MASTERCLASS: BRACHYTHERAPY in PARTIAL BREAST IRRADIATION
Euro-Asian Breast Brachytherapy School

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PERIOPERATIVE BRACHYTHERAPY IN BREAST CARCINOMA (P.O.B.T.)

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After breast conserving surgery, the problem is to localize the tumour bed...

...and to radiate the right margins
Limitations of CT images

- The main problem is to use an image technique (CT) to look for a tumour bed to be irradiated, when no GTV can be seen.
- There will always be differences between observers!!!
- Surgical scar is useful but what we see is only the manipulated area, not the tumour bed.
Limitations of CLIPS

- Clips are useful to know where the surgeon arrived, but they have no a clear correlation with the tumour margins
- There are “irrelevant clips”
- Displacement of the clips along time

Decrease in tumor bed volume as defined by clips. Hepel JT et al

Clips at the beginning of WBI  
Clips after WBI, for the boost
Limitations of endocavitary radiation

- Radiation is only given to the cavity
- No margin can be added
- The cavity is modified by the surgeon to create an sphere
- Skin and chest wall can receive a high dose
- Moreover, intraoperative irradiation misses information about margins
Definition of CTV and missed CTV

- CTV requires 15-20mm free from the tumour border.
- The ideal situation is a tumour in the centre of the lumpectomy but that does not usually happen.
- A safety margin is required, not only based on the cavity, but adding surgical margins and clinical assessment.
- The cavity is a reference to draw the CTV, not the CTV.

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Missed CTV

(Bartelink H. Radiat Oncol August 2012)
ADVANTAGES OF PERIOPERATIVE BRACHYTHERAPY (POBT)

- Precise placement of plastic tubes
- A single procedure and anaesthesia required
- It takes no more than 20-30 minutes.
- The implant can be done while waiting for the result of sentinel node.
- No interference with chemotherapy if needed
- Start at 3-5 days
- Treatment along 4-5 days
- Total treatment, surgery + radiation in <10-12 days.
PERIOPERATIVE BRACHYTHERAPY AS A BOOST
**Perioperative boost with LDR. Mansfield 1994**

655 patients T1-2N0 (1982-1992) 2 planes with 4-5 tubes separated 2cm
4-6 hours later, manual charge with **LDR 192-Ir 20 Gy**
After 10-14 days, EBRT WBI 45Gy
Local failure at 10 y: 369 margin-:7%, 97 margin+:14%, 189 margin?:18%
Acute complications: 11% Late complications: 3%

Perioperative boost with HDR brachytherapy. Results from IVO

- 24 patients with needles
- 4'7 Gy x2 + 46Gy WBI
- 9 involved margin
- 4 resection, 5 WBI 50Gy+6
- Median FU 117 m
- No local failure
- Actuarial local control at 10y 100%
- Cosmetic outcome excellent or good 66%

2005-2010, **100** patients.
The boost treatment was started on the 3rd postoperative day.
Dose: 15 Gy (3Gy x 6 fractions) over 3 days.
Three weeks later, WBI 50 Gy.
**No local recurrence** after median FU 52 months.
Acute toxicity 11 (9/11 breast size >1500 cc.): 4 wound complications, 7 G-III skin toxicity.
Good-excellent cosmesis 87%


**23** patients with high risk breast cancer
neoadjuvant chemotherapy and multifractionated perioperative BT boost
**No local recurrence** after FU of 43 months.
Cosmetic outcome excellent/good: **82.6%**, fair: 13%, poor: 4.4%.

Perioperative brachytherapy as a boost is very effective with low complications rate.
APBI
PERIOPERATIVE
BRACHYTHERAPY
AS SALVAGE
Second Conservative Treatment for Ipsilateral Breast Cancer Recurrence (IBCR): GEC-ESTRO Breast Cancer WG study

Actuarial 2\textsuperscript{nd} local recurrence rate

- @ 5 years: 5.6\% [1.5 - 9.5]
- @ 10 years: 7.2\% [2.1 - 12.1]

217 patients
9-2000/9-2010

Brachytherapy is useful. Better if perioperative?

At 2-3 days **5 fractions x 4.4Gy**, total 22 Gy. 15 patients
At 62 months no failures. 27% distant metastasis.
Excellent/good cosmetic outcome: 73% Asymptomatic fat necrosis: 9 (60%).
IVO Valencia. Salvage POBT 8x4Gy

1 month

4 months

16 months
APBI
PERIOPERATIVE
BRACHYTHERAPY AS
EXCLUSIVE TREATMENT
PROCEDURE OF POSTOPERATIVE BRACHYTHERAPY
Technique IVO: US-guided implant. Closed cavity
PROCEDURE OF PERIOPERATIVE BRACHYTHERAPY
Technique IVO: Perioperative implant. Closed cavity
Technique IVO: Planning CT scan 2-4 days later
• cut every plastic tube at an exact distance
• use the same distance for all tubes.
• Draw marks on the plastic tubes
Constraints:
- D90 > 4Gy
- DNR: <0.35 (V150/V100)
- Skin dose <70%
Relevance of clips placement

Irrelevant clip

Clip marking the bottom of the cavity
Cavities outside of the bed volume: irrelevant
In POBT with closed cavity technique, air cavities are not a reference to draw the CTV and are related to the surgical manipulation but not with the tumour bed.
A small area above the guide-tube was drawn with central clips if present.
A margin of 1.5-2cm was expanded
Avoid 1cm from skin and pectoral muscle.
The resulting volume was adjusted to cover the lateral plastic tubes with a margin of a few mm to obtain the CTV.
Prescription dose: 4 Gy to the CTV = PTV
eight fractions twice a day
PROBLEMS OF PERIOPERATIVE BRACHYTHERAPY (POBT)

- **TECHNICAL**: Small breasts with little tissue to be implanted
- **PATHOLOGIC**: Definitive pathological report delays several days
  - pN1
  - Margin can be involved
  - Risk factors can be present: LVI+, EIC+, Sentinel node +
    
    ...APBI unsuitable...

- **AVAILABILITY**: Centers without radiation facilities cannot use this technique because no radiation oncologist is available...
POSSIBLE SOLUTIONS

- Select cases with enough breast tissue.
- Perioperative biopsy of frozen margins.
- Sentinel lymph node with OSNA technique.
  - “One-step nucleic acid amplification” measures cytokeratin 19 (CK19) mRNA copy numbers in samples of SLN. \((N1_{mac}>5000\) copies\)
- Delay start of sessions until definitive pathological report (collaboration with pathologists)
- Consider brachy as a boost (only 3-4 sessions)
  - In cases with positive margin by DCIS, LVI+, EIC+
- Collaboration with surgeons
  - Technique of guide-tube
PERIOPERATIVE BRACHYTHERAPY WITH A GUIDE-TUBE
• The guide-tube marks the bottom of the surgical cavity
• The surgeon can learn how to insert the guide tube.
• The implant can be completed in other hospital days later.
• The implant will be completed when PR confirms indication.
Pacient with low risk invasive carcinoma

1. Sentinel node (OSNA)
2. Tumorectomy + shaving borders
3. Perioperative implant of 1-2 central needles at the bottom with opened cavity
4. Close cavity
5. Result of sentinel node
   1. If – or N1mic, complete the implant
   2. If +, remove the needles and complete axilar lymphadenectomy
6. At 2-3 days planning CT and dosimetry
7. At 3-4 days start BT at 4 Gy/fx
8. At 5-6 days (before 2 days after BT) pathological report
   a) If free margins, go on APBI
   b) If risk factors, finish with 3x4Gy and two weeks later WBI 2.67Gy x 16
   c) If one margin involved or <2mm finish with 4x4Gy plus WBI
   d) If several positive margins, 2nd surgery and removal of the implant.
Experience with Perioperative APBI with HDR

- Korea. 2000-2006, 48 patients. FU 53 months.
- The treatment was started on the 6-9th postoperative day
- Dose: 34Gy (3.4Gy x 10 fractions)
- 4-6 needles (17p. a single plane) clips Xray
- Two local recurrence at 33 and 40 months.
- DCIS and IDC, both close margin <2mm.
- Good-excellent cosmesis 90%
- Patients with close margin should not be implanted


- 202 patients 46 perioperative. FU 64 months
- Dose: 34Gy (3.4Gy x 10 fractions)
- Five local recurrence (1true 4 elsewhere)
- 5-year local recurrence rate 3%.

Experience with Perioperative APBI with HDR

- February 2003 and January 2010,
- **238** treated breasts
- **Mean V100 239cc**  mean V150 47.5cc
- mean DHI 0.80

- **Fat necrosis**
  - with V150 <65 cc was 15.4%,
  - with V150 =>65 cc was 38.5% (p = 0.011)
- In multivariate analysis, only V150 was significant.
- At 3 years, patients with fat necrosis were more likely to have a fair or poor cosmetic outcome and a larger percentage breast retraction assessment.

The 5-year actuarial rate of fat necrosis was 17.5%

Experience with Perioperative APBI with HDR

- Nice (France) 2005-2013, 70 elder patients. FU 61 months.
- **65 perioperative**
- The treatment was started on the 12th postoperative day
- Dose: 34Gy (3.4Gy x 10 fractions)
- 8 (5-16) needles clips CT

- **One local recurrence.** LRFS 98.1%
- Good-excellent cosmesis **95.7%**
- **Mean V100:** 76.4cc
- **Mean V150:** 36.3cc
- **DHI:** 52.8%

- DHI indicates that 47% of the volume received 150% of the prescribed dose, but the volume was small

**BE CAREFUL WITH THE VOLUME!!!**

Minimally Invasive Intraoperative Multicatheter Breast Implant (MIOMBI) in breast conservative surgery

Clinica Universitaria de Navarra (CUN). Pamplona. Spain

2007-2012, 87 BC patients evaluated for APBI.

Inclusion criteria:
- age > 40 y.o.
- unifocal tumour,
- invasive ductal or DCIS
- tumour size <3 cm
- No lymph node involvement

Operating time 123 min.
- No complications.
- 9 implanted catheters.

Mean age 59 years.
- Patients were discharged from hospital after 4 days.
- Tumour size 11 mm.
- 35 IDC and 13 DCIS.
- 44 adjuvant treatment.

Mean FU 22 months (43m)
- no local or distant recurrence.
- Cosmetic outcome good or excellent in 66% of cases.

Minimally Invasive Intraoperative Multicatheter Breast Implant (MIOMBI) in breast conservative surgery

- Treatment was completed in 48 patients and discarded in 39.

**Reasons to contraindicate exclusive APBI**

- Sentinel node positive 11
- EIC+ 10
- Positive or very close margin 5
- Technical problems 5
- Multicentrality 3
- Benign histology 2
- Invasive lobular carcinoma 1
- Bilateral tumour 1
- Pathological data of bad prognosis 1

Courtesy of Dra Natalia Rodríguez-Spiteri. Clinica Universitaria de Navarra (CUN). Spain
Courtesy of Dra Natalia Rodríguez-Spiteri. Clinica Universitaria de Navarra(CUN). Spain
• Clinica Universitaria de Navarra (CUN). Pamplona. Spain

• 101 perioperative implants
• procedure 25 minutes
• median number of catheter: 9 (4-14).
• When the definitive pathological report arrives, start APBI 3.4 Gy x 10 fractions
• If the patients had risk factors, then the implant is an anticipatory boost: 3.4 Gy x 4 in two days + WBI 39.9 Gy in 15 fractions.

• PHDRBT was delivered as APBI in 64 patients (60%) and as a boost in 34 (40%).
Minimally Invasive Intraoperative Multicatheter Breast Implant (MIOMBI) in breast conservative surgery

Clinica Universitaria de Navarra (CUN). Pamplona. Spain

• No intraoperative complications. bleeding: 1%, infection: 3%, fat necrosis with no symptoms 2%.

• Median CTV (clips zone + 2 cm) 41 cc
• Median D90: 3.27 Gy (96%)
• Median DHI: 0.76
• Median V100: 60 cc
• Median V150: 13 cc.

• no local failure at 22 months FU

• cosmetic outcome excellent 61%, good: 37%, fair: 2%.

LOW RISK CASES ARE NOT AS LOW AS WE THINK…

• In the study of Pamplona, 40% of the patients had risk factors, then the implant is a boost and HFX whole breast irradiation is added.

• The largest APBI trial with intra-beam, TARGIT, with more than three thousand cases, was updated at 5-year follow up at ESTRO-Vienna, and 20% of them need to add whole breast irradiation due to pathological risk factors.

• This proportion of not suitable cases for APBI in low risk women must be taken into account when intraoperative procedures are used.
Perioperative APBI with HDR. Dosimetric advantages

- Valencia (Spain) 2013-2015, **20 patients**. (59-87 y.o.)
- perioperative brachytherapy with negative sentinel node (OSNA)
- Two salvage treatment (previous irradiation)
- Dose: 32Gy (4Gy x 8 fractions)
- 12 (9-15) needles clips CT

- **Mean CTV volume**: 83.9cc (67.7-116.6cc).
- **Mean dose non-uniformity ratio (DNR)**: 0.32 (0.28-0.35)
- Mean dose homogeneity index (DHI): 0.68

- **Mean dose to the 90% of the CTV (D90)**: 4'04Gy.

- Three cases with DCIS in the margin, received 4 fractions and completed EBRT on the whole breast.
- The treatment finished on the 8th postoperative day (6-9)

Dose to lung and heart at 4 Gy per fraction. Maximum dose to heart is minimal, and maximum dose to lung is far less than tangential beams.
Dose to lung and heart with standard tangential beams, 2 Gy per fraction. A small part of the heart and a significant part of the lung volume receive the whole prescribed dose.
## Dose to OAR. Comparison of techniques

<table>
<thead>
<tr>
<th></th>
<th>Dose per fraction</th>
<th>Number of fractions</th>
<th>Total time days</th>
<th>Mean dose to lung</th>
<th>Maximum dose to lung</th>
<th>Maximum dose to heart</th>
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<tbody>
<tr>
<td><strong>Standard EBRT</strong></td>
<td>2Gy</td>
<td>25</td>
<td>33-35</td>
<td>11.4Gy</td>
<td>51.75 Gy</td>
<td>49.75Gy</td>
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<tr>
<td><strong>Hypofractionated EBRT</strong></td>
<td>2.67Gy</td>
<td>16</td>
<td>22</td>
<td>6.41Gy</td>
<td>43.7Gy</td>
<td>42Gy</td>
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<td><strong>POBT APBI</strong></td>
<td>4Gy</td>
<td>8</td>
<td>4-5</td>
<td>1.2Gy</td>
<td>14Gy</td>
<td>8Gy</td>
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CONCLUSIONS

• Interstitial POBT is an optimal treatment to radiate the bed tumour in breast carcinoma
• A close collaboration with surgeons is required
• The technique is simple
• Pathological report as soon as possible
• It is a multi-disciplinary procedure
• The total treatment duration can be shortened to less than 10 days.
• Dose to organs at risk decreases dramatically
• Pay attention to risk factors
Thank you for your attention