Table 17: Studies included in the evidence review for radiotherapy to the internal mammary nodes

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Full citation Matzinger, O., Heimsoth, I., Poortmans, P., Collette, L., Struikmans, H., Van Den Bogaert, W., Fourquet, A., Bartelink, H., Ataman, F., Gulyban, A., Pierart, M., Van Tienhoven, G., Eortc Radiation Oncology, Breast Cancer, Groups, Toxicity at three years with and without irradiation of the internal mammary and medial supraclavicular lymph node chain in stage I to III breast cancer (EORTC trial 22922/10925), Acta oncologica, 49, 24-34, 2010 **Ref Id** 565843 **Country/ies where the study was carried out** Belgium, Netherlands, France, Germany, Switzerland, Poland, United Kingdom, Bosnia and Herzegovina, Italy, Portugal, Chile, Israel, Spain **Study type** RCT **Aim of the study**	**Sample size** 4004 patients randomised **Characteristics** Gender: 100% women Age: Median 54; range 19-75 Ethnicity: NR **Inclusion criteria** Unilateral, histologically confirmed adenocarcinoma (TX-T3, N0-N2, M0). Undergone mastectomy or breast-conserving treatment and axillary dissection. Centrally or medially located tumours could be N- or N+. Externally located tumours had to be N+ **Exclusion criteria** No additional criteria reported **Reported subgroups** None of interest	**Interventions** **Intervention arm:** radiation to internal mammary (IM) and medial supraclavicular (MS) lymph nodes **Control arm:** no radiation to IM and MS lymph nodes	**Details** **Intervention arm (IM RT+):** Prescribed radiotherapy dose was 50 Gy in 25 fractions of 2 Gy - 26 Gy delivered with photons and 24 Gy delivered with electrons. One anterior field for the IM-MS radiation was recommended. **Control arm (IM RT-):** no details reported.	**Results** **Treatment-related morbidity - lung toxicity (3 year follow-up):** IM RT+ 83/1922; IM RT- 26/1944 **Treatment-related morbidity - breast skin toxicity (3 year follow-up)** IM RT+ 262/1922; IM RT- 246/1944 **Treatment-related morbidity - mastitis (3 year follow-up)** IM RT+ 6/1922; IM RT- 7/1944 **Treatment-related morbidity - breast infection (3 year follow-up)** IM RT+ 3/1922; IM RT- 4/1944 **Treatment-related morbidity - radionecrosis (3 year follow-up)** IM RT+ 1/1922; IM RT- 2/1944	**Selection bias: random sequence generation** Not reported: Unclear **Selection bias: allocation concealment** Not reported: Unclear **Selection bias: overall judgement** Unclear **Performance bias** No blinding but unlikely to have a significant impact: Low **Detection bias** Low **Attrition bias** Complete follow-up data available for 95.3% of patients but unclear what percentage available in each arm: Unclear **Selective reporting** Low **Indirectness**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Trial aim: to investigated the potential survival benefit and toxicity of elective irradiation of the internal mammary and medial supraclavicular (IM-MS) nodes. Study aim: to examine toxicity up to three years after treatment. **Study dates** Recruited July 1996 to January 2004 **Source of funding** National Cancer Institute (Bethesda, Maryland, USA)				**Treatment-related morbidity - osteonecrosis (3 year follow-up)** IM RT+ 27/1922; IM RT- 22/1944 **Treatment-related morbidity - oedema (3 year follow-up)** IM RT+ 151/1922; IM RT- 155/1944 **Treatment-related morbidity - breast/chest wall pain (3 year follow-up)** IM RT+ 35/1922; IM RT- 45/1944 **Treatment-related morbidity - retrosternal pain (3 year follow-up)** IM RT+ 2/1922; IM RT- 1/1944 **Treatment-related morbidity - Dysphagia (3 year follow-up)** IM RT+ 4/1922; IM RT- 0/1944 **Treatment-related morbidity - Fatigue (3 year follow-up)** IM RT+ 22/1922; IM RT- 20/1944	None **Limitations** The protocol contained no guidelines which patients were to receive adjuvant treatment (hormonotherapy, chemotherapy). Unclear if rates were equivalent across arms. **Other information** EORTC trial 22922/10925

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
				Treatment-related morbidity - arm/shoulder function impairment (3 year follow-up) IM RT+ 1/1922; IM RT- 8/1944	
Full citation Hennequin, C., Bossard, N., Servagi-Vernat, S., Maingon, P., Dubois, J. B., Datchary, J., Carrie, C., Roullet, B., Suchaud, J. P., Teissier, E., Lucardi, A., Gerard, J. P., Belot, A., Iwaz, J., Ecochard, R., Romestaing, P., Ten-year survival results of a randomized trial of irradiation of internal mammary nodes after mastectomy.[Erratum appears in Int J Radiat Oncol Biol Phys. 2014 Aug 1;89(5):1145], International journal of radiation oncology, biology, physics, 86, 860-6, 2013 **Ref Id** 566242 **Country/ies where the study was carried out** France **Study type** RCT	**Sample size** 1407 patients randomised, 73 lost to follow-up at the beginning of the study, leaving 1334 for analysis. **Characteristics** Gender: 100% women Age: NR Ethnicity: NR **Inclusion criteria** Patients (aged <75) with stage I or II adenocarcinoma of the breast (tumour >1cm) that were undergoing modified radical mastectomy. Must have had positive axillary nodes or a medial/central tumour with or without axillary node involvement. 70% Karnofsky performance scale. **Exclusion criteria**	**Interventions** **Intervention arm:** radiotherapy to chest wall, supraclavicular nodes, apical axillary nodes for pN+ cases, and the internal mammary chain. **Control arm:** radiotherapy to the chest wall, supraclavicular nodes and apical axillary nodes for pN+ cases. No radiotherapy to internal mammary chain.	**Details** **Intervention arm (IM RT+):** Supraclavicular and apical axillary nodes were treated usually with a single-field dose calculated at a 3-cm depth. A posterior axillary field was used to obtain the reference dose at mid-depth. The prescribed dose to the target volume was 50 Gy or equivalent. All patients were treated in the supine position, with addition of wedges when necessary. The ipsilateral parasternal area, including the internal mammary chain, was treated using a combination of photons and electrons up to a total of 12.5 Gy, given in 5 fractions (2.5 Gy per fraction, 4 fractions per week), at a 3-cm depth, and 9-12 MeV electrons up to a total of 32.5 Gy, given in 13 fractions (2.5 Gy per fraction, 4 fractions per week) for a total treatment time of approximately 5	**Results** **DFS (10 year follow-up):** O-E: 12.25; V: 171.69 **OS (10 year follow-up):** O-E: 3.61; V: 203.07 **Treatment-related morbidity - GRADE 3+ on SOMA-LENT scale (10 year follow-up):** IM RT+ 21/672, IM RT- 15/662 **Treatment-related morbidity - cardiac events (10 year follow-up):** IM RT+ 15/672, IM RT- 11/662	**Selection bias: random sequence generation** Not reported: Unclear **Selection bias: allocation concealment** Assigned by coordinating centre: Low **Selection bias: overall judgement** Unclear **Performance bias** No blinding but unlikely to have a significant impact: Low **Detection bias** Low **Attrition bias** 73 lost to follow-up but treatment arm not reported so unclear if this differed between groups: Unclear

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Aim of the study To compare 10 year overall survival of patients who received IMN radiation after postmastectomy with that of patients who did not **Study dates** Recruited January 1991 to December 1997 **Source of funding** Ligue Nationale contre le Cancer and PARCC-ARA	Bilateral breast cancer, history of cancer or severe comorbidity or metastatic disease. **Reported subgroups** None of interest		weeks. The medial border was set on the midline and the lateral border was laid 6-cm lateral from the midline. The field was approximately 14 cm high in order to include the first 5 intercostal spaces. The lateral and superior edges of the IMN field were matched to the field irradiating the chest wall and the supraclavicular field. **Control arm (IM RT-):** Supraclavicular and apical axillary nodes were treated usually with a single-field dose calculated at a 3-cm depth. A posterior axillary field was used to obtain the reference dose at mid-depth. The prescribed dose to the target volume was 50 Gy or equivalent. All patients were treated in the supine position, with addition of wedges when necessary. The internal border of the chest wall field was placed at the external border of a sham internal mammary node field and care was taken to avoid inclusion of the first intercostal spaces in the supraclavicular field.		**Selective reporting** Low **Indirectness** None **Limitations** Risk of IMN involvement overestimated - probably decreased power. **Other information**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Full citation Poortmans, P. M., Collette, S., Kirkove, C., Van Limbergen, E., Budach, V., Struikmans, H., Collette, L., Fourquet, A., Maingon, P., Valli, M., De Winter, K., Marnitz, S., Barillot, I., Scandolaro, L., Vonk, E., Rodenhuis, C., Marsiglia, H., Weidner, N., van Tienhoven, G., Glanzmann, C., Kuten, A., Arriagada, R., Bartelink, H., Van den Bogaert, W., Eortc Radiation Oncology, Breast Cancer, Groups, Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer, New England Journal of MedicineN Engl J Med, 373, 317-27, 2015 **Ref Id** 566650 **Country/ies where the study was carried out** Belgium, Netherlands, France, Germany, Switzerland, Poland, United Kingdom, Bosnia and Herzegovina, Italy, Portugal, Chile, Israel, Spain **Study type** RCT **Aim of the study** To investigate the effect of elective internal mammary and	**Sample size** 4004 randomised **Characteristics** Gender: 100% women Age: Median 54, range 19-75 Ethnicity: NR **Inclusion criteria** Unilateral histologically confirmed breast adenocarcinoma of stage I, II, or III with a centrally or medially located primary tumour, irrespective of axillary involvement, or an externally located tumour with axillary involvement. Eligible patients had undergone mastectomy or breast conserving surgery and axillary dissection. **Exclusion criteria** No additional criteria reported **Reported subgroups** Extent of lymph node metastases (0 [N0], 1-3 [N1], 4+[N2/3]; T stage (1,2,3)	**Interventions** **Intervention arm:** whole breast/thoracic-wall radiation + radiation to internal mammary and medial supraclavicular lymph nodes **Control arm:** whole breast/thoracic-wall radiation only	**Details** **Intervention arm (IM RT+):** Regional nodal irradiation at a dose of 50 Gy in 25 fractions. No further information reported. **Control arm (IM RT-):** No details reported.	**Results** **Whole sample:** **DFS (10 year follow-up):** O-E: -35.96; V: 308.59 **Treatment-related morbidity - pulmonary fibrosis (10 year follow-up):** IM RT+ 85/1922; IM RT- 33/1944 **Treatment-related morbidity - cardiac fibrosis (10 year follow-up):** IM RT+ 23/1922; IM RT- 12/1944 **Treatment-related morbidity - cardiac disease (10 year follow-up):** IM RT+ 125/1922; IM RT- 109/1944 **Treatment-related morbidity - secondary cancer (10 year follow-up):** IM RT+ 191/1922; IM RT- 222/1944	**Selection bias: random sequence generation** Minimisation algorithm: Unclear **Selection bias: allocation concealment** Not reported: Unclear **Selection bias: overall judgement** Unclear **Performance bias** No blinding but unlikely to have significant impact: Low **Detection bias** Low **Attrition bias** 45 and 69 did not receive treatment per protocol in the IM RT- and IM RT+ arms, respectively: Unclear **Selective reporting** Low **Indirectness** None **Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
medial supraclavicular lymph-node irradiation (here termed regional nodal irradiation) on overall survival. **Study dates** Recruited July 1996 to January 2004 **Source of funding** Fonds Cancer				**OS (10 year follow-up):** O-E: -28.41; V: 204.02 **Extent of lymph node metastases: 0** **DFS (10 year follow-up):** O-E: -19.3; V: 115.1 **Extent of lymph node metastases: 1-3** **DFS (10 year follow-up):** O-E: -15.9; V: 135.2 **Extent of lymph node metastases: 4+** **DFS (10 year follow-up):** O-E: -1.17; V: 22.87 **T stage: 1** **DFS (10 year follow-up):** O-E: -10.5; V: 153.7	EORTC trial 22922/10925

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
				T stage: 2 **DFS (10 year follow-up):** O-E: 27.3; V: 143 **T stage: 3** **DFS (10 year follow-up):** O-E: -1.5; V: 14.5	
Full citation Whelan, T. J., Olivotto, I. A., Parulekar, W. R., Ackerman, I., Chua, B. H., Nabid, A., Vallis, K. A., White, J. R., Rousseau, P., Fortin, A., Pierce, L. J., Manchul, L., Chafe, S., Nolan, M. C., Craighead, P., Bowen, J., McCready, D. R., Pritchard, K. I., Gelmon, K., Murray, Y., Chapman, J. A., Chen, B. E., Levine, M. N., M. A. Study Investigators, Regional Nodal Irradiation in Early-Stage Breast Cancer, New England Journal of MedicineN Engl J Med, 373, 307-16, 2015 **Ref Id** 566692	**Sample size** 1832 recruited **Characteristics** Gender: 100% women Age: RT+ Median 54, range 29-84; RT- Median 53, range 26-84 Ethnicity: NR **Inclusion criteria** Women with invasive carcinoma of the breast who were treated with breast-conserving surgery and sentinel lymph node biopsy or axillary node dissection and had positive axillary lymph nodes or negative axillary lymph nodes with	**Interventions** **Intervention arm:** whole breast radiation + radiation to ipsilateral internal mammary, supraclavicular and axillary lymph nodes. **Control arm:** whole breast radiation only	**Details** **Intervention arm (IM RT+):** The breast was treated with a pair of opposed fields tangentially arranged across the chest - dose of 50Gy in 25 fractions. Radiation of the internal mammary nodes (50Gy in 25 fractions) was performed using a modified wide-tangent technique (upper tangents widened to include internal mammary nodes and narrowed inferiorly to reduce dose to heart and lung) or separate internal mammary node field plus tangents (mixed electron and photon field angled to match tangent fields). CT planning was recommended with internal mammary node defined as	**Results** **Whole sample:** **Locoregional recurrence (10 year follow-up):** O-E: -12.24; V: 23.20 **DFS (10 year follow-up):** O-E: -22.55; V: 82.18 **Treatment related morbidity - Grade 2+ fatigue (National Cancer Institute Common Toxicity Criteria; occurring within 3 months following completion of radiation):**	**Selection bias: random sequence generation** Centralized minimization procedure: Unclear **Selection bias: allocation concealment** Not reported: Unclear **Selection bias: overall judgement** Unclear **Performance bias** No blinding but unlikely to have a significant impact: Low **Detection bias** Low

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Country/ies where the study was carried out Canada, USA, Australia **Study type** RCT **Aim of the study** Whether the addition of regional nodal irradiation to whole-breast irradiation following breast-conserving surgery improved outcomes (primarily overall survival) **Study dates** Recruited March 2000 to February 2007 **Source of funding** Canadian Cancer Society Research Institute to the NCIC Clinical Trials Group (021039 and 015469), the Canadian Breast Cancer Research Initiative (010415), the U.S. National Cancer Institute (CA077202, CA32102, and CA27057) and the Cancer Council of Victoria, New South Wales, Queensland, and South Australia (288720).	high-risk features (tumour ≥5cm or ≥2cm with fewer than 10 axillary lymph nodes removed and at least one of the following: grade 3, ER-, or lymphovascular invasion). Level I or II axillary dissection was required for patients with positive SLNB. All patients received adjuvant systemic therapy (chemotherapy and/or endocrine therapy). **Exclusion criteria** Patients were excluded if they had T4 tumours (clinical evidence of direct extension to chest wall or skin) or N2–3 nodes (involvement of axillary nodes that are fixed or of internal mammary nodes), distant metastasis, or serious nonmalignant disease (e.g., cardiovascular or pulmonary) that would preclude definitive radiation therapy. Also excluded if currently pregnant or lactating, had concurrent or previous malignancies, psychiatric or addictive disorders which precluded obtaining informed consent or adherence to protocol, or inability to receive radiotherapy within 8 weeks of completing adjuvant chemotherapy or within 16		1cm around internal mammary vessels in the first three intercostal spaces to be covered by at least the 80% isodose. Supraclavicular and level III axillary nodes (extended to include level I and II nodes for patients who had fewer than 10 axillary nodes removed or more than 3 positive axillary nodes) were treated with a non-divergent anterior field to include the head of the clavicle medially and the coracoid process laterally (50 Gy in 25 fractions as depth of 3cm). For patients who were treated with anterior and posterior fields, a dose of 45Gy in 25 fractions was prescribed at midseparation at the centre of the fields. **Control arm (IM RT-):** the breast was treated with a pair of opposed fields tangentially arranged across the chest - dose of 50Gy in 25 fractions.	IM RT+ 170/893; IM RT- 169/927 **Treatment related morbidity - Grade 2+ pain (National Cancer Institute Common Toxicity Criteria; occurring within 3 months following completion of radiation):** IM RT+ 53/893; IM RT- 40/927 **Treatment related morbidity - Grade 2+ pneumonitis (National Cancer Institute Common Toxicity Criteria; occurring within 3 months following completion of radiation):** IM RT+ 11/893; IM RT- 2/927 **Treatment related morbidity - Grade 2+ radiation dermatitis (National Cancer Institute Common Toxicity Criteria; occurring within 3 months following completion of radiation):**	**Attrition bias** RT+ arm: loss to follow-up 21, withdrew consent 17; RT- arm: loss to follow-up 16, withdrew consent 18: Low **Selective reporting** Low **Indirectness** None **Limitations** Most of the included patients had no more than 3 positive lymph nodes. It is likely that patients with more than three nodes were routinely treated off trial with regional nodal irradiation, which would potentially decrease the probability of detecting a significant effect on overall survival in this trial. Also, since most patients were treated with multiagent chemotherapy containing anthracyclines or taxanes and endocrine therapy, the baseline risk of death and the power to detect a between-group improvement in overall survival were probably further reduced. **Other information** MA.20 trial

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
	weeks after the last surgical breast procedure for patients receiving endocrine therapy only. **Reported subgroups** Extent of lymph node metastases (0, 1-3, 4+); tumour position (medial, lateral)			IM RT+ 442/893; IM RT- 372/927 **Treatment related morbidity - Grade 2+ cardiac events (National Cancer Institute Common Toxicity Criteria; occurring greater than 3 months following completion of radiation):** IM RT+ 8/893; IM RT- 4/927 **Treatment related morbidity - Grade 2+ lymphoedema (National Cancer Institute Common Toxicity Criteria; occurring greater than 3 months following completion of radiation):** IM RT+ 75/893; IM RT- 42/927 **Treatment related morbidity - Grade 2+ pneumonitis or fibrosis (National Cancer Institute Common Toxicity Criteria; occurring greater than 3 months following completion of radiation):** IM RT+ 4/893; IM RT- 3/927	

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
				Treatment related morbidity - secondary cancer (National Cancer Institute Common Toxicity Criteria; occurring greater than 3 months following completion of radiation): IM RT+ 98/893; IM RT- 93/927 **OS (10 year follow-up):** O-E: -7.13; V: 75.64 **Extent of lymph node metastases: 0** **DFS (10 year follow-up):** O-E: -4.97; V: 8.32 **Extent of lymph node metastases: 1-3** **DFS (10 year follow-up):** O-E: -16.26; V: 68.98 **Extent of lymph node metastases: 4+**	

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
				DFS (10 year follow-up): O-E: -2.43; V: 7.10**-O** **Tumour location: medial** **DFS (10 year follow-up):** O-E: -6.50; V: 12.73 **Tumour location: lateral** **DFS (10 year follow-up):** O-E: -13.90; 53.17	
Full citation Choi, J., Kim, Y. B., Shin, K. H., Ahn, S. J., Lee, H. S., Park, W., Kim, S. S., Kim, J. H., Lee, K. C., Kim, D. W., Suh, H. S., Park, K. R., Shin, H. S., Suh, C. O., Radiation Pneumonitis in Association with Internal Mammary Node Irradiation in Breast Cancer Patients: An Ancillary Result from the KROG 08-06 Study, Journal of Breast CancerJ, 19, 275-282, 2016 **Ref Id** 566731	**Sample size** 747 recruited. 25 patients (3.3%) who had not undergone chest X-ray within 6 months of radiotherapy completion were excluded from the analysis, leaving 722 analysable patients. **Characteristics** Gender: NR Age: Median 48, range 28-77	**Interventions** **Intervention arm:** breast radiotherapy + supraclavicular and internal mammary lymph nodes **Control arm:** breast radiotherapy + supraclavicular lymph nodes	**Details** **Intervention arm (IM RT+):** Radiation was administered once per day at a dose of 1.8–2 Gy, up to a total dose of 45–50.4 Gy. The protocol contained no strict guidelines on radiotherapy technique - techniques determined at discretion of physician. Most common technique was partial wide tangent. **Control arm (IM RT-):** Radiation was administered once per day at a dose of	**Results** **Treatment-related morbidity - radiation pneumonitis within 6 months of completing radiotherapy:** RT+ 23/356; RT- 12/366	**Selection bias: random sequence generation** Not reported: Unclear **Selection bias: allocation concealment** Not reported: Unclear **Selection bias: overall judgement** Unclear **Performance bias** No blinding but unlikely to have a significant impact: Low

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Country/ies where the study was carried out Korea **Study type** RCT **Aim of the study** To investigate the effect of internal mammary node irradiation on disease-free survival and toxicity in breast cancer patients. **Study dates** Recruited November 2008 to February 2013 **Source of funding** National R&D Program for Cancer Control, Ministry for Health, Welfare, and Family Affairs, Republic of Korea (0820010)	Ethnicity: NR **Inclusion criteria** Eligible patients were pathologically confirmed to have axillary node-positive breast cancer after surgery (either modified radical mastectomy or breast-conserving surgery). All patients underwent axillary dissection in which eight or more lymph nodes were identified. **Exclusion criteria** Patients who received neoadjuvant systemic therapy or had a previous history of cancer or distant metastasis were excluded. **Reported subgroups** None of interest		1.8–2 Gy, up to a total dose of 45–50.4 Gy. The protocol contained no strict guidelines on radiotherapy technique - techniques determined at discretion of physician. Most common technique was standard tangent method.		**Detection bias** Low **Attrition bias** Not reported: Unclear **Selective reporting** Disease free survival not reported: Unclear **Indirectness** None **Limitations** One drawback of this study is that the chest X-ray follow-up visit could occur at any time within 6 months after RT. Considering that most radiologic changes in this study were found at 2 or 3 months after RT, the heterogeneity of the follow-up time among patients may have caused an underestimation of asymptomatic grade 1 RP. **Other information** KROG 08-06 trial
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Selection:**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Thorsen, L. B., Offersen, B. V., Dano, H., Berg, M., Jensen, I., Pedersen, A. N., Zimmermann, S. J., Brodersen, H. J., Overgaard, M., Overgaard, J., DBCG-IMN: A Population-Based Cohort Study on the Effect of Internal Mammary Node Irradiation in Early Node-Positive Breast Cancer, Journal of clinical oncology, 34, 314-20, 2016 **Ref Id** 566840 **Country/ies where the study was carried out** Denmark, Germany **Study type** Prospective, population-based, cohort study **Aim of the study** To investigate the effect of internal mammary node irradiation (IMNI) in patients with early stage node-positive breast cancer **Study dates**	3377 assessed for eligibility, 3089 patients included **Characteristics** Gender: NR Age: RT+ median 56, range 22-70; RT- median 56, range 27-70 Ethnicity: NR **Inclusion criteria** Patients treated with radiotherapy after surgery (mastectomy or breast-conserving surgery - including axillary lymph node dissection of axillary level I and part of level II) for unilateral, node-positive breast cancer. **Exclusion criteria** Patients who experienced recurrence before radiotherapy, were unfit for standard radiotherapy, only had micro-metastatic nodes, were older than 70 years of age at operation, or had prior malignancy were excluded. **Reported subgroups** None of interest	**Intervention arm:** radiotherapy to the breast/chest wall, scar, supraclavicular and infraclavicular nodes and axillary + internal mammary nodes **Control arm:** radiotherapy to the breast/chest wall, scar, supraclavicular and infraclavicular nodes and axillary.	**Intervention arm (IM RT+ [right sided cancers]):** Radiotherapeutic dose to the breast/chest wall, scar, supraclavicular nodes, infraclavicular nodes, and axillary levels II to III was 48Gy in 24 fractions, administered in five fractions per week. If six or more axillary nodes contained macromtastases. axillary level I was treated. In patients with right-sided breast cancer, the internal mammary nodes in intercostal spaces one to four were treated with anterior electron field or by inclusion in tangential photon fields. **Control arm: (IM RT- [left sided cancers]):** Radiotherapeutic dose to the breast/chest wall, scar, supraclavicular nodes, infraclavicular nodes, and axillary levels II to III was 48Gy in 24 fractions, administered in five fractions per week. If six or more axillary nodes contained macro-mestases. axillary level I was treated.	**OS (8 year follow-up):** O-E: -42.89; V: 216.14	Method of selection appropriate and likely to produce cohort representative of the time. May not be representative of current practice as inclusion stopped with introduction of taxanes. **Comparability:** Differences between groups were adjusted for in analysis. However, groups differed with respect to laterality. **Outcome:** Assessment of outcomes and follow-up were adequate **Indirectness** None **Limitations** Exclusion of patients unfit to receive standard radiotherapy may have led to an overestimation of the treatment effect. Also, there was a lack of radiation-induced morbidity that did not result in death. Further, because IM radiation was avoided in left-side breast cancer, can make no conclusion about cardiotoxicity of radiotherapy in these patients. Due to

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Recruited January 2003 to December 2007 **Source of funding** Danish Cancer Society; the Breast Friends breast cancer campaign; and the Lundbeck Foundation Center for Interventional Research in Radiation Oncology, Max and Inger Wørzners Memorial Foundation					advances in surgery and systemic treatment of early-stage breast cancer, results of this study may not readily apply to current breast cancer patient populations. **Other information** DBCG-IMN trial

DBCG, Danish Breast Cancer Group; EORTC, European Organisation for Research and Treatment of Cancer; Gy, gray; IM, internal mammary; IMN, internal mammary nodes; KROG, Korean Radiation Oncology Group MeV, megaelectronvolt; MS, medial supraclavicular; NR, not reported; RT, radiotherapy; SLNB, sentinel lymph node biopsy