How to Prevent/Avoid Late Side Effects

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Disclosure

Csaba Polgár, MD, PhD, MSc, does not have any financial relationships or products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

Outline of the Presentation

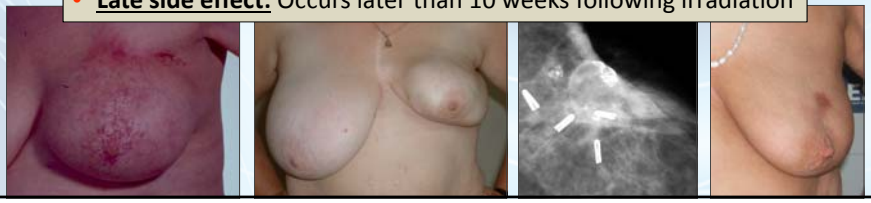
- Overview and background of late side effects
- Critical review of published experience with different accelerated partial-breast irradiation (APBI) techniques
  - Skin side effects
  - Fibrosis
  - Fat necrosis
  - Subsequent mastectomy rate
- Keystones for the prevention of brachytherapy-related late side effects
- Case report with multiple choice question to the audience

Definition of "Early" and "Late" Side Effects

- **Early side effect:** Occurs during the first 10 weeks following irradiation

- **Motto: Before implementation of APBI into routine clinical practice, in addition to non-inferior local control and survival results, at least a comparable toxicity profile should be documented according to each APBI technique!**

- **Late side effect:** Occurs later than 10 weeks following irradiation

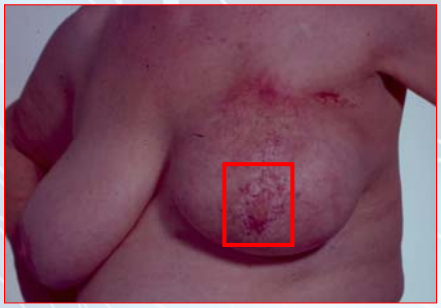


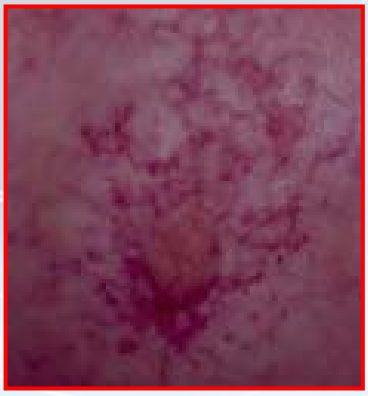
Early and Late Side Effects of Breast Cancer RT

Organ	Early Side Effect	Late Side Effect
Skin	Erythema	Atrophy, scaling
	Pigmentation	Desquamation
	Dry desquamation	Pigmentation
	Moist desquamation	Telangiectasia (2.5%–60%)
		Necrosis-ulceration (<0.5%)
Breast	Edema, cellulitis	Edema (2%–31%)
		Subcutaneous fibrosis (G1-3: 17%–70%)
		Fat necrosis (0%–57%)
Arm		Edema (2%–44%)
		Brachial plexopathy (1%–1.8%)
Lung	Pneumonitis	Fibrosis
Heart	Pericarditis	Ischemic heart disease (0.5%–3.3%)

Skin Telangiectasia – Definition

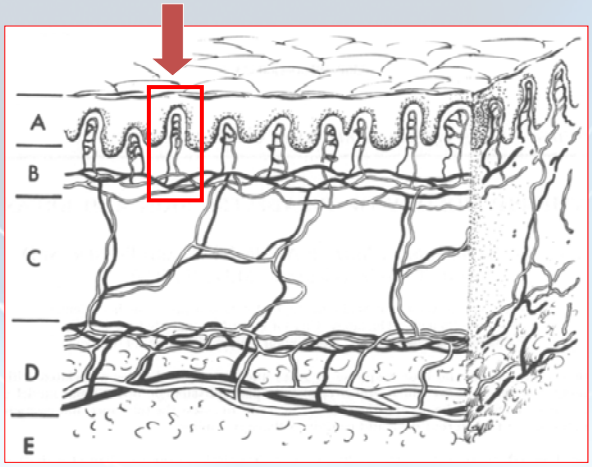
Telangiectasia develops in an atrophic dermis under thinned epidermis as an area of reddish discoloration displaying multiple, prominent, thin-walled, and dilated vessels.





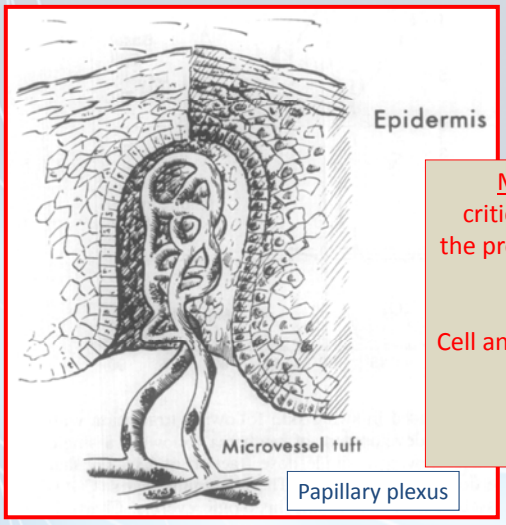
Anatomy of the Skin With Critical Microvessel Components

Skin functional unit (FU)



- Epidermis
- Papillary dermis with the papillary plexus
- Rete dermis with arcuate vessels
- Dermal subcutaneous junction with the dermal plexus
- Subcutaneous layer

Skin Functional Unit = Microvessel With Associated Epidermis and Dermis



Microvessel tuft =
critical tissue controlling
the production of late effects

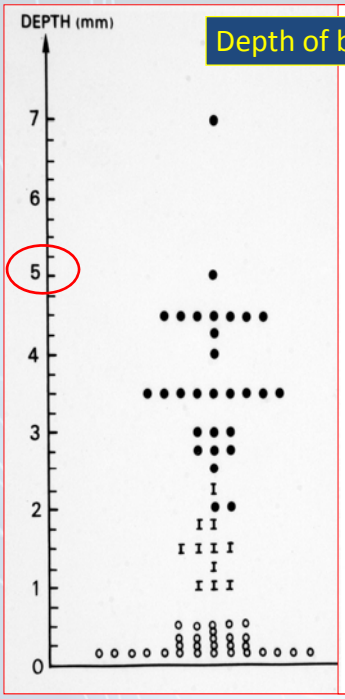
↓

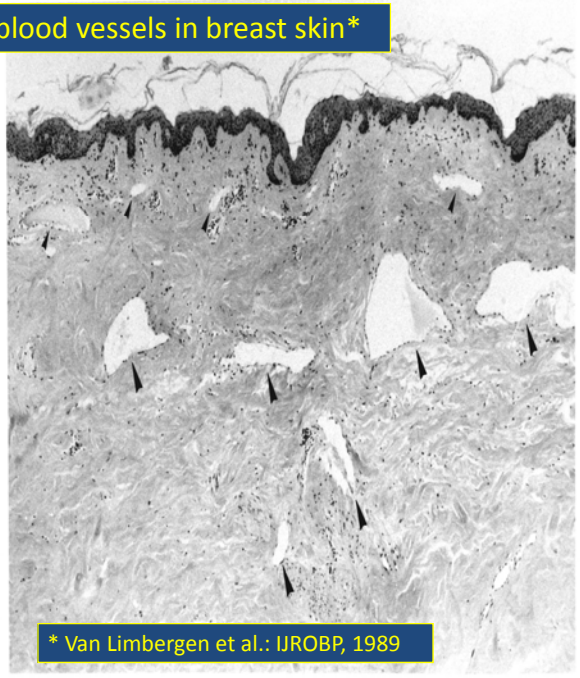
Cell and vessel loss, dilatation

↓

Telangiectasia

Depth of blood vessels in breast skin*





* Van Limbergen et al.: IJROBP, 1989

Skin Tolerance Dose (TD) for 100 cm^2 Field*

Definition:
TD = The dose required to produce a 10%, 30%, or 50% incidence of telangiectasia at 5 years (with conventional fractionation)

$TD_{10/5}$	50 Gy
$TD_{30/5}$	59 Gy
$TD_{50/5}$	65 Gy

*Emami B. et al.: IJROBP 1991;21:109-122

Incidence of Skin Telangiectases (at 5 Years)*

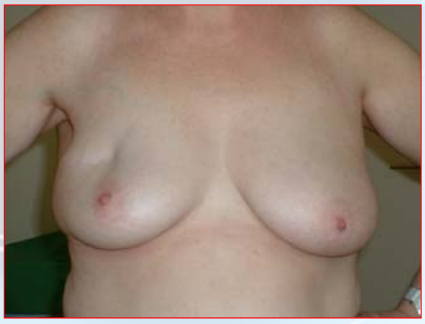
	50 Gy	60 Gy
Score ≥1:	30%	60%
Score ≥2:	12%	30%
Score ≥3:	0%	5%

* Turesson and Notter: IJROBP 1984;10:599-606.

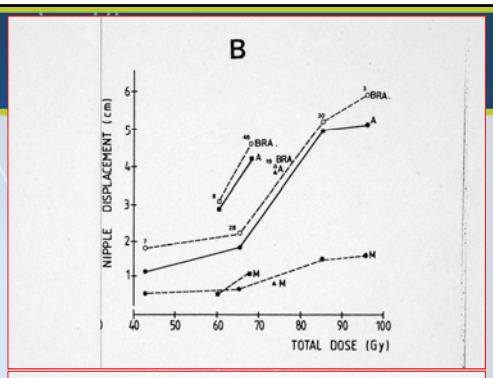
Subcutaneous Fibrosis – Definition

Fibrosis is characterized by a progressive induration, edema formation, and thickening of the dermis and subcutaneous tissues.

Diffuse fibrosis after WBI



Localized fibrosis after APBI



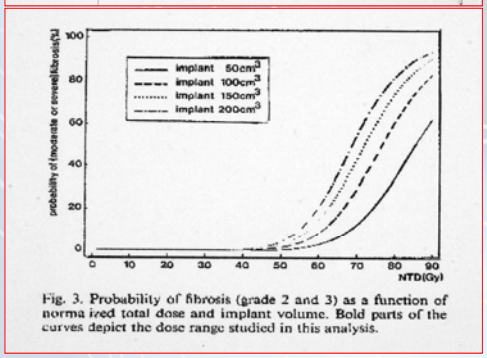


Fig. 3. Probability of fibrosis (grade 2 and 3) as a function of normalized total dose and implant volume. Bold parts of the curves depict the dose range studied in this analysis.

Fibrosis

- Dose dependent

(Leuven 1968–1980)

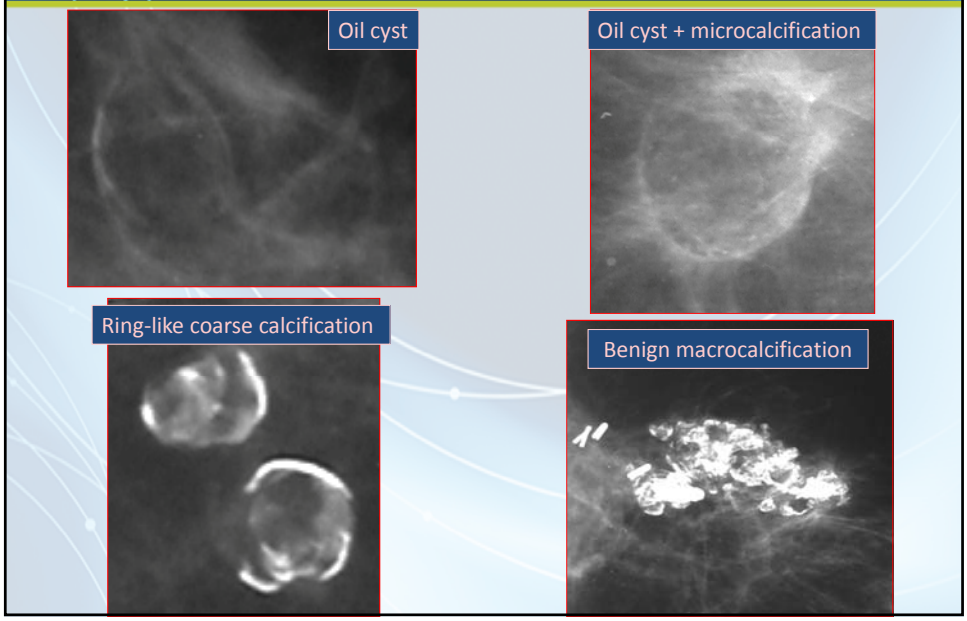
- Dose and volume dependent

(Amsterdam 1985–1989)

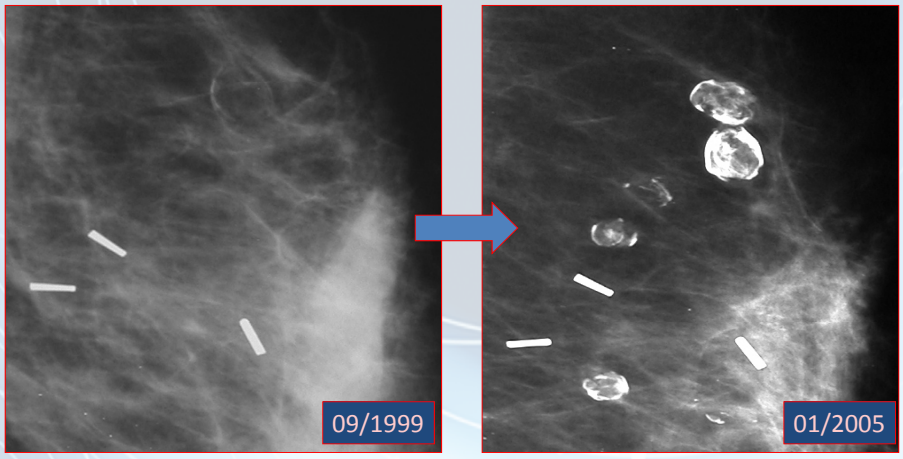
Fat Necrosis: Definition & Etiology

- Fat necrosis = benign inflammatory process that mostly occurs after ANY trauma of the breast
- Etiology:
  - Physical trauma: accidental OR iatrogenic (aspiration citology, core-biopsy, breast surgery, brachytherapy implantation)
  - Radiation therapy (total dose? fractionation? dose inhomogeneity?)
  - Chemotherapy (adriamycin?)
  - Medications (calciphylaxis, anticoagulant therapy)

Mammographic Appearance of Fat Necrosis



Development of Fat Necrosis – From Oil Cyst to Ring-Like Coarse Calcification



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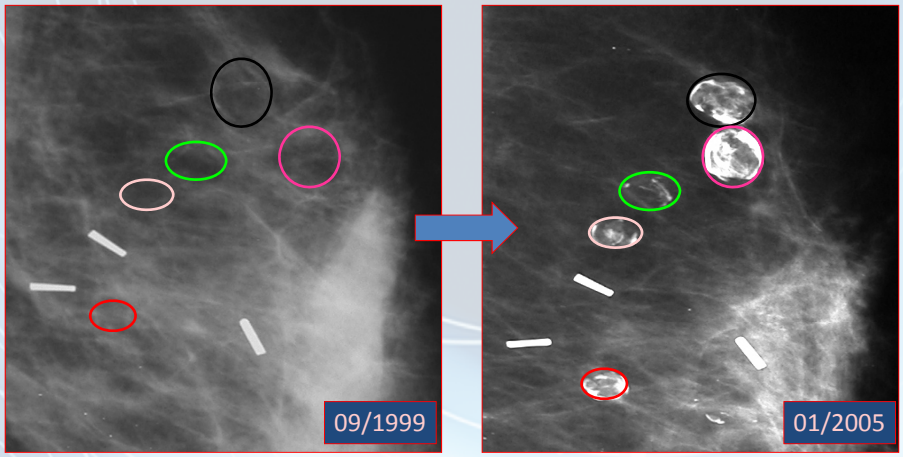
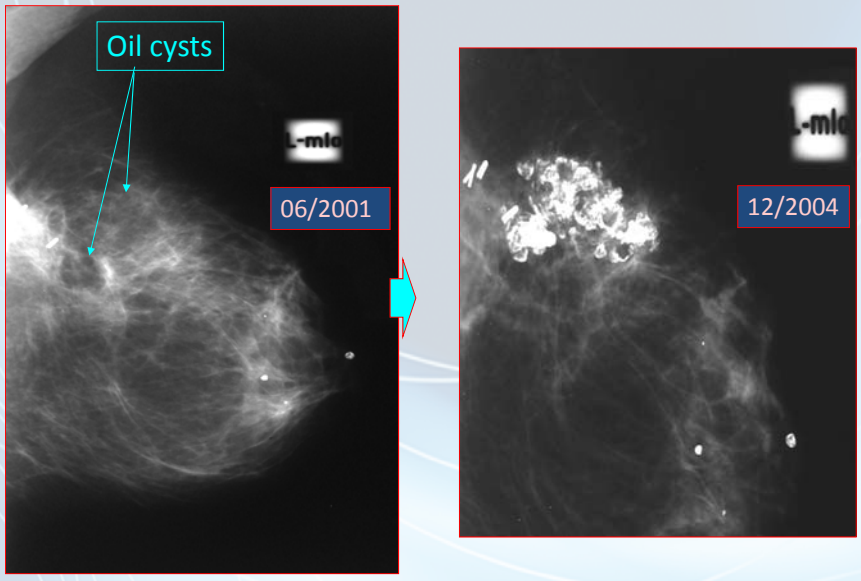
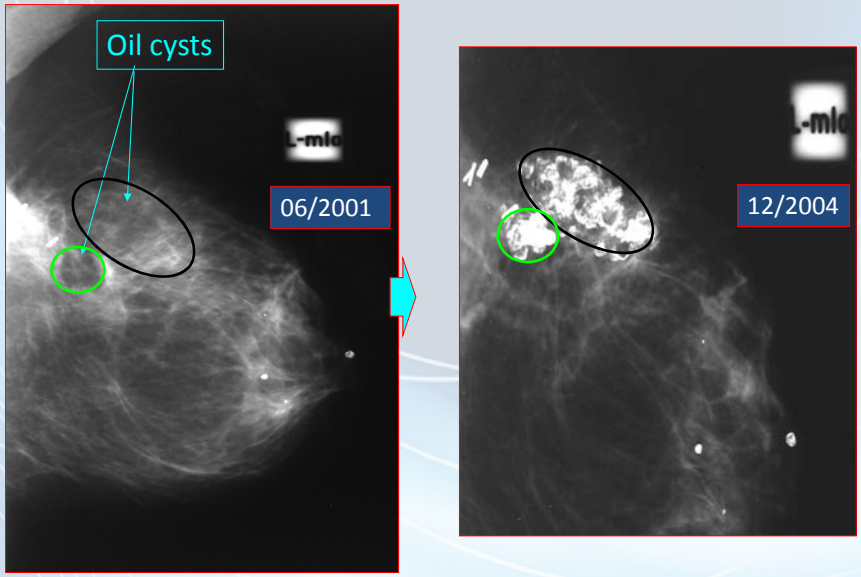


Development of Fat Necrosis – From Oil Cyst to Macrocalcification



Development of Fat Necrosis – From Oil Cyst to Macrocalcification



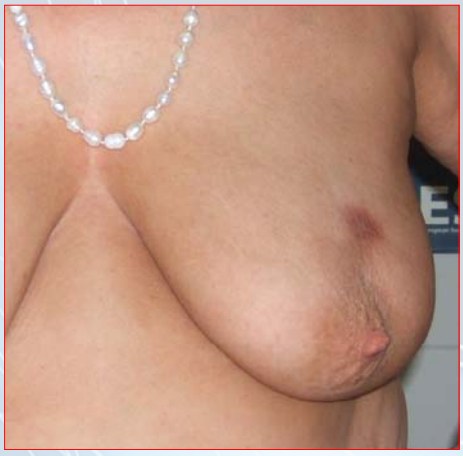
What Is the Clinical Relevance of Fat Necrosis?

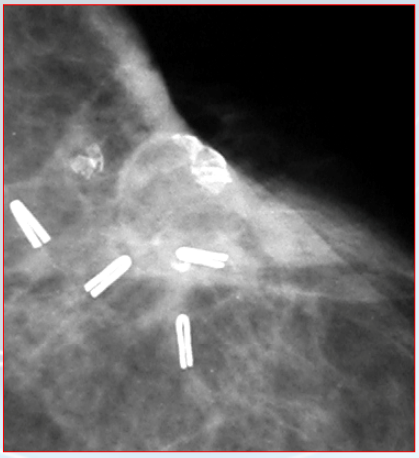
- Clinical distinction:
  - Asymptomatic vs. Symptomatic vs. Requiring surgical intervention
  - Differential diagnosis – fat necrosis OR local recurrence?

Symptomatic Fat Necrosis – Diffuse Fat Necrosis With Progressive Grade 3 Fibrosis

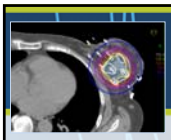
10 years after WBI

Symptomatic Fat Necrosis – Fat Necrosis With Inflammation and Skin Induration





4 years after multicatheter APBI BT



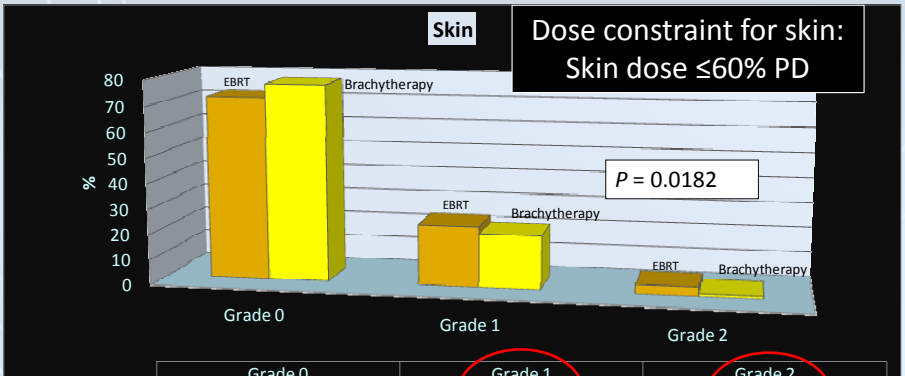
Review of Clinical Results – Skin Side Effects in Multicatheter BT Series

Institute	Patient No.	Median FUP (years)	Dose Constraints for Skin	Telangiectasia,%
Budapest Phase II	45	13.8	Source kept ≥10 mm from the skin Skin dose ≤60% PD	4.4%
Budapest Phase III	87	10.2	Source kept ≥10 mm from the skin Skin dose ≤60% PD	8.2%
Tufts & Virginia University	75	6.1	Source kept 5-7 mm from the skin	4%
University Perugia	100	5	PTV restricted 5 mm from skin	15%
German-Austrian Phase II	274	5.3	PTV restricted 5-10 mm from skin	17%

Budapest Phase III APBI Trial – Late Skin Side Effects

	PBI – HDR BT (N = 85) n (%)	PBI – ELE (N = 40) n (%)	WBI (N = 117) n (%)	*P*-Value
Any grade	11 (12.9%)	16 (40.0%)	24 (20.5%)	HDR BT vs. WBI = NS HDR BT vs. ELE = 0.0009 ELE vs. WBI = NS
G0	74 (87.1%)	24 (60.0%)	93 (79.5%)	
G1	4 (4.7%)	6 (15.0%)	10 (8.5%)	
G2	7 (8.2%)	7 (17.5%)	11 (9.4%)	HDR BT vs. WBI = NS HDR BT vs. ELE = NS ELE vs. WBI = NS
G3	0 (0%)	3 (7.5%)	3 (2.6%)	HDR BT vs. WBI = NS HDR BT vs. ELE = 0.0311

GEC-ESTRO APBI Trial – Late Toxicity at 1 Year FUP

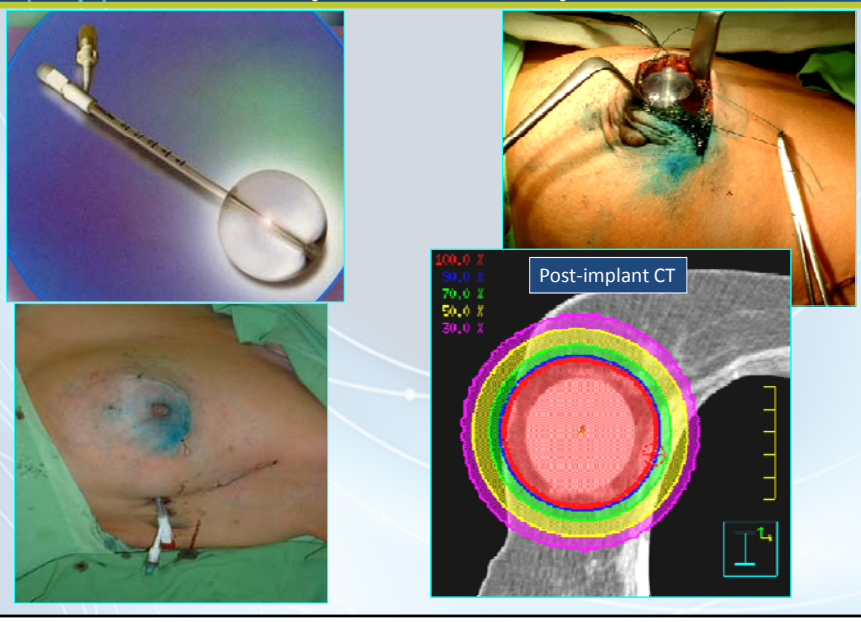


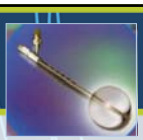
	Grade 0	Grade 1	Grade 2
EBRT	72,3	24	3,7
Brachytherapy	77,8	21,2	1,1

RTOG/EORTC Late Radiation Morbidity Scoring Schema

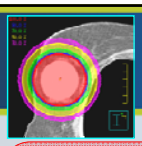
ORGAN TISSUE	0	Grade 1	Grade 2	Grade 3	Grade 4
SKIN	None	Slight atrophy Pigmentation change. Slight telangiectasia (< 1 cm^2); Some hair loss	Patch atrophy; Moderate telangiectasia (1-4 cm^2); Total hair loss	Marked atrophy; Gross telangiectasia (> 4 cm^2)	Ulceration

APBI – Intracavitary Balloon Brachytherapy (MammoSite®)

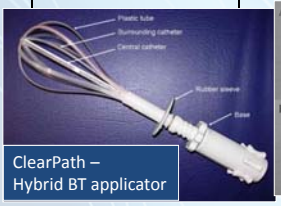




Results of APBI Studies – MammoSite BT Series

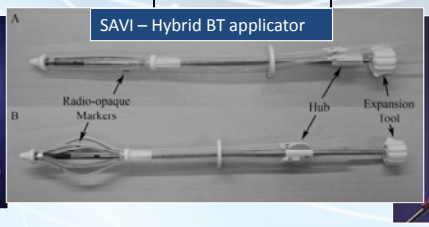


Institute	Patient No.	Median FUP (years)	Crude LR%	Telangiectasia, %
FDA Trial	43	5.5	0	40%
Kiel/Budapest	11	5	0	64%
ASBS Registry Trial	1449	5.3	2.8%	NA
Univ. Pittsburgh	157	5.5	2.5%	27%



ClearPath – Hybrid BT applicator

SAVI – Hybrid BT applicator



Contura – Hybrid BT applicator

Patterns of Use and Short-Term Complications of Breast Brachytherapy in the National Medicare Population From 2008-2009

* Presley et al.: JCO 2012;35:4302-4307.

Table 3. Estimated Adjusted 1-Year Complication Rates for Patients Receiving Brachytherapy and Whole-Breast Irradiation

Treatment	Any Complication		Wound and Skin Complications		Deep-Tissue and Bone Complications	
	% of Patients	95% CI	% of Patients	95% CI	% of Patients	95% CI
Brachytherapy	35.2	28.6 to 41.9	33.7	27.3 to 40.1	4.4	1.3 to 7.6
Whole-breast irradiation	18.4	15.5 to 21.3	16.8	14.0 to 19.5	2.5	1.1 to 3.9
Difference	16.8	9.6 to 24.1	16.9	10.0 to 23.9	1.9	−1.5 to 5.4

NOTE. Rates are adjusted for age at breast-conserving surgery, race, income, comorbidity, type of radiation facility, axillary node dissection, receipt of chemotherapy, prior hospital admission, prior screening mammogram, and prior visit to primary care physician.

Increased Rates of Long-Term Complications after MammoSite Brachytherapy Compared with Whole Breast Radiation Therapy

* Rosenkranz et al.: J Am Coll Surg 2013;2013:217:497-502.

Table 2. Long-Term Complications

Complication	MammoSite APBI		WBRT		p Value
	n	%	n	%	
Patients developed a palpable mass	19/71	26.7	18/245	7.3	<0.001
Palpable masses biopsied	12/19	63	12/18	67	NS
Patients with palpable masses undergoing biopsy	12/71	16.9	12/245	4.9	0.02
Patients with local recurrence	2/71	2.8	4/245	1.6	NS
Patients with ipsilateral in-breast recurrence	3/71	4.2	5/245	2.0	NS
Patients developing telangectasia	17/71	24	10/245	4	<0.001

Extended (5-year) Outcomes of Accelerated Partial Breast Irradiation Using MammoSite Balloon Brachytherapy: Patterns of Failure, Patient Selection, and Dosimetric Correlates for Late Toxicity

Telangiectasia according to different skin dose (SD) cut-offs

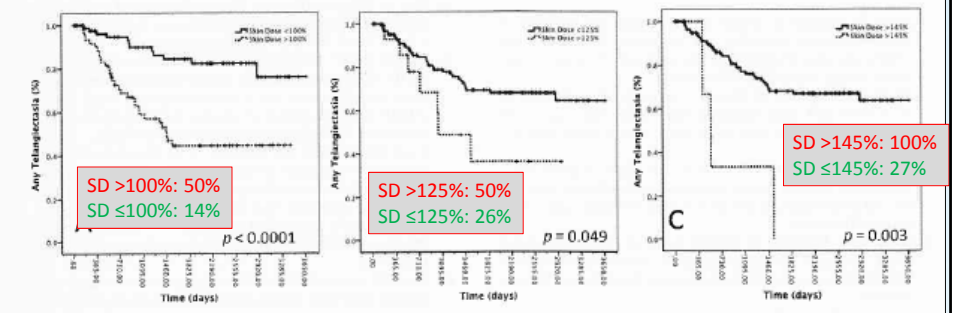
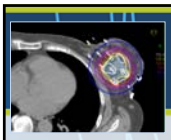


Fig. 2. Impact of skin dose on telangiectasia development. (A) Any telangiectasia as a function of the purposed cutoff of skin dose ≤100%. (B) Prior purposed ideal (21) cutoff of skin dose ≤125% from Contura phase IV trial. (C) NSABP-B39 skin dose constraint ≤145%.

* Vargo et al.: IJROBP 2014;88:285-291.

How to Prevent/Avoid Telangiectasia

- SKIN DOSE MATTERS!
- Skin vessels 5 mm beneath the skin should be avoided from excess dose
- Skin dose should be limited below 60%–70% of the PD
- Keep at least 15 mm balloon-to-skin distance with balloon-based BT applicators
- Image-guided BT and 3D DVH analysis should be implemented in the future



Review of Clinical Results – Fibrosis in Multicatheter BT Series

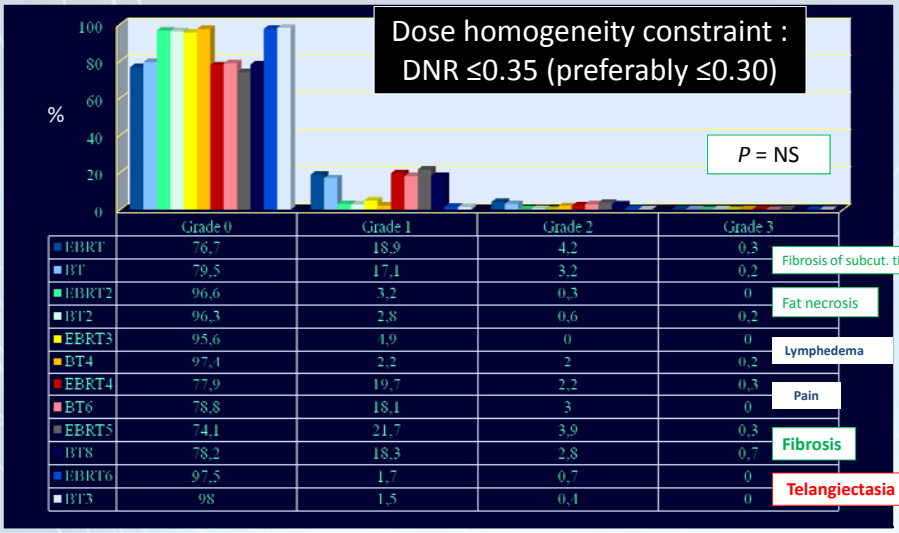
Institute	Patient No.	Median FUP (years)	G3 Fibrosis, %
Budapest Phase II	45	13.8	2.2%
Budapest Phase III	87	10.2	2.4%
Tufts & Virginia University	75	6.1	5%
University Perugia	100	5	0%
German-Austrian Phase II	274	5.3	0.4%
Harvard/Boston	50	11.2	9%
William Beaumont Hospital	199	6.4	1%

0–9%

Budapest Phase III APBI Trial – Fibrosis

	PBI – HDR BT (N = 85) n (%)	PBI – ELE (N = 40) n (%)	WBI (N = 117) n (%)	*P*-Value
Any grade	42 (49.4%)	9 (22.5%)	50 (42.7%)	HDR BT vs. WBI = NS HDR BT vs. ELE = 0.0034 ELE vs. WBI = 0.0166
G0	43 (50.6%)	31 (77.5%)	67 (57.3%)	
G1	26 (30.6%)	7 (17.5%)	40 (34.2%)	
G2	14 (16.5%)	2 (5.0%)	9 (7.7%)	HDR BT vs. WBI = 0.0439 HDR BT vs. ELE = 0.0604

GEC-ESTRO APBI Trial – Late Toxicity at 1 Year FUP



	Grade 0	Grade 1	Grade 2	Grade 3
EBRT	76,7	18,9	4,2	0,3
BT	79,5	17,1	3,2	0,2
EBRT2	96,6	3,2	0,3	0
BT2	96,3	2,8	0,6	0,2
EBRT3	95,6	4,9	0	0
BT4	97,4	2,2	2	0,2
EBRT4	77,9	19,7	2,2	0,3
BT6	78,8	18,1	3	0
EBRT5	74,1	21,7	3,9	0,3
BT8	78,2	18,3	2,8	0,7
EBRT6	97,5	1,7	0,7	0
BT3	98	1,5	0,4	0

Fibrosis of subcut. tissue
Fat necrosis
Lymphedema
Pain
Fibrosis
Telangiectasia

* DNR = Dose Non-uniformity Ratio = V150/V100

Graz-Linz Study (Hammer J et al., n = 420)

	Electrons	Interstitial HDR BT	
Boost dose:	1.8-2 Gy x 5-6	10 Gy x 1	
Boost volume:	70-130 cm^3	21-64 cm^3	
LR rate (5-y):	8.2%	4.3%	
Mean cosmetic score:	1.49	1.15	$P < 0.0005$
Exc./good cosmesis:	70%	88%	$P < 0.001$
Fibrosis:	29%	17%	
Telangiectasia:	28%	9%	

VOLUME MATTERS!

Fibrosis and Dose of BT Harvard/Boston (APBI LDR-BT, n = 75)*

Fibrosis	50 Gy	55 Gy	60 Gy
G0	11%	6%	0%
G1	68%	25%	9%
G2	21%	56%	55%
G3	0%	13%	36%

TOTAL DOSE MATTERS!

* Hattagandi JA et al: IJROBP 2012;83:791-800

Implant-Related Factors for Developing Fibrosis – Tufts/Brown + Virginia University (HDR-BT, n = 75)*

Implant Parameter	G0-1 (n = 52)	>G2 (n = 23)	*P*-Value
Mean V100%	207 cc	179 cc	NS
Mean V150%	47 cc	51 cc	NS
Mean V200%	14 cc	16 cc	NS
Mean DHI*	0.77	0.73	0.02

DOSE HOMOGENEITY MATTERS!

*Wazer DE et al: IJROBP 2006;64:489-495

*DHI = dose homogeneity index

How to Prevent/Avoid Fibrosis

- DOSE, VOLUME, and DOSE HOMOGENEITY MATTERS!
- Limit implant volume to the PTV
  - V100 ≤160 cc
- Dose homogeneity should be controlled
  - DNR (V150/V100) ≤0.35 (preferably ≤0.30)

Literature Review – Controversies on Fat Necrosis

- Some studies do not report incidence of fat necrosis at all
- Some studies report only the incidence of "clinically evident" (symptomatic) fat necrosis
- Some mammography reports do not describe specific findings associated with asymptomatic fat necrosis ("post-therapeutic findings," "postirradiation changes," "benign calcifications")
- Wide range of FUP in different studies
- Lack of data on actuarial rate of fat necrosis
- Lack of comparative studies (brachytherapy vs. teletherapy)
- Limitations of available scoring systems

Limitations of Scoring Systems for Reporting Fat Necrosis

- RTOG/EORTC late radiation morbidity scoring system:
  - ALL fat necrosis should be scored as a Grade 4 side effect
  - NOT suitable to make distinction between symptomatic and asymptomatic fat necrosis
- LENT-SOMA scoring system:
  - Low acceptance (due to its complexity)
  - Fat necrosis = Grade 0–4 side effect (depending on palpable increased density and pain)
  - Asymptomatic fat necrosis (without pain and palpable firmness) should NOT be classified as a side effect

Budapest Scoring System for Reporting Fat Necrosis*

Grade	Definition
Grade 0	No fat necrosis
Grade 1	Asymptomatic fat necrosis (only radiologic and/or cytologic findings)
Grade 2	Symptomatic fat necrosis not requiring medication (palpable mass with or without mild pain)
Grade 3	Symptomatic fat necrosis requiring medication (palpable mass with significant pain)
Grade 4	Symptomatic fat necrosis requiring surgical

Clinical fat necrosis

* Lövey K. et al: IJROBP 2007;69:724-731

Institute	No.	FUP (m)	Dose/Dose Rate	G1	G2-3	G4	Overall
Beaumont	199	77	50 Gy LDR/32-34 Gy HDR	13%	6.5%	1.5%	**21%**
Tufts/Virginia*	75	73	34 Gy HDR	NR	NR	NR	**13%**
Ochsner	51	75	45 Gy LDR/32 Gy HDR	NR	20%	4%	**24%**
Massachusetts	48	84	50-60 Gy LDR	NR	NR	6%	**50%**
Örebro*	50	86	50 Gy PDR	8%	10%	2%	**20%**
London Reg.	39	91	37.2 Gy HDR	5%	8%	0	**13%**
Erlangen	274	32	32 Gy HDR/49.8 Gy PDR	5%	0%	0	**5%**
Tufts/Brown I.*	33	33	34 Gy HDR	NR	24%	0	**24%**
Tufts/Brown II.	33	83	34 Gy HDR	NR	NR	NR	**52%**
			34 Gy HDR	5-40%	0-24%	**0-6%**	**5-57%**

*Including analysis of DVH parameters

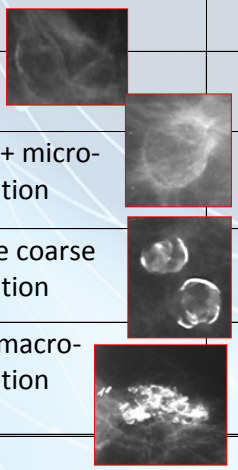
Substudy of Budapest Phase III PBI Study – Fat Necrosis After PBI vs. WBI: 4-Year Results of a Randomized Trial*

- Systematic review of all control mammography films
- Incidence of fat necrosis (crude and 4-year actuarial rates)
- Accompanying clinical symptoms
- Accompanying radiologic features
- Need for additional diagnostic procedures
- Risk factors for developing fat necrosis:
  - Radiation-related factors
  - Non-radiation-related factors

* Lövey K. et al: IJROBP 2007;69:724-731

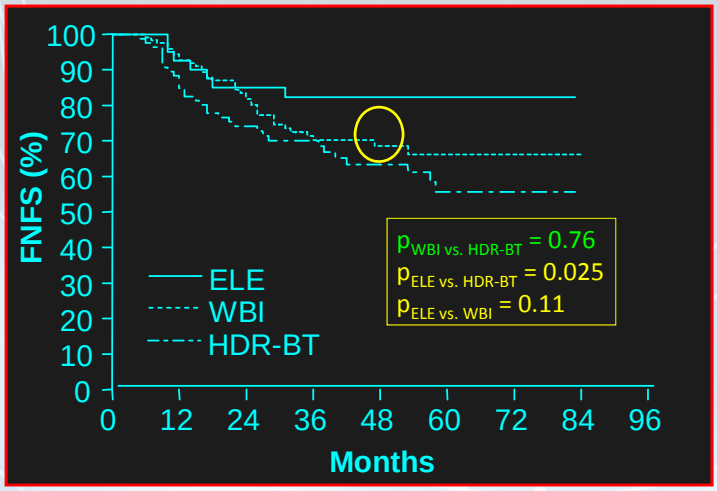
Crude Rate and Radiologic Features of Fat Necrosis by Treatment Arm

	PBI (n = 127)	WBI (n = 129)	All Patients (n = 256)
Crude rate of fat necrosis	**39 (31%)**	**37 (29%)**	**76 (30%)**
• Oil cyst	18 (46%)	13 (35%)	31 (41%)
• Oil cyst + micro-calcification	10 (26%)	11 (30%)	21 (28%)
• Ring-like coarse calcification	4 (10%)	4 (11%)	8 (11%)
• Benign macro-calcification	7 (18%)	9 (24%)	16 (21%)



P = N S

Probability of Fat Necrosis-Free Survival (FNFS) by Treatment



4-y actuarial rate of fat necrosis: WBI: 32% (n = 37 of 129)
HDR-BT: 36% (n = 32 of 87)
ELE: 18% (n = 7 of 40)

Crude Rate and Grade of Fat Necrosis by Treatment

Median FUP: 4 years

	WBI (n = 129)	HDR-BT (n = 87)	ELE (n = 40)
Any fat necrosis (G1-4)	37 (29%)	32 (37%)	7 (18%)
G1: Asymptomatic fat necrosis (radiologic/cytologic findings)	26 (20%)	22 (25%)	4 (10%)
G2-3: Symptomatic fat necrosis not requiring surgery (palpable mass with/without pain)	11 (9%)	9 (10%)	3 (8%)
G4: Fat necrosis requiring surgical intervention	0 (0%)	1 (1%)	0 (0%)

P = N S

Crude Rate and Grade of Fat Necrosis by Treatment

Median FUP: 6.8 years*

	WBI (n = 108)	HDR-BT (n = 87)	ELE (n = 39)
Any fat necrosis (G1-4)	55 (51%)	50 (57%)	11 (28%)
G1: Asymptomatic fat necrosis (radiologic/cytologic findings)	39 (36%)	35 (40%)	8 (20%)
G2-3: Symptomatic fat necrosis not requiring surgery (palpable mass with/without pain)	16 (15%)	14 (16%)	3 (8%)
G4: Fat necrosis requiring surgical intervention	0 (0%)	1 (1%)	0 (0%)

P = N S

*Unpublished data

Crude Rate and Grade of Fat Necrosis by Treatment

Median FUP: 10.2 years

	WBI (N = 117) n (%)	PBI-HDR BT (N = 86) n (%)	PBI – ELE (N = 40) n (%)	*P*-Value
Any fat necrosis	61 (52.1%)	51 (59.3%)	12 (30.0%)	HDR BT vs. WBI = NS HDR BT vs. ELE = 0.0019 ELE vs. WBI = 0.0119
Symptomatic fat necrosis requiring surgery	0 (0%)	1 (1.2%)	0 (0%)	HDR BT vs. WBI = NS HDR BT vs. ELE = NS ELE vs. WBI = NS

Possible Risk Factors for Developing Fat Necrosis – Non-Radiation-Related Factors (n = 256)

Patient age, menopausal status, adjuvant chemo- and hormonal therapy, tumor size and tissue volume excised by surgery had no impact on the incidence of fat necrosis!!

Bra Cup Size	Incidence of Fat Necrosis N (%)
A-B	26 of 145 (25%)
C-D	40 of 111 (36%)

P = 0.036

Bra Cup Size	WBI (n = 129)	HDR-BT (n = 87)	ELE (n = 40)
A-B	75 (58%)	41 (47%)	29 (73%)
C-D	54 (42%)	46 (53%)	11 (27%)

$p_{HDR-BT/ELE} = 0.006$
$p_{HDR-BT/WBI} = 0.07$
$p_{WBI/ELE} = 0.07$

Possible Risk Factors for Developing Fat Necrosis – Implant-Related Parameters (HDR-BT, n = 87)

Implant Parameter	Fat Necrosis (n = 32)	No Fat Necrosis (n = 55)
Median N° catheters (range)	9 (5-13)	9 (4-13)
Mean V100% (range)	63 cc (28-120)	63 cc (27-107)
Mean V150% (range)	25 cc (8-56)	24 cc (7-46)
Mean DHI* (range)	0.61 (0.37-0.78)	0.62 (0.45-0.79)

P = NS

* DHI = dose homogeneity index

Implant-Related Factors for Developing Fat Necrosis – Örebro University Hospital (PDR-BT, n = 51)*

Implant Parameter	Median	Range
N° catheters	12	4-18
V 100%	160 cc	53-300 cc
V 150%	31 cc	17-95 cc
V 200%	12 cc	6-28 cc
DHI	0.80	0.65-0.84

"No significant correlation between different dosimetric parameters and fat necrosis."

* Johansson et al.: Radiother. Oncol 2009;90:30-35

Implant-Related Factors for Developing Fat Necrosis – Tufts/Brown University (HDR-BT, n = 30)*

Implant Parameter	Fat Necrosis n = 8	No Fat Necrosis n = 22	*P*-Value
Mean N° catheters	18	15	NS
Mean V100%	234 cc	148 cc	0.03
Mean V150%	69 cc	36 cc	0.01
Mean V200%	21 cc	11 cc	0.01
Mean DHI	0.82	0.85	NS

* Wazer DE et al: IJROBP 2001;50:107-11

Implant-Related Factors for Developing Fat Necrosis – Tufts/Brown + Virginia University (HDR-BT, n = 75)*

Implant Parameter	Fat Necrosis n = 10	No Fat Necrosis n = 65	*P*-Value
Mean V100%	236 cc	185 cc	NS
Mean V150%	69 cc	44 cc	0.02
Mean V200%	22 cc	13 cc	0.01
Mean DHI	0.71	0.75	NS

* Wazer DE et al: IJROBP 2006;64:489-495

Implant-Related Factors for Developing Fat Necrosis – University Wisconsin-Madison (HDR-BT, n = 172)*

Implant Parameter	Fat Necrosis n = 25	No Fat Necrosis n = 147	*P*-Value
Median N° catheters	23	23	NS
PTV	168 cc	135 cc	0.006
Mean V100%	202 cc	184 cc	NS
Mean V150%	45 cc	41 cc	0.004
Mean V200%	16 cc	13 cc	0.001
Mean DHI	0.80	0.79	NS

* Christensen M. et al: ASTRO 2007

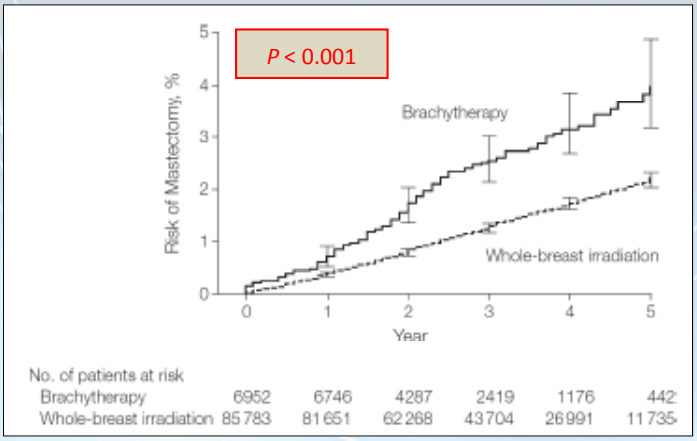
Conclusions on Fat Necrosis

- Asymptomatic fat necrosis is a common adverse event after breast-conserving therapy, having no significant clinical relevance in the majority of cases
- The incidence of fat necrosis is similar after accelerated partial breast HDR-BT and conventional WBI
- Routine FUP examinations (mammography, US, aspiration cytology; MRI) are sufficient for the differential diagnosis of fat necrosis
- Open surgical biopsy should be avoided when possible, because additional core biopsy and MRI are useful for differentiating fat necrosis from local recurrence

How to Prevent/Avoid Fat Necrosis

- Within the range of small-intermediate volume implants (up to 160 cc), neither implant volume (V100), nor volume of high-dose region (V150, V200), nor dose inhomogeneity (DHI) are associated with an increased risk of fat necrosis
- At large volume implants (>160 cc), larger high-dose regions are correlated with a higher incidence of fat necrosis
- The absolute volume of the high-dose region seems to be associated with the risk of fat necrosis
- Image-guided BT and 3D CT-planning are suggested
  - To minimize the overall volume of breast implants
  - To control the volume of "hot spots"

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



Mastectomy rate is significantly higher after balloon-based BT!

* Smith GL. et al: JAMA 2012;307:1827-1837

Crude LR and Subsequent Mastectomy Rates in the Budapest Phase III APBI Trial

Median FUP: 10.2 years

	WBI (N = 130) n (%)	PBI-HDR BT (N = 88) n (%)	PBI – ELE (N = 40) n (%)	*P*-Value
Local recurrence	6 (4.6%)	5 (5.7%)	2 (5.0%)	NS
Subsequent mastectomy	3 (2.3%)	1 (1.1%)	0 (0%)	NS

Mastectomy rate is definitely NOT higher after multicatheter BT!

No mastectomy was performed as a consequence of side effects!

Summary – Keystones of the Prevention of BT-Related Side Effects

For multicatheter BT:

- Limit the skin dose below 70% of the PD
- Avoid large volume implants (e.g., >160-200 cc)
- Limit dose non-uniformity ratio below 0.35
- Limit the volume of high-dose region as low as possible

For balloon-based BT:

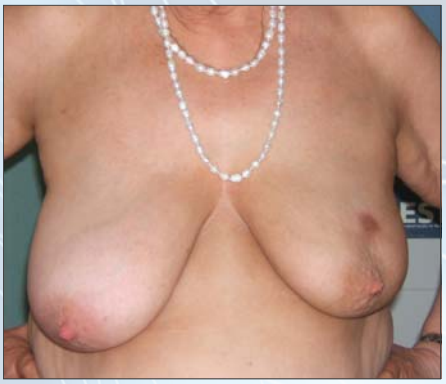
- A balloon-to-skin distance of at least 15 mm is advised

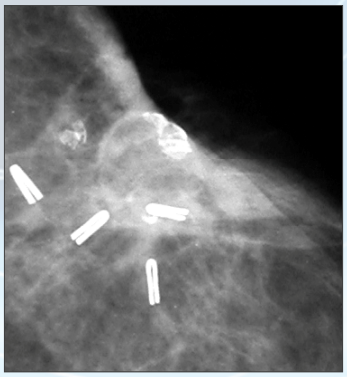
- **Conclusion:** Long-term results of multiple clinical trials prove that APBI with multicatheter BT is a safe alternative to WBI for low-risk breast cancer patients.

Case Report With Multiple Choice Question to the Audience

67-year-old patient with left-sided breast IDC underwent left BCS and APBI multicatheter BT in 2009

At 4-year FUP: painless palpable mass in the tumor bed with skin retraction and pigmentation





Case Report With Multiple Choice Question to the Audience

- What kind of diagnostic/therapeutic procedures are needed?

A) Nothing special, observation with annual FUP mammography
B) Diagnostic excision of the palpable mass
C) Aspiration cytology, if not conclusive breast MRI
D) Mastectomy
E) US-guided core-biopsy

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Thank you for your kind attention!