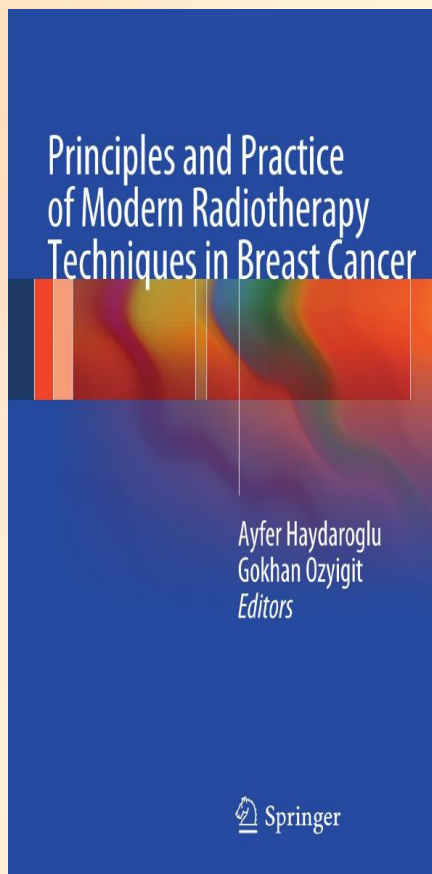




Erken Evre Meme Kanserinde Radyoterapi Gerekmeyen Hasta Var mıdır?

Dr. Gökhan Özyiğit
Hacettepe Üniversitesi, Tıp Fakültesi
Radyasyon Onkolojisi Anabilim Dalı



*Dedicated to the memory of Professor Ibtisam
Lale Atahan, M.D. (1945–2007)*

Chapter 18 **Forward Planning Intensity Modulated Radiation Therapy Techniques**

Ferah Yildiz, Gozde Yazici, Pervin Hurmuz, and Ali Dogan

Chapter 13 **Chest Wall and Regional Lymphatics**

Gokhan Ozyigit, Melis Gultekin, and Ferah Yildiz

Chapter 14 **Breast and Tumor Bed**

Aylin Fidan Korcum and Melek Nur Yavuz

2 Erken Evre Meme ca olgusu

- **GERÇEK**

- 41 yaş, premen.
- Sol MRM
 - 4 cm tümör
 - LVI(+)
 - Grad III
 - 3 LN(+)
 - ECE(+)
 - Triple (-)



Radyoterapi önermemek mümkün mü?

- **SANAL**

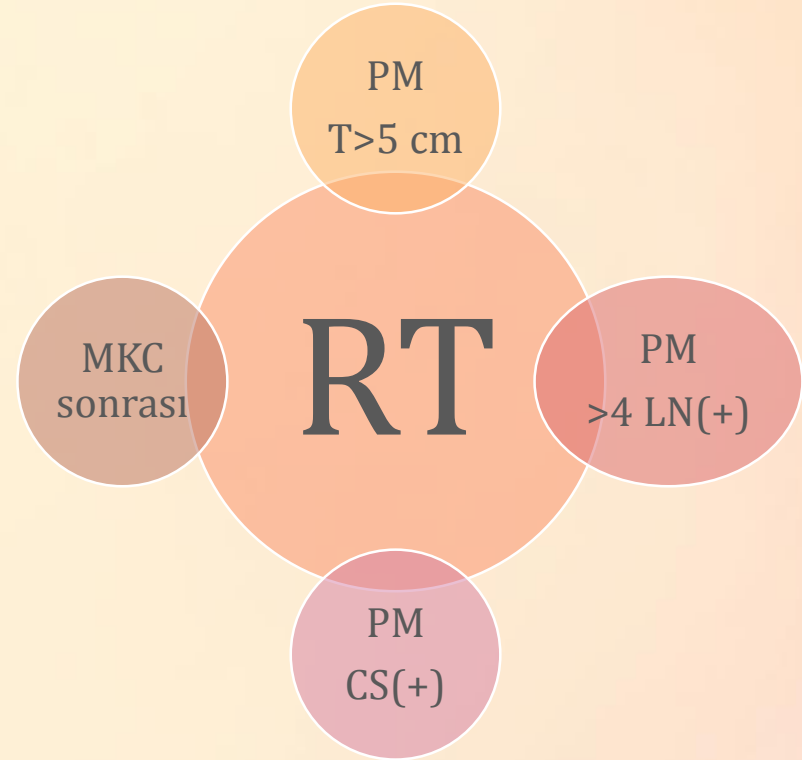
- 41 yaş, premen.
- Sol MRM ve rekonstrüksiyon
 - 1.8 cm tümör
 - Grad II
 - LVI (-)
 - 1 LN (+), odak 8 mm
 - ECE(-)
 - ER (+)/PR(+) %90
 - cerB2 (-)



Radyoterapi önerelim mi?

Erken Evre Meme Kanserinde Radyoterapinin Yeri

- Cerrahi
 - MKC
 - Mastektomi
- Aksilla LN durumu
- Tümör boyutu ve cerrahi sınır



EBCTCG Metaanalizi-Postmastektomi RT

- Bireysel veri analizi:
 - 1964-1989 arası randomize çalışmalar
 - 8135 meme ca
 - Ortalama 11 yıl izlem
 - 1-3 LN(+):1314 olgu
 - ≥ 4 LN(+): 1772 olgu
 - %54 Aksiller diseksiyon, %44 aksiller örnekleme
 - En sık CMF ve TMX

EBCTCG Metaanalizi: SONUÇ

- LN(-) (n=700 olgu)
 - RT gereksiz
- 1-3 LN (+)'de Postmastektomi RT
 - Relapsta %32 azalma
 - Meme kanseri mortalitesinde %20 azalma
 - 1 LN(+) ve 2-3 LN(+) olgularda benzer fayda.
 - KT ve HT'den bağımsız fayda.
- ≥ 4 LN (+)'de Postmastektomi RT
 - Relapsta %21 azalma
 - Meme kanseri mortalitesinde %13 azalma
 - 1 LN(+) ve 2-3 LN(+) olgularda benzer fayda.
 - KT ve HT'den bağımsız fayda.

EBCTCG Metaanalizi: SONUÇ

- 1-3 LN (+) varlığında Postmastektomi RT
 - 10. yılda 100 kadında **12** daha az relaps
 - 20. yılda 100 kadında **8** daha az ölüm
- ≥ 4 LN (+) varlığında Postmastektomi RT:
 - 10. yılda 100 kadında **9** daha az relaps
 - 20. yılda 100 kadında **9** daha az ölüm

EBCTCG Metaanalizi: TARTIŞMA

- Eski çalışmalar, eski RT tekniği
 - Yeni modern teknikler bu katkıyı daha arttırabilir mi?
- Eski kemoterapi rejimleri (CMF)
 - CA ve taksanlar/trastuzumab vb modern rejimler bu katkıyı gölgeleyebilir mi?

EBCTCG/2011, Metaanalizi-MKC Sonrası RT

EBCTCG, Lancet 2011

- IPD meta-analiz: **MKC vs MKC+RT**
- 17 faz III çalışma, 10801 hasta
- Ortanca izlem: 9.5 yıl

Effect of radiotherapy after breast-conserving surgery on
10-year recurrence and 15-year breast cancer death:
meta-analysis of individual patient data for 10 801 women
in 17 randomised trials



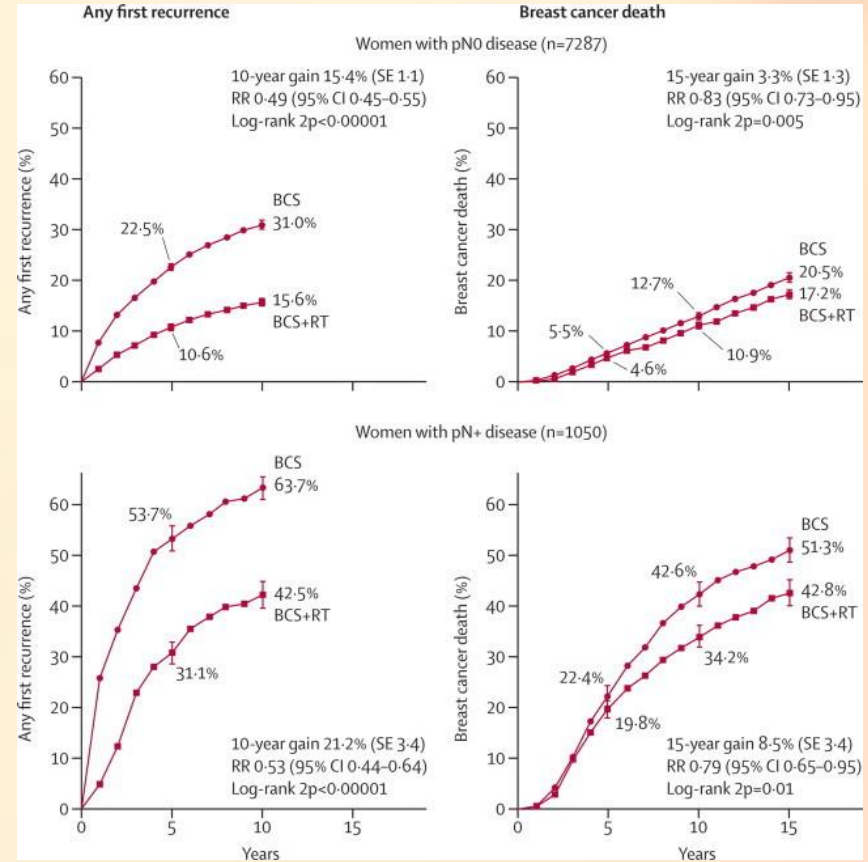
EBCTCG/2011, Metaanalizi-MKC Sonrası RT

- MKC sonrası RT ile:
 - Herhangi nüks: %35 → %19
 <0.00001
 - MK den ölüm: %25.3 → %21.4
 0.00005
 - Herhangi ölüm: %37.6 → %34.6
 0.03
- İlk relaps yeri:
 - RT (-): %25 lokal-bölgesel
 - RT (+): %8 lokal-bölgesel

EBCTCG, 2011

- pN0 7287 hasta

	<u>ilk nüks</u>	<u>MK ölüm</u>
RT(-)	%31	%20.5
RT(+)	%15.6	%17.2
p	<0.0001	0.005



*Yaş, grad, T, ER, risk grubundan
bağımsız etki*

EBCTCG, 2011

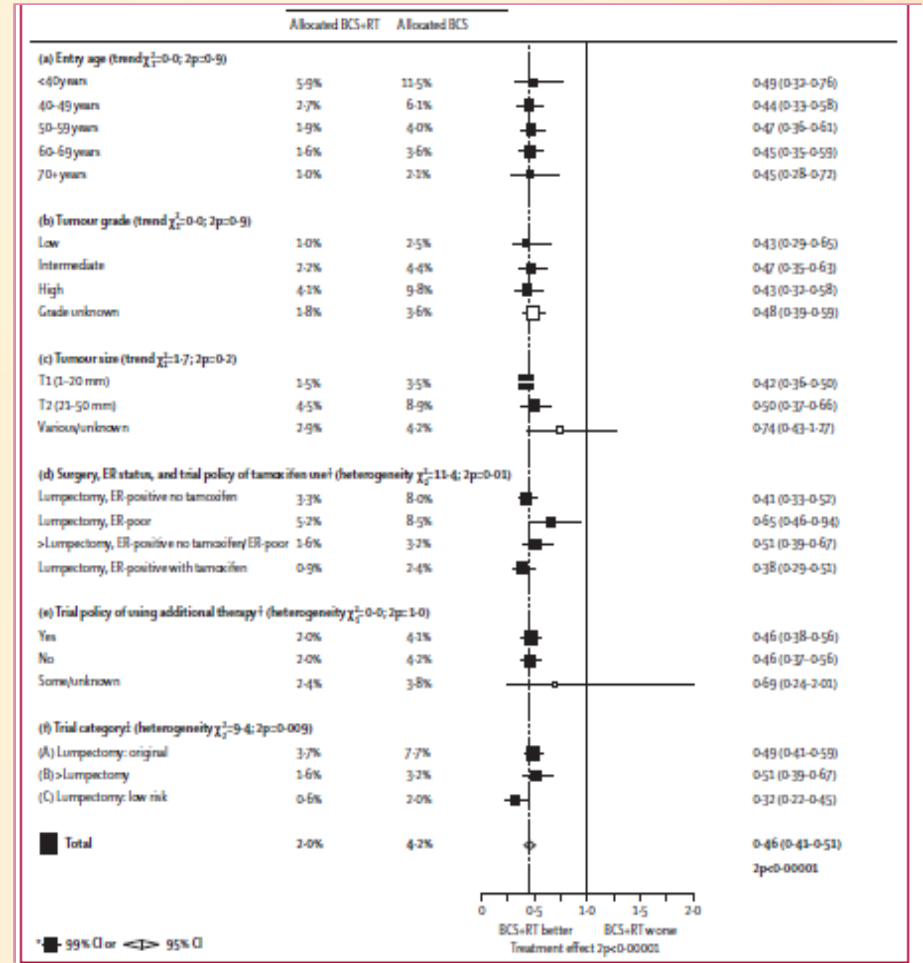
- pN0, düşük risk hasta

Herhangi nüks/yıl

MKC %2/yıl

MKC+TMI %0.6/yıl

$p < 0.00001$



EBCTCG, 2011

- *‘.....the overall findings from the trials show that RT after BCS not only substantially reduces the risk of recurrence **but also moderately reduces the risk of death from BC.** These results suggest that the killing microscobic tumor foci in the conserved breast with RT reduces the potential for both LR and DM. There appears to be little adverse effect on non BC mortality’*

EBCTCG 2011

- En düşük risk grubu
 - İleri yaş
 - HR (+)
 - T<2 cm
 - pN0
 - Düşük grad



Herhangi nüks riskini

%19.9 → %6.3

Net kazanç: %13.6

Sağkalım katkısı:

Net % 3.3

MKC sonrası RT'nin gereksiz olduğu bir grup var mı?

Çalışma

Hasta Seçim Kriterleri

CALGB 9343

≥ 70 y, T1N0M0, ER(+), cNo

PRIME
gr1-2

≥ 65 y, $T \leq 3$ cm, HR(+), pN0,

KANADA

≥ 50 y, T1-T2, cN0

BASO II

< 70 y, T1, pN0, grad 1

ABCCSG 8A
(+), pN0

postmen, $T < 3$ cm, gr 1-2, ER

Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

Kevin S. Hughes[†], Lauren A. Schnaper, Jennifer R. Bellon, Constance T. Cirrincione, Donald A. Berry, Beryl McCormick, Hyman B. Muss, Barbara L. Smith, Clifford A. Hudis, Eric P. Winer and William C. Wood

- 636 hasta, ≥ 70 y, T1N0M0, ER (+)
- Faz III: TMI+TMX vs TMX
- İzlem : 12.6 yıl
- 10y LRFS: %98 vs %90 $p < 0.001$
- 10y GS: fark yok
- Mastektomiye kadar geçen süre: fark yok

S2-01

The PRIME 2 trial: Wide local excision and adjuvant hormonal therapy ± postoperative whole breast irradiation in women ≥ 65 years with early breast cancer managed by breast conservation

Dr. Kunkler: Nothing to disclose.

Dr. Williams: Nothing to disclose.

Dr. Jack: Nothing to disclose.

Dr. Canney: Nothing to disclose.

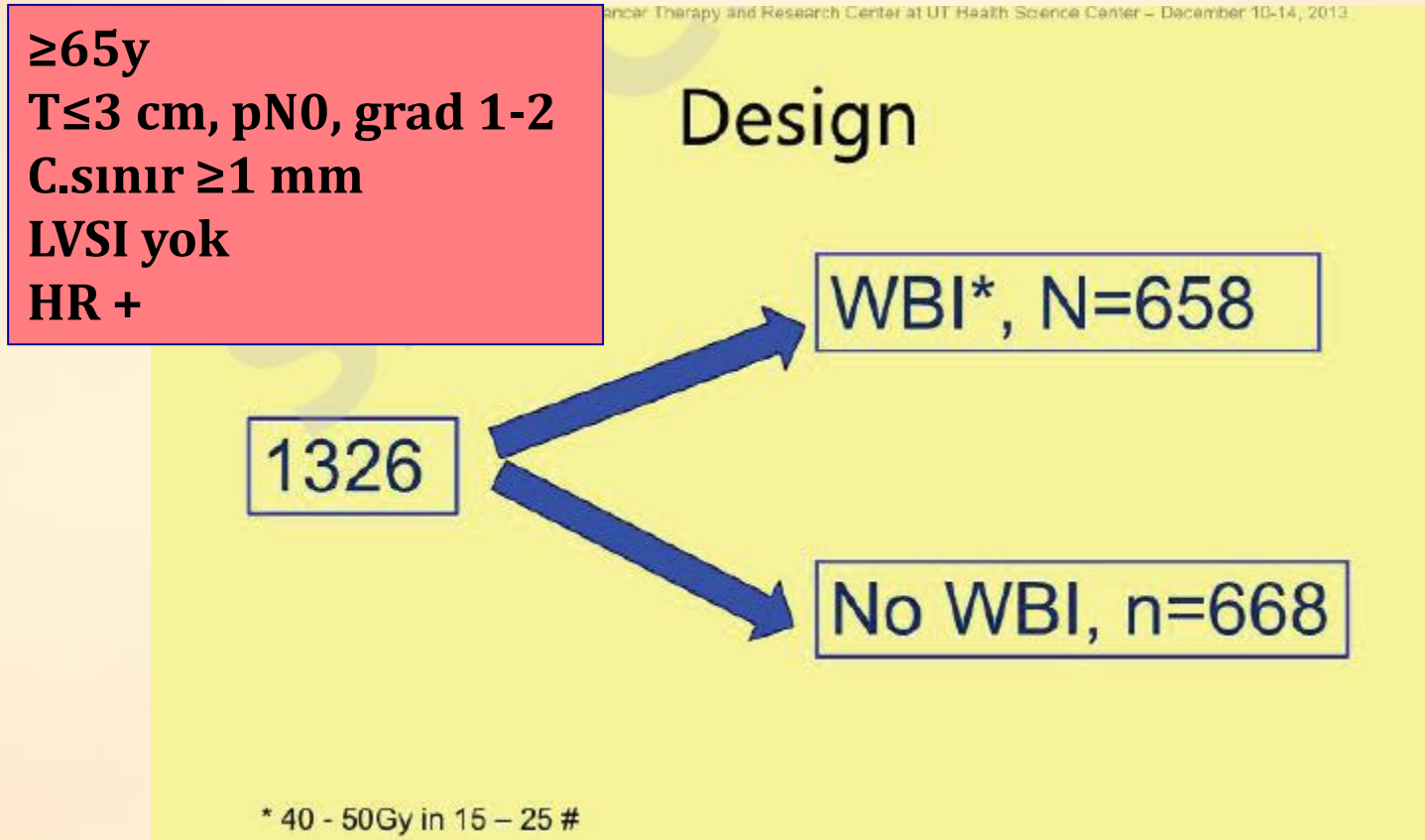
Dr. Prescott: Nothing to disclose.

Dr. Dixon: Nothing to disclose.

Post-operative Radiotherapy In
Minimum-risk Elderly – PRIME
II

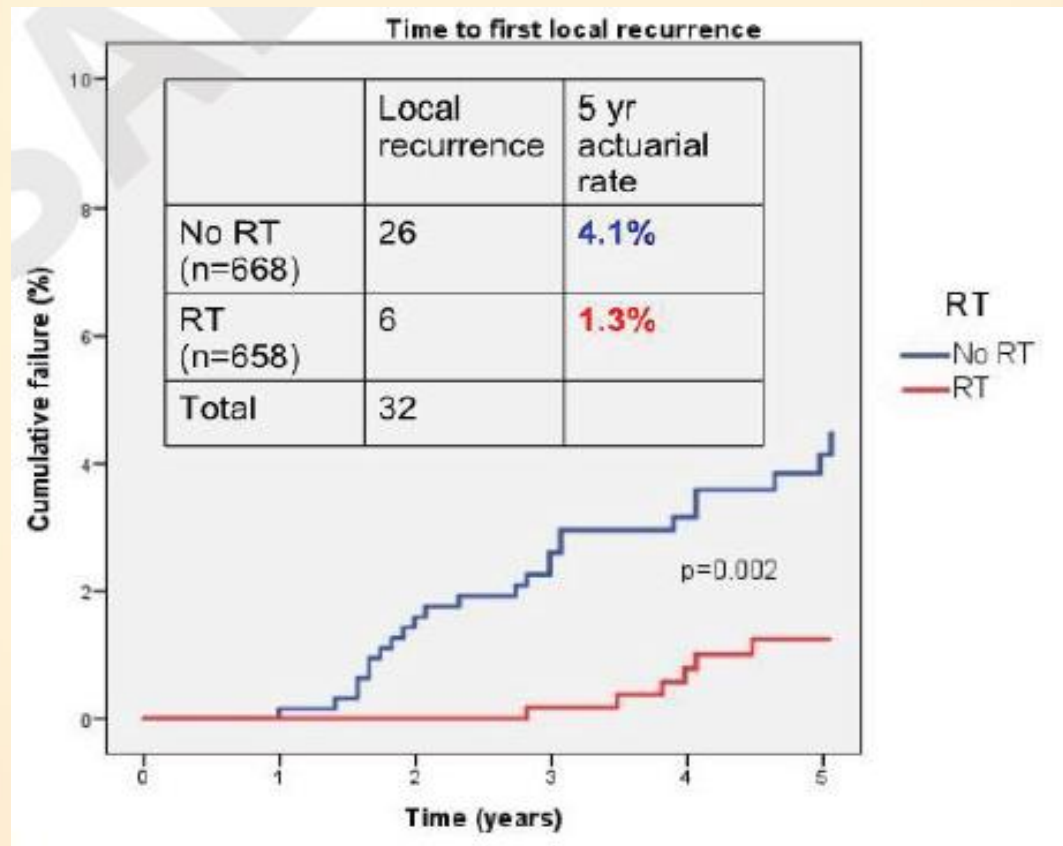


PRIME 2: 98 merkez, 6 ülke



Primer hedef: Lokal Kontrol

Lokal Kontrol



Çok değişkenli analiz

Variable	HR (95% CI)	p-value
T size (ref 0-10mm)	1	
10.1-20mm	0.53 (0.23, 1.22)	0.14
20.1-30mm	1.17 (0.43, 3.20)	0.76
Margins (ref >5mm)	1	
<1mm	1.99 (0.25, 16.04)	0.52
1-5mm	0.89 (0.40, 1.98)	0.78
Re-excision	1.05 (0.38, 2.89)	0.92
Radiotherapy (ref Yes)	1	
No	5.08 (1.95, 13.24)	0.001

Variable	HR (95% CI)	p-value
Age (ref 65-69)	1	
70+	2.08 (0.95, 4.55)	0.07
Grade (ref G1)	1	
G2	1.31 (0.59, 2.90)	0.51
G3	3.48 (0.89, 13.65)	0.07
LVI (ref No)	1	
Yes	1.28 (0.29, 5.59)	0.75
ER status (ref High)	1	
Low	2.84 (1.21, 6.65)	0.02

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 2, 2004

VOL. 351 NO. 10

Tamoxifen with or without Breast Irradiation in Women 50 Years of Age or Older with Early Breast Cancer

Anthony W. Fyles, M.D., David R. McCready, M.D., Lee A. Manchul, M.D., Maureen E. Trudeau, M.D.,
Patricia Merante, R.N., Melania Pintilie, M.Sc., Lorna M. Weir, M.D., and Ivo A. Olivetto, M.D.

- 769 hasta,
 - $\geq 50y$, T1-T2, N0
- MKC+TMX vs. MKC+TMX+TMI

Characteristic	Tamoxifen + Radiotherapy (N=386)	Tamoxifen (N=383)
<i>no. of women (%)</i>		
Age at diagnosis		
50-59 yr	98 (25.4)	85 (22.2)
60-69 yr	117 (30.3)	144 (37.6)
≥ 70 yr	171 (44.3)	154 (40.2)
Tumor size*		
≤ 1 cm	128 (33.2)	139 (36.3)
>1-2 cm	193 (50.0)	179 (46.7)
>2-5 cm	64 (16.6)	64 (16.7)
Hormone receptor status†		
Positive	313 (81.1)	308 (80.4)
Negative	25 (6.5)	21 (5.5)
Unknown	48 (12.4)	54 (14.1)
Pathological grade		
1	84 (21.8)	81 (21.1)
2	179 (46.4)	181 (47.3)
3	57 (14.8)	67 (17.5)
Unknown	66 (17.1)	54 (14.1)
Nodal assessment		
Pathological	320 (82.9)	316 (82.5)
Clinical	66 (17.1)	67 (17.5)

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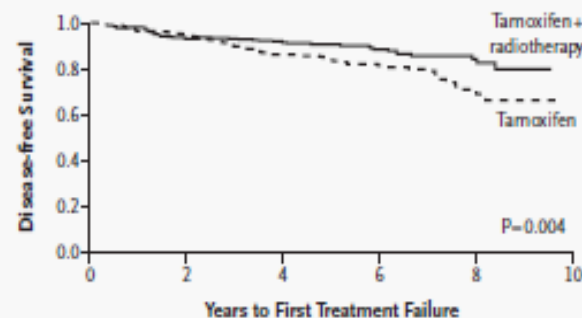
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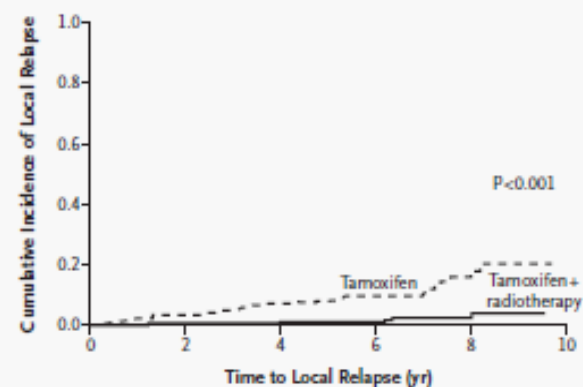
	TMX(%)	TMX+RT(%)
5y LRR	7.7	0.6
8y LRR	17.6	3.5

5y DFS 84 91



No. at Risk					
Tamoxifen+radiotherapy	386	354	282	157	51
Tamoxifen	383	344	264	138	33

Figure 2. Disease-free Survival.



No. at Risk						
Tamoxifen + radiotherapy	386	359	285	161	52	0
Tamoxifen	383	348	271	140	34	0



Radiotherapy or tamoxifen after conserving surgery for breast cancers of excellent prognosis: British Association of Surgical Oncology (BASO) II trial [☆]

R.W. Blamey^{a,j}, T. Bates^b  , U. Chetty^{c,j}, S.W. Duffy^{d,j}, I.O. Ellis^{a,j}, D. George^{a,j}, E. Mallon^{e,j}, M.J. Mitchell^{a,j}, I. Monypenny^{a,j}, D.A.L. Morgan^{a,j}, R.D. Macmillan^{a,j}, J. Patnick^{a,j}, S.E. Pinder^{f,j}

- <70y, T1, pN0, grad 1
- 1135 hasta: TMX vs TMX+RT vs RT vs İzlem
- İzlem: 167 ay
- Yıllık LRR
 - MKC %1.9
 - MKC+RT: %0.7
 - MKC+TMX %0.8
 - MKC+TMX+RT %0

CLINICAL INVESTIGATION

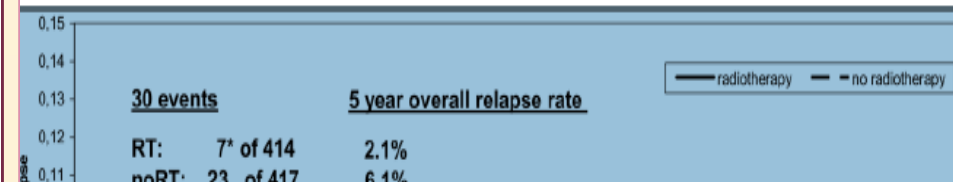
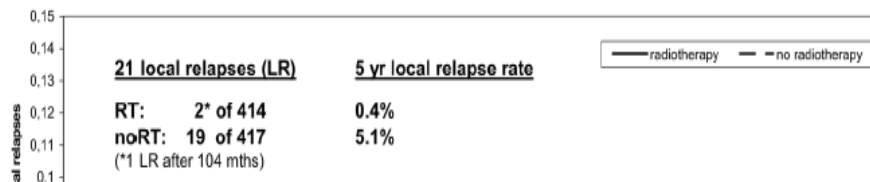
Breast

**LUMPECTOMY PLUS TAMOXIFEN OR ANASTROZOLE WITH OR
WITHOUT WHOLE BREAST IRRADIATION IN WOMEN WITH FAVORABLE
EARLY BREAST CANCER**

RICHARD PÖTTER, M.D.,* MICHAEL GNANT, M.D.,* WERNER KWASNY, M.D.,[†]
CHRISTOPH TAUSCH, M.D.,[‡] LEONORE HANDL-ZELLER, M.D.,* BRIGITTE PAKISCH, M.D.,[†]
SUSANNE TAUCHER, M.D.,* JOSEF HAMMER, M.D.,[‡] GERO LUSCHIN-EBENGREUTH, M.D.,[§]
MARIANNE SCHMID, M.D.,[§] FELIX SEDLMAYER, M.D.,** MICHAEL STIERER, M.D.,^{||}
GEORG REINER, M.D.,[¶] KARIN KAPP, M.D.,[§] FRIEDRICH HOFBAUER, M.D.,[#]
ANDREA ROTTENFUSSER, M.D.,* SABINE PÖSTLBERGER, M.D.,[‡] KARIN HAIDER, M.D.,[†]
WOLFGANG DRAXLER, M.Sc.,^{††} AND RAIMUND JAKESZ, M.D.,* ON BEHALF OF THE AUSTRIAN BREAST
AND COLORECTAL CANCER STUDY GROUP

- 831 hasta, postmenapozal, pN0,gr 1-2, ER (+)
- %70 hasta >60y, en genç: 46y
- MKC sonrası 2yT→A vs HT+RT

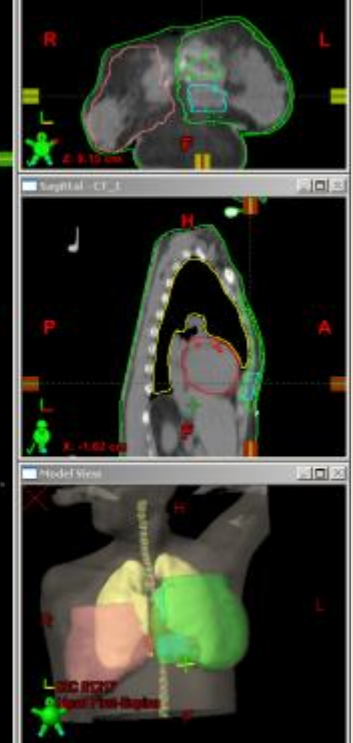
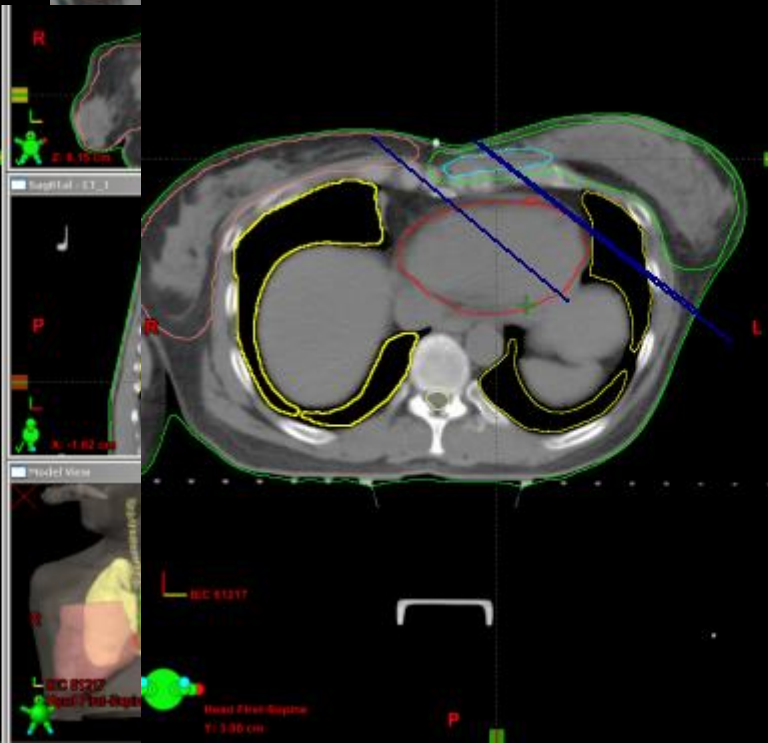
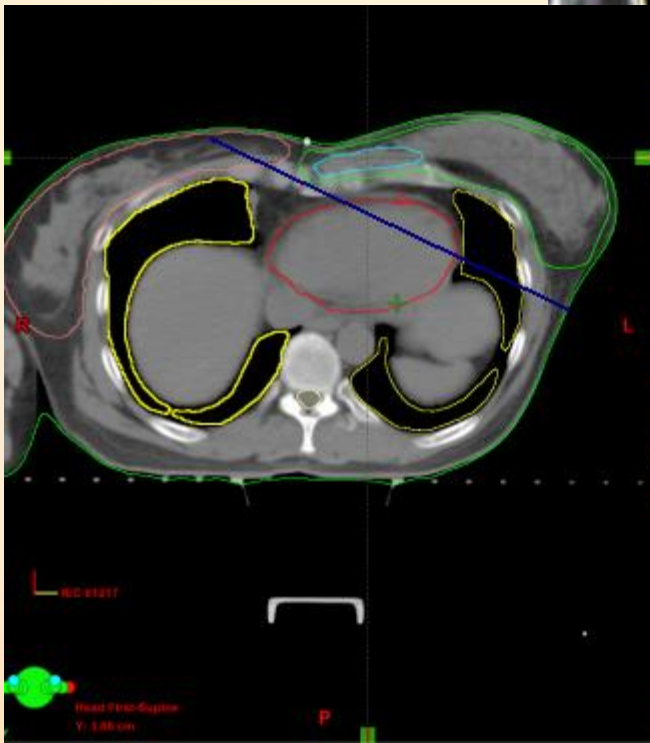
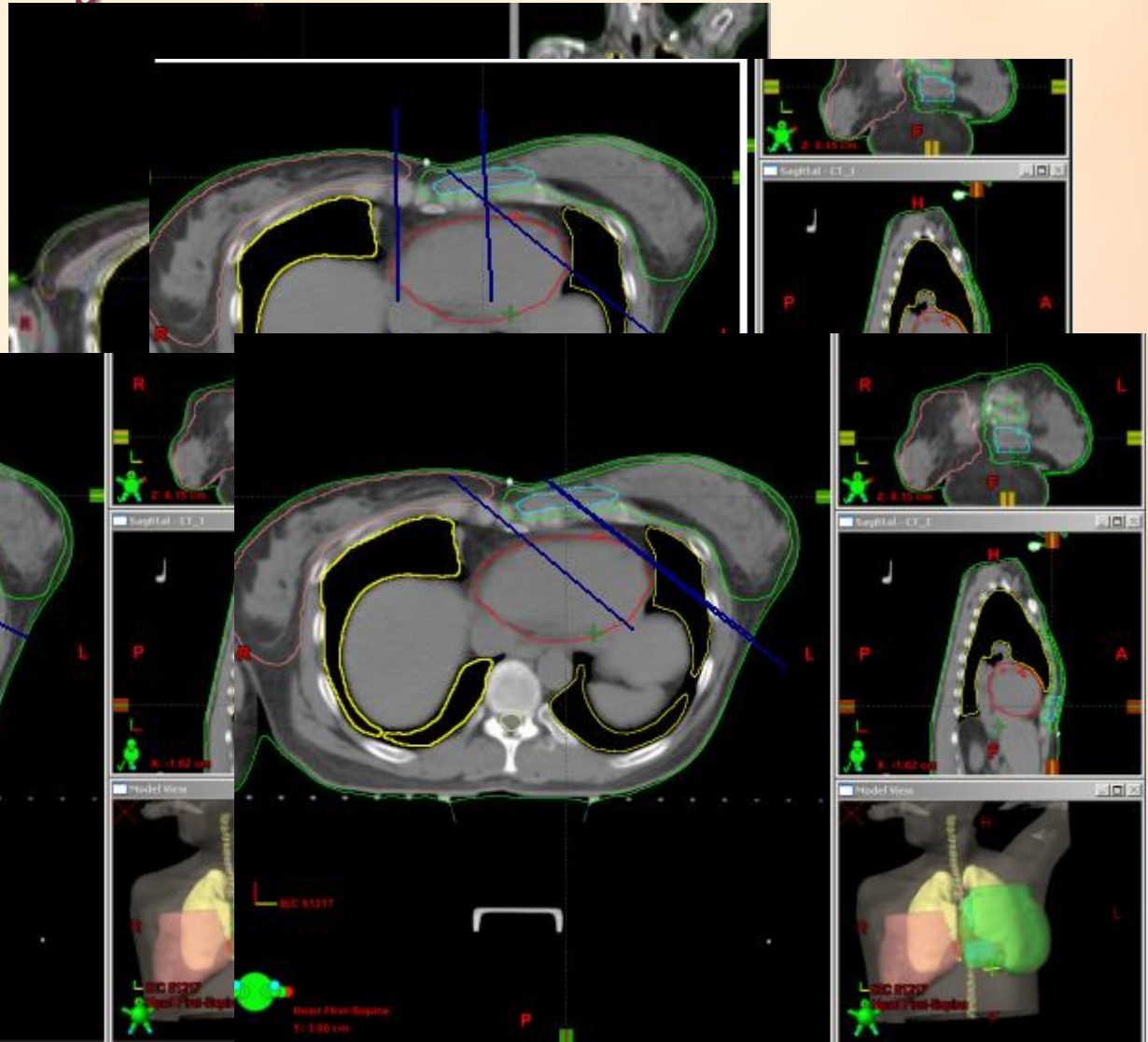
ABCCSG, Poetter ve ark 2007

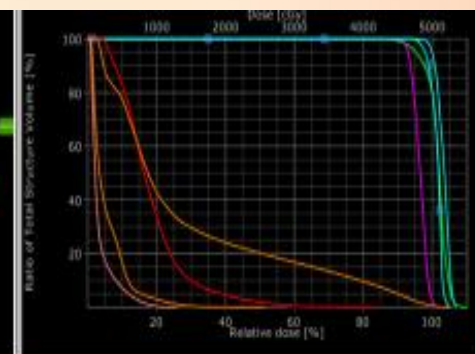
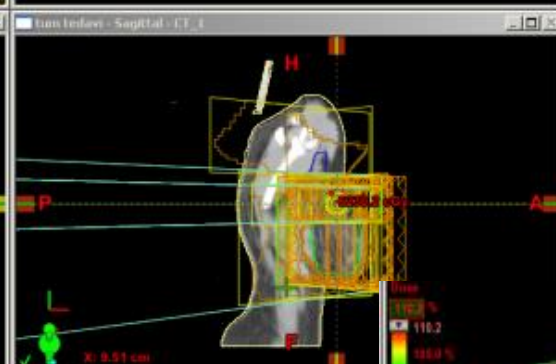
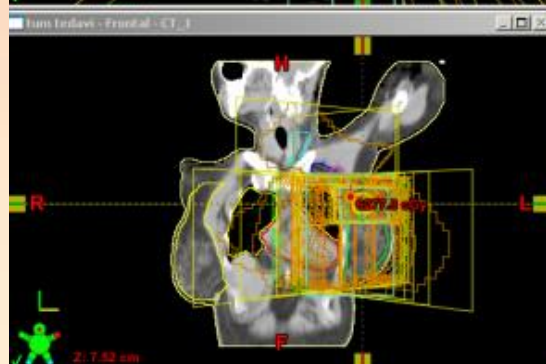
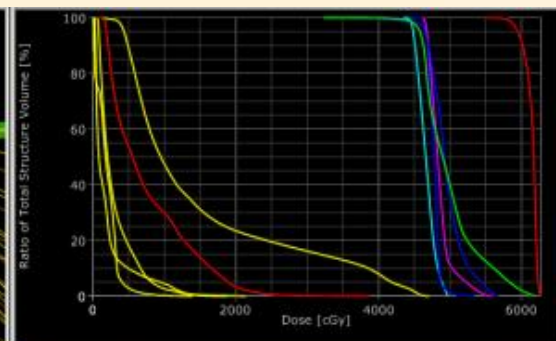
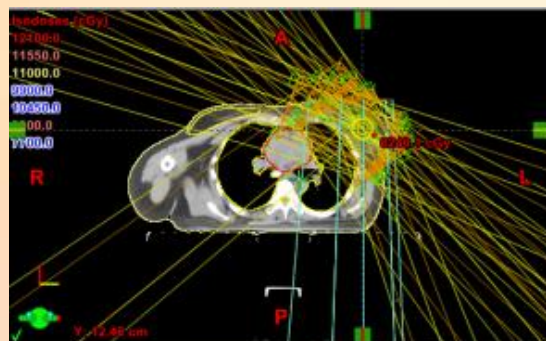


In conclusion, for patients with favorable early breast cancer as addressed in this randomized trial, further evidence is provided to indicate that whole-breast radiotherapy remains the major integral part of adjuvant treatment in breast-conserving treatment, even if tamoxifen is replaced partly by aromatase inhibitors. It is a matter of future research, to investigate

İzlem: 53.8 ay

Neden kardiyovasküler ölüm?





IMPORT LOW Çalışması: MKC Sonrası sadece yatak IMRT

- Kriterler:
 - >50 yaş
 - Herhangi bir grad
 - ≤ 3 cm
 - LN+/-
- Çalışma Grubunun %90'ı:
 - Ortalama 60 yaş
 - Grad 1/2 tümör
 - LN(-)
 - <2 cm



IMPORT LOW Çalışması



SONUÇ: Ortanca 71 ay izlemde tüm kollar benzer. 5-y lokal relaps ~%1, 10. yılda tahmin ~%2

ÖZET

- Mastektomi sonrası:
 - <5 cm ve LN(-), RT gerek yok.
 - 1-3 LN (+), RT önerilir.
- MKC sonrası:
 - Mutlak kontraendikasyonlar dışında –ki bunlara MKC önerilmemekte- RT önerilir.
 - Ancak PMI seçilmiş ileri yaş düşük riskli olgularda önerilebilir.

Önemli bir bilgilendirme...

- Ülkemizde gerek kamuda gerekse özelde merkezlerde modern radyoterapi tekniklerini uygulama kabiliyetinde cihazlar vardır.
- Bu bağlamda cihazların yeni olması iyi bir (meme) radyoterapi uygulayacağının garantisini vermez.
- Çünkü cihazlar sadece radyasyon onkolojisi ekibinin planladığı RT'yi uygular.
- 'Onların cihazları eski yakar.' söylemi doğru değildir.
- Radyoterapi cihazları arıza yapar. Hatta en yeni cihaz bile arıza yapar.
- En önemli husus eğitimli ve tecrübeli RT ekibidir.





Teşekkür ederim...