

**Table 14: Studies included in the evidence review for heart sparing radiotherapy**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
<p><b>Full citation</b></p> <p>Bartlett, F. R., Colgan, R. M., Donovan, E. M., McNair, H. A., Carr, K., Evans, P. M., Griffin, C., Locke, I., Haviland, J. S., Yarnold, J. R., Kirby, A. M., The UK HeartSpare Study (Stage IB): Randomised comparison of a voluntary breath-hold technique and prone radiotherapy after breast conserving surgery, Radiotherapy and Oncology, 114, 66-72, 2015</p> <p><b>Ref Id</b></p> <p>670601</p> <p><b>Country/ies where the study was carried out</b></p> <p>United Kingdom</p> <p><b>Study type</b></p>	<p><b>Sample size</b></p> <p>28</p> <p><b>Characteristics</b></p> <p>Median age: 57 years(range 25-79 years)</p> <p><b>Inclusion criteria</b></p> <p>Women with left BC who had undergone breast-conserving surgery for invasive ductal or lobular carcinoma (pT1-3b,N0-1,M0), who required radiotherapy to the breast alone (<math>\pm</math> tumour bed boost) without nodal irradiation, and who had an estimated breast volume of <math>&gt;750</math> cm<sup>3</sup></p> <p><b>Exclusion criteria</b></p> <p>Not described</p>	<p><b>Interventions</b></p> <p><b>Voluntary Breath Hold</b></p> <p>The patients were asked to breathe in and out twice before taking a deep breath in and holding. The reference mark on the patient's skin should rise up to the level of the laser. They repeated the breath-hold procedure a couple of times to confirm reproducibility before proceeding with patient setup.</p> <p>Patients performed a breath-hold and the midline tattoo was aligned to the isocenter position superior/inferior and</p>	<p><b>Details</b></p> <p>Patients were randomised to receive one or other technique for fractions 1–7, before switching techniques for fractions 8–15.</p>	<p><b>Results</b></p> <p>Mean Heart Dose: VBH: 0.44(0.38-0.51)Gy</p> <p>Mean Heart Dose: Prone: 0.66(0.61-0.71)Gy</p> <p>Median target tissue coverage was <math>\geq 95\%</math> for both techniques</p>	<p><b>Limitations</b></p> <p>Small sample size. Because of use of MLC/beam angle alterations to avoid cardiac tissue likely to result in lower coverage.</p> <p><b>Other information</b></p> <p>Selection Bias: Low risk</p> <p>Performance Bias: Low risk</p> <p>Detection Bias: Low risk</p>

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
<p>Single centre randomized non blinded cross over study</p> <p><b>Aim of the study</b></p> <p>To compare mean heart and left anterior descending coronary artery (LAD) doses and positional reproducibility in larger-breasted women receiving left breast radiotherapy using supine voluntary deep-inspiratory breath-hold (VBH) and free-breathing prone techniques.</p> <p><b>Study dates</b></p> <p>January 2013 to April 2014</p> <p><b>Source of funding</b></p> <p>National Institute of Health Research (NIHR)</p>		<p>set the focus-to-surface distance (FSD) at the midline.</p> <p><b>Prone radiotherapy</b></p> <p>Prone positioning was reproduced at treatment by aligning tattoos to lasers and using CT-planning photographs to check consistency.</p>			<p>(Objective Outcome)</p> <p>Attrition Bias:Low risk</p> <p>Reporting Bias: Low risk (Published protocol available)</p> <p>Indirectness: Only patients with breast volume &gt;750 cm<sup>3</sup> were included</p>
<p><b>Full citation</b></p> <p>Bartlett, F. R., Donovan, E. M., McNair, H. A., Corsini, L. A., Colgan, R. M., Evans, P. M., Maynard, L., Griffin, C., Haviland, J. S., Yarnold, J. R., Kirby, A. M., The UK HeartSpare Study (Stage II): Multicentre Evaluation of a Voluntary Breath-hold</p>	<p><b>Sample size</b></p> <p>93 from 10 UK centres</p> <p><b>Characteristics</b></p> <p>Median age: 56 years( 27-78 yrs)</p> <p>80(79%) Breast conserving surgery</p>	<p><b>Interventions</b></p> <p><b>Voluntary Breath Hold</b></p> <p>The patients were asked to breathe in and out twice before taking a deep breath in and holding. The reference mark on the patient's</p>	<p><b>Details</b></p>	<p><b>Results</b></p> <p>Mean Heart Dose: VBH: 1.04(0.97-1.12)</p> <p>Mean Heart Dose: Free breathing Prone: 1.79(1.66-1.91)Gy</p>	<p><b>Limitations</b></p> <p>Non randomized study</p> <p><b>Other information</b></p> <p>Selection</p>

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<p>Technique in Patients Receiving Breast Radiotherapy, Clinical Oncology, 29, e51-e56, 2017</p> <p><b>Ref Id</b></p> <p>670653</p> <p><b>Country/ies where the study was carried out</b></p> <p>United Kingdom</p> <p><b>Study type</b></p> <p>Multicenter non randomised prospective study</p> <p><b>Aim of the study</b></p> <p>To evaluate the heart-sparing ability and feasibility of the VBH technique in a national multicentre setting</p> <p><b>Study dates</b></p> <p>Recruitment from January to October 2014</p> <p><b>Source of funding</b></p> <p>National Institute of Health Research (NIHR)</p>	<p>11(11%): mastectomy±reconstruction</p> <p>10(10%):Operation data missing:</p> <p><b>Inclusion criteria</b></p> <p>1) underwent left breast conserving surgery or mastectomy for early stage invasive ductal or lobular carcinoma (pT1-3b N0-1 M0) or ductal carcinoma in situ</p> <p>2) Recommended adjuvant radiotherapy to the whole breast or chest wall without nodal irradiation.</p> <p>3)Women whose free-breathing planning computed tomography (CT) scan showed the presence of any heart tissue within tangential radiotherapy fields placed according to standard anatomical borders (i.e. any heart within the 50% isodose)</p> <p><b>Exclusion criteria</b></p> <p>Not separately described</p>	<p>skin should rise up to the level of the laser. They repeated the breath-hold procedure a couple of times to confirm reproducibility before proceeding with patient setup.</p> <p>Patients performed a breath-hold and the midline tattoo was aligned to the isocenter position superior/inferior and set the focus-to-surface distance (FSD) at the midline.</p> <p><b>Free Breathing</b></p> <p>Prone positioning was reproduced at treatment by aligning tattoos to lasers and using CT-planning photographs to check consistency.</p>		<p>Median target tissue coverage was ≥95% for both techniques</p>	<p>Method of selection appropriate and likely to produce representative cohort</p> <p>Comparability: Comparable</p> <p>Outcome Outcome and follow-up adequate</p> <p>Indirectness Only women with larger breast volume included</p> <p>Other information</p>
<b>Full citation</b>	<b>Sample size</b>	<b>Interventions</b>	<b>Details</b>	<b>Results</b>	<b>Limitations</b>

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
<p>Chi, F., Wu, S., Zhou, J., Li, F., Sun, J., Lin, Q., Lin, H., Guan, X., He, Z., Dosimetric comparison of moderate deep inspiration breath-hold and free-breathing intensity-modulated radiotherapy for left-sided breast cancer, <i>Cancer/Radiotherapie</i>, 19, 180-186, 2015</p> <p><b>Ref Id</b> 671586</p> <p><b>Country/ies where the study was carried out</b> China</p> <p><b>Study type</b> Prospective</p> <p><b>Aim of the study</b> This study determined the dosimetric comparison of moderate deep inspiration breath-hold using active breathing control and free-breathing intensity-modulated radiotherapy (IMRT) after breast-conserving surgery for left-sided breast cancer.</p> <p><b>Study dates</b> January 2008-July 2011</p>	<p>31</p> <p><b>Characteristics</b> Median age 39.5 yrs, Tumour stage T1 &amp; T2</p> <p><b>Inclusion criteria</b> 1)female patient aged 18 years or older 2)Pathologically-confirmed breast cancer 3)axillary lymph node dissection or sentinel lymph node biopsy-confirmed pathology-negative lymph nodes 4)stage I or II (pT1N0M0, pT2N0M0) according to the 2009 7th edition of the American Joint Committee on Cancer (AJCC) TNM staging 5) cardiac capacity and good cognitive ability based on active breathing control technology 6)informed consent</p> <p><b>Exclusion criteria</b> Not described separately</p>	<p>Intervention: Two field-in-field-IMRT moderate deep inspiration breath-holding plans were compared in the dosimetry to target volume coverage of the glandular breast tissue and organs at risks for each patient.</p> <p>Control: Free breathing</p>		<p>There was no significant difference between the free-breathing and moderate deep inspiration breath-holding in the target volume coverage. The dose to ipsilateral lung, coronary artery and heart in the field-in-field-IMRT were significantly lower for the free-breathing plan than for the two moderate deep inspiration breath-holding plans (all <math>P &lt; 0.05</math>)</p>	<p>Small sample size</p> <p><b>Other information</b> Selection Method of selection appropriate and likely to produce representative cohort</p> <p>Comparability: Comparable</p> <p>Outcome Outcome and follow-up adequate</p>

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
<p><b>Source of funding</b></p> <p>National Natural Science Foundation of China (No. 81402527), the Sci-Tech Office of Guangdong Province (No. 2013B021800157) and the Education Scientific Research Project of Young Teachers in Fujian Province (No. JB13131).</p>					
<p><b>Full citation</b></p> <p>Czeremyszynska, B., Drozda, S., Gorzynski, M., Kepka, L., Selection of patients with left breast cancer for deep-inspiration breath-hold radiotherapy technique: Results of a prospective study, Reports of Practical Oncology and Radiotherapy, 22, 341-348, 2017</p> <p><b>Ref Id</b></p> <p>671669</p> <p><b>Country/ies where the study was carried out</b></p> <p>Poland</p> <p><b>Study type</b></p> <p>Prospective study</p>	<p><b>Sample size</b></p> <p>31</p> <p><b>Characteristics</b></p> <p>Age: 24-70 yrs (Mean 55.5 yrs)</p> <p><b>Inclusion criteria</b></p> <p>1) Early stage left breast cancer: Invasive ductal carcinoma in situ</p> <p>2) Age 18-70 years</p> <p>3) Informed consent</p> <p><b>Exclusion criteria</b></p> <p>1) Did not agree to participate</p> <p>2) Unable to cooperate in DIBH training</p>	<p><b>Interventions</b></p> <p>Prescribed radiation dose: 39.9 Gy</p> <p>Intervention: Align RT system used for alignment and coregistration, and breath hold during treatment.</p> <p>Control: Free breathing</p>	<p><b>Details</b></p> <p>Patients that had no sufficient improvement of treatment plan with DIBH, or those who were unable to breath hold steadily were given FB plan</p>	<p><b>Results</b></p> <p>Intervention (DIBH): Mean heart dose (Gy): 1.06 (0.60 to 1.73)</p> <p>Control (Free breathing): Mean heart dose (Gy): 2.57 (0.66 to 7.92)</p>	<p><b>Limitations</b></p> <p>Small sample size</p> <p>Selection</p> <p>Selection bias likely due to more chances of people with respirator fitness to be included</p> <p>Comparability: Comparable</p> <p>Outcome</p>

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
<p><b>Aim of the study</b></p> <p>To assess prospectively which patients with left breast cancer have the dosimetric benefit from the use of deep-inspiration breath-hold radiotherapy (DIBH-RT).</p> <p><b>Study dates</b></p> <p>June 2014 to June 2015</p> <p><b>Source of funding</b></p> <p>Not financially supported</p>	<p>3) Respiratory function impairment precluding them from deep inspiration maintenance</p>				<p>Outcome and follow-up adequate</p> <p>Indirectness</p> <p>Subjects with poor respiratory function were excluded</p> <p><b>Other information</b></p>
<p><b>Full citation</b></p> <p>Eldredge-Hindy, H., Lockamy, V., Crawford, A., Nettleton, V., Werner-Wasik, M., Siglin, J., Simone, N. L., Sidhu, K., Anne, P. R., Active Breathing Coordinator reduces radiation dose to the heart and preserves local control in patients with left breast cancer: Report of a prospective trial, Practical Radiation Oncology, 5, 4-10, 2015</p> <p><b>Ref Id</b></p>	<p><b>Sample size</b></p> <p>86</p> <p><b>Characteristics</b></p> <p>Women with Stages 0-III left breast cancer</p> <p>Median age(Range): 52(25-80 years)</p> <p><b>Inclusion criteria</b></p> <p>1) Adjuvant RT to the breast or chest wall</p> <p>2) Could tolerate mDIBH</p>	<p><b>Interventions</b></p> <p>mDIBH with ABC device</p>	<p><b>Details</b></p> <p>ABC device (Elekta Oncology, Stockholm, Sweden) was used for intervention.</p>	<p><b>Results</b></p> <p>Absolute reduction in MHD : 1.7 Gy</p> <p>Relative reduction in MHD : 62%</p>	<p><b>Limitations</b></p> <p>Small sample size</p> <p><b>Other information</b></p> <p>Selection</p> <p>Method of selection appropriate and likely to produce representative cohort</p>

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671820	3) Greater than 5 cc heart within the tangential field.				Comparability: Comparable
<b>Country/ies where the study was carried out</b>	<b>Exclusion criteria</b>				
United States	1) Unwilling to undergo device training				Outcome
<b>Study type</b>	2) Unable to perform a breath hold for 20 seconds.				Outcome and follow-up adequate
Prospective trial	3) Patients who were non-English speaking or who had poor hearing				Indirectness
<b>Aim of the study</b>					None
To determine if radiotherapy with active breathing coordinator can reduce mean heart dose (MHD) by $\geq 20\%$ and dose to the lung					
<b>Study dates</b>					
October 2002 to August 2011					
<b>Source of funding</b>					
NCI Cancer Center Support Grant (P30 CA 56036)					

ABC: Active breathing coordinator; AJCC: American Joint committee on Cancer; BC: Breast cancer; CT: Computed tomography; DIBH: deep inspiration breath hold; FSD: Focus-to-surface distance; Gy: Gray; FB: Free breathing; IMRT: Intensity-modulated radiotherapy; LAD: Left anterior descending; mDIBH: Moderate deep inspiration breath hold; MHD: Mean heart dose; NCI: National Cancer Institute; NIHR: National Institute of Health Research; RT: Radiotherapy; VBH: Voluntary breath holding