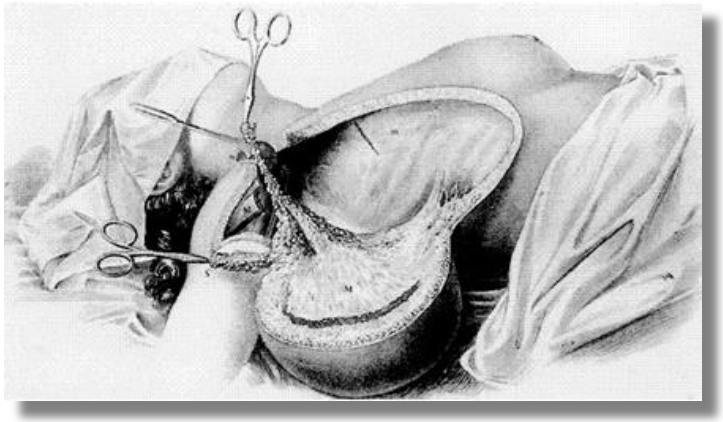
Irradiation partielle du sein - POUR

Jean-Philippe Pignol
Erasmus MC – Cancer Institute

Historical perspective

1907



‘Halsted’ radical mastectomy

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Historical perspective

1907 1971

Fisher, NSABP-B04
Modified Radical Mastectomy

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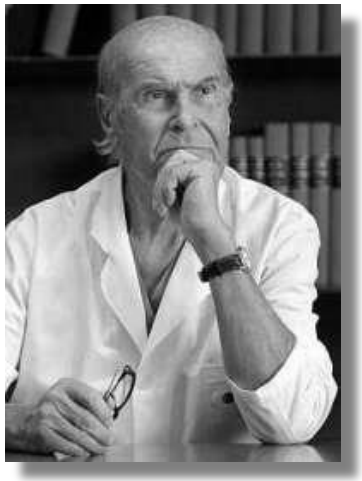
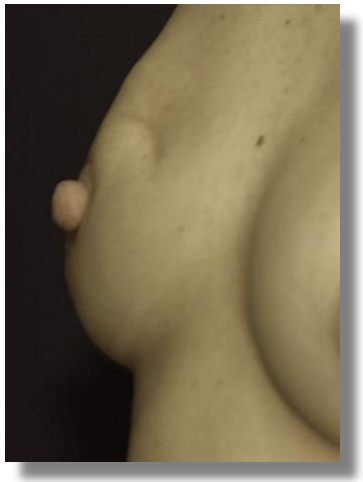
Historical perspective





Breast conserving therapy
Veronesi, Milan I/II
Fisher, NSABP-B06

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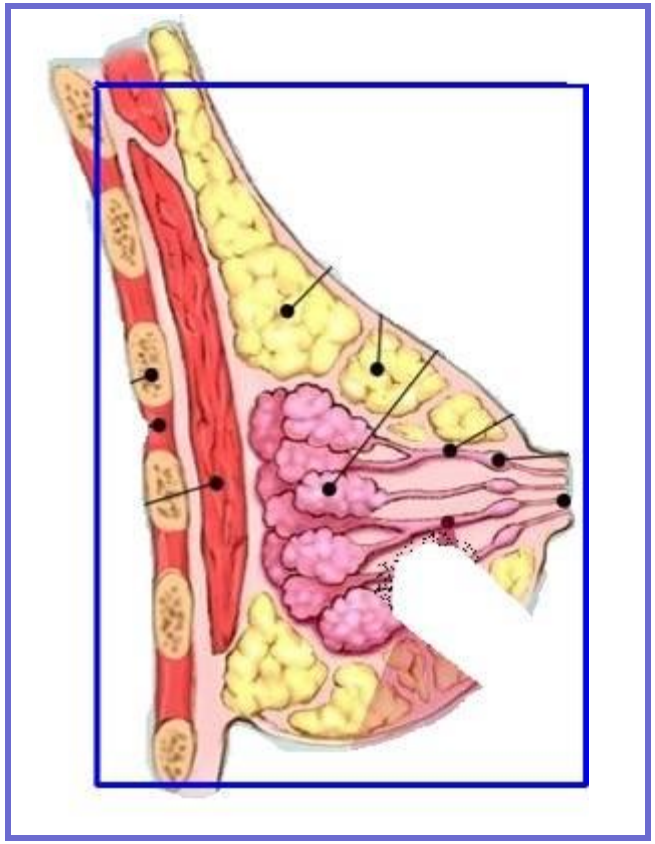
Standard treatment

- Surgery
- Radiotherapy
- Chemotherapy or Hormone

] BCS



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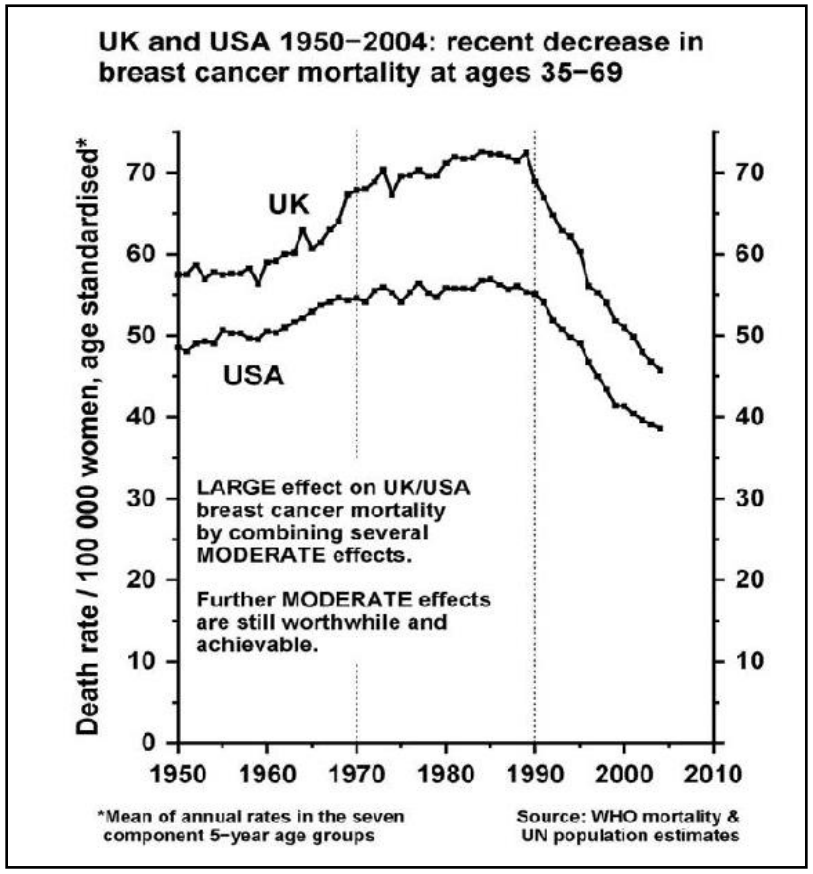
Mammography = earlier stages



Stage at Diagnosis	Frequency	5-year Relative Survival
Localized (confined to primary site)	60%	98.6%
Regional (spread to regional lymph nodes)	33%	83.6%
Distant (cancer has metastasized)	5%	23.4%
Unknown (unstaged)	2%	57.9%

SEER, 2010
www.seer.cancer.gov/statfacts/html/breast.html

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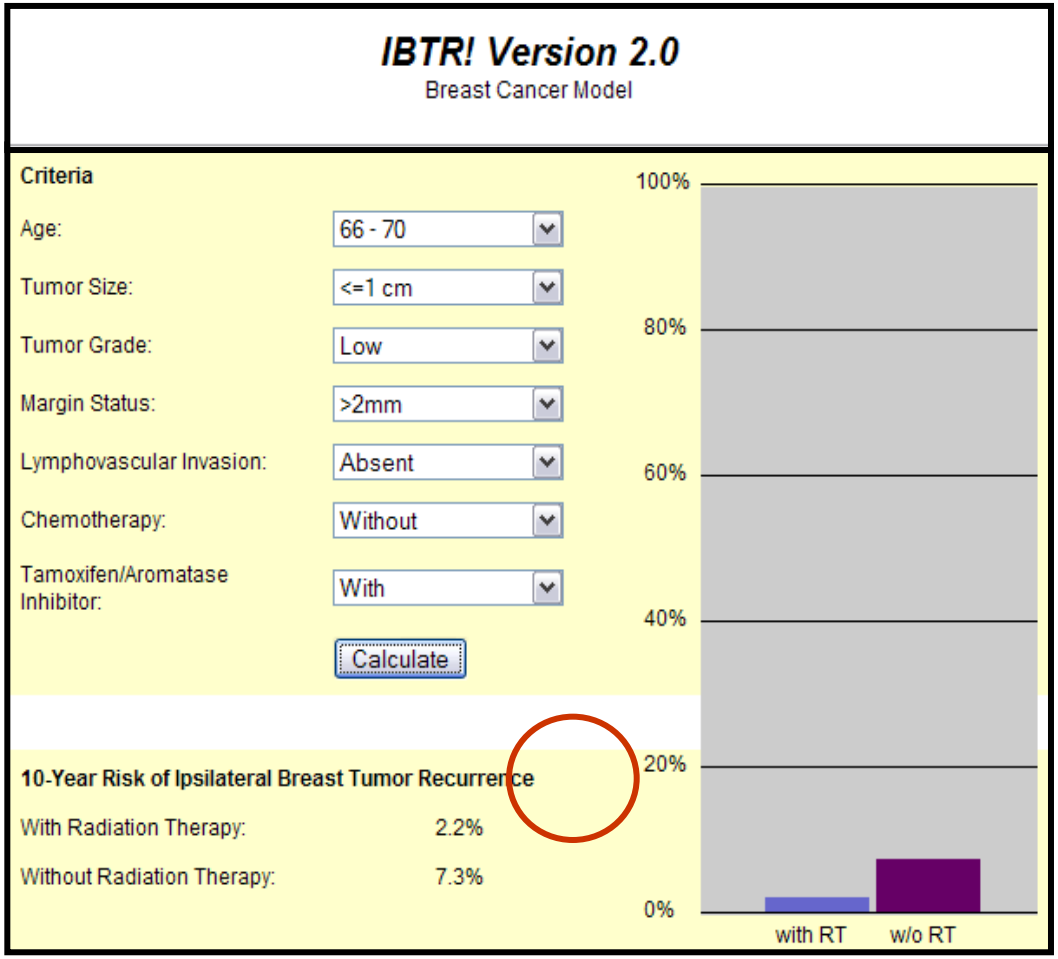
Could we de-escalate further?



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Breast Radiotherapy

- 3.5 to 6.5 weeks of XRT
- Acute and delayed skin toxicities

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Could we omit XRT ?

- Liljegren (JCO 1999)
  - Lumpectomy versus lumpectomy + XRT
  - 381 women with To mammography detected
  - At 5 years 2.3% ~ 18.4%
- Fyles (NEJM 2004)
  - 769 women Surgery + TAM ± XRT
  - LRR 7.7% versus 0.6% at 5 years
    17.6% versus 3.5% at 8 years
- Hughes (NEMJ 2004)
  - 636 women > 70 years stage I
  - Surgery + TAM ± XRT
  - LRR 4% versus 1% at 5 years

Chia (British Columbia)
San Antonio 2009:
Less than 40% TAM observance

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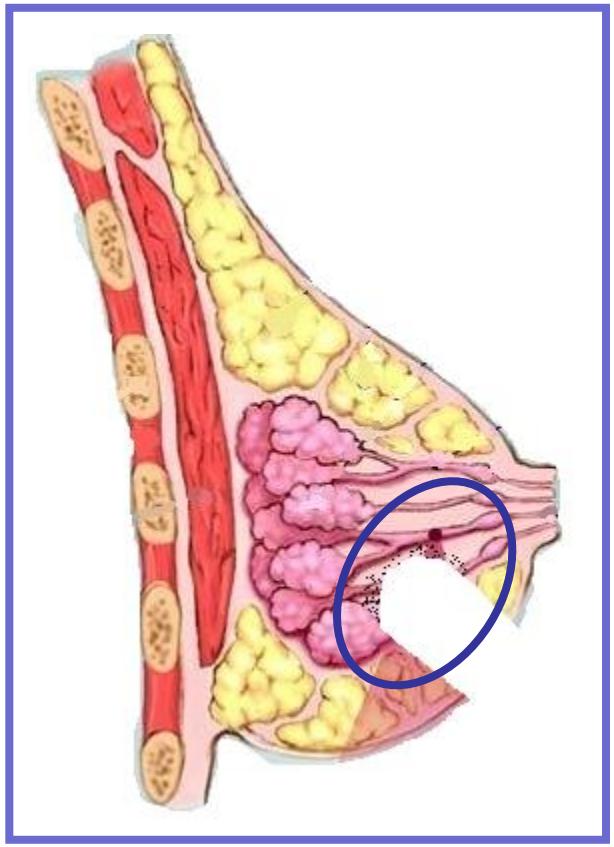
NSABP-B06

- Three forms of recurrences
  - Around surgical cavity 86%
  - Pseudo inflammatory 14%
  - Skin or scar 0.5%
- Factors: LVI+, grade and >2cm

Fisher ER *Cancer* **57**:1717-1754, 1986



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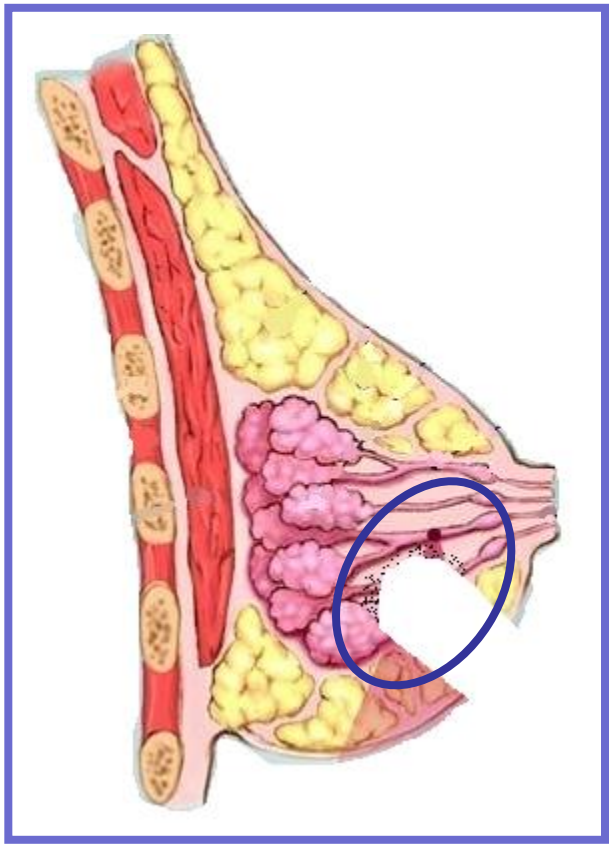
Accelerated Partial Breast Irradiation

- Permanent side effects are related to volume and dose per fraction
- Smaller volume
  = higher dose per fraction
  = treatment acceleration



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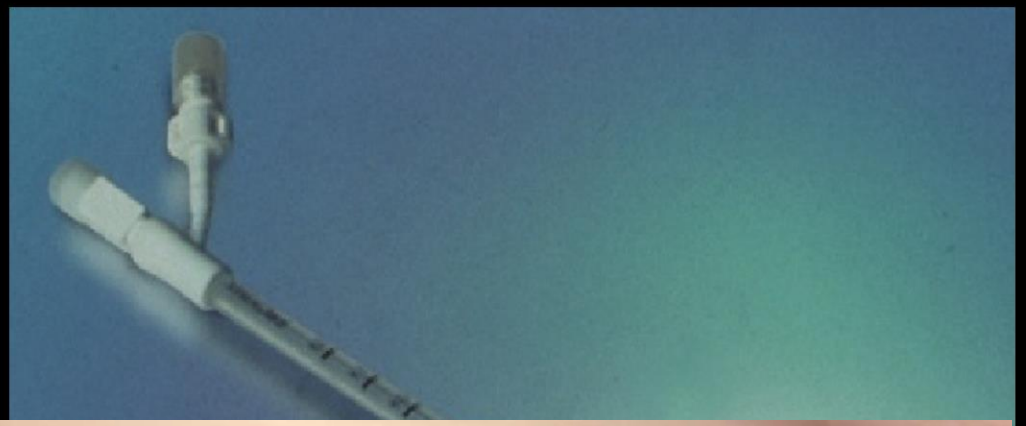
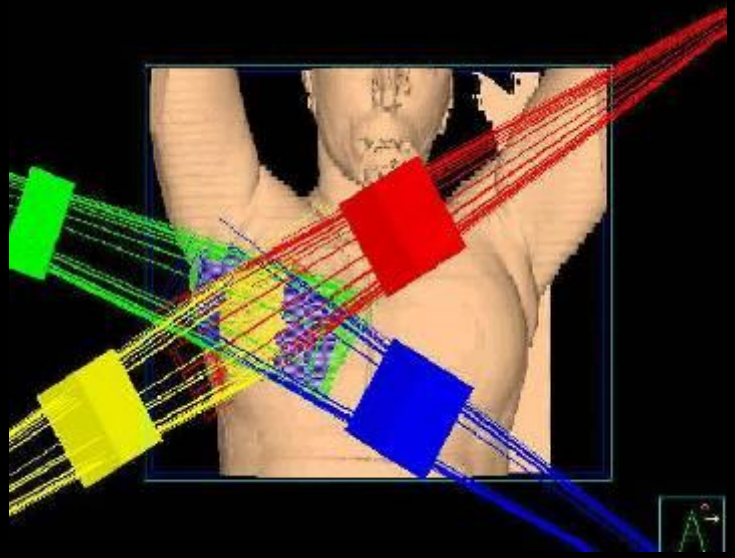
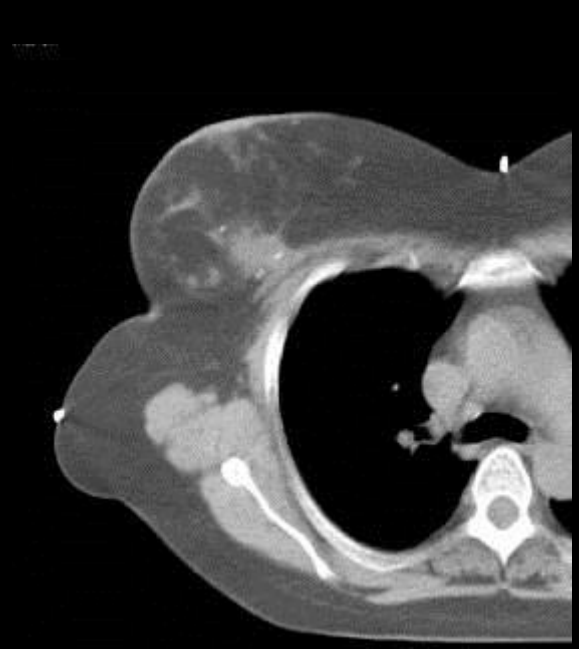
HDR brachytherapy

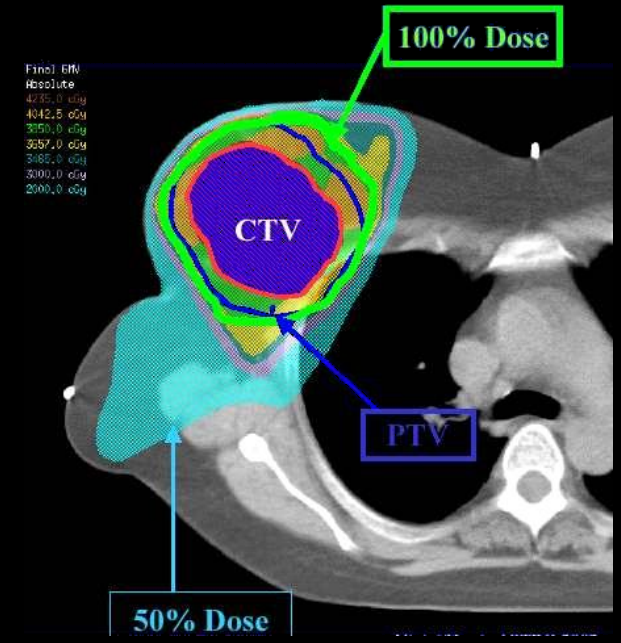
Mammosite™



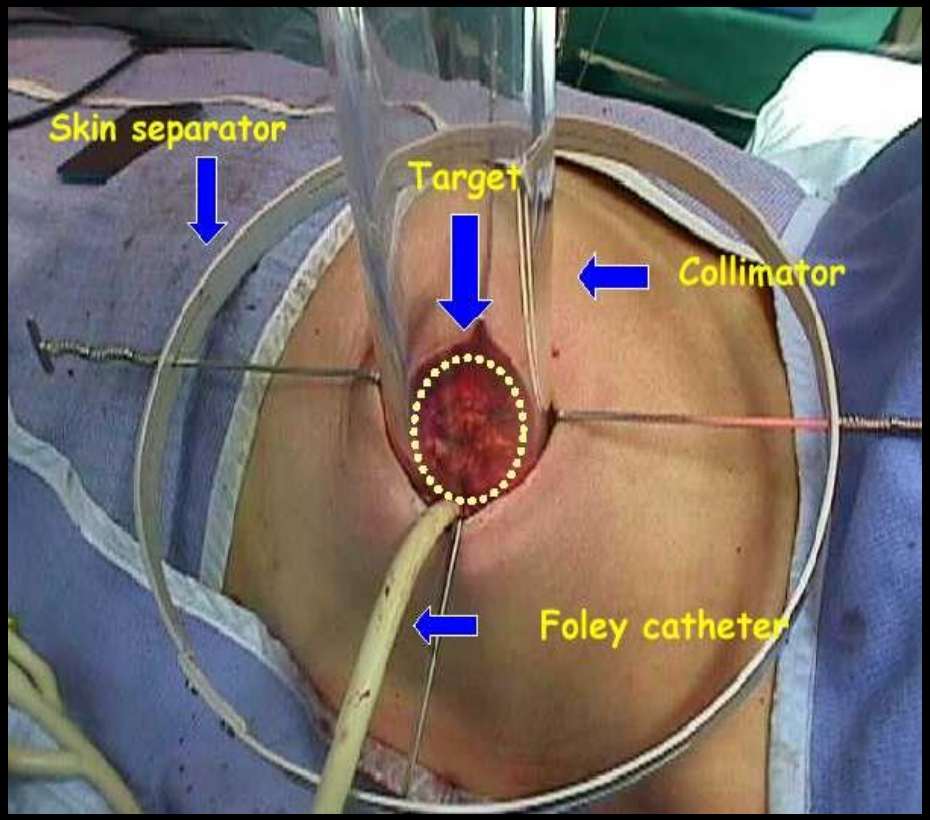


3D-CRT/IMRT
partial breast irradiation

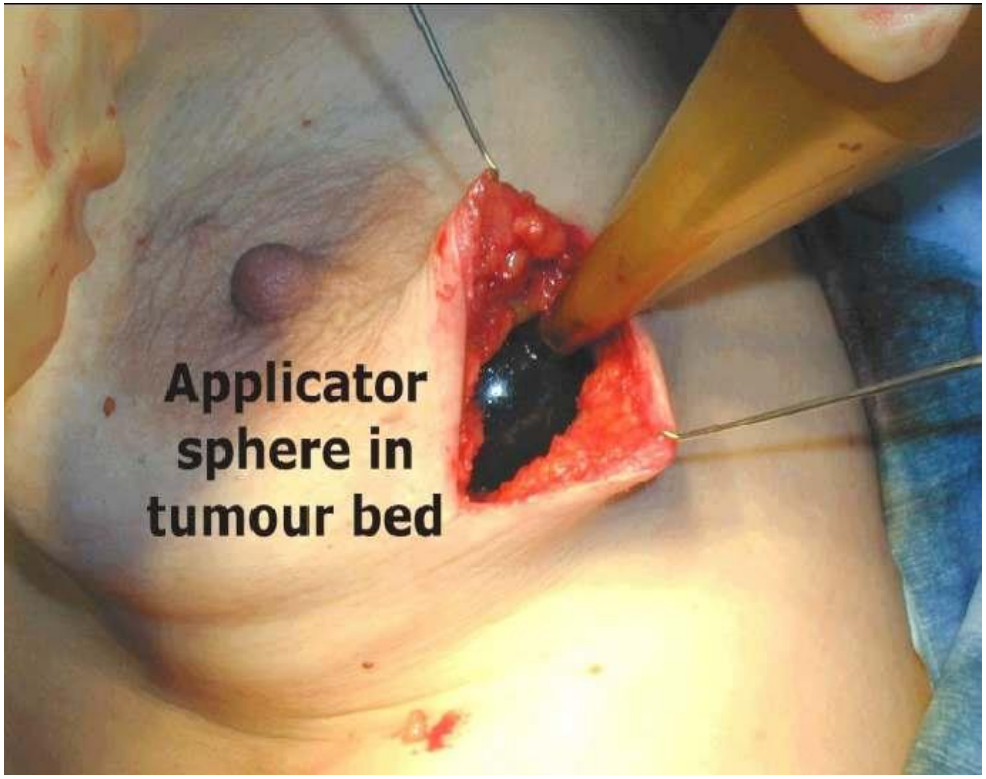




European Institute of Oncology, Véronesi
IEO trial



TARGIT-A Phase III trial



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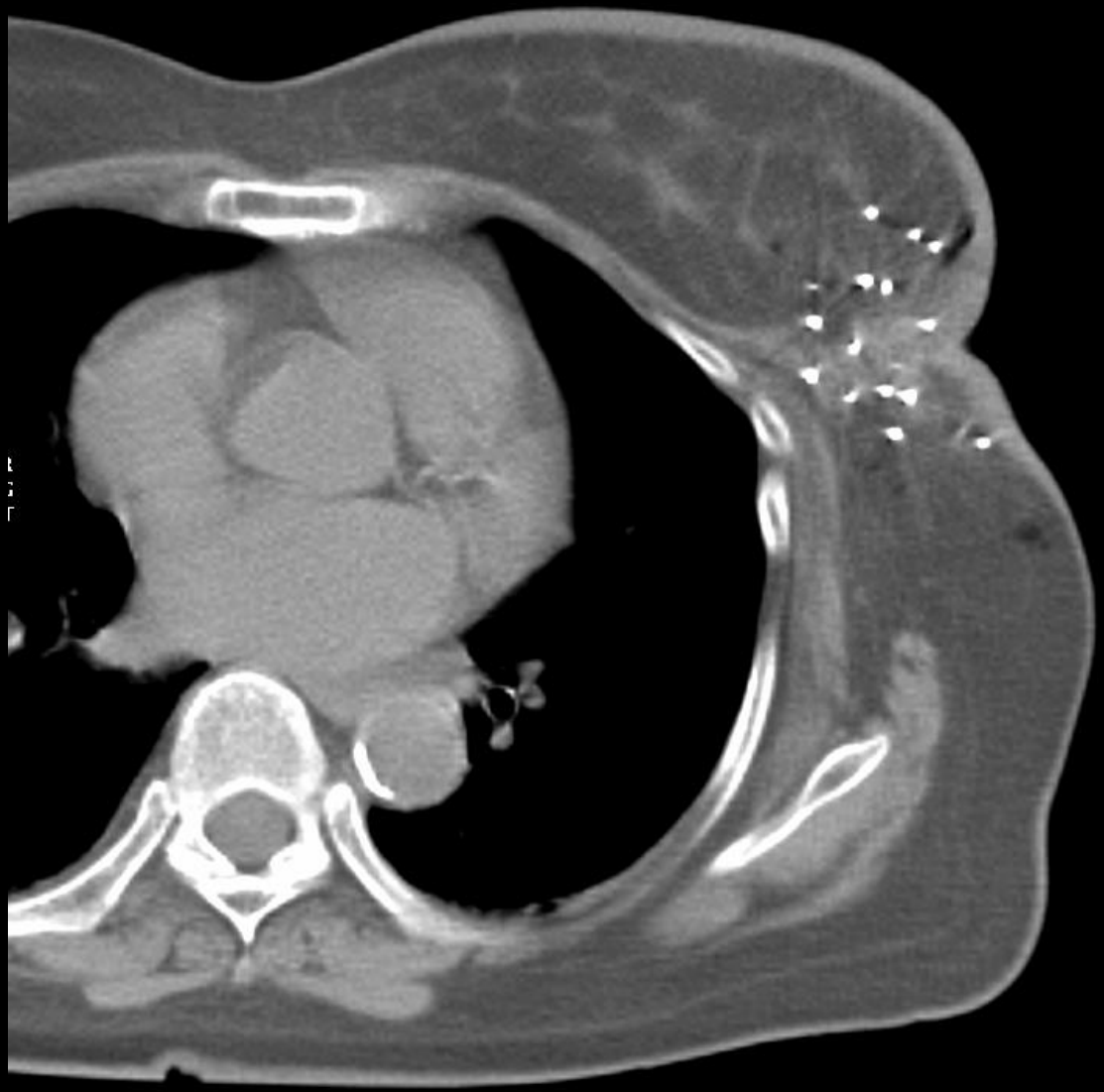
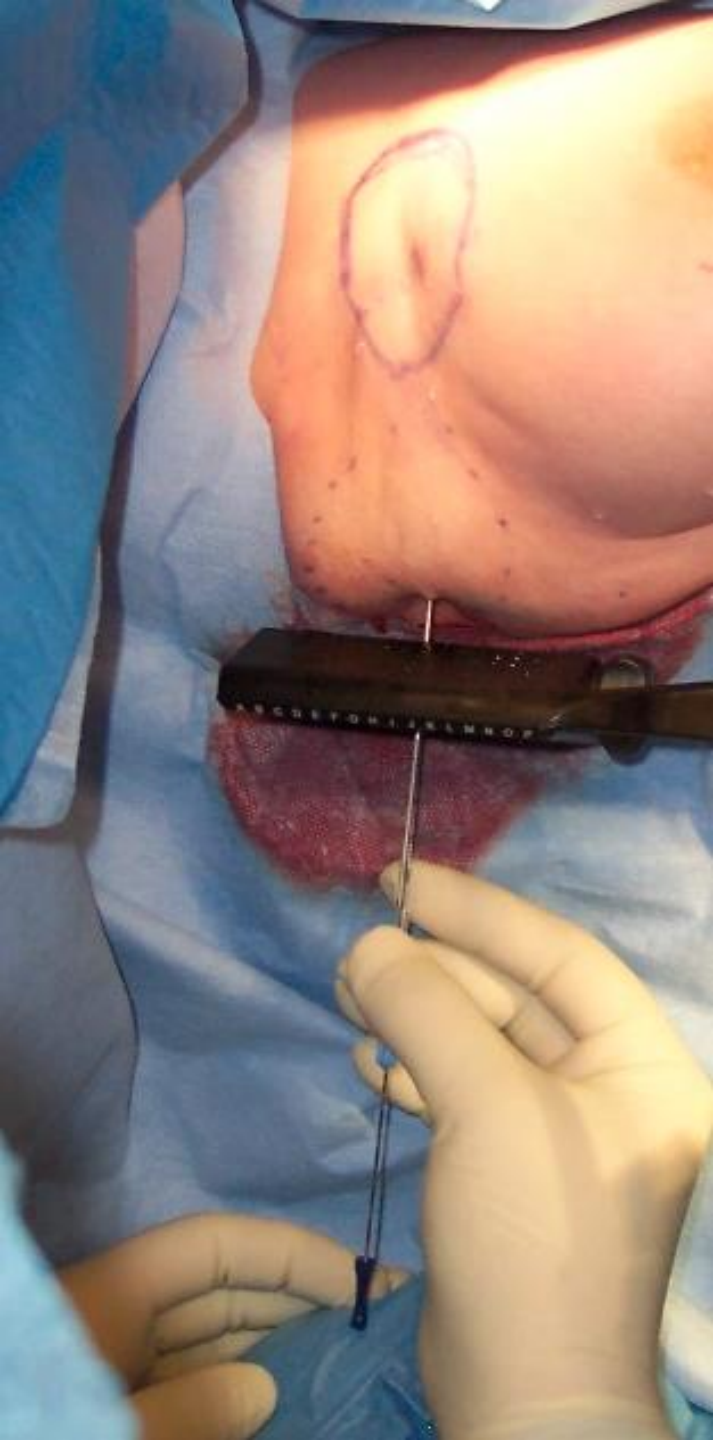
Permanent Breast Seed Implant

Permanent Breast Seed Implant





Results and controversies

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ARTICLES

Limited-Field Radiation Therapy in the Management of Early-Stage Breast Cancer

Frank A. Vicini, Larry Kestin, Peter Chen, Pamela Benitez, Neal S. Goldstein, Alvaro Martinez

On matched-pair analysis, the rate of local recurrence was not statistically significantly different between the patient groups (1% [95% CI = 0% to 2.4%] for the whole-breast radiation therapy patients versus 1% [95% CI = 0% to 2.8%] for the limited-field radiation therapy patients; $P = .65$). *Conclusions:* Limited-field radiation therapy administered to the region of the tumor bed has comparable 5-year local control rates to whole-breast radiation therapy in selected patients. [J Natl Cancer Inst 2003; 95:1205–11]

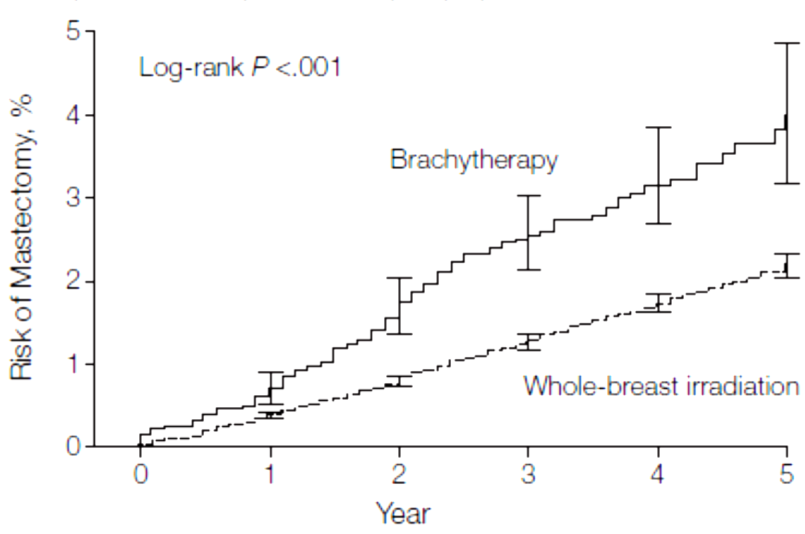
Journal of the National Cancer Institute, Vol. 95, No. 16, August 20, 2003

JAMA, May 2, 2012—Vol 307, No. 17

Association Between Treatment With Brachytherapy vs Whole-Breast Irradiation and Subsequent Mastectomy, Complications, and Survival Among Older Women With Invasive Breast Cancer

Grace L. Smith, MD, PhD, MPH
Ying Xu, MD, MS
Thomas A. Buchholz, MD
Sharon H. Giordano, MD, MPH
Jing Jiang, MS
Ya-Chen Tina Shih, PhD
Benjamin D. Smith, MD

Infections 16.5% vs 10.3%
Pain 14.5% vs 11.9%
Fat necrosis 8.26% vs 4.0%



No. of patients at risk

Brachytherapy	6952	6746	4287	2419	1176	442
Whole-breast irradiation	85783	81651	62268	43704	26991	11735

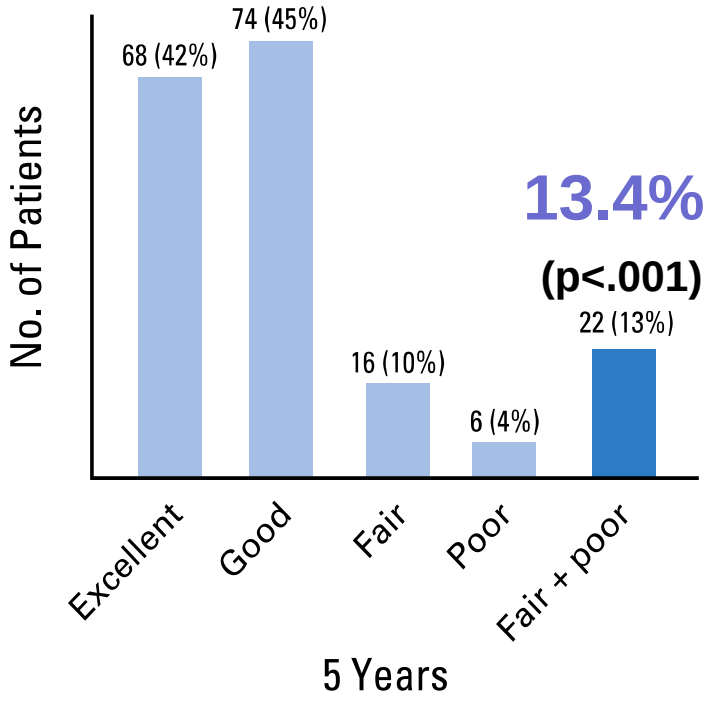
3.95%

2.18%

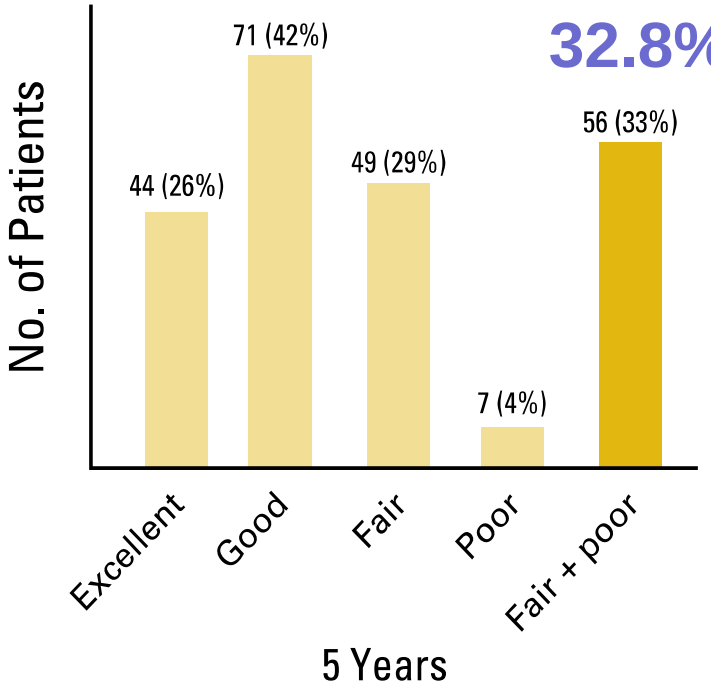
p<0.001

Olivotto I et al. J Clin Oncol 2013

WBI

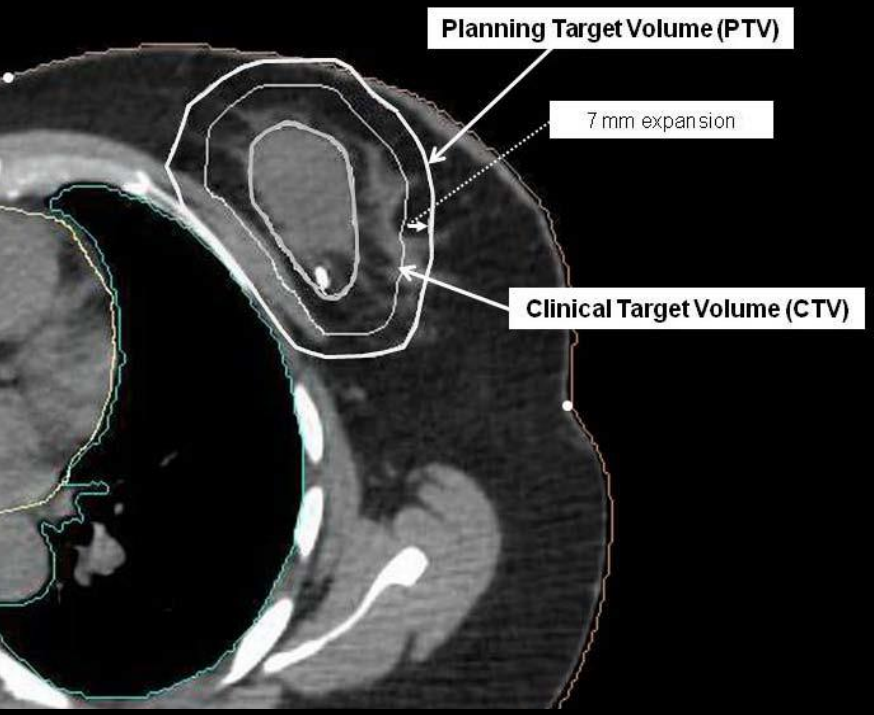


APBI



5 year assessment on 335 out of 2,135 patients randomised

Target volume

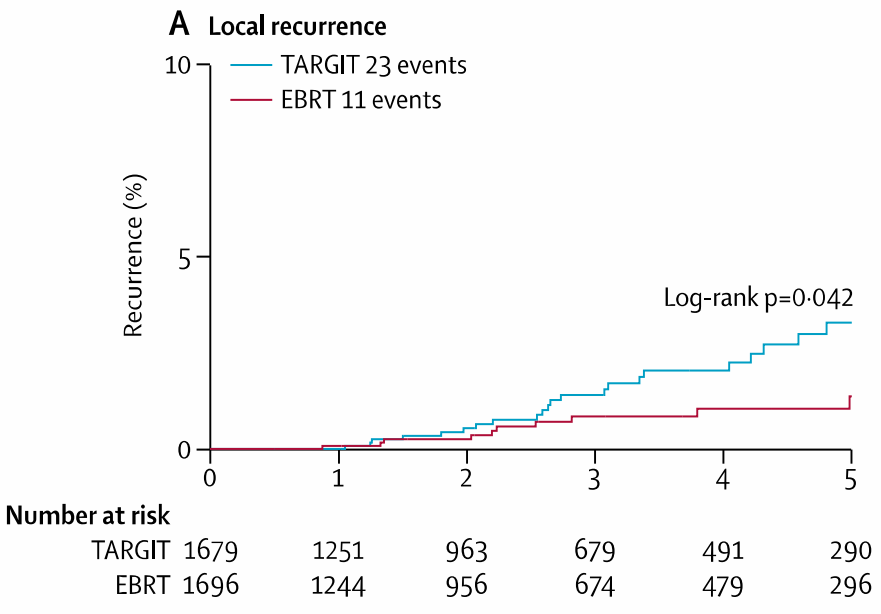


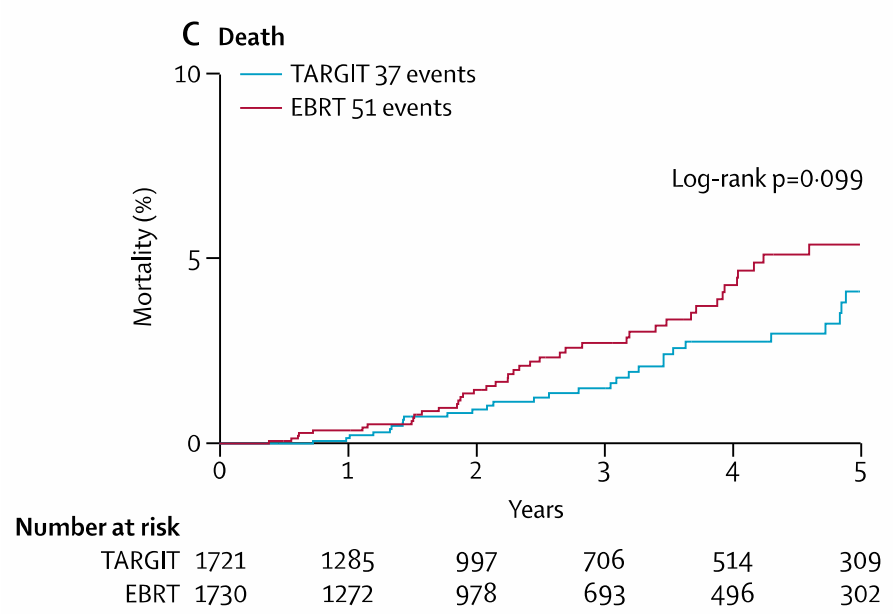
	NSABP-B39	RAPID
CTV	Ser + 1.5 cm	Ser + 1 cm
PTV	CTV + 1 cm	CTV + 1 cm
3 cm seroma (~14cc)	268 cc	179 cc

ELIOT Randomized Trial. LF

	External radiotherapy RT (n=601)		Intraoperative radiotherapy ELIOT (n=585)		
Person-years until last visit	3,615		3,323		
Person-years until last contact	3,780		3,583		
	N (rate/100-year)	*5-year event rate% (95% CI) ***	*N (rate/100-year)*	*5-year event rate % (95% CI) ***	*Log-rank P*
Local relapse + Ipsilateral breast cancer	5 (0.14)	0.7 (0.0-1.4)	37 (1.11)	5.3 (3.3-7.3)	<0.0001
Local relapse	5 (0.14)	0.7 (0.0-1.4)	23 (0.69)	3.2 (1.7-4.8)	0.0002
Ipsilateral breast cancer	0 (0.00)	0.0	14 (0.42)	2.1 (0.9-3.4)	<0.0001
Axillary/regional LN metastasis	2 (0.06)	0.4 (0.0-0.9)	9 (0.27)	1.1 (0.2-2.1)	0.02

TARGIT trial 5 years data





Vaidya JS *Lancet* **383**: 603–13, 2014

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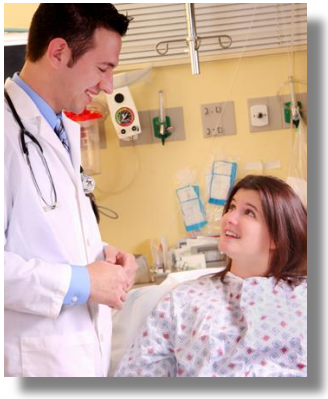
Canadian Breast Cancer Foundation®

creating a future without breast cancer



PBSI clinical trials

- Phase I/II for IDC – 2004 to 2007
- Multicentre Registry study – 2009 to current
- Phase II multicentre DCIS – 2010 to current

131 patients

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Efficiency

- FU range 1 month to over 10 years,
  49.6% over 5 years
- 5 years Overall Survival 97%
  5 years **ipsilateral relapse free 98.5%**
  5 years contralateral free 95.6%
- Most event after 5 years
  - 5 ipsilateral recurrences
  - 1 regional recurrence (the only node positive patient)
  - 1 metastatic patient (lung or breast?)
  - 6 controlateral cancers

IBTR ~ 98.2%

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Tolerance

- Acute side effects
  - Mainly grade I acute skin reactions – 42% redness
  - 16.5% moist desquamation (compares to 31 ~ 48%)
- Delayed side effects
  - telangiectasia – 21% at 2 years, 23% at 5 years
  - indurations – 24% at 2 years, 40% at 5 years
  - skin pigmentation – 10%

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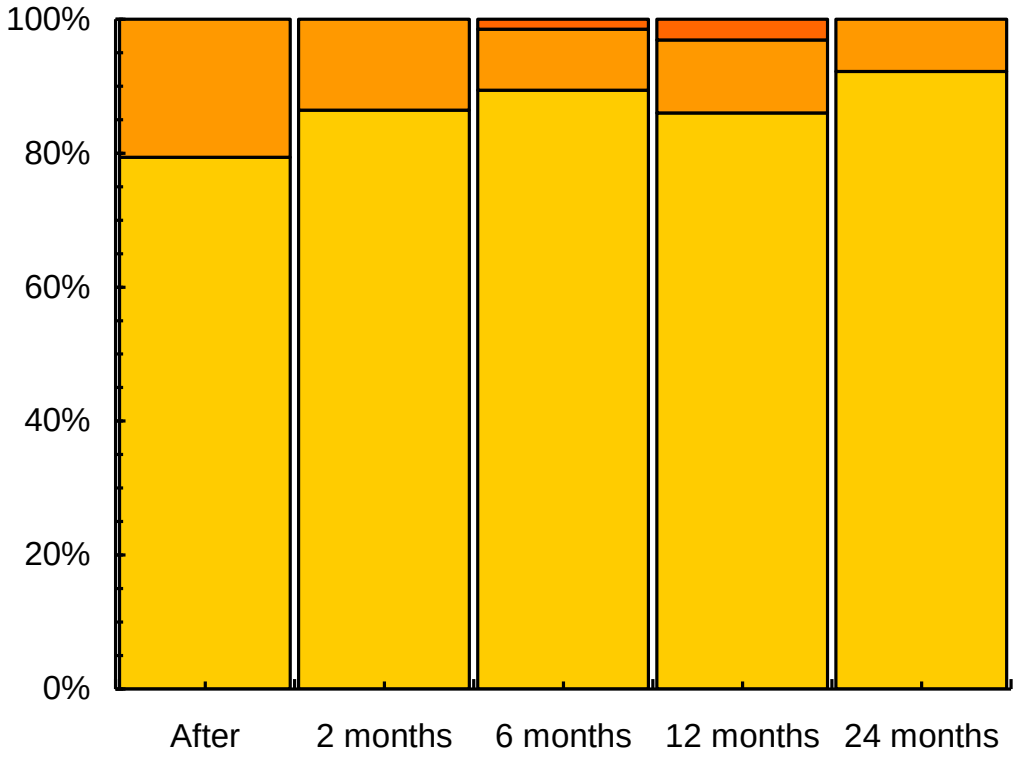
Satisfaction – RTOG 95-17



98% satisfied

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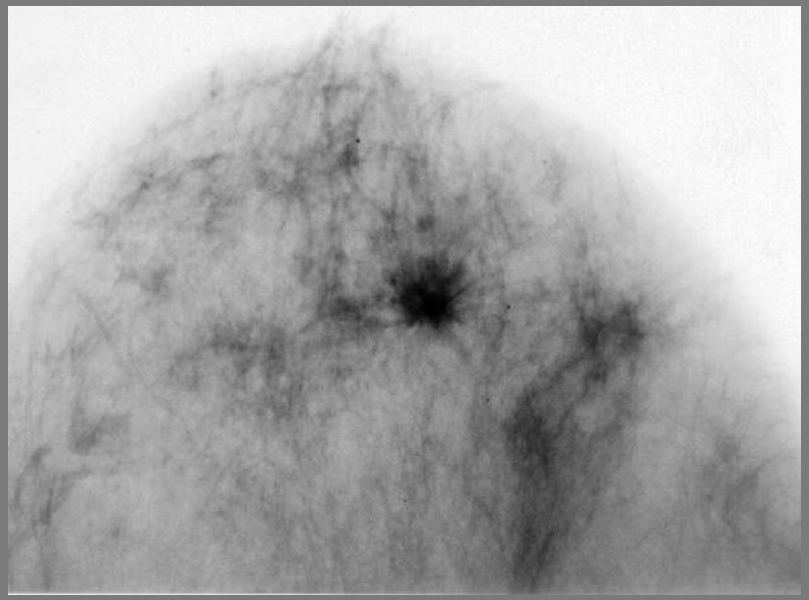
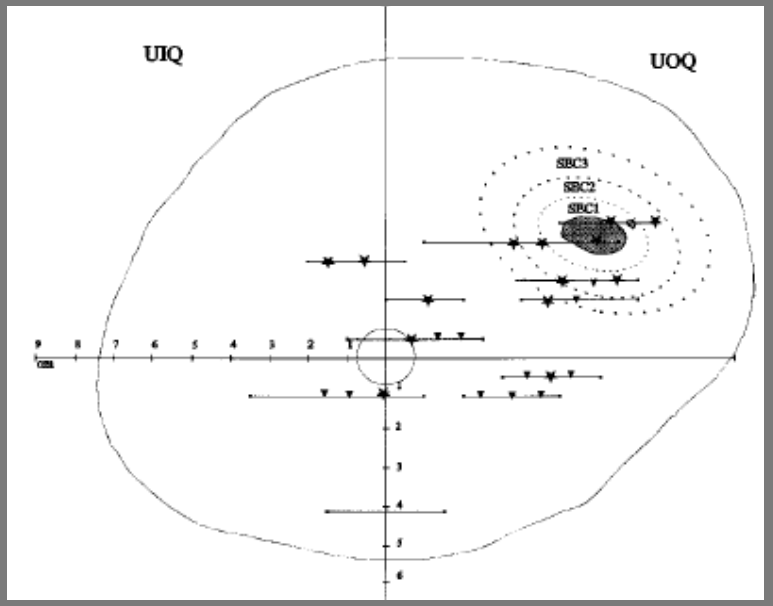
Multifocality/Multicentricity





Holland R, *Cancer* 56:979-990, 1985

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IHC subtypes

	Luminal subtype	HER2 subtype	Basal subtype
Gene expression	ER+, CK8-18	ER-, HER2+ ERBB2+	ER-, HER2-, CK5,6,14,17
Pathology	Grade 1-2	Grade 2-3	Grade 3 pushing borders, mitoses, geographic necrosis, associated with medullary and metaplastic
IHC surrogates	Luminal A: ER+, PR+, HER2- Luminal B: ER+, PR+, HER2+	ER-, PR-, HER2+	Triple negative, CK5/6+, EGFR+
Clinical features	50~70% tumors Luminal A excellent prognosis, Luminal B intermediate Endocrine therapy Poor CT response	15~20% tumors Poor prognosis Good response to Trastuzumab and CT	10~15% tumors 35% of pre-menopausal and Afro-americans, associated with BRCA1 Neo-adjuvant CT

LUMINA trial
>60 years old
10 years LRR 4.1% vs 5.6%

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Conclusions

- Outcomes comparable to WBI
- Much shorter treatment
- Patients love it
- Open new opportunities

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