**Supplementary Table 1: side effects, especially wound healing disorders after preoperative radiotherapy**

| **Author** | **Year of publication** | **Journal** | **Number of patients** | **RT Technique/ dose/ fractions** | **Surgical procedure** | **Simultaneous Chemotherapy** | **time interval between end of neoadjuvant therapy and surgery** | **Acute toxicity (up to three months after surgery) + Subacute toxicity (three months until one year after surgery)** | **Late toxicity (from one years after surgery)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
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| Gerlach et al. [1] | 2003 | Strahlentherapie und Onkologie | n=134: CT (chemotherapy)-PRT (preoperative radiotherapy)  n=194 with 198 biopsy-proven invasive breast tumors, n=64 (CT)-group and adjuvant radiotherapy | PRT:  50 Gy/ Gy SD  whole breast external irradiation, boost of 6-11 Gy, all but n=5 electron boost, ipsilateral internal mammary lymph nodes irradiated in 9 patients, supraclavicular fossa irradiated: 50 Gy in n=137 | Type of surgery : tumorectomy,tumorectomy+LAT flap, MRM, MRM+TRAM flap  LAT=latissimus dorsi myocutaneous flap TRAM=trans-rectus abdominis myocutaneous flap MRM=modified radical mastectomy | n=2 in this group received preoperative chemo-and radiotherapy simultaneously | PRT group: 3 to 38 weeks (median 16 weeks)  CT and adjuvant radiotherapy group: 4 to 24 weeks (median 8 weeks) | In one case necrosis of a myocutaneous flap after preoperative chemo-and radiotherapy occurred | See below [2] |
| Matuschek et al [2] | 2019 | Strahlentherapie und Onkologie | n=315 LABC receiving PRT (study group partially [1]).  After a median follow-up of 17.7 years (14-21 years) n=203 were alive. n=107 were investigated in the follow up (n=64 after BCS and 43 after ME) | Preoperative RT: external-beam RT of 50 Gy/2 Gy SD to the breast and the supra-/ infraclavicular lymph nodes,  N=101 patients: interstitial boost of 10 Gy | ME (+/- reconstruction) and in 50.8% BCS with a tumor-specific immediate reconstruction.  n=1 refused surgery after complete response. | simultaneously in 113 patients | 2-11 months (median 4.5 months) | [1] | **No grade III and IV** late side effects were detected.  Grade II: BCS:  pigmentation change °II: 2%, teleangiectasia° II: 7%  Grad: II: ME:  Pigmentation change°II: 6,3%, teleangiectasia°II: 6.3% |
| Calitchi et al. [3] | 2001 | Int. J. Cancer | n=74 | external beam irradiation with cobalt or 4 MV accelerator, 45 Gy in 5 weeks to  -chest wall -lower axillary lymph nodes and internal mammay nodes  -boost of 15 Gy to internal mammary nodes, using direct 10 MeV electron beam -after tumorectomy postoperative boost of 20 Gy using iridium-192 low dose rate (LDR)-afterloading interstitial techniques | n=72 (96%):secondary tumorectomy,  n=3 (4%): reduction mammaplasty, secondary tumorectomy followed by postoperative boost of 20 Gy (range 15 to 25 Gy), axillary lymph node dissection in 50 cases (67%) | n=0 patients received neoadjuvant CT | NR | none | **Late complications:**  -n= 2 (3%) of lymphoedema -n=2 **fibrosis** (3%) -no radiation-induced malignancy  -no cardiac complications |
| Bollet et al. [4] | 2012 | Radiotherapy and Oncology | n=59 | PRT (cobalt-60 or 4-6 MV) -RT 50 Gy to whole breast -internal mammary chain (combination of photons and electrons) and supra/infra-clavicular areas irradiated to 46 Gy in 23 daily fractions and 4.6 weeks | tumorectomy or modified radical mastectomy, axillary lymph node dissection of the first 2 levels | yes | minimal 6 weeks after PRT | Acute toxicities: -n=5: wound infections after tumorectomy, n=2: surgical drainage -n=2 voluminous hematoma after tumorectomy, n=1 surgical drainage | Late toxicities with median follow-up of 7 years -n= 4 (8%) at least one grade III toxicity (1 telangectasia and 3 fibrosis)  -n=16 (31%) at least one grade II (11 fibrosis, 10 telangectasia, one lymphoedema, and one dyspnea) |
| Baltodano et al. [5] | 2017 | Plast Reconstr Surg Glob Open | n=341 (data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQUP) 2005-2011 containing n=77,902 data sets | NR | **PRT:**  ME-only: n=266  ME+immediate breast reconstruction: n=75  **No PRT:**  ME-only: n=61039 (78,4%)  ME+immediate breast reconstruction: n=16863 (21,6%) | NR | NR | **surgical site morbidity:**  ME-only group:  PRT: n= 12 (4.5%)vs. n= 1.637 (2.7%) not receiving PRT  Immediate Reconstruction Group (Mastectomy with Concurrent Reconstruction) :  PRT: n=4 (5.3%) vs. n=895 (5,3%) with no PRT  **Systemic Morbidity**  **Mastectomy-only Group** (**No Reconstruction**)  PRT: n=17 (6.4%) vs. n=5.469 (9.0%) with no PRT  Immediate Reconstruction Group (Mastectomy with Concurrent Reconstruction) :  PRT: n= 8 (10.7%) vs. n=1.463 (8.7%) with no PRT  **Overall morbidity:**  Mastectomy-only Group:  PRT: n= 25 (9.4%) vs. n=6711 (11,1%) with no PRT  Immediate Reconstruction Group (Mastectomy with concurrent Reconstruction):  PRT: n=11 (14.7%) vs. 1.873 (11.2%) with no PRT  **Conclusion: PRT is not significantly correlated with higher postoperative 30-day morbidity** | NR |
| Brooks et al. [6] | 2011 | The Breast Journal | n= 560  RT: n=97 (13%)  PRT: n=27 (partial ME+RT defined as PRT | NR | PRT: NR  n= 385: unilateral, n=174 bilateral tissue expander/ implant reconstructions | NR | NR.  The PRT-group is defined by former irradiation after partial mastectomy. The surgical procedure is performed after recurrence | Patients with RT: total complication rate: 58.8% and major complication rate 45.4%  Patients with no PRT : 27.6% complications, 21.2% major complication rate  PRT: is not analyzed | |
| Nahabedian et al. [7] | 2003 | Plastic and Reconstructive Surgery | n=130  RT: n=23 (13,7%),  PRT: before implant reconstruction: n=13 (57%)  Adjuvant RT: after implant reconstruction: n=10 (43%) | NR | n=168 breast reconstructions in n=130  PRT: NR | NR | NR | Infectious complications: n=10/130 (7.7%)  PRT: n=1 (7,7%) infected of total implants (n=13) | |
| Colwell et al. [8] | 2011 | Plastic and Reconstructive Surgery | n=211  RT: n=51  PRT: n=33  Adjuvant RT: n=18 | NR | n=331 direct-to-implant reconstructions  120 bilateral, 91 unilateral procedures | NR | NR | All patients:10 infections (3.0%), 5 seromas (1.5%), 4 hematomas (1.2%)  9.1%, skin necrosis leading to 5 implant losses (1.5%)  Early complication rate in PRT: Single-Stage: 24,2%, Two-Stage: 41,1%.  Postoperative RT: Single-Stage: 16,7%, Two-Stage: 23%  Conclusion: highest complication rate in PRT and Two-Stage reconstruction | PRT: NR |
| Sbitany [9] | 2014 | Plastic and Reconstructive Surgery | n=580: 903 breast reconstructions following total skin-sparing mastectomy  Cohort 1: total SSM and reconstruction with no RT  n=727 breasts  Cohort 2: prior history of radiation before SSM and reconstruction  n=63 breasts  Cohort 3:  Adjuvant RT  n=113 breasts | PRT: NR  Adjuvant RT to fully inflated tissue expander, before expander-implant exchange | Immediate breast reconstruction with tissue expander placement | Cohort 1: Neoadjuvant CTX: n=226 (31.1%), adjuvant CTX: n=113 (15.5%)  Cohort 2: neoadjuvant n=13 (20.6%), adjuvant n=9 (14.3%)  Cohort 3: n=83 neoadjuvant CTX (73.5%), n=28 adjuvant CTX (24.8%) | NR | Cohort 1: 20 Hematoma (2.8%), 36 seroma (5.0%), 95 infections requiring PO antibiotics (13.1%), 53 infections requiring IV antibiotics (7.3%), 24 infections requiring procedure (3.3%), 3 partial nipple necrosis (0.4%), 6 complete nipple necrosis (0.8%), 12 partial-thickness skin necrosis (1.7%), 27 full-thickness necrosis (3.7%), 23 incisional breakdowns (7.2%), 33 expander/ implant exposure (4.5%), 37 expander/ implant removal (5.1%)  Cohort 2: 0 hematoma (0%), 7 seroma (11.1%), 17 infections requiring PO antibiotics (27.0%), 13 infections requiring IV antibiotics (20.6%), 6 infections requiring procedure (9.5%), 1 partial nipple necrosis (1.6%), 1 complete nipple necrosis (1.6%), 2 partial-thickness skin necrosis (3.2%), 5 full-thickness necrosis (7.9%), 6 incisional breakdowns (24.0%), 7 expander/ implant exposure (11.1%), 13 expander/ implant removal (20.6%)  Cohort 3: 3 hematoma (2.7%), 7 seroma (6.2%), 30 infections requiring PO antibiotics (26.5%), 25 infections requiring IV antibiotics (22.1%), 7 infections requiring procedure (6.2%), 0 partial nipple necrosis (0%), 0 complete nipple necrosis (0%), 4 partial-thickness skin necrosis (3.5%), 13 full-thickness necrosis (11.5%), 2 incisional breakdowns (6.1%), 12 expander/ implant exposure (10.6%), 20 expander/ implant removal (17.7%)  Conclusion: Cohort 2 (PRT) had a higher complication rate | |
| Selber et al. [10] | 2006 | Annals of Plastic Surgery | n=500  n=100 adjuvant RT  PRT: NR | NR | n= 500 TRAM flap reconstruction, n=69 had bilateral free flap reconstructions | NR | NR | -overall complication rate: 20.9% (119)  -fat necrosis in 3.3% (19 ) of patients -neuroma in 1.9% (11 patients) -partial flap loss in 1.6% (9)  -abdominal hernia in 1.9% (11)  -total flap loss in 0.3% (2)  -wound infection in 3.5% (20) -abdominal flap necrosis in 3.3% (19) -mastectomy flap necrosis in 3.0% (17)-seroma in 1.2% (7) -hematoma in 0.5% (3) -arterial thrombosis in 0.2% (1)  **Frequency of Flap Complications by Risk Factor Preoperative Radiation:** -Fat necrosis: 2 (0.4%) -Neuroma: 2 (0.4%)  -Lymphedema: 0 (0%) -Hernia: 2 (0.4%) -Free-flap necrosis: 0 (0%) -Wound infection: 1 (0.2%) -Abdominal-flap necrosis: 3 (0.6%) -Mastectomy-flap necrosis: 3 (0.6%) -Hematoma: 0 (0%)  -Seroma: 2 (0.4%) -Arterial thrombosis: 0 (0%)  Conclusion: Patients with PRT had more seromas (p=0,043) | NR |
| Reish et al. [11] | 2015 | Plastic and Reconstructive Surgery | n=605: immediate breast reconstructions,  n=517 no RT,  n=88 treated with RT:  n=43 PRT,  n= 45 adjuvant RT | irradiation of tissue expander (in 10 patients) or final silicone implant (in 35 patients) | nipple-sparing mastectomy and immediate reconstruction | adjuvant RT: neoadjuvant CT n= 10 adjuvant CT: n=35  PRT: NR | NR | Breast Reconstructions with PRT vs. no Radiation Therapy:  Infection: 3 (7.0%) vs. 15 (2.9%) p=0,153  Hematoma: 1 (2.3%) vs. 9 (1.7%), p=0,533  Seroma: 0 (0.0%) vs. 9 (1.7%), p=1  PRT or adjuvant RT vs.  no RT  Infection:  6 (6,8%) vs. 15 (2,0%), p=0,064  Hematoma:  1 (1,1%) vs. 9 (1,7%), p=1  Seroma:  1 (1,1%) vs. 9 (1,7%), p=1 | Breast Reconstructions with PRT vs.no Radiation Therapy:  Nipple-areola complex necrosis:  3 (7.0%) vs. 20 (3.9%), p=0,409  Mastectomy skin flap necrosis:  4 (9.3%) vs. 28 (5.4%), p=0,296  Explant secondary to complications:  2 (4.7%) vs. 5 (1.0%), p=0,095  Malposition: 1 (2.3%) vs. 7 (1.4%), p=0,475  Oncologic margins: 1 (2.3%) vs. 15 (2.9%), P=1  Capsular contracture:  4 (9.3%) vs. 12 (2.3%), p=0,028  Fat grafting 11 (25.6%) vs. 20 (3.9%), p<0,001  PRT or adjuvant RT vs.  no RT  Nipple-areola complex necrosis:  4 (4.6%) vs. 20 (3.9%), p=0,767  Mastectomy skin flap necrosis:  7 (8%) vs. 28 (5.4%), p=0,346  Explant secondary to complications:  6 (6,8%) vs. 5 (1.0%), p=0,001  Nipple removal/Malposition: 1 (1,1,%) vs. 7 (1.4%), p=1  Oncologic margins: 4 (4,6%) vs. 15 (2.9%), P=0,503  Capsular contracture:  11 (12,5%) vs. 12 (2.3%), p<0,001  Fat grafting 12 (13.6%) vs. 20 (3.9%), p<0,001 |

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