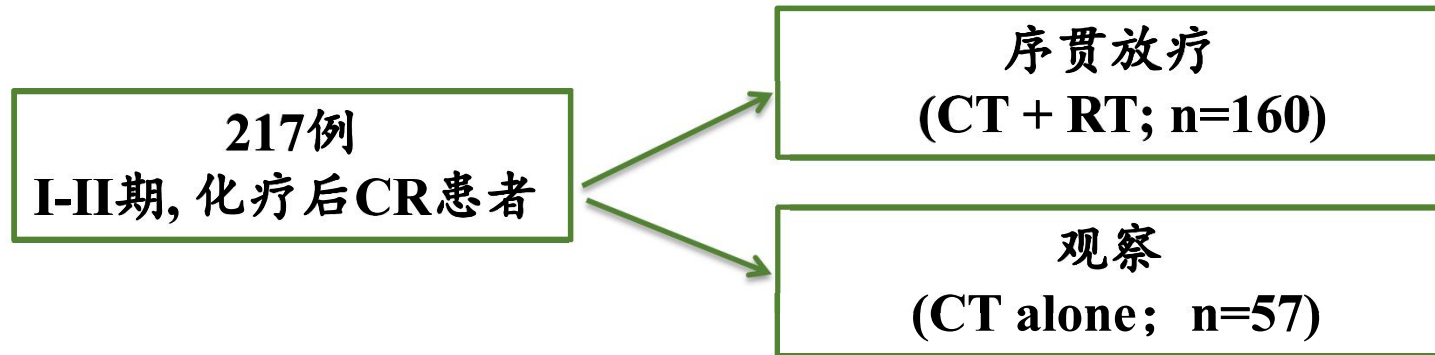


Yong Y, et al. Blood, 2015;126:1424-32

早期NKTCL化疗CR后是否需要放疗



治疗方案



◆ 化疗方案:

CHOP-like 160例 (74%)

L-asp-based 49例 (23%)

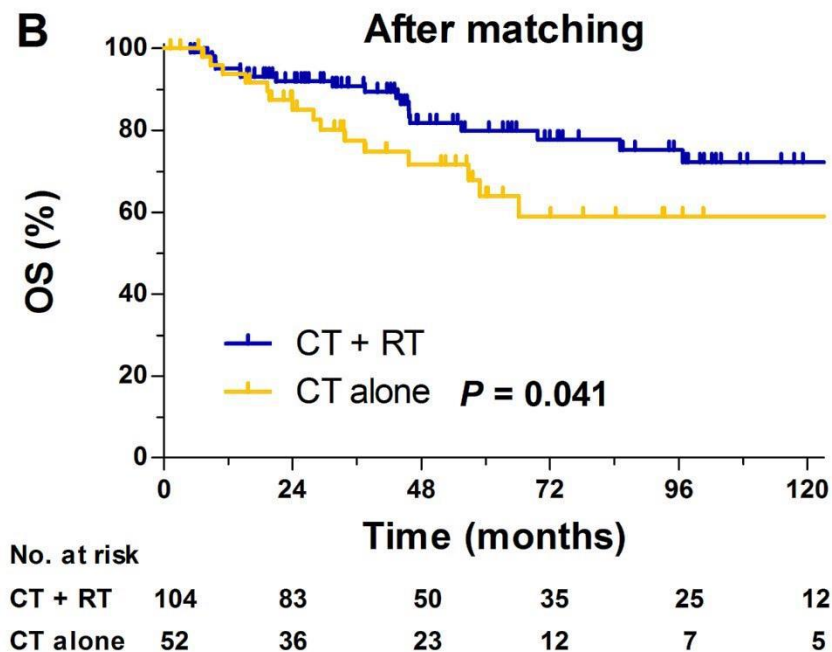
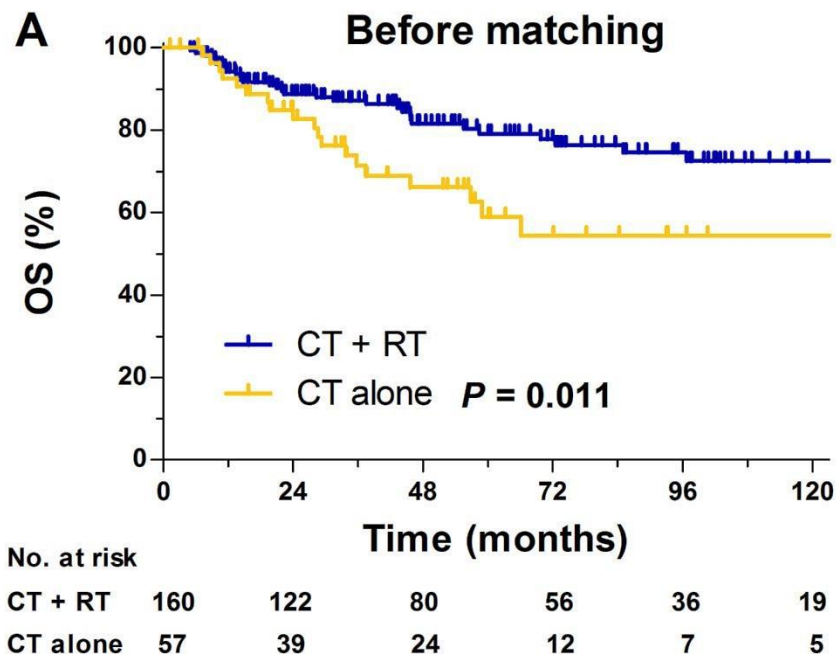
◆ 中位周期数为4 (1-14)

◆ 放疗:

扩大受累野照射

DT 50 Gy (16-60 Gy)

结果-配比前后OS



5年OS

CT alone

CT + RT

P值

配比前

58.8%

79.1%

0.011

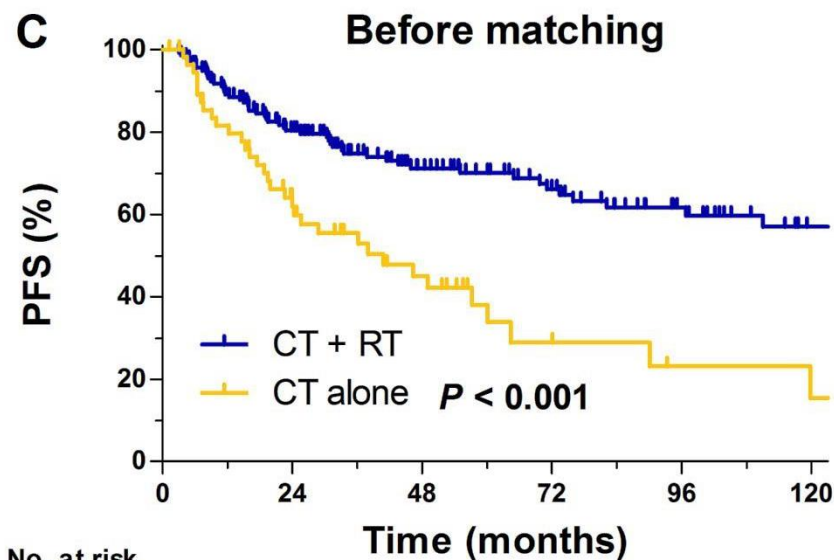
配比后

63.8%

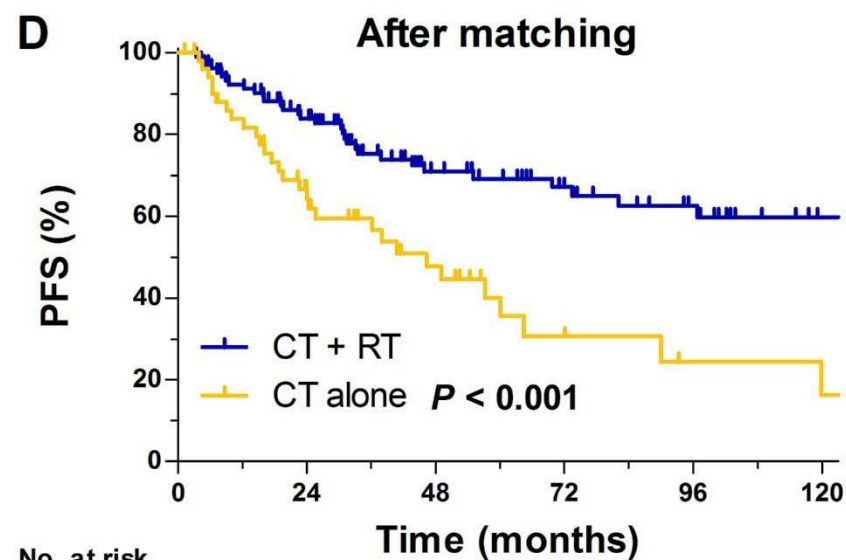
79.9%

0.041

结果-配比前后PFS



No. at risk						
CT + RT	160	111	72	49	31	17
CT alone	57	29	16	6	3	2



No. at risk						
CT + RT	104	76	45	32	22	11
CT alone	52	27	15	6	3	2

5年PFS

CT alone

CT + RT

P值

配比前

37.9%

70.0%

< 0.001

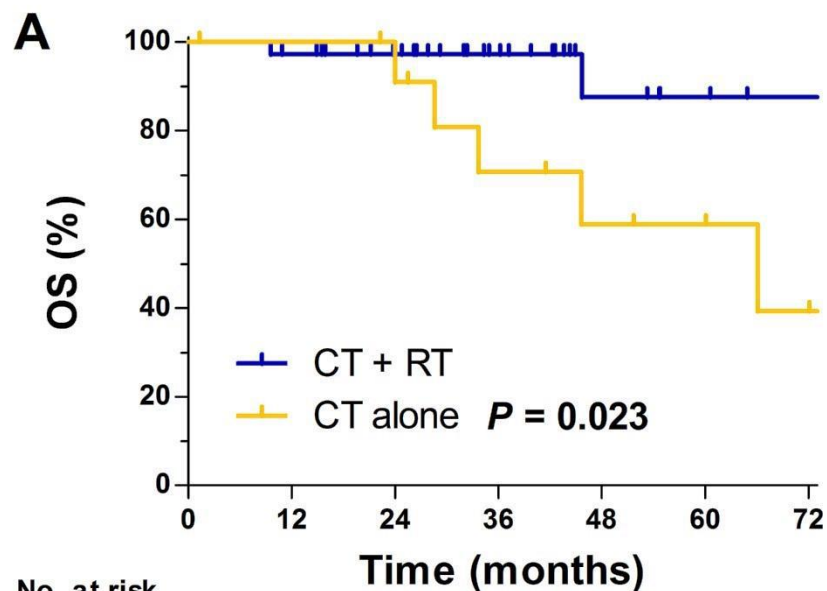
配比后

40.0%

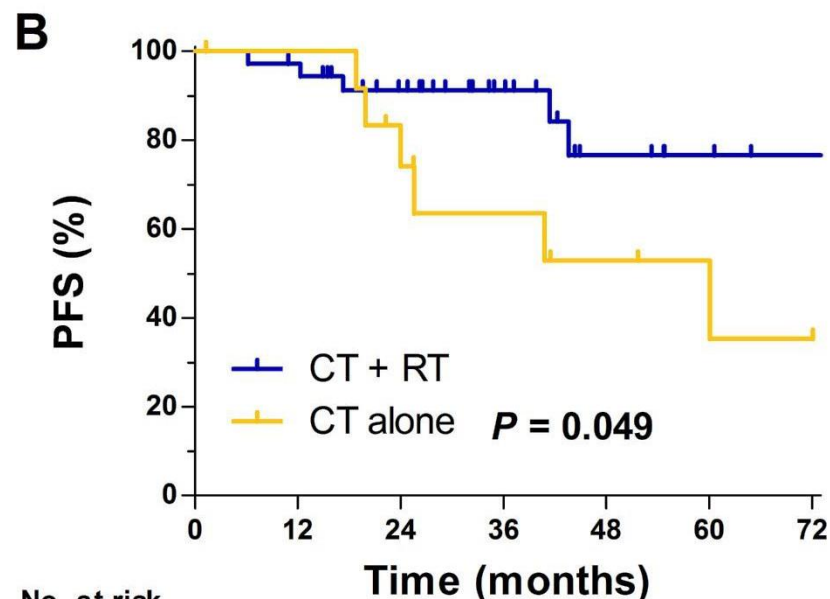
69.2%

< 0.001

结果-L-asp化疗亚组 (n=49)



No. at risk							
	0	12	24	36	48	60	72
CT + RT	36	34	28	18	9	6	4
CT alone	13	12	10	7	5	4	2



No. at risk							
	0	12	24	36	48	60	72
CT + RT	36	34	26	16	8	5	3
CT alone	13	12	8	6	4	3	1

CT alone

CT + RT

P值

5年 OS

58.9%

87.5%

0.023

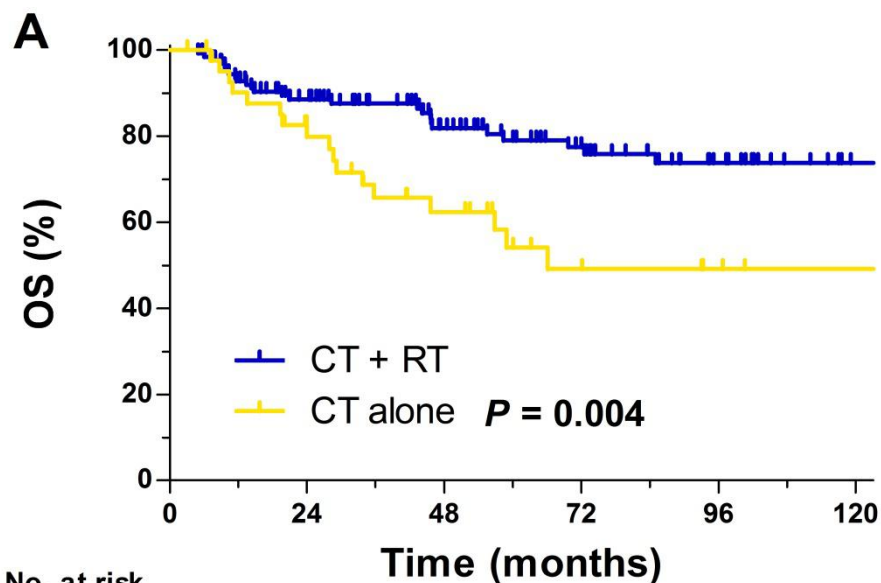
5年 PFS

35.3%

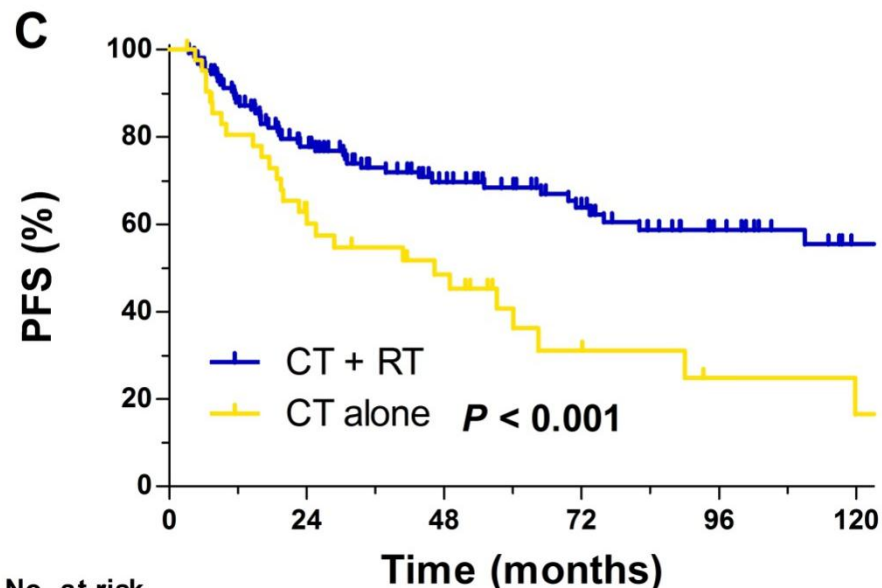
76.5%

0.049

结果- ≥ 4 周期化疗亚组 (n=170)



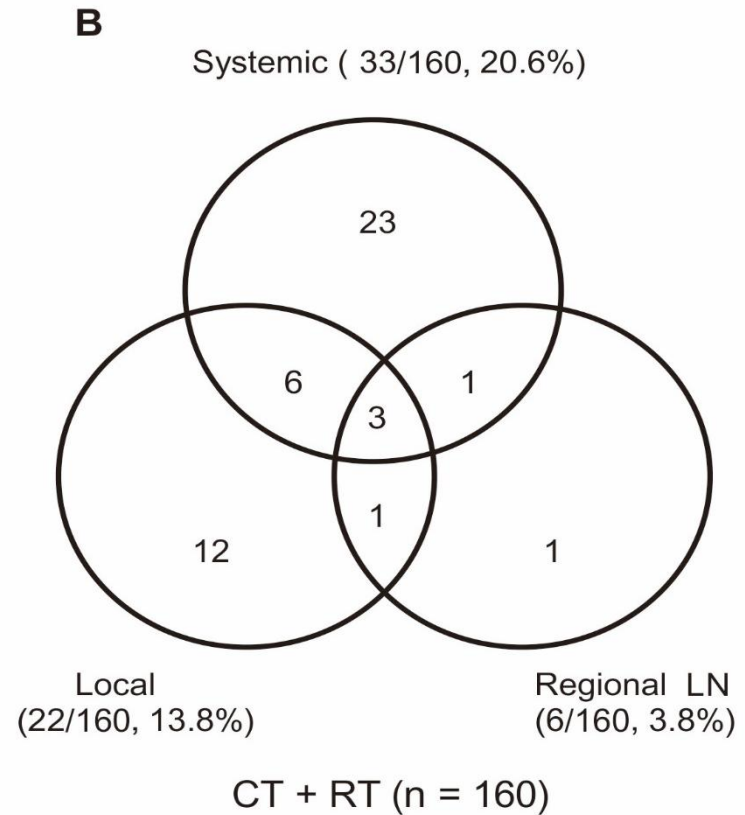
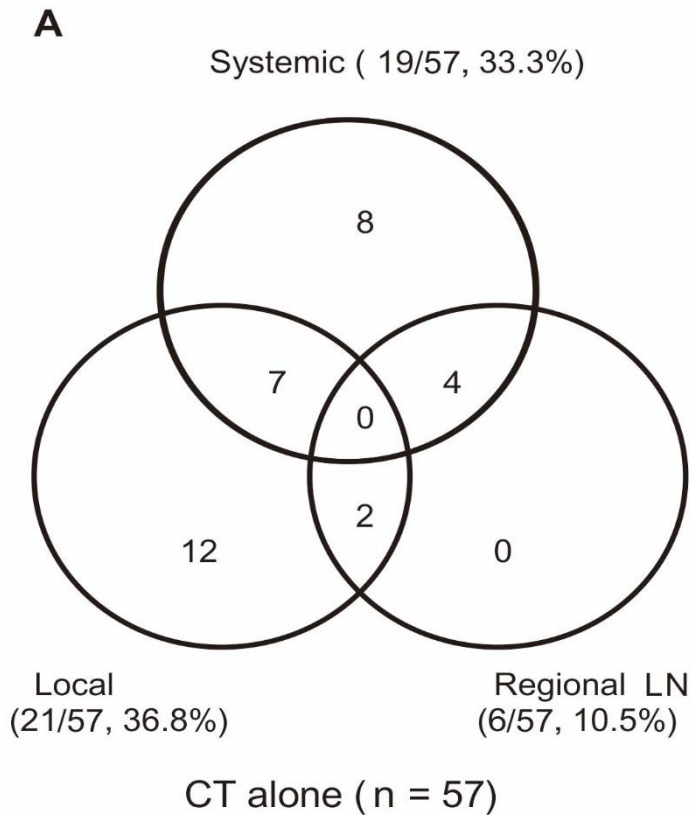
No. at risk						
CT + RT	127	98	67	47	29	15
CT alone	43	19	19	10	7	5



No. at risk						
CT + RT	127	87	60	40	24	13
CT alone	43	22	15	6	3	2

	CT alone	CT + RT	P值
5年 OS	54.1%	79.0%	0.004
5年 PFS	40.8%	68.4%	< 0.001

结果-失败模式



◆左图：单纯化疗组总失败率58%，以局部失败和系统失败为主

◆右图：化疗+放疗组总失败率29%，以系统失败为主

结 论



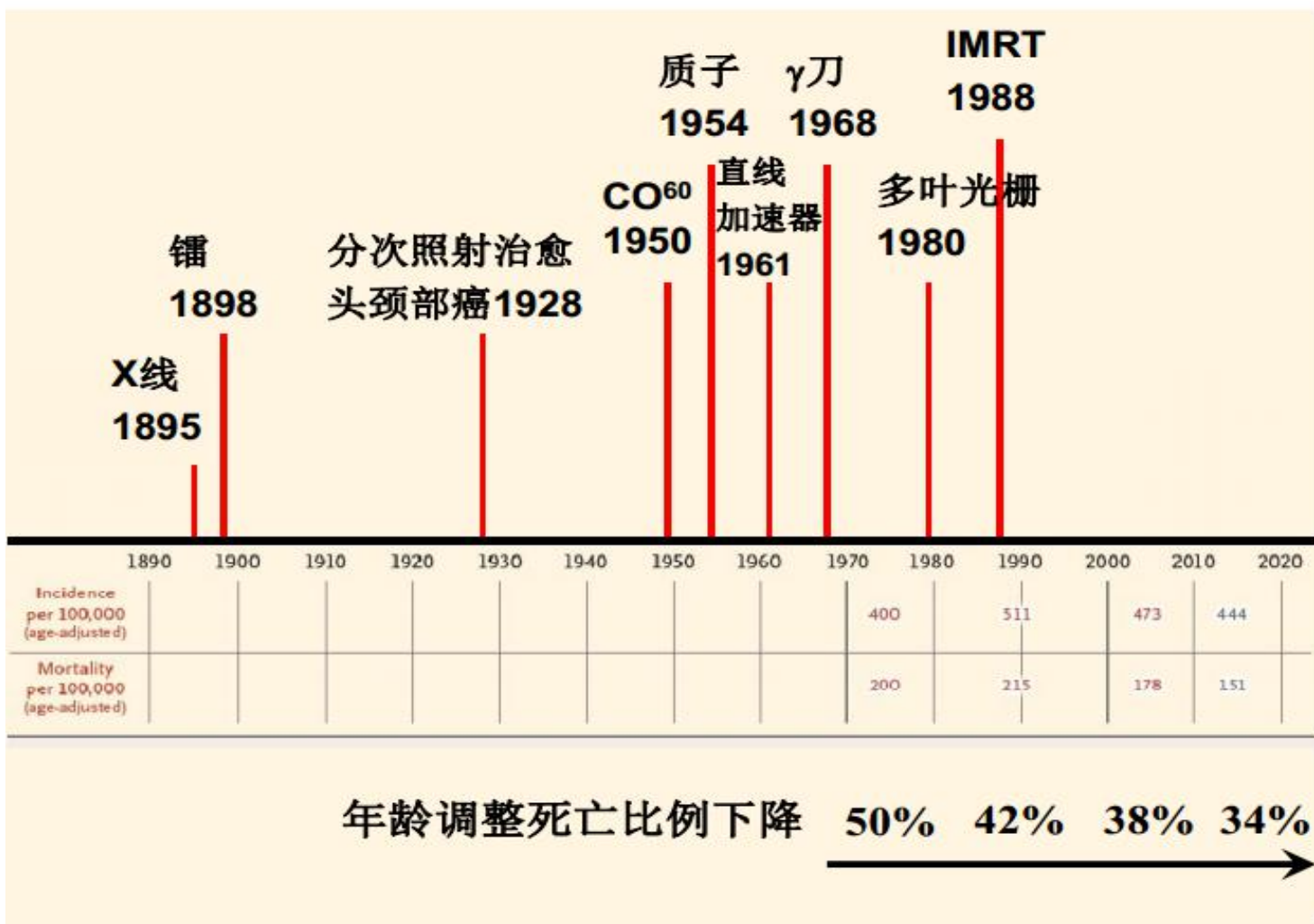
- ✓ 早期NKTCL行单纯化疗即使达到完全缓解，局部区域失败和系统失败率仍然很高，
- ✓ 放疗可以改善总生存和无进展生存，减少局部区域及远处失败

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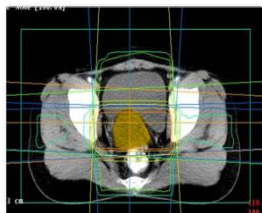


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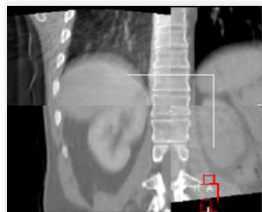
肿瘤放疗的120年发展历程



近代放疗技术快速发展



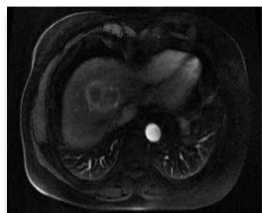
三维适形放疗



图像引导放疗

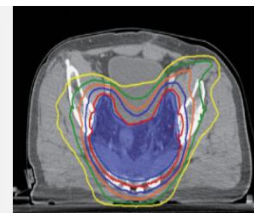


四维模拟CT定位

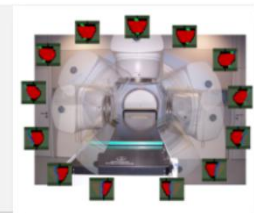


MRI模拟定位

逆向调强放疗



动态旋转调强放疗



立体定向放疗



术中放疗



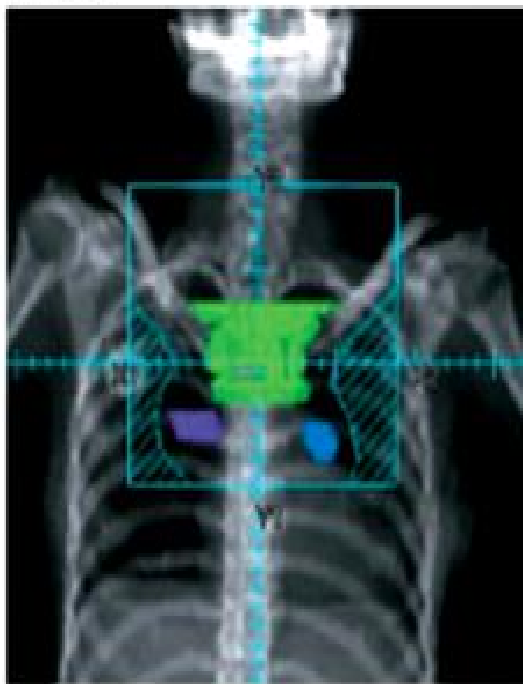
放疗野



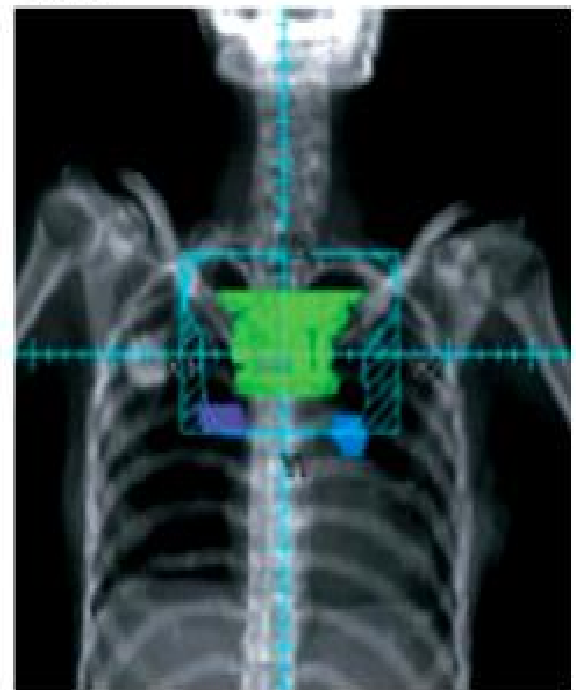
Mantle



IFRT



INRT



HD放疗野缩小&剂量降低



2-3 ABVD
+
IN/ISRT
20 Gy

预后好早期HD

4 ABVD或
2 ABVD + 2
BEACOPP+
IN/ISRT 30 Gy

预后不良早期HD

6-8 周期化疗
±放疗

晚期HD

NHL放疗剂量降低



英国多中心，III期，RCT研究

惰性淋巴瘤：40-45Gy/20-23f vs 24Gy/12f

侵袭性淋巴瘤：40-45Gy/20-23f vs 30Gy/15f

- 入组标准：
- 1、 ≥ 18 岁
- 2、所有病理类型 NHL
- 3、所有包含放疗的患者（根治性、辅助性、姑息性、挽救性）

	Indolent (n = 289)	Aggressive (n = 476)
FL Grade 1/2	171 (59%)	11 (2%)
Grade 3	14 (5%)	11 (2%)
MZL including MALT lymphoma	56 (19%)	4 (1%)
CLL/SLL	10 (3%)	0
LPL	2 (1%)	
MCL	8 (3%)	7 (2%)
DLBCL	20 (7%)	391 (82%)
HG transformation of FL	6 (2%)	15 (3%)
Burkitt's	0	3 (1%)
T-NHL	1 (<1%)	24 (5%)
Other	1 (<1%)	10 (2%)

Lowry L, et al. Radiother Oncol. 2011;100(1):86-92.

NHL放疗剂量降低



Baseline characteristics and indications for therapy.

	Indolent		Aggressive		Total
	24 Gy N = 180	40–45 Gy N = 181	30 Gy N = 319	40–45 Gy N = 321	
Age median (range)	62 (29–85)	64 (30–89)	65 (18–91)	65 (23–92)	64 (18–92)
Male gender N (%)	84 (47)	97 (54)	179 (56)	168 (52)	528 (53)
First-line treatment: stage N (%)					
I	69 (40)	72 (41)	77 (24)	68 (21)	286 (29)
IE	38 (22)	47 (27)	55 (17)	56 (18)	196 (20)
II/III	11 (6)	13 (7)	79 (25)	93 (30)	216 (20)
III/IV	6 (3)	12 (7)	45 (14)	45 (14)	108 (11)
Relapsed/refractory; any stage N (%)	50 (29)	30 (17)	44 (14)	41 (13)	165 (17)
Not known N	6	7	19	18	50
B symptoms N (%)	13 (8)	4 (2)	43 (15)	40 (15)	100 (11)
Time from diagnosis to randomisation; median months (range)	3.1 (0.2–220)	2.8 (0–179)	4.6 (0–352*)	4.5 (0–164)	4.1 (0–352)
Indication for RT radical	119 (66)	130 (72)	36 (12)	35 (12)	320 (32)
Palliation	56 (31)	46 (25)	25 (8)	29 (9)	156 (16)
Consolidation	5 (3)	5 (3)	257 (81)	255 (79)	522 (52)
Previous/contemporaneous chemotherapy N (%)	46 (26)	36 (20)	256 (80)	252 (79)	590 (59)
Previous radiotherapy N (%)	15 (8)	24 (13)	32 (10)	29 (9)	100 (10)
Previous rituximab exposure N (%)	2 (1)	2 (1)	34 (11)	33 (10)	71 (7)
Karnofsky scale N (%)					
60–80	16 (12)	16 (11)	67 (30)	61 (30)	160 (23)
90	44 (34)	34 (24)	66 (29)	67 (32)	211 (30)
100	70 (53)	90 (64)	92 (41)	80 (38)	332 (47)
Not known	50	41	94	113	298

* The single patient 352 months from original diagnosis represented a recent aggressive transformation of indolent lymphoma.

Lowry L, et al. Radiother Oncol. 2011;100(1):86-92.

NHL低剂量放疗未降低反应率



惰性NHL: ORR 高剂量 vs 低剂量=93% vs 92% ($p = 0.72$);
侵袭性NHL: ORR 均为91% ($p = 0.87$)

Response	Indolent		Aggressive		Total
	24 Gy	40-45 Gy	30 Gy	40-45 Gy	
CR	145 (82%)	138 (79%)	249 (82%)	251 (83%)	783 (82%)
PR	18 (10%)	24 (14%)	29 (9%)	24 (8%)	95 (10%)
SD/ progression	14 (8%)	12 (7%)	25 (8%)	24 (8%)	75 (8%)
Death	0 (0%)	0 (0%)	1 (<1%)	3 (1%)	4 (<1%)
Not assessable	2	2	0	3	7
No RT received	1	1	5	3	10
Missing	0	4	10	13	27
Total	180	181	319	321	1001

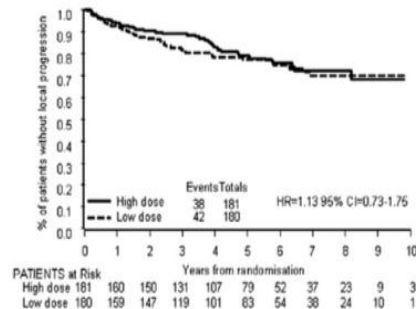
Lowry L, et al. Radiother Oncol. 2011;100(1):86-92.

NHL低剂量放疗未降低疗效

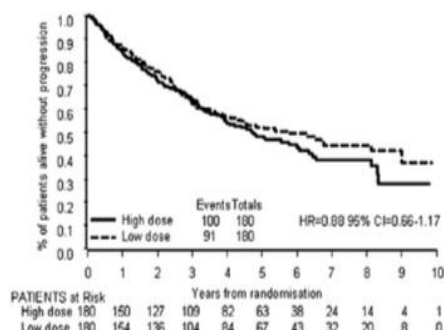


Indolent group

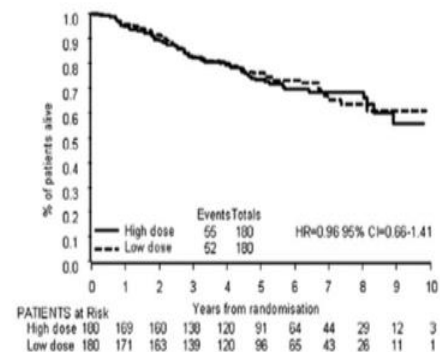
(a) Freedom from local progression



(b) Progression-free survival

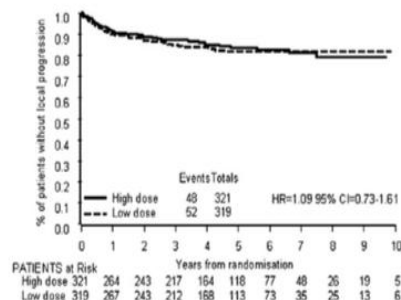


(c) Overall survival

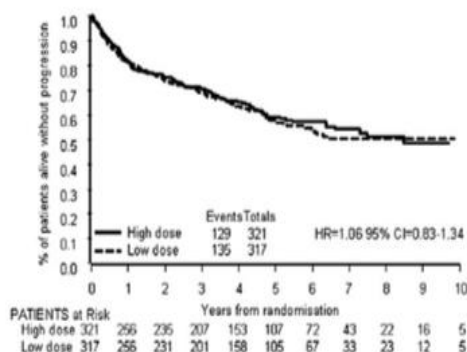


Aggressive group

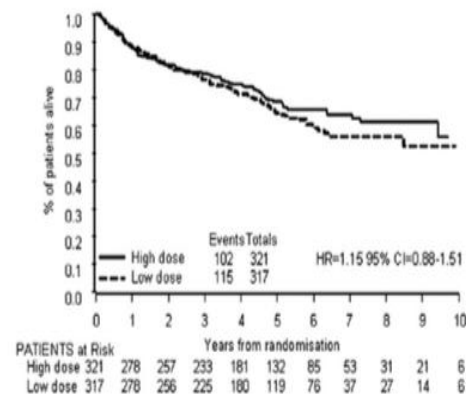
Freedom from local progression



Progression-free survival



Overall survival



Lowry L, et al. Radiother Oncol. 2011;100(1):86-92.

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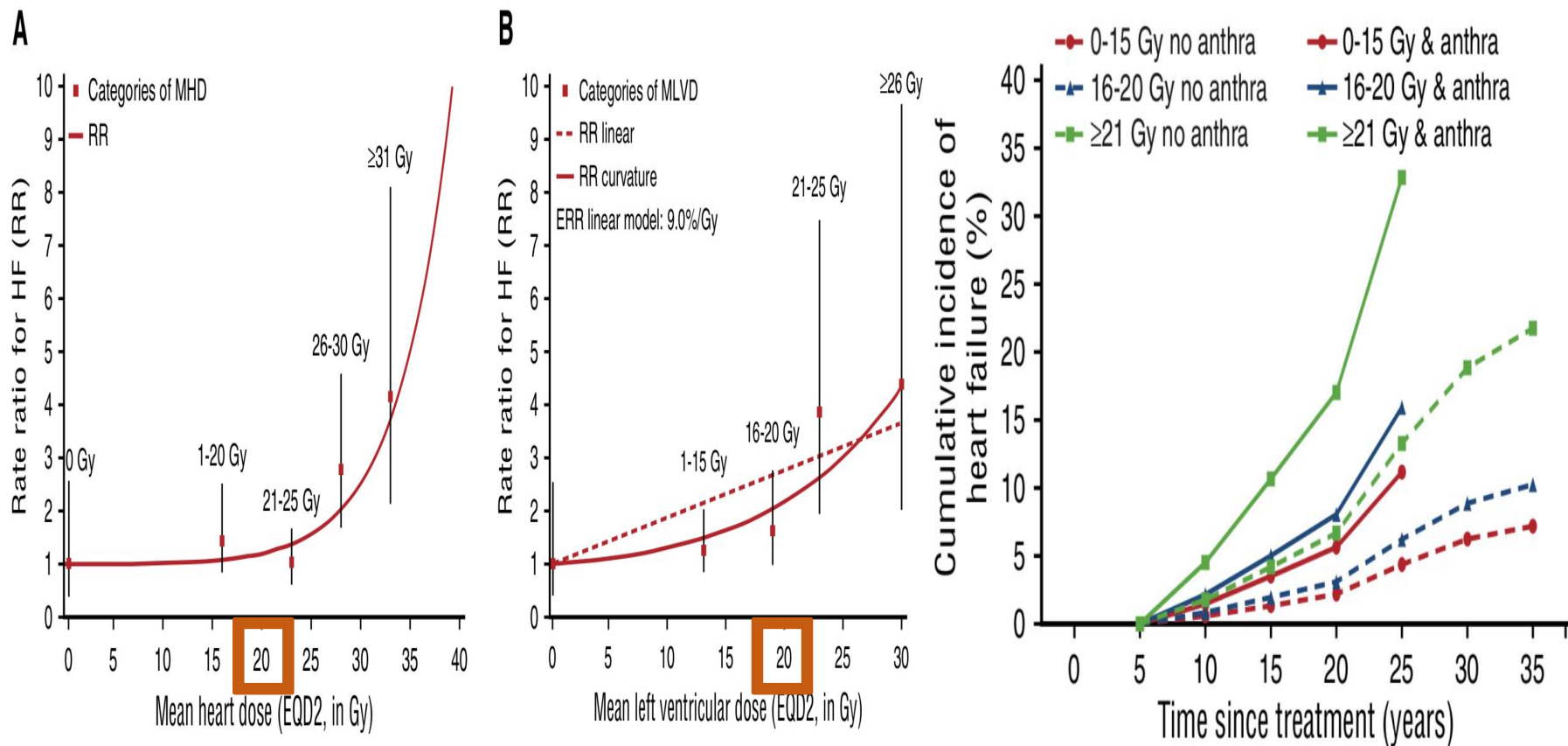


- 放疗在DLBCL治疗中的作用
- 放疗在PMBCL治疗中的作用
- 放疗在FL治疗中的作用
- 放疗在MALT治疗中的作用
- 放疗在NKTCL治疗中的作用
- 放疗技术进步、剂量降低
- 放疗远期不良反应
- 典型病例实战

HD治疗后心衰发生风险



与阿霉素累积剂量和照射剂量相关

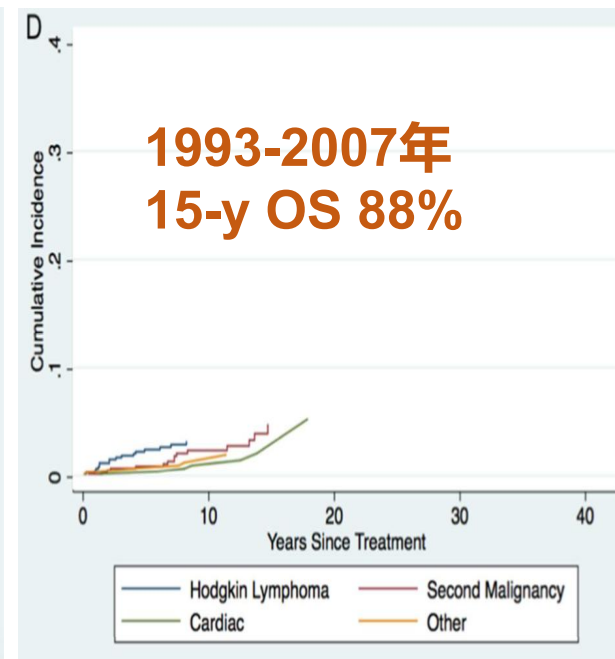
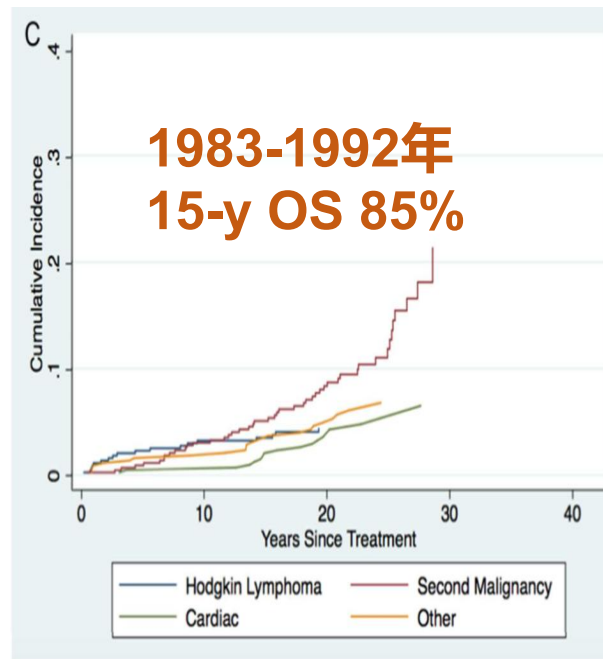
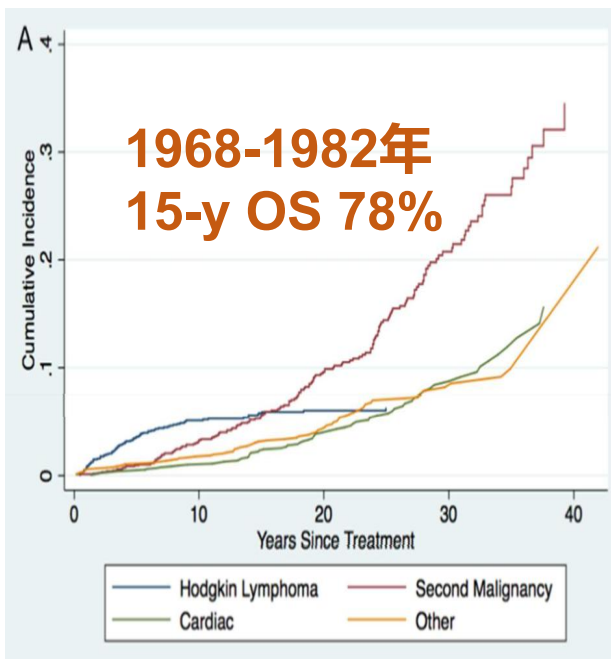


van Nimwegen FA, et al. Blood. 2017;129(16):2257-2265.

HD心脏和第二原发肿瘤风险下降



- 1541例早期HD 接受放疗/综合治疗 中位年龄27岁 中位随访15年



Patel CG, et al. Int J Radiat Oncol Biol Phys. 2018;100(2):498-506.

放疗未增加NHL第二原发肿瘤风险



			SIR (95% CI)	
	病种	病例数	未放疗	放疗
BNLI	NHL	2456	1.0 (0.7–1.4)	1.2 (0.8–1.7)
SEER	NHL	77823	1.13 (1.1–1.2)	1.18 (1.1–1.2)
GISL	DLBCL	1280	1.16 (0.79–1.63)	0.92 (0.42–1.75)
SEER	HD, >20岁	12467	15.0% (化疗) *	14.5% (放+化) *

*第二原发肿瘤发生率

Mudie NY, et al. J Clin Oncol. 2006;24(10):1568-74.

Tward JD, et al. Cancer. 2006;107(1):108-15.

Sacchi S, et al. Haematologica. 2008;93(9):1335-42.

Koshy M, et al. Int J Radiat Oncol Biol Phys. 2010;78(3): S65–S66.

第二原发性肿瘤主要与生活方式/遗传相关



The proportion of second cancers attributable to radiotherapy treatment in adults: a prospective cohort study in the US SEER cancer registries

Amy Berrington de Gonzalez, DPhil¹, Rochelle E Curtis, MA¹, Stephen F Kry, PhD², Ethel

Interpretation—A relatively small proportion of second cancers are related to radiotherapy in adults, suggesting that most are due to other factors, such as lifestyle or genetics.

Berrington de Gonzalez A, et al. Lancet Oncol. 2011,12(4): 353–360.

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眼眶粘膜相关淋巴组织淋巴瘤



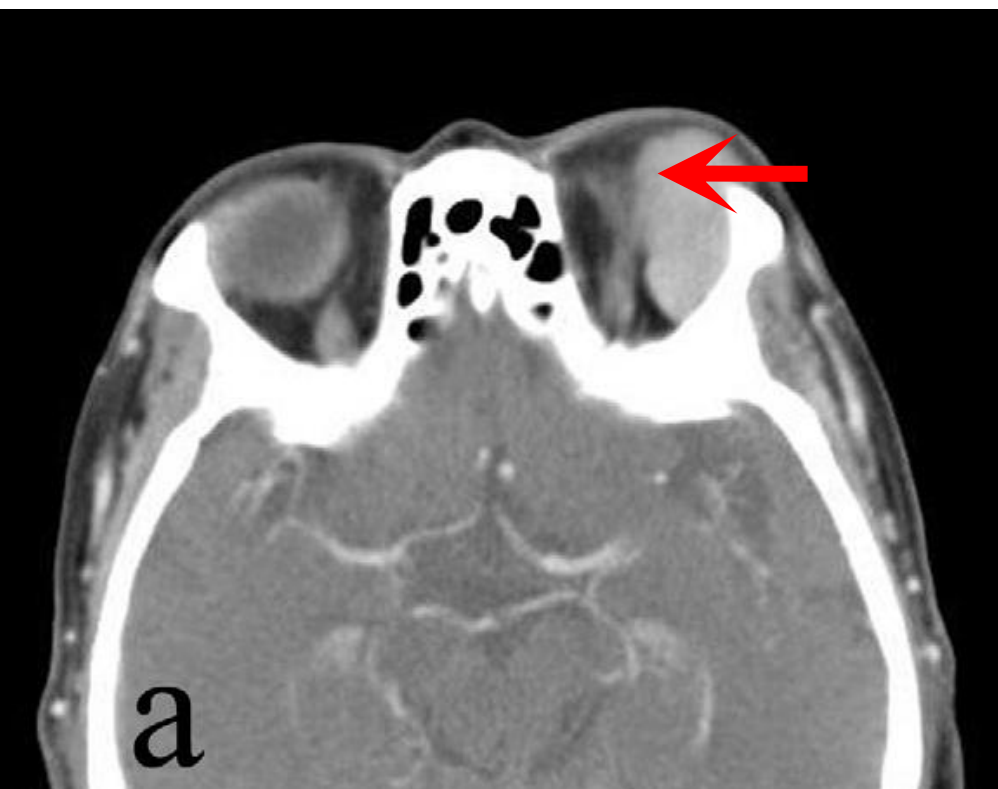
- ✓ 85%-90%为I期
- ✓ 区域淋巴结受累5%
- ✓ 10%-15%双侧发生

(80%同时发生, 20%先后发生)

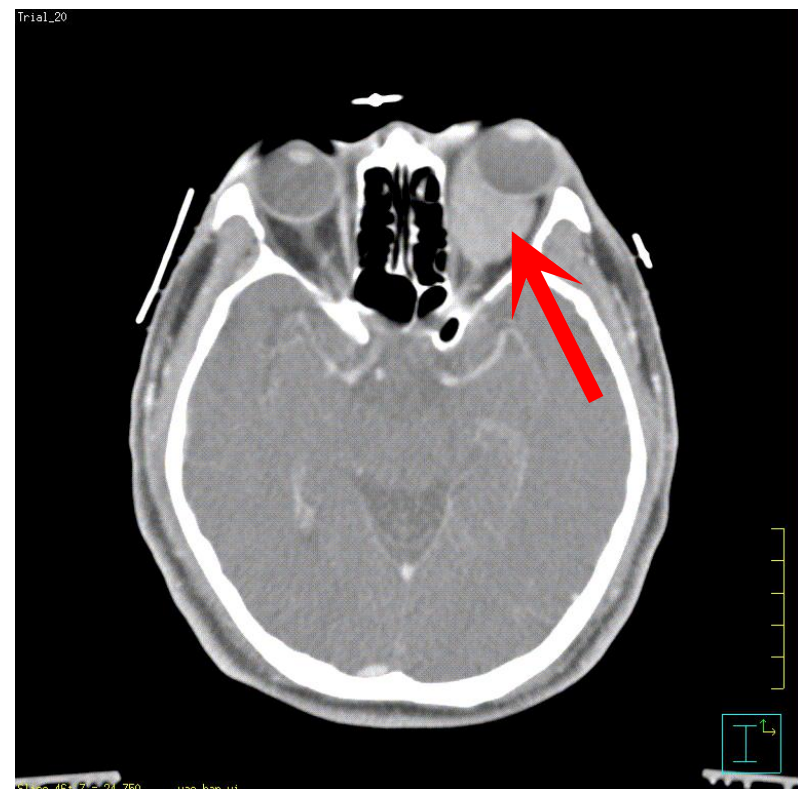
影像学表现



原发泪腺



原发球后

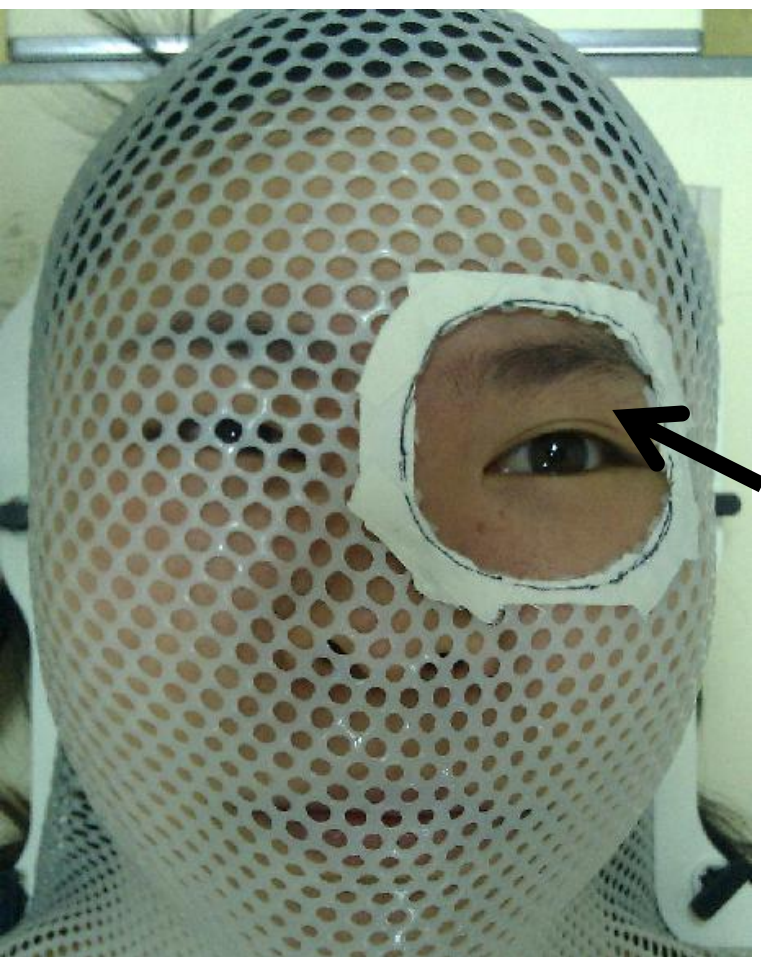


放疗实例 -原发结膜

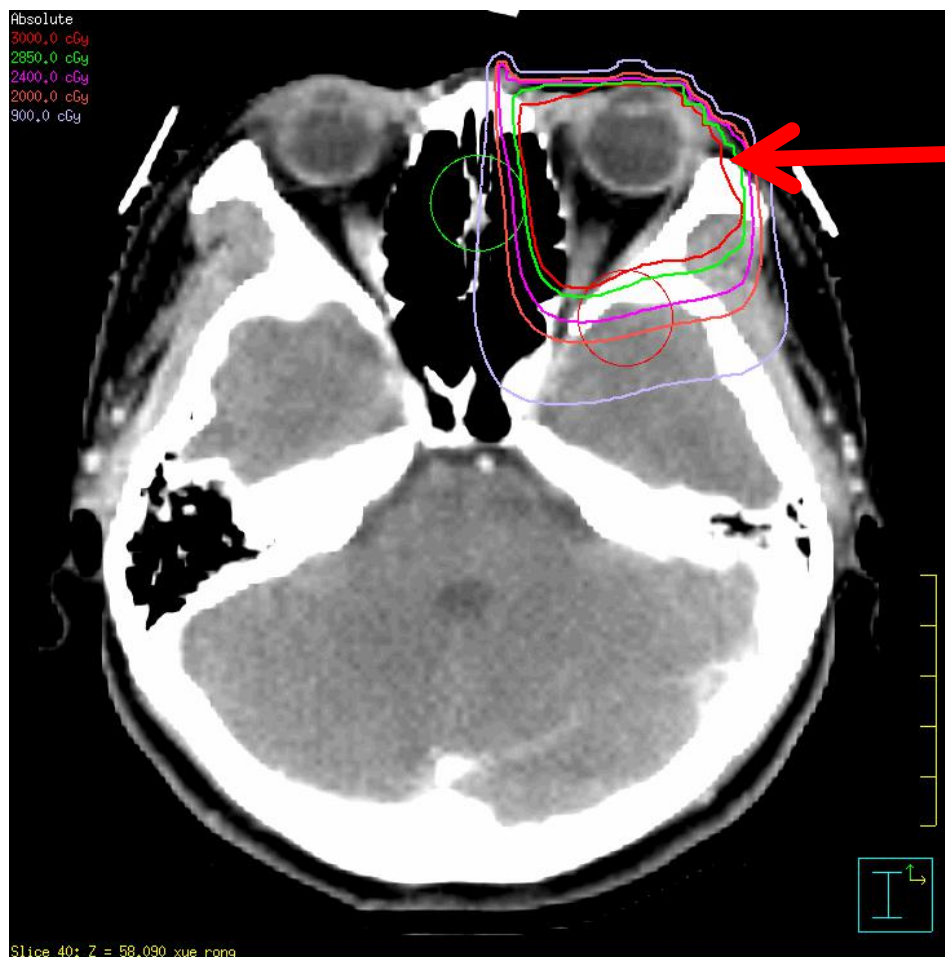


黑色实线：
放疗范围

特制电子
线铅块



放疗实例 -原发结膜



单前野电子线
30Gy处方
剂量线

眼眶MALT淋巴瘤的放疗



Study	No. of patients	Clinical stage	Median dose(Gy)	5-y LC (%)	5-y OS (%)
Le et al, 2002	31	IE	(mean, 34)	100	73
Uno et al., 2003	50	IE	36	98 (at 2-y)	91
Fung et al., 2003	39	IE	31.8	96	94
Ejima et al., 2006	42	IE	36	100	97
Monzen et al., 2006	14	IE	not available	100	NA
Nam et al., 2009	66	IE	30	95	96
Hata et al., 2011	30	IE-IIIE	30	100	100

LC=局部控制 OS=总生存率

晚期并发症



- ✓ 30%左右的患者出现白内障, 在保护角膜和晶体的情况下, 其发生率降低
- ✓ 发生白内障后行人工晶体植入后视力可以恢复

胃MALT淋巴瘤放疗适应症



- 抗HP无效的I期胃MALT淋巴瘤
- IIE期以上胃MALT淋巴瘤
- 有t(11;18)(q21;q21)易位
- 转化型胃MALT淋巴瘤

放疗方案

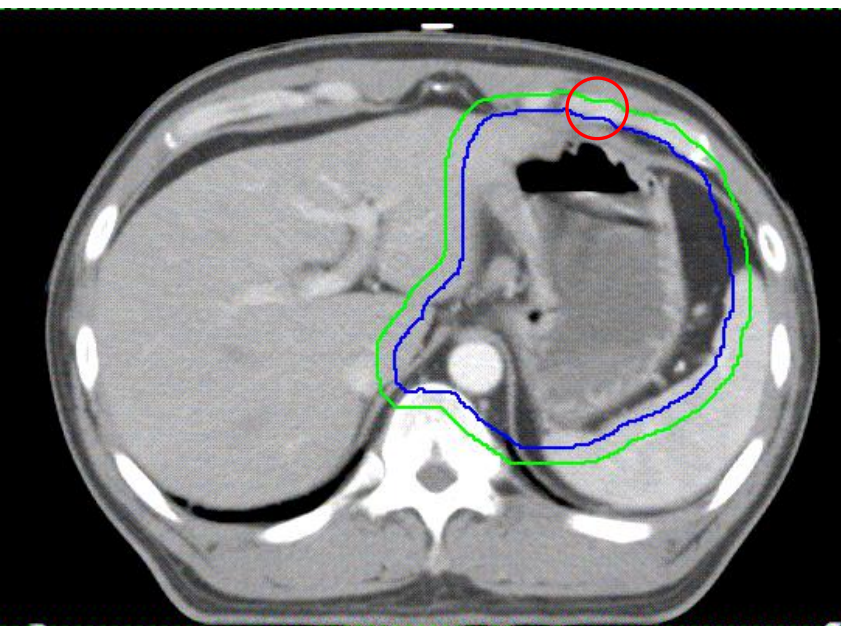


- 射野范围：胃和区域淋巴结
- 照射剂量：30Gy

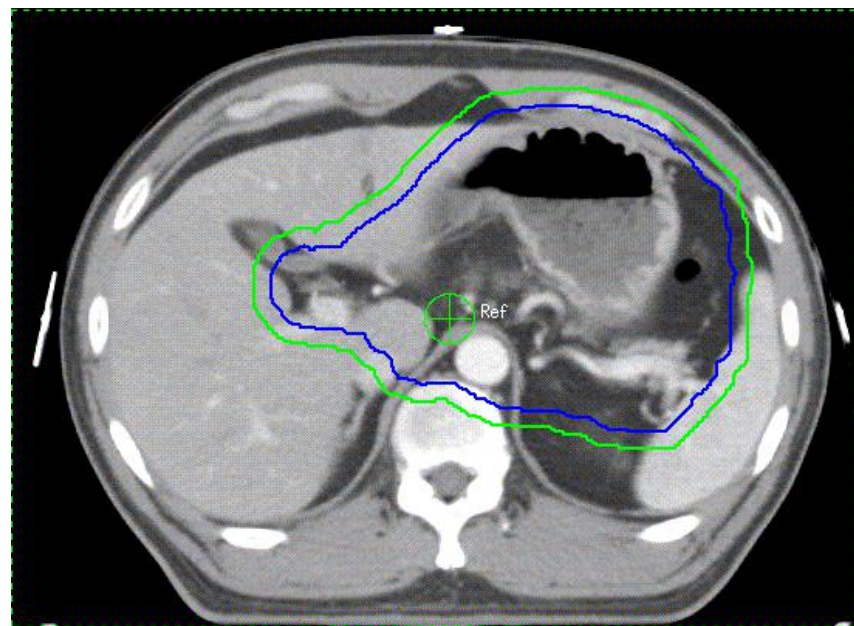
原发胃MALT淋巴瘤



- 射野范围：胃和区域淋巴结
- 照射剂量：30Gy



CTV=临床靶体积



PTV=计划靶体积

放疗实例



ID No. :

Name :

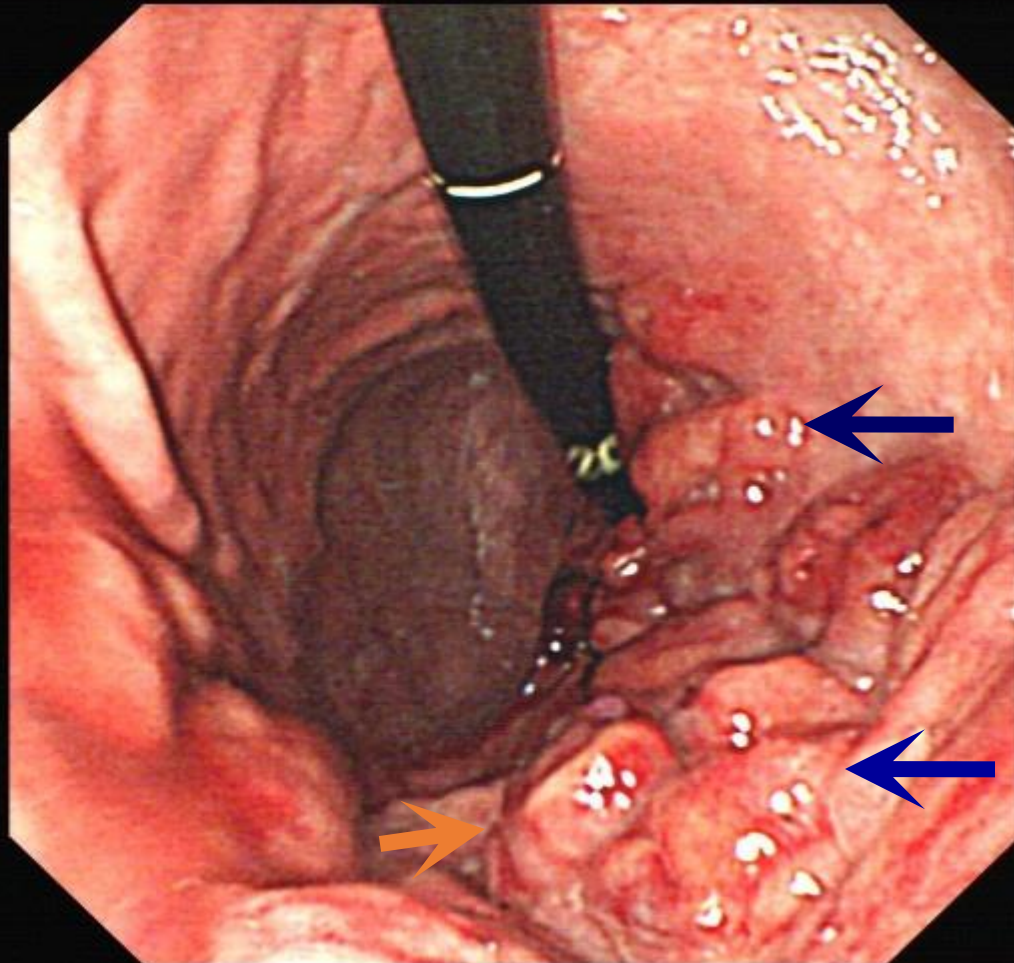
Sex : Age :

D.O.Birth :

24/04/2009

12:20:18

SCV-4



Comment :

放疗实例



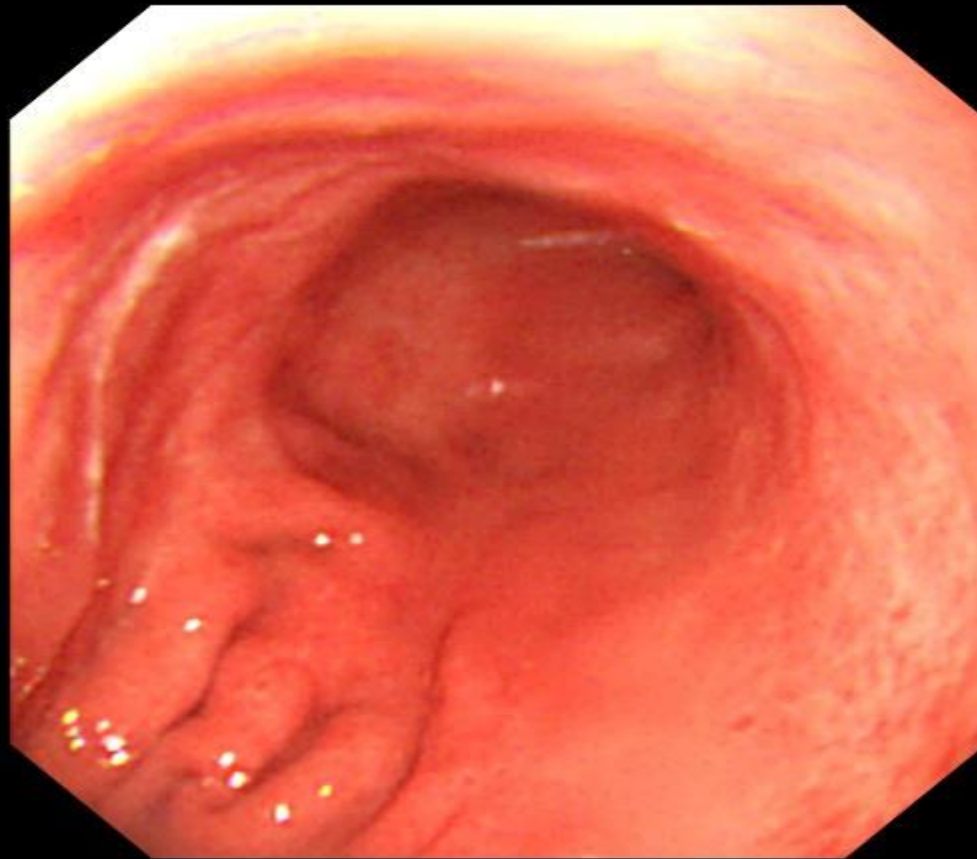
ID No. :
Name :

Sex : Age :
D.O.Birth :

17 02 2011
09:06:53

Ct: N E: A3
Ce: O

Physician :
Comment :



小结



- 照射野缩小：受累部位或淋巴结照射
- 照射剂量降低：
- 照射技术进步：3维适形或调强放疗
- 放疗是低度恶性淋巴瘤根治性治疗，侵袭性淋巴瘤综合治疗重要组成部分

早期疗效更好

毒性更小

Thank you for attention !



北京大学肿瘤医院

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Beijing Institute For Cancer Research