Clinical studies

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery?		
Study	Reason for exclusion	
TARGIT-B:An international randomised controlled trial to compare targeted intra-operative radiotherapy boost with conventional external beam radiotherapy boost after lumpectomy for breast cancer in women with a high risk of local recurrence (Project record), Health Technology Assessment Database, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development	
Abo-Madyan, Y., Welzel, G., Sperk, E., Neumaier, C., Keller, A., Ehmann, M., Wenz, F., Intraoperative (IORT) versus whole breast radiotherapy (WBRT) for early breast cancer: Single centre results from the randomized phase III trial TARGIT-A, Strahlentherapie und Onkologie, 192 (1 Supplement 1), 18-19, 2016	Intrabeam has not been included in this review, as there is a NICE TA in development	
Alvarado, M., Gallant, E., Rice, J. S., Grobmyer, S. R., Harris, E. E., Holmes, D., Pavord, D., Small, W., TARGIT-U.S.: A registry trial of targeted intraoperative radiation therapy following breast-conserving surgery, Journal of Clinical Oncology, 33, no pagination, 2015	Intrabeam has not been included in this review, as there is a NICE TA in development	
Andersen, K. G., Gartner, R., Kroman, N., Flyger, H., Kehlet, H., Persistent pain after targeted intraoperative radiotherapy (TARGIT) or external breast radiotherapy for breast cancer: a randomized trial, Breast, 21, 46-9, 2012	Intrabeam has not been included in this review, as there is a NICE TA in development	
Anonymous, Vaidya et al. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. Lancet 2014. (2), International Journal of Radiation Oncology Biology Physics, 89, 497-498, 2014	Intrabeam has not been included in this review, as there is a NICE TA in development	
Baum, M., The targeted intraoperative radiotherapy (TARGIT) trial for breast cancer: A review after the first 10 years of clinical application, European Journal of Cancer, Supplement, 8, 129-130, 2010	Intrabeam has not been included in this review, as there is a NICE TA in development	
Baum, M., Targit-a trial (targeted intraoperative radiotherapy): Updated analysis of local recurrence, Breast, 22, S95, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development	
Baum, M., Joseph, D. J., Tobias, J. S., Wenz, F. K., Keshtgar, M. R., Alvarado, M., Bulsara, M., Eiermann, W., Williams, N. R., Vaidya, J. S., Safety and efficacy of targeted intraoperative radiotherapy (TARGIT) for early breast cancer: First report of a randomized controlled trial at 10-years maximum follow-up, Journal of Clinical Oncology, 28, no pagination, 2010	Intrabeam has not been included in this review, as there is a NICE TA in development	

Study	Reason for exclusion
Baum, M., Vaidya, J. S., Targeted intra-operative radiotherapy-TARGIT for early breast cancer, Annals of the new york academy of sciences, 1138, 132-5, 2008	Intrabeam has not been included in this review, as there is a NICE TA in development
Baum, M., Vaidya, J. S., Bulsara, M. K., Wenz, F., Tobias, J. S., Eiermann, W., Joseph, D., Insights into the natural history of subclinical breast cancer: A biological fall out from the TARGIT-a trial, Annals of Oncology, 23, ix3, 2012	Intrabeam has not been included in this review, as there is a NICE TA in development
Baum, M., Vaidya, J. S., Tobias, J. S., Keshtgar, M., Williams, N. R., Wenz, F., Bulsara, M., Saunders, C., Joseph, D., Targit (targeted intra-operative radiotherapy for early stage breast cancer): Results from the targit a randomized controlled trial, European Journal of Cancer, Supplement, 8, 19, 2010	Intrabeam has not been included in this review, as there is a NICE TA in development
Coles, C, Donovan, E, Venables, K, Rowlings, C, Maylex, H, Bentzen, S, Sydenham, M, Bliss, J, Yarnold, J, Randomised trial testing intensity modulated radiotherapy and partial organ radiotherapy in early breast cancer (import trial), British journal of cancer, 91, S80, 2004	Abstract
Coles, C., Agrawal, R., Ah-See, M. L., Algurafi, H., Alhasso, A., Brunt, A. M., Chan, C., Griffin, C., Harnett, A., Hopwood, P., Kirby, A., Sawyer, E., Syndikus, I., Titley, J., Tsang, Y., Wheatley, D., Wilcox, M., Yarnold, J., Bliss, J. M., Partial breast radiotherapy for women with early breast cancer: First results of local recurrence data for IMPORT LOW (CRUK/06/003), European Journal of Cancer, 57, S4, 2016	Abstract.
Coles, C., Griffin, C., Kirby, A., Titley, J., Tsang, Y., Harnett, A., Chan, H., Sawyer, E., Bliss, J., Yarnold, J., Partial breast radiotherapy for women with early breast cancer: First analysis of late cosmesis adverse events from IMPORT LOW (CRUK/06/003), European Journal of Cancer, 50, S103, 2014	Abstract.
Corica, T., Nowak, A. K., Saunders, C. M., Bulsara, M., Taylor, M., Vaidya, J. S., Baum, M., Joseph, D. J., Cosmesis and Breast-Related Quality of Life Outcomes After Intraoperative Radiation Therapy for Early Breast Cancer: A Substudy of the TARGIT-A Trial, International Journal of Radiation Oncology Biology Physics, 96, 55-64, 2016	Intrabeam has not been included in this review, as there is a NICE TA in development
Dodwell, D. J., Dyker, K., Brown, J., Hawkins, K., Cohen, D., Stead, M., Ash, D., A randomised study of whole-breast vs tumour-bed irradiation after local excision and axillary dissection for early breast cancer, Clinical Oncology, 17, 618-622, 2005	Intervention does not fit inclusion criteria.
Engel, D., Schnitzer, A., Brade, J., Blank, E., Wenz, F., Suetterlin, M., Schoenberg, S., Wasser, K., Are mammographic changes in the tumour bed more pronounced after intraoperative radiotherapy for breast cancer? Subgroup analysis from a randomized trial (TARGIT-A), Breast Journal, 19, 92-95, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery?	
Study	Reason for exclusion
Hanna, Samir A, Marta, Gustavo N, Riera, Rachel, da, Silva Joao Lf, de, Andrade Carvalho Heloisa, De, Barros Alfredo Carlos Sd, Intensity-modulated versus conventional radiotherapy for breast cancer, Cochrane Database of Systematic Reviews, 2013	Systematic Review Protocol.
Holmes, D. R., Baum, M., Joseph, D., The TARGIT trial: targeted intraoperative radiation therapy versus conventional postoperative whole-breast radiotherapy after breast-conserving surgery for the management of early-stage invasive breast cancer (a trial update), American journal of surgery, 194, 507-510, 2007	Intrabeam has not been included in this review, as there is a NICE TA in development
Jain, A. K., Vallow, L. A., Gale, A. A., Buskirk, S. J., Does Three-Dimensional External Beam Partial Breast Irradiation Spare Lung Tissue Compared With Standard Whole Breast Irradiation?, International Journal of Radiation Oncology Biology Physics, 75, 82-88, 2009	Non-RCT.
Joseph, D. J., Targit, Radiotherapy and Oncology, 103, S4, 2012	Intrabeam has not been included in this review, as there is a NICE TA in development
Julian, T. B., Costantino, J. P., Vicini, F. A., White, J. R., Cecchini, R. S., Winter, K. A., Arthur, D. W., Kuske, R., Rabinovitch, R., Parda, D. S., Mamounas, E. P., Curran Jr, W. J., Wolmark, N., A randomized phase III study of conventional whole breast irradiation (WBI) vs partial breast irradiation (PBI) for women with stage 0, 1, or 2 breast cancer: NSABP B-39/RTOG 0413, Cancer Research, 71, no pagination, 2011	Abstract.
Keshtgara, M., Vaidyab, J., Tobiasc, J., Williamsd, N., Baumdon, M., TARGIT (Targeted intra-operative radiotherapy for early stage breast cancer): Early results from the multi-centre randomized controlled trial, European Journal of Surgical Oncology, 36, 1098, 2010	Intrabeam has not been included in this review, as there is a NICE TA in development
Livi, L., Meattini, I., Marrazzo, L., Pallotta, S., Simontacchi, G., Saieva, C., Scotti, V., De Luca Cardillo, C., Bastiani, P., Nori, J., Orzalesi, L., Bianchi, S., Accelerated partial breast irradiation using intensity modulated radiotherapy versus whole breast irradiation: 5-year survival results of a phase 3 randomized trial, Cancer Research, 75, no pagination, 2015	Abstract
Livi, L., Meattini, I., Saieva, C., Franceschini, D., Meacci, F., Franzese, F., Scotti, V., De Luca Cardillo, C., Greto, D., Biti, G., Accelerated partial breast irradiation with IMRT: 3-years interim analysis of a Phase III randomized clinical trial, Radiotherapy and Oncology, 103, S51, 2012	Abstract.
Livi, L., Meattini, I., Saieva, C., Scotti, V., De Luca Cardillo, C., Meacci, F., Nori, J., Bianchi, S., Orzalesi, L., Biti, G., Accelerated partial breast irradiation with intensity-modulated radiotherapy (IMRT): The florence phase III randomized clinical trial at 3 years median follow-up, European Journal of Cancer, 48, S183, 2012	Abstract.

Study	Reason for exclusion
Livi, L., Saieva, C., Borghesi, S., Paoletti, L., Meattini, I., Rampini, A., Petrucci, A., Scoccianti, S., Paiar, F., Cataliotti, L., Leonulli, B. G., Bianchi, S., Biti, G. P., Concurrent Cyclophosphamide, Methotrexate, and 5-Fluorouracil Chemotherapy and Radiotherapy for Early Breast Carcinoma, International Journal of Radiation Oncology Biology Physics, 71, 705-709, 2008	Not a RCT.
Livi, L., Scotti, V., Saieva, C., Meattini, I., Detti, B., Simontacchi, G., Cardillo, C. D., Paiar, F., Mangoni, M., Marrazzo, L., Agresti, B., Cataliotti, L., Bianchi, S., Biti, G., Outcome after conservative surgery and breast irradiation in 5,717 patients with breast cancer: implications for supraclavicular nodal irradiation, International journal of radiation oncology, biology, physics, 76, 978-83, 2010	Intervention does not fit the inclusion criteria.
Marta, G. N., Macedo, C. R., Carvalho, H. D. A., Hanna, S. A., Da Silva, J. L. F., Riera, R., Accelerated partial irradiation for breast cancer: Systematic review and meta-analysis of 8653 women in eight randomized trials, Radiotherapy and Oncology, 114, 42-49, 2015	All studies included in the Hickey (2016) Cochrane systematic review.
Marta, G. N., Macedo, C. R., De Andrade Carvalho, H., Hanna, S. A., Da Silva, J. L. F., Riera, R., Erratum: Accelerated partial irradiation for breast cancer: Systematic review and meta-analysis of 8653 women in eight randomized trials (Radiotherapy and Oncology (2015) 114 (42-49)), Radiotherapy and Oncology, 115, 436-437, 2015	All studies included in the Hickey (2016) Cochrane systematic review.
McCormick, B., Partial breast radiation for early-stage breast cancer, Current Opinion in Obstetrics and Gynecology, 24, 31-37, 2012	Non-RCT.
Meattini, I., Marrazzo, L., Saieva, C., Pallotta, S., Simontacchi, G., Scotti, V., Furfaro, I., Meacci, F., Orzalesi, L., Livi, L., APBI versus whole breast irradiation in women age 70 years or older: A subgroup analysis of a phase 3 randomised trial, Radiotherapy and Oncology, 115, S20, 2015	Abstract.
Meattini, I., Saieva, C., Desideri, I., De Luca Cardillo, C., Scotti, V., Miccinesi, G., Bonomo, P., Orzalesi, L., Bernini, M., Casella, D., Sanchez, L. J., Nori, J., Bianchi, S., Livi, L., Accelerated partial breast irradiation versus whole breast radiotherapy: Quality of Life results from a phase 3 randomized trial and focus on patients aged 70 years or older, European Journal of Cancer, 57, S47, 2016	Abstract.
Meattini, I., Saieva, C., Desideri, I., Miccinesi, G., Francolini, G., Meacci, F., Muntoni, C., Scotti, V., De Luca Cardillo, C., Marrazzo, L., Simontacchi, G., Pallotta, S., Sanchez, L., Casella, D., Bernini, M., Orzalesi, L., Nori, J., Bianchi, S., Livi, L., Accelerated partial breast irradiation versus whole breast irradiation: Health-related quality of life analysis from a phase 3 trial, Cancer Research. Conference: 39th Annual CTRC AACR San Antonio Breast Cancer Symposium. United States, 77, 2017	Abstract.

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery? Study **Reason for exclusion** Meattini, I., Saieva, C., Desideri, I., Simontacchi, G., Marrazzo, L., Scoccianti, S., De Luca Cardillo, C., Scotti, V., Bonomo, Abstract. P., Mangoni, M., Rossi, F., Nori, J., Casella, D., Bernini, M., Sanchez, L., Orzalesi, L., Pallotta, S., Bianchi, S., Livi, L., Accelerated partial breast irradiation for Luminal-A breast cancer: Analysis from a phase 3 trial, Radiotherapy and Oncology, 119, S242, 2016 Meattini, I., Saieva, C., Marrazzo, L., Di Brina, L., Pallotta, S., Mangoni, M., Meacci, F., Bendinelli, B., Francolini, G., Abstract. Desideri, I., De Luca Cardillo, C., Scotti, V., Furfaro, I. F., Rossi, F., Greto, D., Bonomo, P., Casella, D., Bernini, M., Sanchez, L., Orzalesi, L., Simoncini, R., Nori, J., Bianchi, S., Livi, L., Accelerated partial breast irradiation using intensitymodulated radiotherapy technique compared to whole breast irradiation for patients aged 70 years or older: subgroup analysis from a randomized phase 3 trial. Breast Cancer Research & TreatmentBreast Cancer Res Treat. 153, 539-47. 2015 Murawa, D., Rutten, H., Maluta, S., Electron IORT APBI: What does the data tell us at 5 years?, European journal of Abstract. surgical oncology, 42 (9), S137, 2016 Olivotto, I., What have we learned from the randomized trials of partial breast RT?, Cancer Research, 75, no pagination, Abstract. 2015 Ott, O. J., Hildebrandt, G., Potter, R., Hammer, J., Hindemith, M., Resch, A., Spiegl, K., Lotter, M., Uter, W., Kortmann, R. Control/Comparator of interest D., Schrauder, M., Beckmann, M. W., Fietkau, R., Strnad, V., Accelerated partial breast irradiation with interstitial implants: does not fit inclusion criteria. risk factors associated with increased local recurrence, International Journal of Radiation Oncology, Biology, Physics, 80, 1458-63, 2011 Ott, O. J., Hildebrandt, G., Potter, R., Hammer, J., Lotter, M., Resch, A., Sauer, R., Strnad, V., Accelerated partial breast Control/Comparator of interest irradiation with multi-catheter brachytherapy: Local control, side effects and cosmetic outcome for 274 patients. Results of does not fit inclusion criteria. the German-Austrian multi-centre trial, Radiotherapy & Oncology, 82, 281-6, 2007 Ott, O. J., Lotter, M., Fietkau, R., Strnad, V., Accelerated partial-breast irradiation with interstitial implants. Analysis of Outcomes of interest does not fit factors affecting cosmetic outcome, Strahlentherapie und Onkologie, 185, 170-6, 2009 inclusion criteria. Ott, O. J., Lotter, M., Sauer, R., Strnad, V., Accelerated partial-breast irradiation with interstitial implants: the clinical Control/Comparator of interest relevance of the calculation of skin doses, Strahlentherapie und Onkologie, 183, 426-31, 2007 does not fit inclusion criteria. Ott, O. J., Potter, R., Hildebrandt, G., Hammer, J., Lotter, M., Beckmann, M. W., Sauer, R., Strnad, V., [Partial breast Not in English language. irradiation for early breast cancer with favorable prognostic factors: 3-year results of the German-Austrian phase II-trial, Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der NuklearmedizinROFO Fortschr Geb Rontgenstr

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery? Study **Reason for exclusion** Ott, O. J., Schulz-Wendtland, R., Uter, W., Pfahlberg, A., Beckmann, M. W., Sauer, R., Strnad, V., Fat necrosis after Non-RCT. conserving surgery and interstitial brachytherapy and/or external-beam irradiation in women with breast cancer. Strahlentherapie und Onkologie, 181, 638-44, 2005 Ott, O. J., Strnad, V., Stillkrieg, W., Uter, W., Beckmann, M. W., Fietkau, R., Accelerated partial breast irradiation with Non-RCT. external beam radiotherapy : First results of the German phase 2 trial. Strahlentherapie und Onkologie, 193, 55-61, 2017 Pan, X. B., Huang, S. T., Jiang, Y. M., Ma, J. L., Zhu, X. D., Secondary malignancies after partial versus whole breast All studies included in the Hickey irradiation: A systematic review and meta-analysis, Oncotarget, 7, 71951-71959, 2016 (2016) Cochrane systematic review. Picot, J., Copley, V., Colquitt, J. L., Kalita, N., Hartwell, D., Bryant, J., The INTRABEAM photon radiotherapy system for All studies included in the Hickey the adjuvant treatment of early breast cancer: A systematic review and economic evaluation, Health Technology (2016) Cochrane systematic Assessment, 19, 1-190, 2015 review. Polgar, C., Fodor, J., Orosz, Z., Major, T., Takacsi-Nagy, Z., Csaba Mangel, L., Sulyok, Z., Somogyi, A., Kasler, M., Intervention does not fit the Nemeth, G., Electron and high-dose-rate brachytherapy boost in the conservative treatment of stage I-II breast cancer: inclusion criteria. First results of the randomized Budapest boost trial, Strahlentherapie und Onkologie, 178, 615-623, 2002 Polgar, C., Kahan, Z., Orosz, Z., Gabor, G., Hadijev, J., Cserni, G., Kulka, J., Jani, N., Sulyok, Z., Lazar, G., Boross, G., Systematic review with non-Diczhazi, C., Szabo, E., Laszlo, Z., Pentek, Z., Major, T., Fodor, J., The role of radiotherapy in the conservative treatment RCTs. of ductal carcinoma in situ of the breast, Pathology Oncology ResearchPathol Oncol Res, 14, 179-92, 2008 Polgar, C., Limbergen, E. V., Potter, R., Kovacs, G., Polo, A., Lyczek, J., Hildebrandt, G., Niehoff, P., Guinot, J. L., Abstract. Guedea, F., Johansson, B., Ott, O. J., Major, T., Strnad, V., Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Europeen de Curietherapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). Radiotherapy and Oncology, 94, 264-273, 2010 Polgar, C., Major, T., Fodor, J., [Modern radiotherapy after breast-conserving surgery], Orvosi HetilapOrv Hetil, 153, 45-55, Not in English language. 2012 Polgar, C., Major, T., Fodor, J., Sulyok, Z., Takacsi-Nagy, Z., Nemeth, G., Kasler, M., Breast-conserving therapy with Abstract. partial or whole breast RT: 10-year results of the Budapest randomized trial, Radiotherapy and Oncology, 103, S35, 2012 Polgar, C., Major, T., Somogyi, A., Fodor, J., Toth, J., Sulyok, Z., Forrai, G., Takacsi-Nagy, Z., Mangel, L. C., Nemeth, G., Non-RCT. Sole brachytherapy of the tumour bed after breast conserving surgery: A new radiotherapeutic strategy for patients at low risk of local relapse, Neoplasma, 46, 182-189, 1999

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery? Study **Reason for exclusion** Polgar, C., Major, T., Sulvok, Z., Takacsi-Nagy, Z., Fodor, J., Long-term toxicity and cosmetic results of partial versus Abstract. whole breast irradiation: 10-year results of a phase jii APBI trial. International Journal of Radiation Oncology Biology Physics, 90, S133-S134, 2014 Polgar, C., Major, T., Sulyok, Z., Takacsi-Nagy, Z., Fodor, J., Toxicity and cosmetic results of partial vs whole breast Abstract. irradiation: 10-year results of a randomized trial. Radiotherapy and Oncology, 111, S60, 2014 Polgar, C., Orosz, Z., Kahan, Z., Gabor, G., Jani, N., Cserni, G., Hadijev, J., Kulka, J., Sulyok, Z., Boross, G., Lazar, G., Not in English language. Laszlo, Z., Diczhazi, C., Udvarhelyi, N., Szabo, E., Pentek, Z., Major, T., Fodor, J., Combined surgery and radiotherapy in the treatment of ductal carcinoma in situ of the breast: preliminary results of the Hungarian multicentre prospective randomised study. [Hungarian], Magyar onkologia, 52, 269-277, 2008 Not a systematic review. Polgar, C., Strnad, V., Kovacs, G., Partial-breast irradiation or whole-breast radiotherapy for early breast cancer: a metaanalysis of randomized trials, Strahlentherapie und Onkologie, 186, 113-4, 2010 Polgar, C., Strnad, V., Major, T., Brachytherapy for partial breast irradiation: the European experience. Seminars in Not a systematic review. Radiation Oncology, 15, 116-22, 2005 Polgar, C., Strnad, V., Ott, O., Hildebrandt, G., Kauer-Dorner, D., Knauerhase, H., Major, T., Lyczek, J., Guinot, J., Dunst, Abstract. J., Gutierrez Miguelez, C., Slampa, P., Allgauer, M., Lossl, K., Polat, B., Kovacs, G., Fischedick, A., Wendt, T., Hindemith, M., Resch, A., Niehoff, P., Guedea, F., Potter, R., Gall, C., Uter, W., Late toxicity and cosmesis after APBI with brachytherapy vs WBI: 5-year results of a phase III trial, Radiotherapy and Oncology, 119, S230-S231, 2016 Polgar, C., Van Limbergen, E., Potter, R., Kovacs, G., Polo Rubio, J. A., Lyczek, J., Hildebrandt, G., Niehoff, P., Guinot, J. Abstract. L., Guedea, F., Johansson, B., Ott, O. J., Major, T., Strnad, V., Selection criteria for brachytherapy in partial breast irradiation - Recommendations of the GEC-ESTRO Breast Cancer Working Group, Radiotherapy and Oncology, 96, S134, 2010 Polgar, C., Van Limbergen, E., Potter, R., Kovacs, G., Polo, A., Lyczek, J., Hildebrandt, G., Niehoff, P., Major, T., Strnad, Systematic review includes non-V., Patient selection for accelerated partial breast irradiation after breast-conserving surgery. Recommendations of the RCTs. groupe europeen de curietherapie-european society for therapeutic radiology and oncology (GEC-ESTRO) breast cancer working group. International Journal of Radiation Oncology Biology Physics, 78, S243, 2010 Rodriguez De Dios, N., Sanz, X., Dengra, J., Foro, P., Reig, A., Membrive, I., Lozano, J., Fernandez-Velilla, E., Iglesias. Abstract. P., Algara, M., Interim cosmetic results and toxicity using 3d conformal external beam radiation therapy to deliver accelerated partial breast irradiation in patients with early-stage breast cancer, International Journal of Radiation Oncology Biology Physics, 84, S87, 2012

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery? Study **Reason for exclusion** Rodriguez, N., Sanz, X., Dengra, J., Foro, P., Perez, P., Fernandez-velilla, E., Membrive, I., Reig, A., Quera, J., Lio, J., Abstract. Pera, O., Algara, M., Long-term toxicity and cosmetic results using 3D-CRT to deliver accelerated partial breast irradiation in earlystage breast cancer, Reports of Practical Oncology and Radiotherapy, 18, S60-S61, 2013 Rodriguez, N., Sanz, X., Foro, P., Reig, A., Membrive, I., Lozano, J., Fernandez-Velilla, E., Quera, J., Pera, O., Algara, M., Abstract. Phase III study comparing accelerated partial breast irradiation vs whole breast radiation therapy using 3D-CRT. Radiotherapy and Oncology, 103, S400, 2012 Silverstein, M. J., Fastner, G., Maluta, S., Reitsamer, R., Goer, D. A., Vicini, F., Wazer, D., Intraoperative Radiation Intrabeam has not been included Therapy: A Critical Analysis of the ELIOT and TARGIT Trials. Part 2-TARGIT, Annals of surgical oncology, 21, 3793-3799, in this review, as there is a NICE 2014 TA in development Silverstein, M. J., Fastner, G., Maluta, S., Reitsamer, R., Goer, D. A., Vicini, F., Wazer, D., Intraoperative Radiation Intrabeam has not been included Therapy: A Critical Analysis of the ELIOT and TARGIT Trials, Part 1-ELIOT, Annals of surgical oncology, 21, 3787-3792. in this review, as there is a NICE 2014 TA in development Smith, B. D., Arthur, D. W., Buchholz, T. A., Haffty, B. G., Hahn, C. A., Hardenbergh, P. H., Julian, T. B., Marks, L. B., Systematic review with non-Todor, D. A., Vicini, F. A., Whelan, T. J., White, J., Wo, J. Y., Harris, J. R., Accelerated partial breast irradiation consensus RCTs. statement from the American Society for Radiation Oncology (ASTRO), International Journal of Radiation Oncology, Biology, Physics, 74, 987-1001, 2009 Sperk, E., Vaidya, J., Bulsara, M., Sutterlin, M., Ataseven, B., Pigorsch, S., Feyer, P., Blohmer, J. U., Kaufmann, M., Intrabeam has not been included Rodel, C., Friese, K., Belka, C., Solomayer, E. F., Fleckenstein, J., Park-Simon, T. W., Bremer, M., Joseph, D., Tobias, J., in this review, as there is a NICE Baum, M., Wenz, F., Updates from the TARGIT A trial for the German centers: Local recurrence and survival, Oncology TA in development Research and Treatment, 37, 16-17, 2014 Sperk, E., Welzel, G., Keller, A., Kraus-Tiefenbacher, U., Gerhardt, A., Sutterlin, M., Wenz, F., Late radiation toxicity after Intrabeam has not been included intraoperative radiotherapy (IORT) for breast cancer: Results from the randomized phase III trial TARGIT A, Breast Cancer in this review, as there is a NICE Research and Treatment, 135, 253-260, 2012 TA in development Strnad, V., Multicatheter brachytherapy is the best for APBI, Radiotherapy and Oncology, 119, S141, 2016 Abstract. Strnad, V., Hildebrandt, G., Potter, R., Hammer, J., Hindemith, M., Resch, A., Spiegl, K., Lotter, M., Uter, W., Bani, M., Control/Comparator of interest Kortmann, R. D., Beckmann, M. W., Fietkau, R., Ott, O. J., Accelerated partial breast irradiation: 5-year results of the does not fit inclusion criteria. German-Austrian multicentre phase II trial using interstitial multicatheter brachytherapy alone after breast-conserving surgery, International Journal of Radiation Oncology Biology Physics, 80, 17-24, 2011

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery? Study **Reason for exclusion** Strnad, V., Ott, O. J., Hildebrandt, G., Potter, R., Fietkau, R., Lyczek, J., Uter, W., Major, T., Lotter, M., Polgar, C., First Abstract. clinical results of the GEC-ESTRO breast WG phase III multicentric APBI trial. Radiotherapy and Oncology, 103, S35-S36. 2012 Tobias, J. S., Vaidya, J. S., Keshtgar, M., Douek, D., Metaxas, M., Stacey, C., Sainsbury, R., D'Souza, D., Baum, M., Intrabeam has not been included Breast-conserving surgery with intra-operative radiotherapy: The right approach for the 21st century? Clinical Oncology. in this review, as there is a NICE 18, 220-228, 2006 TA in development Vaidya, A., Vaidya, P., Both, B., Brew-Graves, C., Vaidya, J., Cost effectiveness analysis of targeted intraoperative Intrabeam has not been included radiotherapy alone (TARGIT-A) in early breast cancer patients, Value in Health, 17, A640, 2014 in this review, as there is a NICE TA in development Vaidya, J. S., Baum, M., Tobias, J. S., D'Souza, D. P., Naidu, S. V., Morgan, S., Metaxas, M., Harte, K. J., Sliski, A. P., Intrabeam has not been included Thomson, E., Targeted intra-operative radiotherapy (Targit): An innovative method of treatment for early breast cancer. in this review, as there is a NICE Annals of oncology, 12, 1075-1080, 2001 TA in development Vaidya, J. S., Baum, M., Tobias, J. S., Massarut, S., Wenz, F., Murphy, O., Hilaris, B., Houghton, J., Saunders, C., Corica, Intrabeam has not been included T., Roncadin, M., Kraus-Tiefenbacher, U., Melchaert, F., Keshtgar, M., Sainsbury, R., Douek, M., Harrison, E., Thompson, in this review, as there is a NICE A., Joseph, D., Targeted intraoperative radiotherapy (TARGIT) yields very low recurrence rates when given as a boost, TA in development International Journal of Radiation Oncology Biology Physics, 66, 1335-1338, 2006 Vaidya, J. S., Baum, M., Tobias, J. S., Morgan, S., D'Souza, D., The novel technique of delivering targeted intraoperative Intrabeam has not been included radiotherapy (Targit) for early breast cancer, European journal of surgical oncology, 28, 447-454, 2002 in this review, as there is a NICE TA in development Intrabeam has not been included Vaidya, J. S., Baum, M., Tobias, J. S., Wenz, F., Massarut, S., Keshtgar, M., Hilaris, B., Saunders, C., Williams, N. R., Brew-Graves, C., Corica, T., Roncadin, M., Kraus-Tiefenbacher, U., Sutterlin, M., Bulsara, M., Joseph, D., Long-term in this review, as there is a NICE results of TARGeted Intraoperative radioTherapy (Targit) boost during breast-conserving surgery, International Journal of TA in development Radiation Oncology Biology Physics, 81, 1091-1097, 2011 Vaidya, J. S., Baum, M., Wenz, F., Bulsara, M., Tobias, J., Alvarodo, M., Saunders, C., Williams, N., Joseph, D., The Intrabeam has not been included TARGIT-a trial update confirms no increase in local recurrence. Cancer Research. Conference: 34th Annual CTRC AACR in this review, as there is a NICE San Antonio Breast Cancer Symposium, San Antonio, TX United States, Conference Publication:, 71, 2011 TA in development Vaidya, J. S., Bulsara, M., Wenz, F., Coombs, N., Singer, J., Ebbs, S., Massarut, S., Saunders, C., Douek, M., Williams, N. All studies included in the Hickey R., Joseph, D., Tobias, J. S., Baum, M., Reduced Mortality With Partial-Breast Irradiation for Early Breast Cancer: A Meta-(2016) Cochrane systematic Analysis of Randomized Trials, International Journal of Radiation Oncology Biology Physics, 96, 259-265, 2016 review.

Excluded studies -8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery? Study **Reason for exclusion** Vaidya, J. S., Bulsara, M., Wenz, F., Massarut, S., Joseph, D., Tobias, J., Williams, N. R., Baum, M., Fewer non-breast Intrabeam has not been included cancer deaths in targit-a trial: Systemic benefit of targit or lack of EBRT toxicity. Breast, 22, S97, 2013 in this review, as there is a NICE TA in development Vaidya, J. S., Bulsara, M., Wenz, F., Massarut, S., Joseph, D., Tobias, J., Williams, N. R., Baum, M., Omitting whole breast Intrabeam has not been included radiotherapy does not increase axillary recurrence-data from targit-a trial. Breast, 22, S96, 2013 in this review, as there is a NICE TA in development Vaidya, J. S., Bulsara, M., Wenz, F., Massarut, S., Joseph, D., Tobias, J., Williams, N., Baum, M., The lower non-breast Intrabeam has not been included cancer mortality with targit in the targita trial could be a systemic effect of targit on tumour microenvironment, International in this review, as there is a NICE Journal of Radiation Oncology Biology Physics, 87, S240, 2013 TA in development Vaidya, J. S., Joseph, D. J., Tobias, J. S., Bulsara, M., Wenz, F., Saunders, C., Alvarado, M., Flyger, H. L., Massarut, S., Intrabeam has not been included Eiermann, W., Keshtoar, M., Dewar, J., Kraus-Tiefenbacher, U., Sutterlin, M., Esserman, L., Holtveg, H. M. R., Roncadin, in this review, as there is a NICE M., Pigorsch, S., Metaxas, M., Falzon, M., Matthews, A., Corica, T., Williams, N. R., Baum, M., Targeted intraoperative TA in development radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): An international, prospective, randomised, non-inferiority phase 3 trial, The Lancet, 376, 91-102, 2010 Vaidya, J. S., Joseph, D., Tobias, J. S., Wenz, F., Keshtgar, M., Bulsara, M., Saunders, C., Williams, N., Baum, M., Single Intrabeam has not been included dose targeted intra-operative radiotherapy (TARGIT) for early breast cancer compared with external beam radiotherapy in this review, as there is a NICE First report of a randomized controlled trial (TARGIT-A) at 10 years maximum follow up, European Journal of Surgical TA in development Oncology, 36, 829-830, 2010 Vaidya, J. S., Massarut, S., Tobias, J. S., Wenz, F., Bulsara, M., Keshtgar, M., Saunders, C., Alavarado, M., Williams, N., Intrabeam has not been included Joseph, D., Baum, M., Targeted intra-operative radiotherapy boost-TARGIT-B trial: A randomized trial for young and high in this review, as there is a NICE risk patients including those after post-neoadjuvant systemic therapy lumpectomy, European Journal of Surgical Oncology, TA in development 36, 820, 2010 Vaidya, J. S., Tobias, J. S., Baum, M., Wenz, F., Kraus-Tiefenbacher, U., D'Souza, D., Keshtgar, M., Massarut, S., Hilaris, Not an RCT. B., Saunders, C., Joseph, D., TARGeted Intraoperative radiotherapy (TARGIT): An innovative approach to partial-breast irradiation, Seminars in Radiation Oncology, 15, 84-91, 2005 Vaidya, J. S., Walton, L., Dewar, J., Single dose targeted intraoperative radiotherapy (TARGIT) for breast cancer can be Not an RCT. delivered as a second procedure under local anaesthetic, World Journal of Surgical Oncology, 4, 2, 2006

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Study	Reason for exclusion
Vaidya, J. S., Wenz, F., Bulsara, M., Erratum: Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial (Lancet (2014) 383 (603-613)), The Lancet, 383, 602, 2014	Intrabeam has not been included in this review, as there is a NICE TA in development
Vaidya, J. S., Wenz, F., Bulsara, M., Joseph, D., Tobias, J. S., Keshtgar, M., Flyger, H., Massarut, S., Alvarado, M., Saunders, C., Eiermann, W., Metaxas, M., Sperk, E., Sutterlin, M., Brown, D., Esserman, L., Roncadin, M., Thompson, A., Dewar, J. A., Holtveg, H., Pigorsch, S., Falzon, M., Harris, E., Matthews, A., Brew-Graves, C., Potyka, I., Corica, T., Williams, N. R., Baum, M., Targeted intraoperative radiotherapy for early breast cancer: TARGIT-A trial-updated analysis of local recurrence and first analysis of survival, Cancer Research, 72, no pagination, 2012	Intrabeam has not been included in this review, as there is a NICE TA in development
Vaidya, J. S., Wenz, F., Bulsara, M., Tobias, J. S., Joseph, D. J., Keshtgar, M., Flyger, H. L., Massarut, S., Alvarado, M., Saunders, C., Eiermann, W., Metaxas, M., Sperk, E., Sutterlin, M., Brown, D., Esserman, L., Roncadin, M., Thompson, A., Dewar, J. A., Holtveg, H. M. R., Pigorsch, S., Falzon, M., Harris, E., Matthews, A., Brew-Graves, C., Potyka, I., Corica, T., Williams, N. R., Baum, M., Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer:5-year results for local control and overall survival from the TARGIT-A randomised trial, The Lancet, 383, 603-613, 2014	Intrabeam has not been included in this review, as there is a NICE TA in development
Vaidya, J. S., Wenz, F., Bulsara, M., Tobias, J. S., Joseph, D. J., Saunders, C., Brew-Graves, C., Potyka, I., Morris, S., Vaidya, H. J., Williams, N. R., Baum, M., An international randomised controlled trial to compare TARGeted Intraoperative radioTherapy (TARGIT) with conventional postoperative radiotherapy after breast-conserving surgery for women with early-stage breast cancer (the TARGIT-A trial), Health Technology Assessment, 20, vii-188, 2016	Intrabeam has not been included in this review, as there is a NICE TA in development
Vaidya, J. S., Wenz, F., Bulsara, M., Tobias, J. S., Massarut, S., Joseph, D., Baum, M., Case selection for targeted intraoperative radiotherapy (TARGIT), European Journal of Cancer, 49, S451, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development
Vaidya, J., Bulsara, M., Wenz, F., Tobias, J. S., Joseph, D. J., Massarut, S., Flyger, H., Eiermann, W., Saunders, C., Alvarado, M., Brew-Graves, C., Potyka, I., Williams, N. R., Baum, M., Whole breast radiotherapy does not affect growth of cancer foci in other quadrants: Results from the TARGIT A trial, Radiotherapy and Oncology, 115, S232-S233, 2015	Intrabeam has not been included in this review, as there is a NICE TA in development
Vaidya, Js, Baum, M, Tobias, Js, Houghton, J, Keshtgar, M, Sainsbury, R, Taylor, I, Morgan, S, Metaxas, M, D'Souza, D, Targeted intraoperative radiotherapy for breast cancer-a randomised trial, Breast Cancer Research and Treatment, 69, 228, 2001	Intrabeam has not been included in this review, as there is a NICE TA in development

Study	Reason for exclusion
Vaidya, Js, Joseph, Dj, Tobias, Js, Wenz, Fk, Bulsara, M, Alvarado, M, Abstract PD06-01: A Single Treatment with Targeted Intraoperative Radiotherapy (TARGIT) Is Similar to Several Weeks of External Beam Radiotherapy (EBRT) with Respect to Efficacy and Safety, and Has Obvious Advantages to the Patient and the Economy, 70, 2010	Intrabeam has not been included in this review, as there is a NICE TA in development
Valachis, A., Mauri, D., Polyzos, N. P., Mavroudis, D., Georgoulias, V., Casazza, G., Partial breast irradiation or whole breast radiotherapy for early breast cancer: A meta-analysis of randomized controlled trials, Journal of clinical oncology, 27, CRA532, 2009	All studies included in the Hickey (2016) Cochrane systematic review.
Valachis, A., Mauri, D., Polyzos, N. P., Mavroudis, D., Georgoulias, V., Casazza, G., Partial breast irradiation or whole breast radiotherapy for early breast cancer: a meta-analysis of randomized controlled trials, Breast Journal, 16, 245-51, 2010	All studies included in the Hickey (2016) Cochrane systematic review.
Veronesi, U., Orecchia, R., Maisonneuve, P., Viale, G., Rotmensz, N., Sangalli, C., Luini, A., Veronesi, P., Galimberti, V., Zurrida, S., Leonardi, M. C., Lazzari, R., Cattani, F., Gentilini, O., Intra, M., Caldarella, P., Ballardini, B., Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial, Lancet OncologyLancet Oncol, 14, 1269-77, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development
Welzel, G., Boch, A., Blank, E., Kraus-Tiefenbacher, U., Keller, A., Hermann, B., Sutterlin, M., Wenz, F., Radiation-related quality of life parameters after targeted intraoperative radiotherapy vs. Whole breast radiotherapy in patients with breast cancer: Results from the randomized phase iii trial TARGIT-A, International Journal of Radiation Oncology Biology Physics, 81, S206-S207, 2011	Intrabeam has not been included in this review, as there is a NICE TA in development
Welzel, G., Boch, A., Blank, E., Kraus-Tiefenbacher, U., Keller, A., Hermann, B., Sutterlin, M., Wenz, F., Radiation-related quality of life parameters after targeted intraoperative radiotherapy versus whole breast radiotherapy in patients with breast cancer: Results from the randomized phase III trial TARGIT-A, Journal of cancer research and clinical oncology, 138, 82, 2012	Intrabeam has not been included in this review, as there is a NICE TA in development
Welzel, G., Boch, A., Sperk, E., Hofmann, F., Kraus-Tiefenbacher, U., Gerhardt, A., Suetterlin, M., Wenz, F., Radiation- related quality of life parameters after targeted intraoperative radiotherapy versus whole breast radiotherapy in patients with breast cancer: results from the randomized phase III trial TARGIT-A, Radiation Oncology, 8, 9, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development
Wenz, F., TARGIT E(Iderly) - Prospective phase II study of Intraoperative Radiotherapy (IORT) in elderly patients with small breast cancer, Strahlentherapie und Onkologie, 192 (1 Supplement 1), 17-18, 2016	Intrabeam has not been included in this review, as there is a NICE TA in development

Study	Reason for exclusion
Wenz, F. K., TARGIT E(Iderly): Prospective phase II study of intraoperative radiotherapy (IORT) in elderly patients with small breast cancer, Journal of Clinical Oncology, 34, no pagination, 2016	Intrabeam has not been included in this review, as there is a NICE TA in development
Wenz, F. K., Vaidya, J. S., Bulsara, M., Suetterlin, M., Sperk, E., Ataseven, B., Pigorsch, S., Feyer, P. C., Blohmer, J. U., Kaufmann, M., Roedel, C., Friese, K., Belka, C., Solomayer, E., Fleckenstein, J., Park-Simon, T. W., Bremer, M., Joseph, D. J., Tobias, J. S., Baum, M., TARGIT-A trial: Updated results for local recurrence and survival for the German centers, Journal of Clinical Oncology, 31, no pagination, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development
Wenz, F., Vaidya, J. S., Pigorsch, S., Feyer, P., Roedel, C., Belka, C., Fleckenstein, J., Bremer, M., Joseph, D., Baum, M., Local recurrence and survival for the german centers in the targit-a (targeted intraoperative radiation therapy-alone) trial, International Journal of Radiation Oncology Biology Physics, 87, S241, 2013	Intrabeam has not been included in this review, as there is a NICE TA in development
Williams, N. R., Keshtgar, M., Corica, T., Saunders, C., Joseph, D., Bulsara, M. K., Early breast cancer and cosmetic outcome one, two, three and four years after intra-operative radiotherapy compared with external beam radiotherapy: An objective assessment of patients from a randomised controlled trial (on behalf of the targit trialists' group), European Journal of Cancer, 47, S365, 2011	Intrabeam has not been included in this review, as there is a NICE TA in development
Zhang, L., Zhou, Z., Mei, X., Yang, Z., Ma, J., Chen, X., Wang, J., Liu, G., Yu, X., Guo, X., Intraoperative radiotherapy versus whole-breast external beam radiotherapy in early-stage breast cancer, Medicine (United States), 94, e1143, 2015	All studies included in the Hickey (2016) Cochrane systematic review.
Zhang, L., Zhou, Z., Yu, X., Mei, X., Yang, Z., Chen, X., Guo, X., Intraoperative radiation therapy versus whole-breast external beam radiation therapy in early-stage breast cancer: A systematic review and meta-analysis, International Journal of Radiation Oncology Biology Physics, 93, E10, 2015	All studies included in the Hickey (2016) Cochrane systematic review.

NICE, National Institute of Health and Care Excellence; RCT, randomised controlled trial; TA, technology appraisal