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# Neues zur lokoregionären Therapie

# Strahlentherapie

Dr. med. Kathrin Hering

Strahlentherapie Universität Leipzig

San Antonio Breast Cancer Symposium®, December 10-14, 2019

# Accelerated partial breast or whole breast irradiation after breast conservation surgery for patients with early breast cancer

# 10-year follow up results of the APBI IMRT Florence randomized phase 3 trial

**Icro Meattini**[1,2], Calogero Saieva[3], Sara Lucidi[1], Monica lo Russo[1], Vieri Scotti[2], Isacco Desideri[1,2], Livia Marrazzo[2], Gabriele Simontacchi[2], Monica Mangoni[1,2], Carlotta Becherini[1], Lisa Paoletti[4], Erika Moretti[5], Luca Triggiani[6], Marco Bernini[2], Lorenzo Orzalesi[1,2], Luis Sanchez[2], Jacopo Nori[2], Stefania Pallotta[1,2], Simonetta Bianchi[1,2], and Lorenzo Livi[1,2]

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# Deeskalation der adjuvanten Strahlentherapie!

# Hintergrund - Akzelerierte Teilbrustbestrahlung APBI

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- Welche Patientinnen?
- Welche Fraktionierung?
- Welche Technik?
- Welches Zielvolumen?

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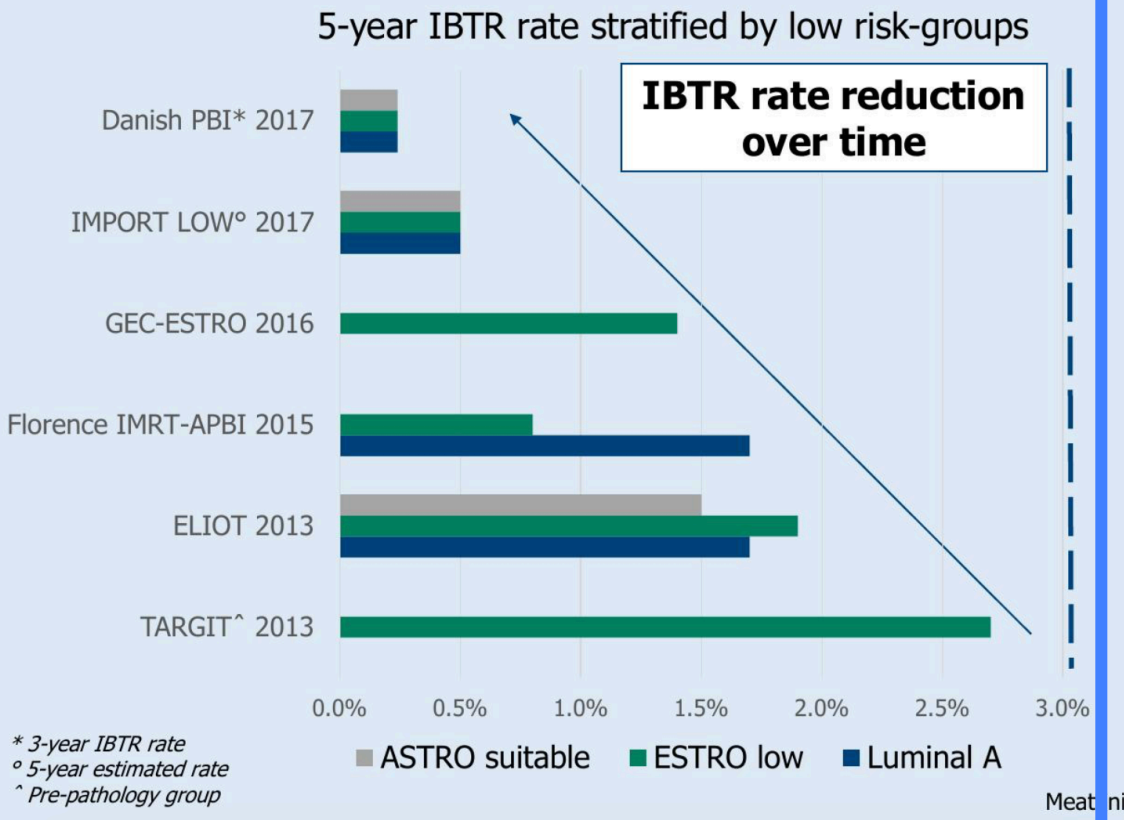
# Local relapse in low-risk patients – Selection of patients




Adapted from
Meattini I, et al. Breast 2018

**RAPID trial**
8-year IBTR
**3.0% vs 2.8%**

**NSABP B39/RTOG 0413 trial**
10-year IBTR
**4.6% vs 3.9%**

- Very low long-term IBTR rates
- Safety concerns on twice-daily schedule (RAPID)

Vicini F, et al. Lancet 2019
Whelan T, et al. Lancet 2019

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# Background

## ESTRO and ASTRO recommendation identified suitable patients for PBI outside clinical trials

| Patient Group | Risk Factor | 2009 | 2016 Update |
|---|---|---|---|
| ASTRO Suitable | Age | ≥60 | ≥50 |
| | Margins | ≥ 2 mm | ≥ 2 mm |
| | Nodal status | pN0 | pN0 |
| | T stage | T1 | Tis or T1 |
| | ER/PgR | Positive | |
| | DCIS<br>Lobular invasive | Not allowed<br>Not allowed | G1-2; ≤2.5 cm |

| Patient Group | Risk Factor | 2010 |
|---|---|---|
| ESTRO Low Risk | Age | ≥ 50 |
| | Margins | ≥ 2 mm |
| | Nodal status | pN0 |
| | T stage | T1-2 |
| | ER/PgR | Any |
| | DCIS<br>Lobular Invasive | Not allowed<br>Not allowed |

Polgar C, et al. R&O 2010
Smith BD, et al. IROBP 2009
Correa C, et al. PRO 2016

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# Akzelerierte Teilbrustbestrahlung APBI

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- Welche Patientinnen?
- Welche Fraktionierung?
- Welche Technik?
- Welches Zielvolumen?

# Technik und Fraktionierung APBI

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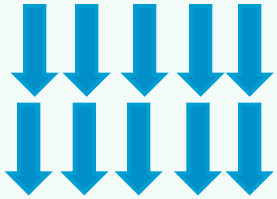
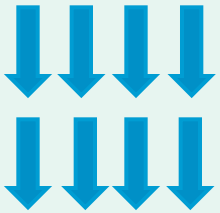
| Technik / (Studie) | Fraktionierung | Volumen | Toxizität |
|---|---|---|---|
| **Externe Radiatio**<br>Moderate Hypofraktionierung<br>Moderate Akzelerierung<br>**(UK-IMPORT-LOW; Coles 2017)** | <br>2,67 Gy - 40 Gy;<br>15 Fraktionen<br>3 Wochen | Tumorbett (Clips)<br>+ 15 mm<br>+ 10 mm | |
| **Externe Radiatio**<br>Starke Hypofraktionierung<br>Sehr starke Akzelerierung<br>**(RAPID-Studie; Whelan 2019)** |  <br>3,85 Gy - 38,5 Gy;<br>10 Fraktionen<br>1 Woche | Tumorbett (Clips)<br>+ 10mm<br>+ 10mm | |
| **Multikatheter Brachytherapie**<br>Starke Hypofraktionierung<br>Starke Akzelerierung<br>**(GEC-ESTRO-APBI-Studie; Strnad 2015)** |  <br>4 Gy - 32 Gy; 8 Fraktionen<br>4 Tage | Tumorbett (Clips)<br>+ individuell;<br>mind. 10mm | |
| **IORT**; Extreme Hypofraktionierung<br>Extreme Akzelerierung<br>**(TARGIT Vaidya 2014, ELIOT Veronesi 2013)** | <br>20 Gy; 1 Fraktion; 1 Tag | Tumorbett | |

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# Accelerated partial breast or whole breast irradiation after breast conservation surgery for patients with early breast cancer

## 10-year follow up results of the APBI IMRT Florence randomized phase 3 trial

**Icro Meattini**[1,2], Calogero Saieva[3], Sara Lucidi[1], Monica lo Russo[1], Vieri Scotti[2], Isacco Desideri[1,2], Livia Marrazzo[2], Gabriele Simontacchi[2], Monica Mangoni[1,2], Carlotta Becherini[1], Lisa Paoletti[4], Erika Moretti[5], Luca Triggiani[6], Marco Bernini[2], Lorenzo Orzalesi[1,2], Luis Sanchez[2], Jacopo Nori[2], Stefania Pallotta[1,2], Simonetta Bianchi[1,2], and Lorenzo Livi[1,2]

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UNIVERSITÀ DEGLI STUDI FIRENZE

FONDAZIONE FIRENZE RADIOTERAPIA ONCOLOGICA

Azienda Ospedaliero Universitaria Careggi

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# Trial design – APBI IMRT Florence *(NCT 02104895)*

**Einzeldosis 6 Gy; 10 Tage**

**Mo – Mi – Fr – Mo - Mi**

**Phase III trial**
**(n=520 patients)**

- Breast conserving surgery
- pT <25 mm
- Final surgical margins ≥5 mm
- Age >40 years

**APBI using IMRT**
30 Gy in 5#
non-consecutive

**1:1 randomization**

**CF-WBI**
50 Gy in 25#
+
10 Gy in 5# boost

**Follow Up**

**Primary endpoint**
- IBTR

**Secondary endpoints**
- Overall (OS) and breast cancer specific-survival (BCSS)
- Contralateral breast cancer (CBC)
- Early and late toxicity
- Physician-rated cosmesis

Livi L, et al. EJC 2015

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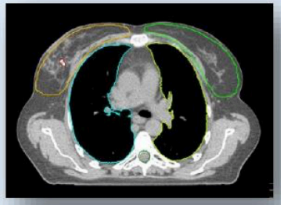
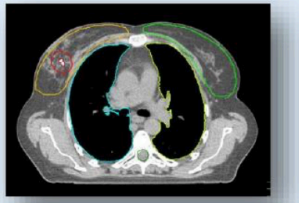
# APBI USING S&S IMRT TECHNIQUE

*Target Delineation and OARs dose thresholds*

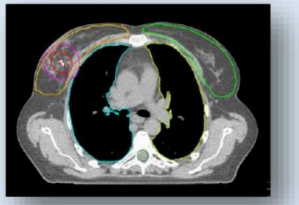
**Surgical Clips**
(4 mandatory)
CTV identification



**CTV**
Surgical Clips + 1 cm



**PTV**
CTV + 1 cm
limiting to 3 mm from skin and to 4 mm intrusion in homolateral lung



| OAR | Constraint |
|---|---|
| **Contralateral Lung** | V5 <10% |
| **Homolateral Lung** | V10 <20% |
| **Heart** | V3 <10% |
| **Homolateral breast** (uninvolved tissue) | V15 <50% |
| **Contralateral Breast** | Max 1 Gy in each point |

Livi L, et al. IJROBP 2010
Livi L, et al. EJC 2015

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# Patients features

| | APBI N (%) | WBI N (%) |
|---|---|---|
| **Age** | | |
| <50 | 41 (15.8) | 45 (17.3) |
| 51-59<br>60-69<br>≥70 | **84.2** | **82.7** |
| **Grade** | | |
| G1-2 | **90.0** | **87.3** |
| G3 | 26 (10) | 33 (12.7) |
| **pT stage** | | |
| pTis | 23 (8.8) | 32 (12.3) |
| pT1 | **85.8** | **81.9** |
| pT2 | 14 (5.4) | 15 (5.8) |
| **No. N+** | | |
| None | **89.2** | **81.9** |
| 1-3 | 19 (7.3) | 33 (12.7) |
| No ALDN | 9 (3.5) | 14 (5.4) |
| **ER status** | | |
| Positive | **95.4** | **95.8** |
| Negative | 12 (4.6) | 11 (4.2) |

| | APBI N (%) | WBI N (%) |
|---|---|---|
| **Ki67 index** | | |
| <20% | 193 (72.2) | 174 (72.2) |
| ≥20% | 50 (20.6) | 67 (27.8) |
| **Molecular Subtype** | | |
| Luminal A-like<br>Luminal B-like | **94.9** | **92.8** |
| HER2+ (non luminal) | 6 (2.8) | 13 (6.2) |
| Triple negative | 5 (2.3) | 2 (1) |
| **Systemic treatment** | | |
| None | **35.8** | **28.8** |
| Endocrine therapy (ET) only | 155 (59.6) | 162 (62.3) |
| Chemotherapy (CT) only | 5 (1.9) | 3 (1.2) |
| CT and ET | 7 (2.7) | 20 (7.7) |
| **Risk Class** | | |
| ASTRO Suitable | 133 (51.2) | 113 (43.5) |
| ASTRO Intermediate-Unsuitable | 127 (48.8) | 147 (56.5) |
| ESTRO Low Risk | 190 (73.1) | 166 (63.8) |
| ESTRO Medium-High Risk | 70 (26.9) | 94 (36.2) |

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# Results – 5- and 10-year

## 5- and 10-year event rate according to allocated group *(ITT population)*

| | | 5-year | | | | | 10-year | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | APBI | | WBI | | | APBI | | WBI | | |
| | Total° | N | % | N | % | P-value | N | % | N | % | P-value |
| **Ipsilateral breast tumour recurrence** | **17** | **6** | **2.4** | **3** | **1.2** | **0.31** | **9** | **3.3** | **6** | **2.6** | **0.39** |
| Local relapse | 10 | 3 | 1.2 | 3 | 1.2 | 0.99 | 5 | 2.2 | 4 | 1.8 | 0.69 |
| New ipsilateral breast cancer | 7 | 3 | 1.2 | 0 | - | 0.08 | 4 | 1.7 | 2 | 0.8 | 0.39 |
| **Locoregional tumour recurrence** | **19** | **6** | **2.4** | **4** | **1.6** | **0.52** | **9** | **3.9** | **7** | **3.0** | **0.56** |
| **Contralateral breast tumour** | **10** | **1** | **0.4** | **4** | **1.6** | **0.18** | **2** | **0.9** | **8** | **3.5** | **0.07** |
| **Distant metastasis** | **16** | **4** | **1.6** | **5** | **2.0** | **0.74** | **7** | **3.1** | **7** | **3.1** | **0.95** |
| **Deaths** | **40** | **5** | **2.0** | **8** | **3.1** | **0.41** | **15** | **7.3** | **16** | **6.7** | **0.97** |
| Breast cancer | 13 | 2 | 0.8 | 3 | 1.2 | 0.66 | 5 | 2.4 | 6 | 2.5 | 0.82 |
| Other cause | 27 | 3 | 1.2 | 5 | 1.9 | 0.48 | 10 | 4.3 | 10 | 5.0 | 0.90 |
| **Other primary tumour** | **13** | | | | | | **4** | **2.5** | **3** | **1.8** | **0.70** |

°at time of analysis

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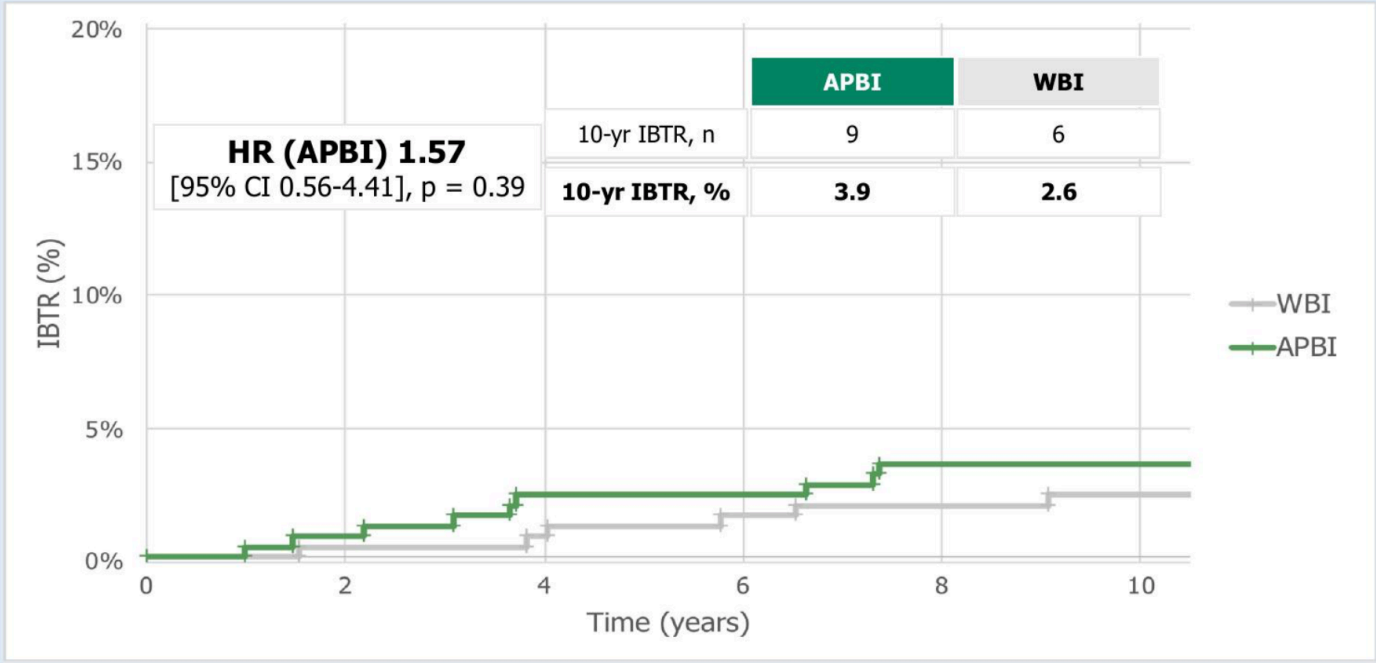
# Results – Ipsilateral Breast Tumour Recurrence

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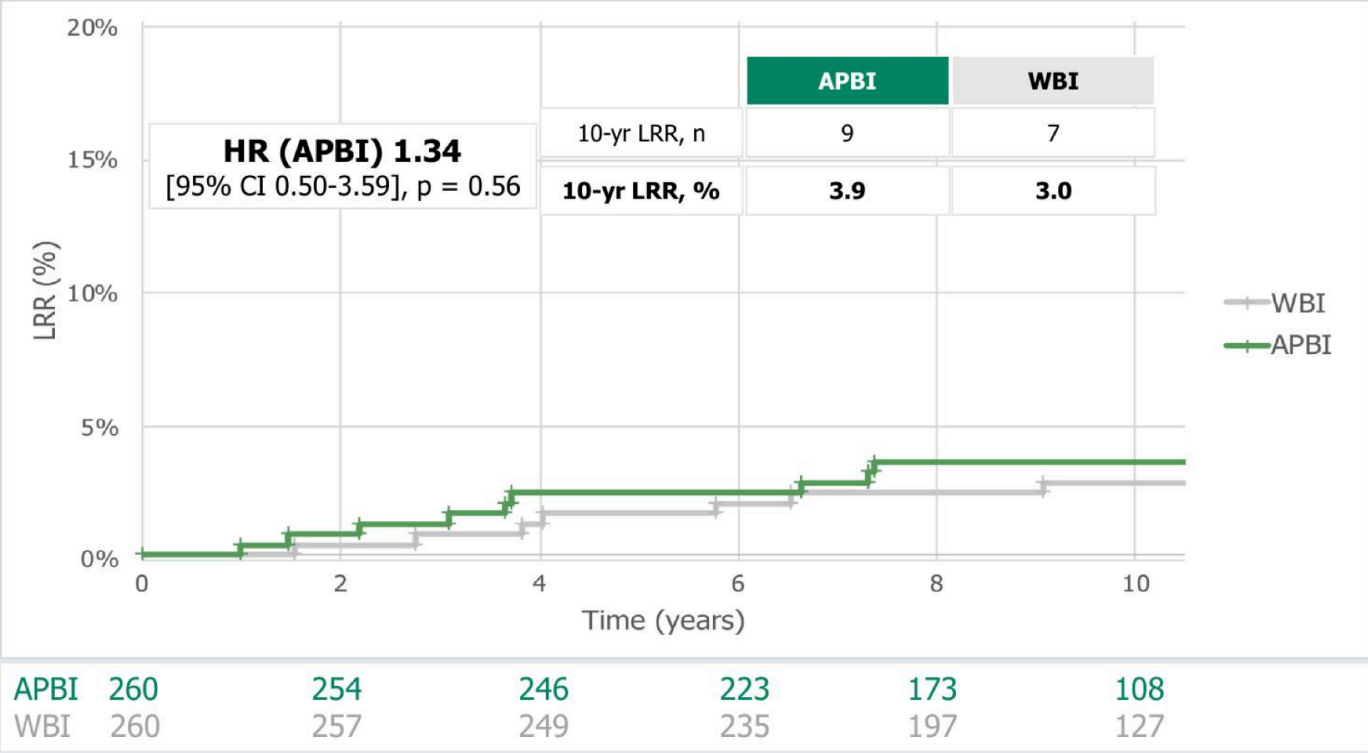
# Results – Locoregional Recurrence

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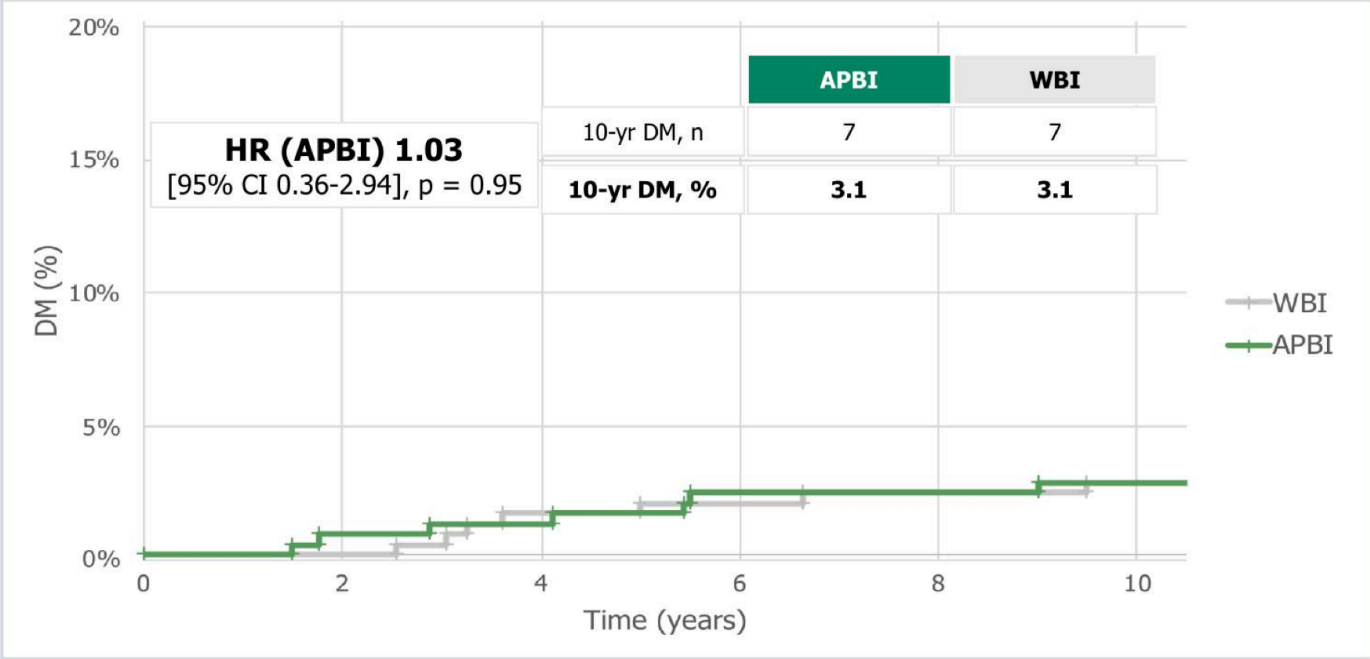
# Results – Distant Metastases

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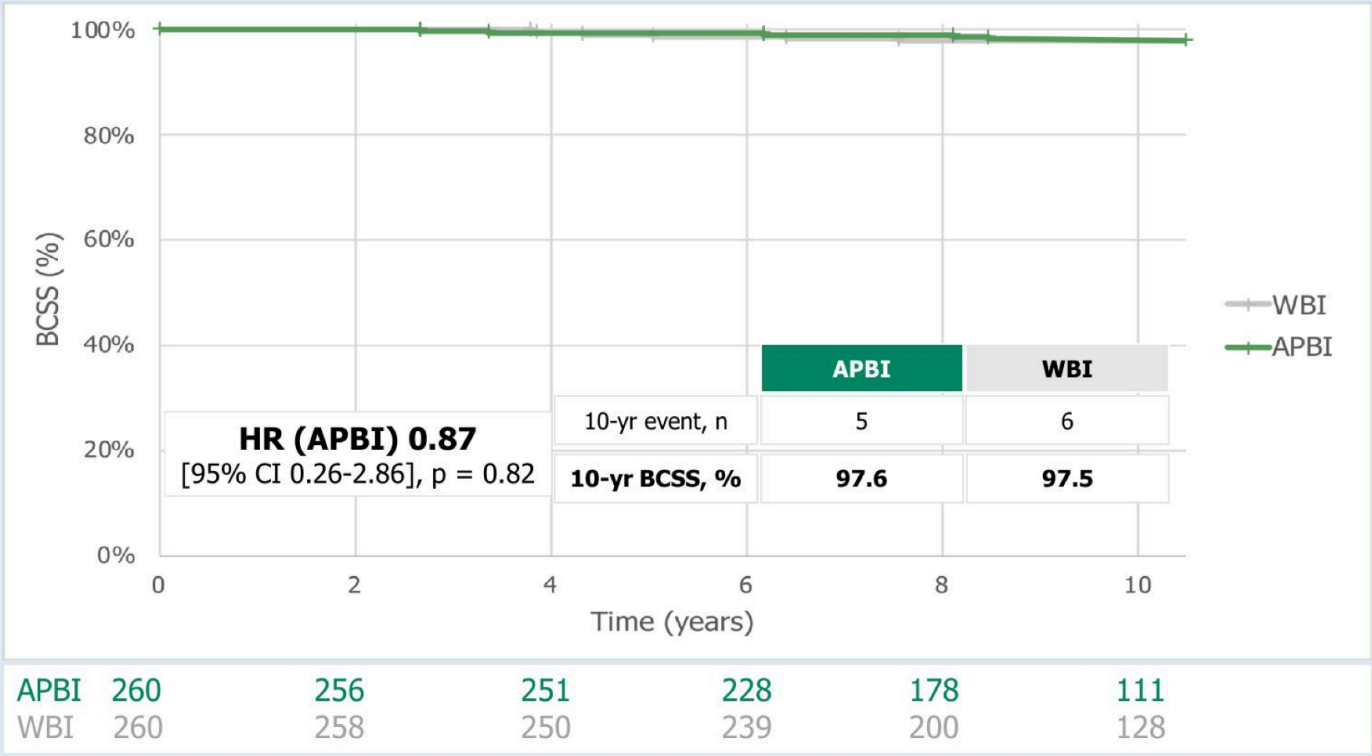
# Results – Breast Cancer Specific Survival




| | | | | | | |
|---|---|---|---|---|---|---|
| APBI | 260 | 256 | 251 | 228 | 178 | 111 |
| WBI | 260 | 258 | 250 | 239 | 200 | 128 |

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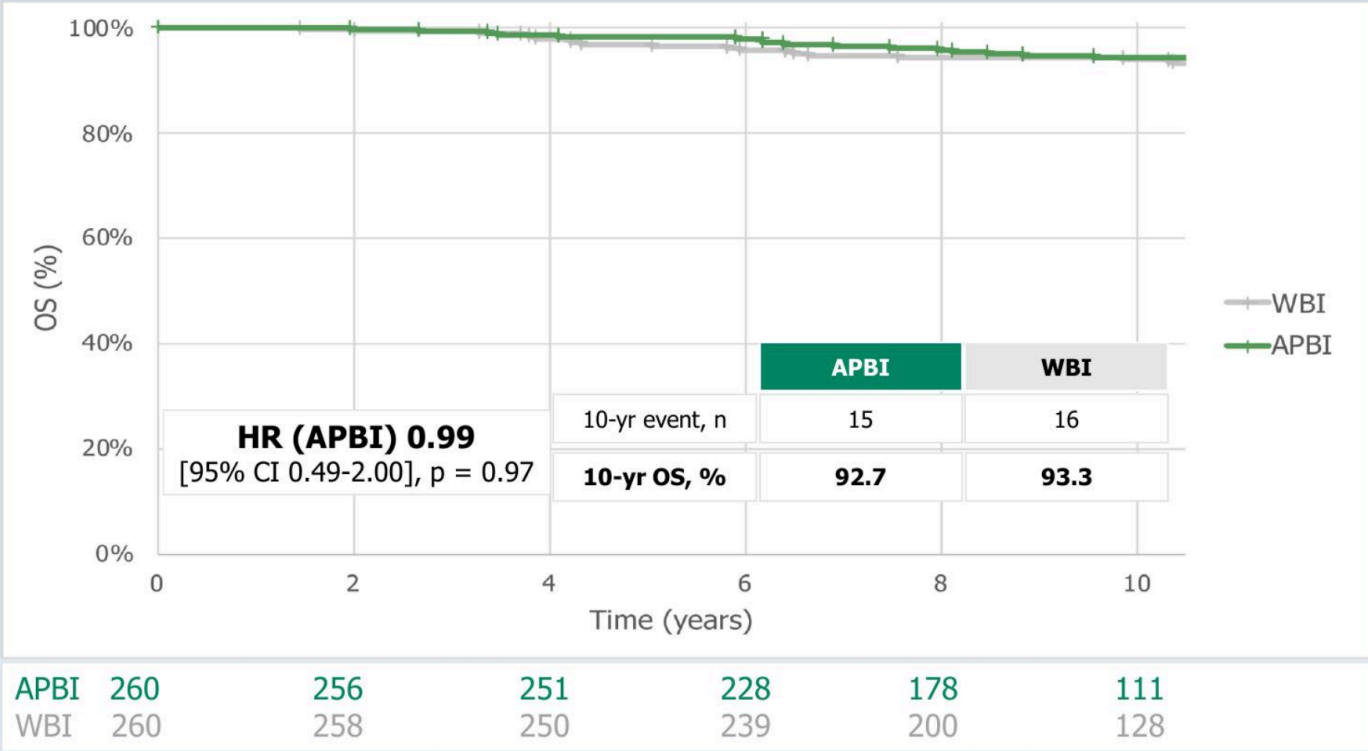
# Results – Overall Survival

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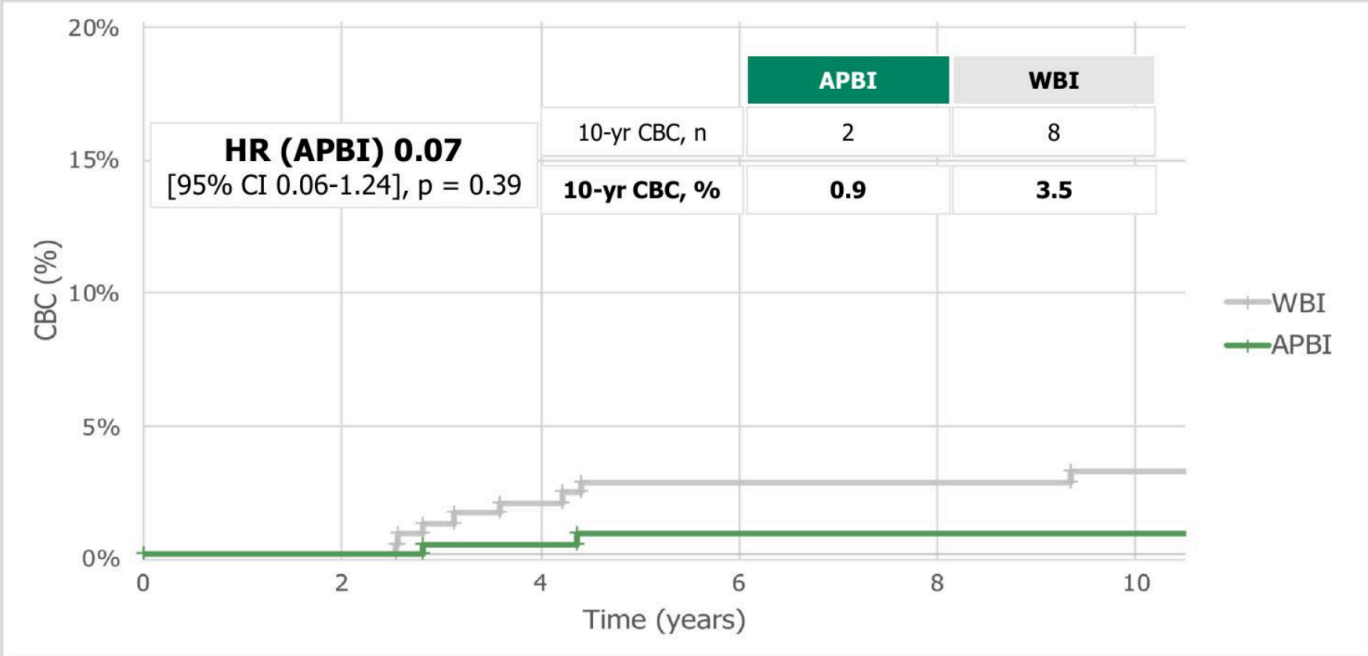
# Results – Contralateral Breast Cancer

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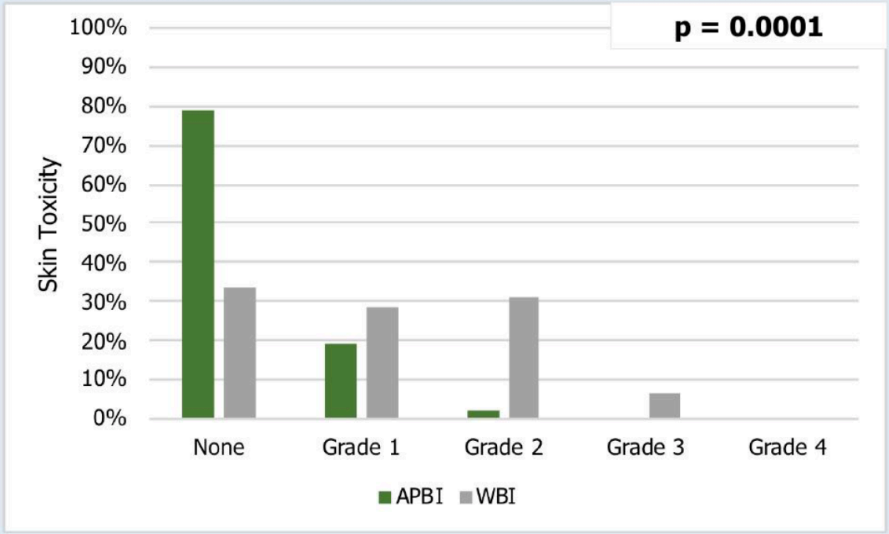
# Results - Acute Adverse Events

## RTOG & EORTC acute toxicity scale

| | APBI (n=246) N | % | WBI (n=274) N | % | p-value |
|---|---|---|---|---|---|
| **Any skin toxicity** | | | | | |
| None | 194 | 78.9 | 87 | 33.5 | |
| Yes, any Grade | 52 | 21.1 | 173 | 66.5 | **0.0001** |
| | | | | | |
| None | 194 | 78.9 | 87 | 33.5 | |
| Grade 1 | 47 | 19.1 | 75 | 28.8 | |
| Grade 2 | 5 | 2.0 | 81 | 31.2 | |
| Grade 3 | - | - | 17 | 6.5 | |
| Grade 4 | - | - | - | - | **0.0001** |
| | | | | | |
| Grade 0-1 | 241 | 98.0 | 162 | 62.3 | |
| Grade ≥2 | 5 | 2.0 | 98 | 37.7 | **0.0001** |

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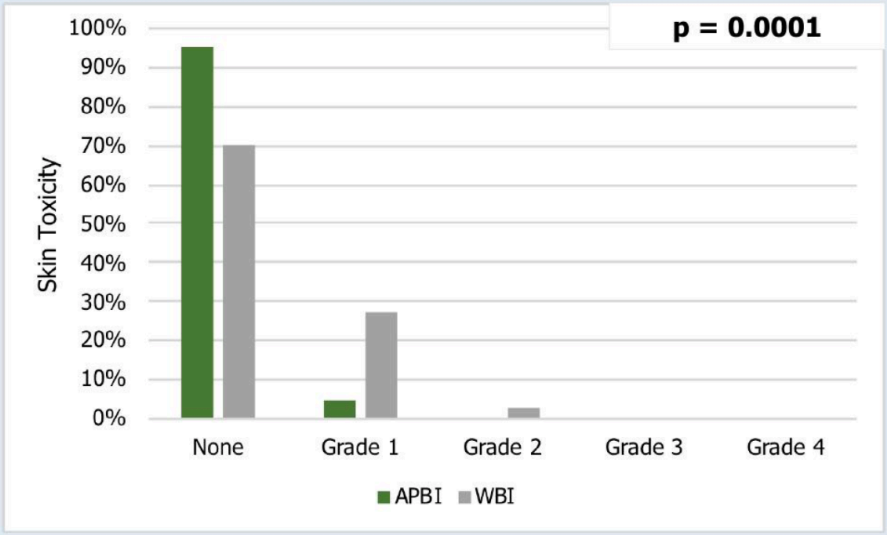
# Results - Late Adverse Events

## RTOG & EORTC late toxicity scale

| | APBI (n=246) N | APBI (n=246) % | WBI (n=274) N | WBI (n=274) % | p-value |
|---|---|---|---|---|---|
| **Any skin toxicity** | | | | | |
| None | 235 | 95.5 | 182 | 70.0 | |
| Yes, any Grade | 11 | 4.5 | 78 | 30.0 | **0.0001** |
| | | | | | |
| None | 235 | 95.5 | 182 | 70.0 | |
| Grade 1 | 11 | 4.5 | 71 | 27.3 | |
| Grade 2 | - | - | 7 | 2.7 | |
| Grade 3 | - | - | - | - | |
| Grade 4 | - | - | - | - | **0.0001** |
| | | | | | |
| Grade 0-1 | 246 | 100 | 253 | 97.3 | |
| Grade ≥2 | 0 | - | 7 | 2.7 | **0.015** |

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# Zusammenfassung

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- 10 Jahre nach Operation und Teilbrustbestrahlung sind die kumulativen **Inzidenzen von IBTR niedrig** (WBI 2,6 %; PBI 3,9%)
- Zwischen WBI und PBI gibt es **keinen signifikanten Unterschied** (LRR, DM, OS)
- Akute und **chronische Nebenwirkungen** niedriger bei PBI

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KLINIK UND POLIKLINIK FÜR FRAUENHEILKUNDE
in Zusammenarbeit mit dem St. Elisabeth-Krankenhaus Leipzig und dem Klinikum St. Georg

3. Leipziger Post-SABCS

Neues zur Behandlung des Mammakarzinoms

Mittwoch, 22. Januar 2020
16:30 – 20:00 Uhr

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# Was würden Sie ab morgen ändern?

## Bei selektionierten Patienten

## Teilbrustbestrahlung

## Gleiche Effektivität
## Reduktion Toxizität

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KLINIK UND POLIKLINIK FÜR FRAUENHEILKUNDE
in Zusammenarbeit mit dem St. Elisabeth-Krankenhaus Leipzig und dem Klinikum St. Georg

## 3. Leipziger Post-SABCS

Neues zur Behandlung des Mammakarzinoms

Mittwoch, 22. Januar 2020
16:30 – 20:00 Uhr

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# Vielen Dank!