Concept of Accelerated Partial Breast Irradiation (APBI)

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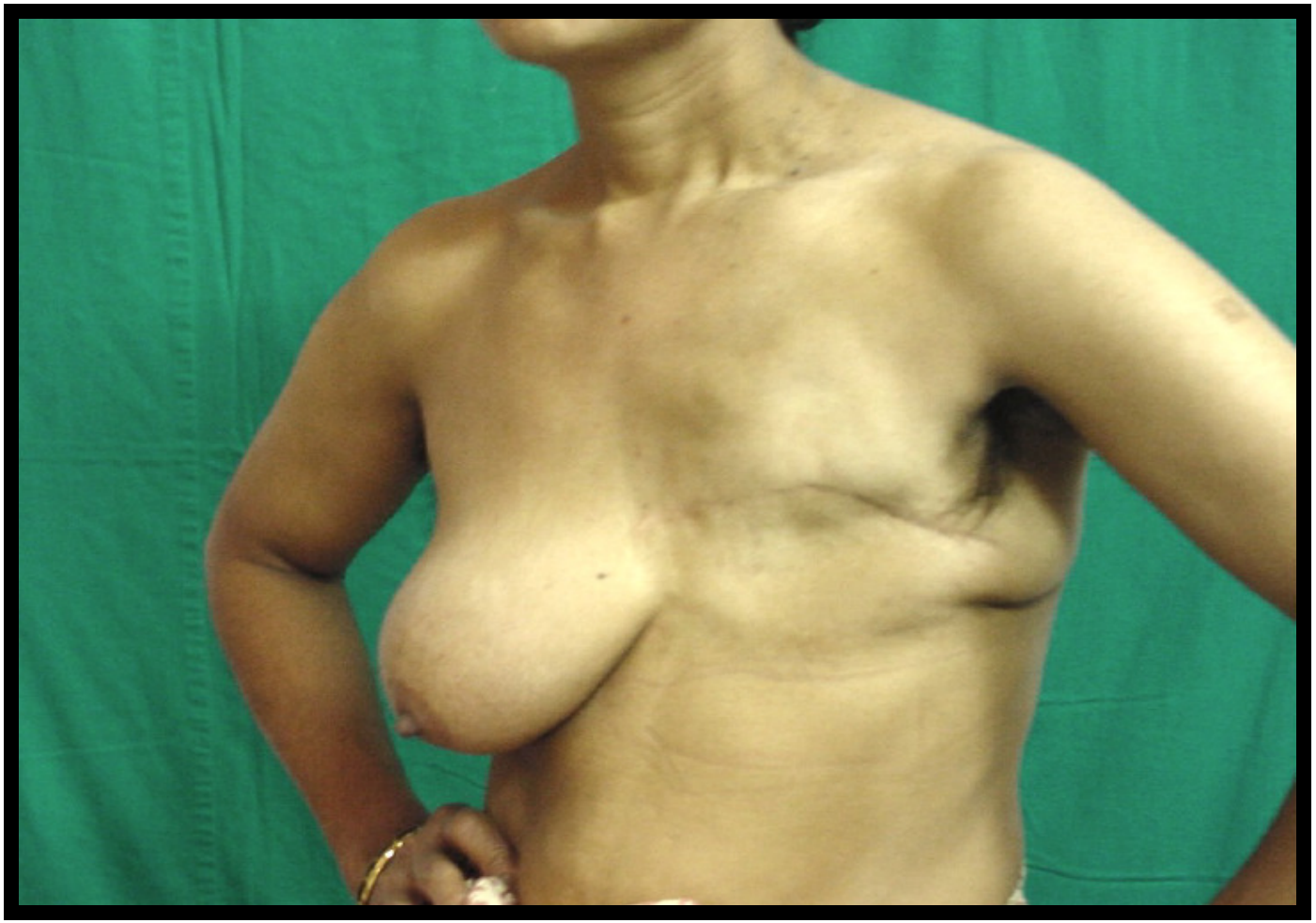
Modified Radical Mastectomy



Modified Radical Mastectomy was considered as the Gold Standard for long period

Early Breast Cancer
Breast Conservative Treatment equivalent to Mastectomy

Trial	No. of Patients (Median FU)	Survival		Local Recurr.	
		MRM	BCT +RT	MRM	BCT + RT
NCI Milan *1973-80*	701 (13 yrs)	69%	71%	2%	4%
NSABP-06 *1976-84*	1444 (12 yrs)	62%	62%	6%	10%
EORTC *1980-86*	903 (7 yrs)	75%	75%	9%	13%
Danish *1983-87*	905 (6 yrs)	82%	79%	7%	3%

MRM Vs BCT

Randomized trials

Meta-analysis

↓

Comparable local control, Overall survival

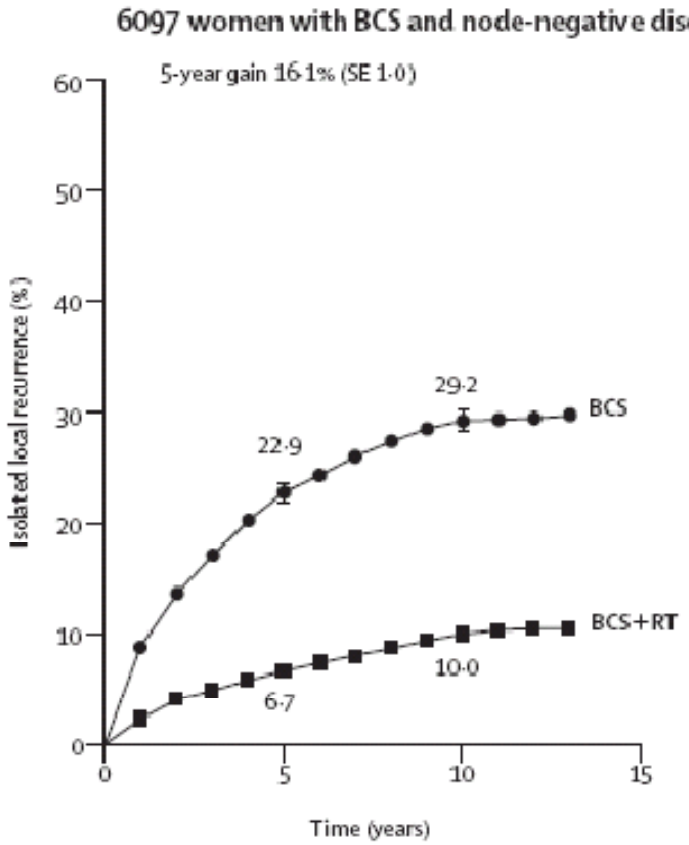
Better cosmetic outcome

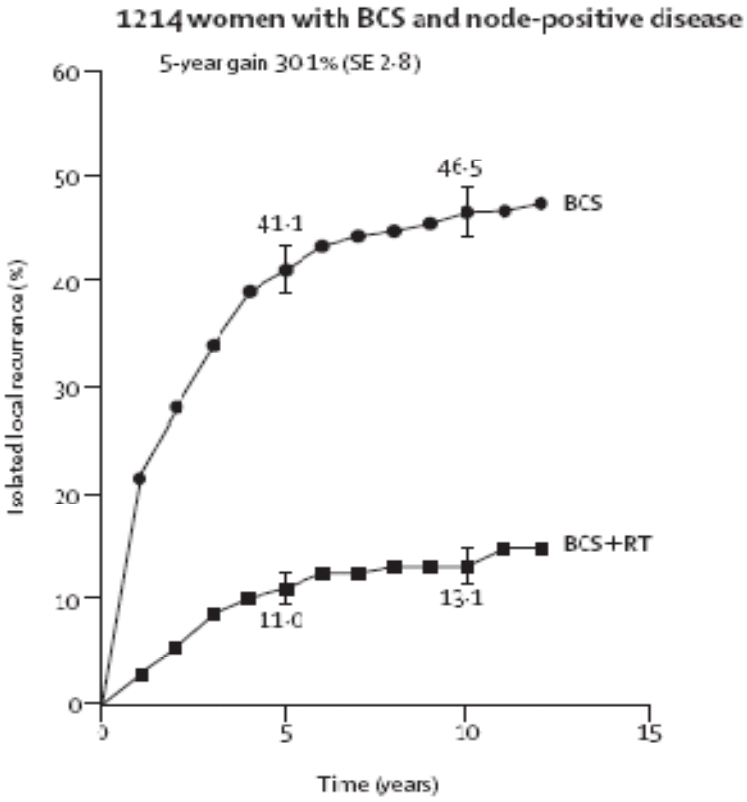
Early Breast Cancer

RT is Necessary after Breast Conserving Surgery

Trials (Period)	No. of Patients (Median FU)	Local Rec.		Survival	
		BCS	BCS +RT	BCS	BCS + RT
NSABP 06 (1976-84)	1450 (12 yrs)	35%	10% (*p <0.001*)	58%	63% (*NS*)
Swedish 1981-88	381 (5 yrs)	18%	2% (*p <0.0001*)	90%	91% (*NS*)
Ontario (1984-89)	837 (4 yrs)	26%	6% (*p <0.0001*)	85%	87% (*NS*)

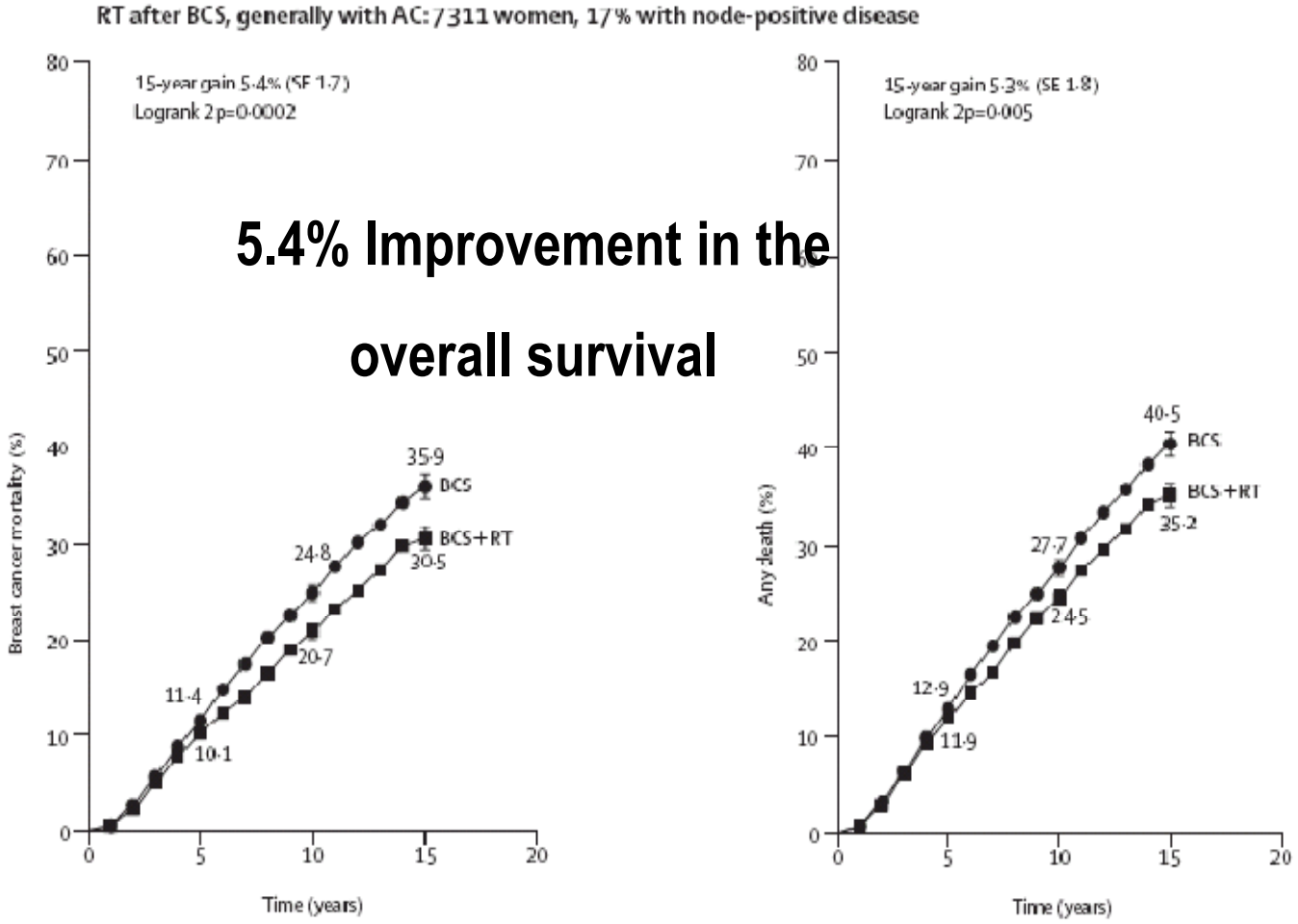
Breast Conserving Therapy: Whole breast radiation-Why?





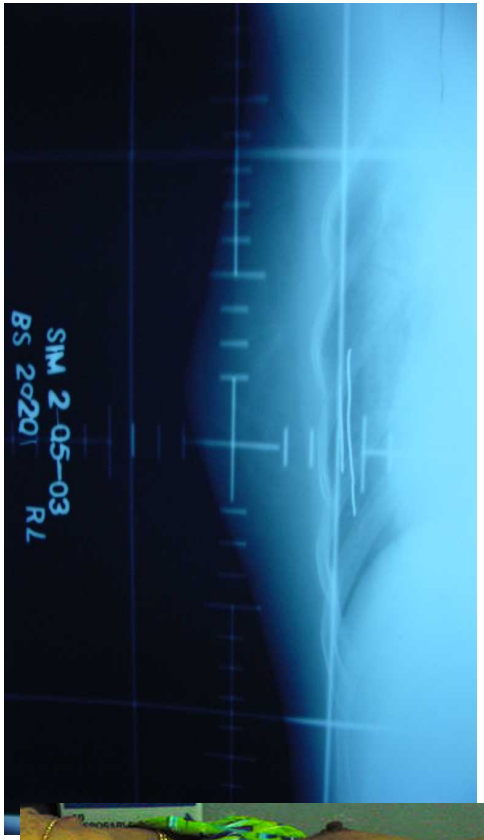
***EBCTCG meta-analysis. Lancet* 2005; 366: 2087–2106**

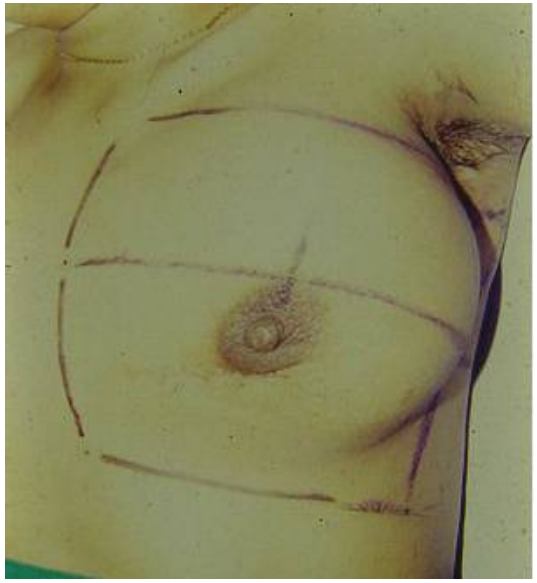
Breast Conserving Therapy: Whole breast radiation-Why?

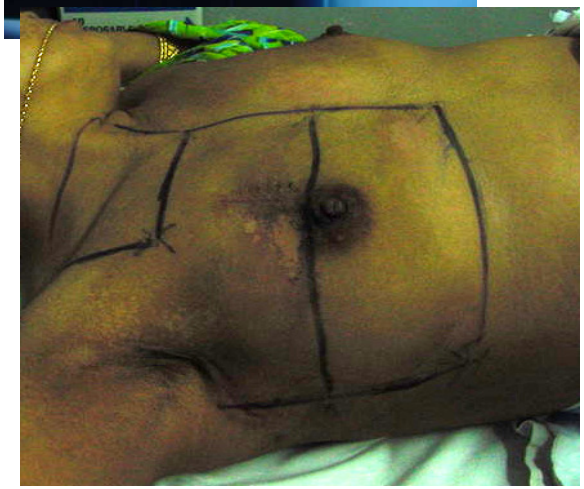


5.4% Improvement in the overall survival

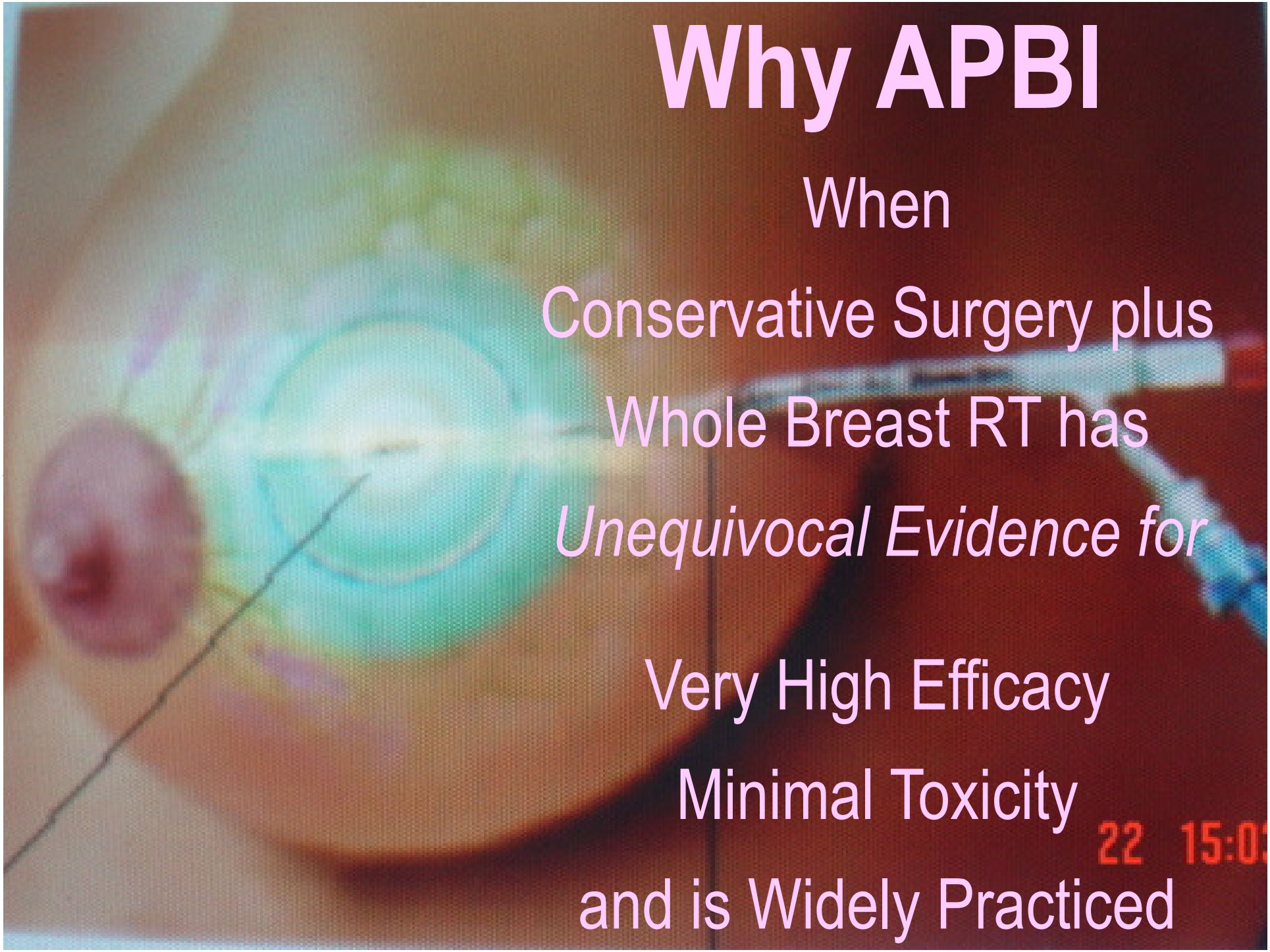
EBCTCG meta-analysis. Lancet 2005; 366: 2087–2106







Budrukkar et al. Mammology 05


Why APBI
When
Conservative Surgery plus
Whole Breast RT has
Unequivocal Evidence for
Very High Efficacy
Minimal Toxicity
and is Widely Practiced

Is BCT (BCS + WBI) a Universal Practice & Standard of Care

Only 43% of women with
Stage I and II Breast cancer in
North America were treated
with Breast Conservative Surgery
and of these
14% did not receive post op RT

Morrow et al JCO 2001

Why BCT (BCS + WBI) is not a Universal Practice?

Multifactorial Problem

Non believers

Expertise

Facilities

Need for daily hospital visits for 6-7 weeks

Local Recurrence Patterns

Vast majority (75-90%) of all breast recurrences after whole breast RT are in the index quadrant (same as without RT after breast conserving surgery)

Only 1-3% women have recurrences in other quadrants (same as contra-lateral Breast Cancer rates)

Approaches for Partial Breast Treatment

- Wide Excision + Partial Breast Irradiation (PBI) of tumour bed + 1-2 cm

  Increasing body of evidence supporting the safety of this approach in selected cases

- Wider Wide Excision in selected cases

  Excess recurrences even after quadrentectomy when RT is omitted

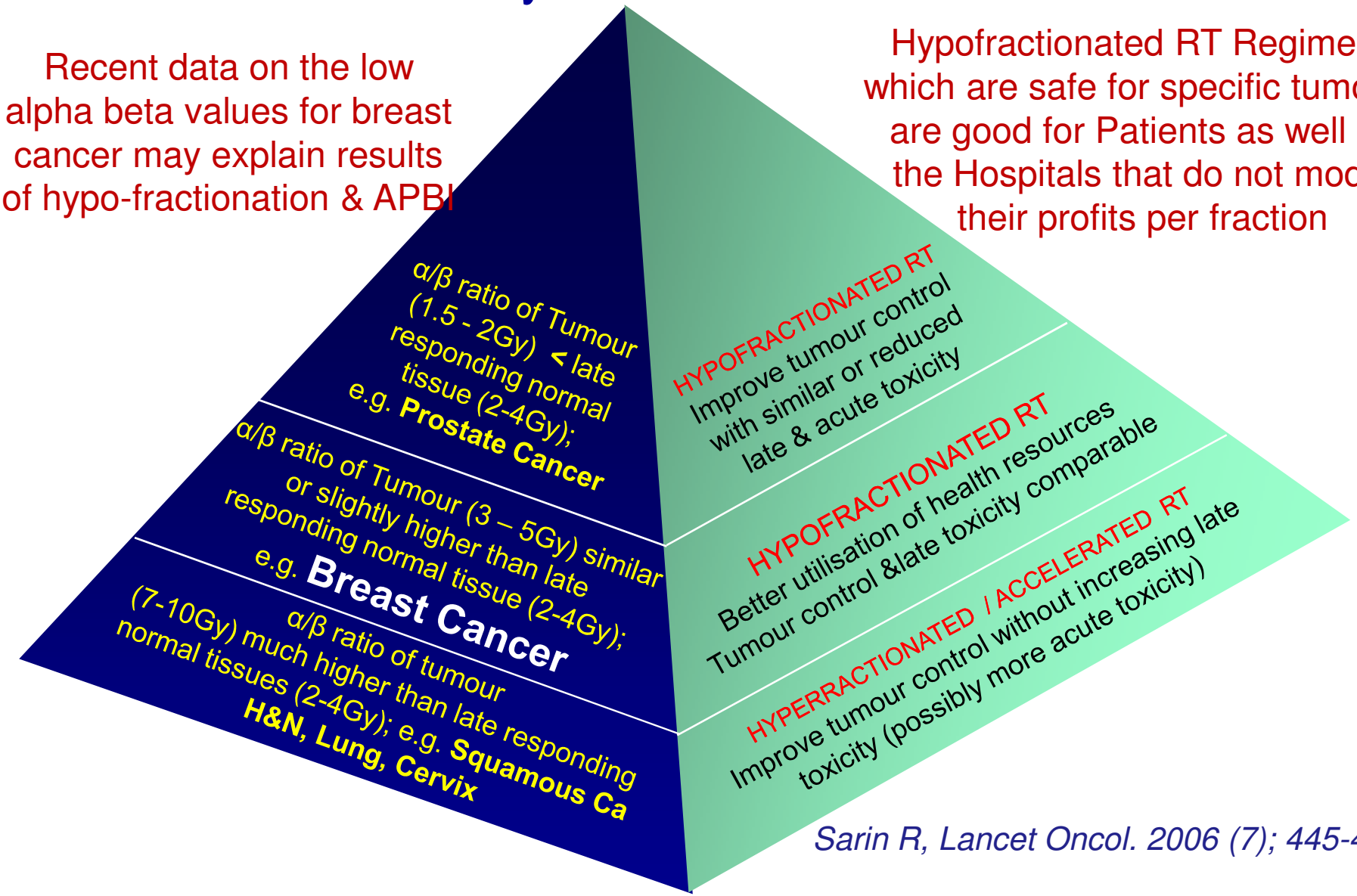
‘Accelerating’ Partial Breast Irradiation

- *Smaller volumes of normal tissues can tolerate ‘biologically equivalent’ doses of radiation in much shorter time period*
- *Radiobiological modelling predicted safety of doses equivalent to 45- 50Gy /25 # / 5 wks with Brachytherapy – HDR (High Dose Rate) 34Gy / 10# / 5 days OR 45Gy/ 5 days LDR OR Highly Conformal External Beam RT*
- *Short treatment time- Logistic advantages*

Clinico-Radiobiological Fractionation Pyramid: Why APBI may work in Breast Ca

Recent data on the low alpha beta values for breast cancer may explain results of hypo-fractionation & APBI

Hypofractionated RT Regimens which are safe for specific tumours are good for Patients as well as the Hospitals that do not model their profits per fraction

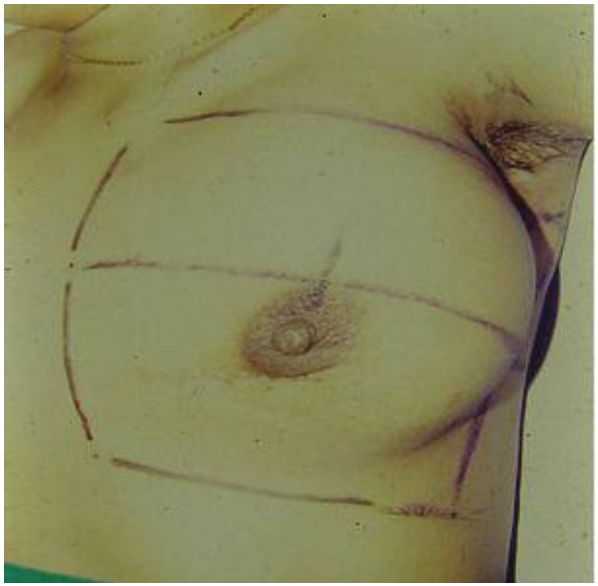


Sarin R, Lancet Oncol. 2006 (7); 445-47

Partial breast irradiation: Attractive alternative

Accelerated RT: shorter treatment duration

APBI: Accelerated Partial Breast Irradiation



5-6 Weeks of RT

Whole breast

1 week of RT

Tumor bed with adequate margin

Omitting Whole Breast Treatment
'Oncological Safety Issues'

Concerns

Microscopic extensions of Cancer, which may sometimes not be evident on routine Histopathology

Multi-centric Foci (pre-malignant or Malignant) which could progress and manifest during the patient's lifetime

Whole organ versus Partial Organ Treatment (RT / Sx/ Both)
ONCOLOGICAL SAFETY ISSUES

Is Partial resection / irradiation of
Tongue, Thyroid, Lung, Bladder, Brain, Liver etc

'Oncologically Safe'

for '<u>selected</u>' cancers
of these organs?

If partial organ treatment is routinely practiced for cancers in other organs, why treat early breast cancers differently?

As in other organs,

Pre-malignant or malignant multi-centric foci occur in Breast Cancer also

But the key to successful Partial Organ Treatment here too is ‘Case Selection’

When to consider APBI?

- Minimal Risk for recurrence outside the index quadrant. Risk categorization based on conventional biological & pathological criteria
- Volume of breast requiring radiation (lumpectomy cavity + 1-2 cm) is sufficiently small to tolerate accelerated radiation delivery without serious radiation sequelae
- Technical feasibility & Means to deliver APBI

Recommended Selection Criteria for APBI

Criteria	American Brachytherapy Society	American Society of Breast Surgeons
Patient age	45 years or more	50 years or more
Tumour size	Up to 3cm	Up to 2cm
Node	Negative	Negative
Histology	IDC	IDC or DCIS
Margins	Microscopically negative	Microscopically -ve (>2mm)

Several ongoing RCTs are also including ILC, EIC

At TMH we are now also excluding women with hereditary breast cancer

Phase III data
Hungarian Randomized trial: 5 year results

1998-2004 (N=258)

$T_1N_{0\text{-}1mi}$ breast cancer, low risk

Non lobular cancers, Clear margins,
No EIC

	Whole Breast RT(N=130) 50Gy/25#	Partial Breast Irradiation (N=128) Interstitial brachytherapy (N=88) Electrons (50Gy/25#) (N=40)
LR	3.4 %	4.7 %
OAS	91.8 %	94.6 %
Cosmesis	62.9%	77.6 %

Median FU: 66 months

Polgar C etal. IJROBP 2007; 69(3):694-702

Importance of patient selection
APBI studies in optimally selected patients

Study	N	Median FU (yrs)	Local Rec %
Polgar (2009) NIO, Budapest	45	12	8.9
Johansson (2009) Orebro Medical Centre	51	7.2	5.9
King T (2000) Ochsner Clinic,New Orleans	51	6.25	2
Arthur DW (2008) RTOG 95-17	99	7	6.1
Mark (2009) J Arrington Cancer Centre	192	5.4	4.2
Antonucci (2009) William Beaumont Hospital, Detroit	199	9.6	5

Strnad V. IJROBP 2010 (In press), Sarin R Nature Oncol 2005

APBI in suboptimally selected patients

Institution APBI technique	No of patients (Median FU yrs)	Criticism	Breast Recurrence
Christie Hospital RCT External Electrons 40Gy/8#/10days	353 (8)	Lobular ca -15%Margin NK or+ve 19% Inadequate coverage	25%
Guys Hospital LDR 55 Gy over 5 days	27 (6)	Positive margins 55%, EIC+VE 40%	37%
Uzsoki Hospital Budapest LDR 50Gy in 10-22 hrs	70 (12)	Cut margin NK, single plane, unacceptable dose rate	24%
London Regional Cancer Centre Ontario	39 (7.5)	Av. Implant vol:30cc	16%
Tufts New England	33 (5)	55% EIC	6%
University of Kansas	25 (4)	Inadequate LDR dose	0%

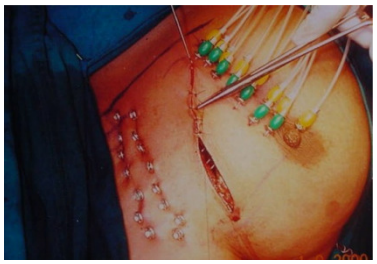
Sarin R, Nature Oncology 2005

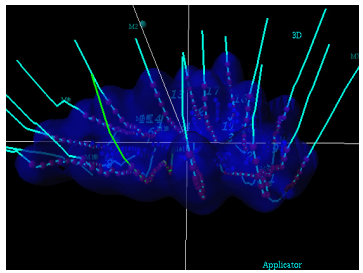
ASTRO Consensus statement :APBI outside clinical trial

Factor	Suitable group	Cautionary	Unsuitable
Patient Factors Age	 >60years	 50-59	 Age <50 years
Pathologic factors Tumor size T stage Margins Grade LVSI ER status Multicentricity Multifocality	 <2cm T1 Negative (> 2 mm) Any No Positive Unicentric only Unifocal	 2.1-3 T0, T2 Close (<2mm) Limited/focal Negative	 >3cm T3,T4 Positive Present extensive Present >3cm
Histology Pure DCIS EIC	Invasive ductal ,favorable Not allowed Not alowed	Invasive lobular	 >3cm
Nodal factors N stage Nodal surgery	 pNo SN Bx or ALND		 PN1, N2, N3
Treatment factors Neoadjuvant therapy	 Not allowed		 Used

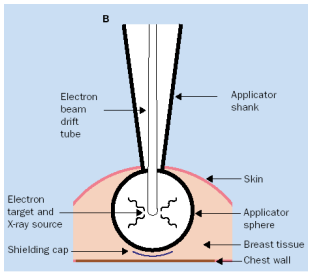
Smith BD. IJROBP 2009;74:987-1001

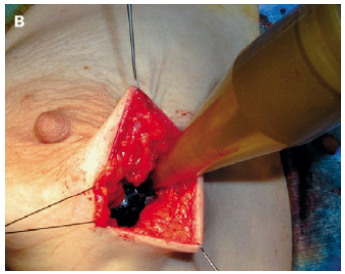
Methods of APBI





Interstitial brachytherapy





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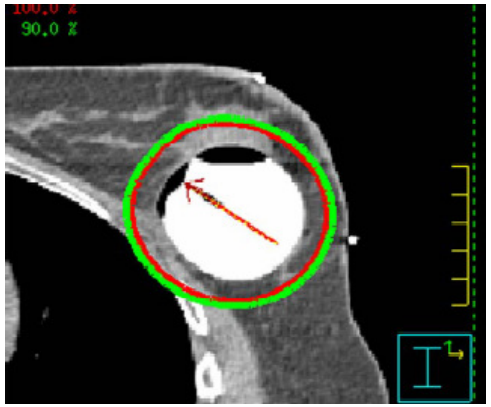
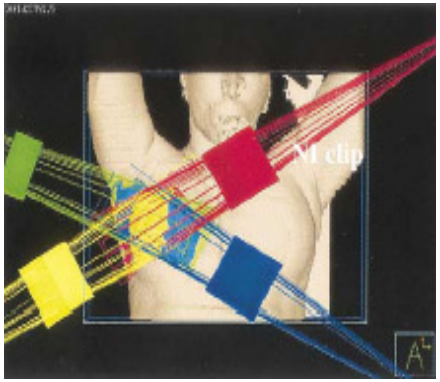
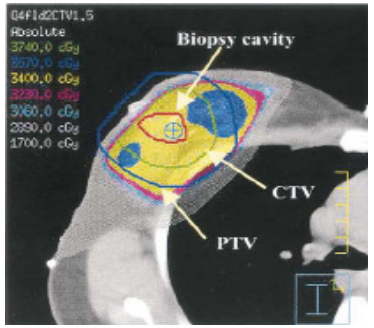


Mammosite



3DCRT



IMRT

Summary and recommendations for APBI in early breast cancers

PARTIAL BREAST TREATMENT APPROACH	CLINICAL OUTCOME	RECOMMENDATION
Inappropriate Case selection or Inadequate target coverage or suboptimal radiobiology	Excess breast recurrence rates and or late radiation sequelae	APBI should not be considered
Appropriate case selection as per ASTRO/GEC ESTRO guidelines. Treated with optimal technique and radiobiology	5-7 year breast recur. rates and cosmesis comparable to matched controls treated with whole breast irradiation	APBI may be considered as an alternative to WBI

Sarin, Nature Oncol; 2 (1), 2005