

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Surgical Clips for Breast Biopsy: Comparative Clinical Effectiveness, Cost- Effectiveness, and Guidelines

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Authors: Humaira Nakhuda, Sarah Jones

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Research Questions

1. What is the comparative clinical effectiveness of breast biopsy with and without surgical clips in patients with suspected breast cancer or undergoing breast cancer treatment?
2. What is the comparative clinical effectiveness of surgical breast clips in patients undergoing breast biopsy for suspected breast cancer or undergoing breast cancer treatment?
3. What is the comparative cost-effectiveness of breast biopsy with and without surgical clips in patients with suspected breast cancer or undergoing breast cancer treatment?
4. What is the comparative cost-effectiveness of surgical clips in patients undergoing breast biopsy for suspected breast cancer or undergoing breast cancer treatment?
5. What are the guidelines informing best practice for patients undergoing breast biopsy for suspected breast cancer or undergoing breast cancer treatment?

Key Findings

Two systematic reviews without meta-analysis, six non-randomized studies, and one evidence-based guideline were identified regarding the use of surgical clips for breast biopsy. No relevant health technology assessments, randomized controlled trials, or economic evaluations were identified.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1 2013 and May 14 2018. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1-Q5: Adults (including men or women) undergoing breast biopsy for suspected breast cancer, or breast cancer treatment after breast biopsy
Intervention	Q1, Q3, Q5: Breast biopsy with surgical clips Q2, Q4: One type of surgical breast clip
Comparator	Q1, Q3, Q5: Breast biopsy without surgical clips Q2, Q4: Another type of surgical breast clip
Outcomes	Q1, Q2: Clinical effectiveness i.e., benefit (e.g., correct identification/treatment of diseased tissue; cancer survival), harm/safety (e.g., unintended identification/treatment of healthy tissue; need for repeat biopsy), Q3, Q4: Cost-effectiveness Q5: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

Two systematic reviews without meta-analysis, six non-randomized studies, and one evidence-based guideline were identified regarding the use of surgical clips for breast biopsy. No relevant health technology assessments, randomized controlled trials, or economic evaluations were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Two systematic reviews (SR)^{1,2} without meta-analysis, six non-randomized studies (NRS),³⁻⁸ and one evidence-based guideline⁹ were identified regarding the clinical and cost-effectiveness of using surgical clips for adult breast biopsy for suspected breast cancer or breast cancer treatment. Study details for the NRSs are included in Table 2.

The authors of one SR² reported that surgical clips combined with standardized guidelines significantly improve delineation ability by an observer, and that it is the standard in ongoing trials for external-beam accelerated partial breast irradiation. The authors of a second SR¹ noted meta-analysis and comparative analysis is missing for all of the various breast lesion location techniques.

The authors of two NRSs^{3,5} noted that surgical clips allow for more accurate margins and targeting of at-risk tissue and less normal tissue in the radiotherapy field, reducing re-excision rates. Furthermore, the authors of one NRS⁷ concluded margins smaller than 8 mm cannot be safely used without clip-based image-guided radiotherapy. HydroMARK biopsy clips were concluded to be a feasible and safe alternative to traditional preoperative wire-localized excision⁴, and as effective as standard markers with regards to re-excision rates and specimen volume from partial mastectomy.⁷ Additionally, the authors of one

NRS⁵ concluded that sonographically visible clips achieved a reduction in re-excision rates and an increase in clear margins when compared with radiopaque clips for preoperative localization for breast conserving surgery. Lastly, the authors of one NRS⁶ found the volume variability to delineate based on using seroma, clips, or both clips and seroma, which resulted in variability for dosimetry for at-risk organs.

One evidence-based guideline was identified.⁹ The National Institute for Health and Care Excellence (NICE) concluded Intrabeam, a radiotherapy system, as not advantageous in radiotherapy delivery, and noted that the use of clips to guide electron boost radiotherapy is recommended as best practice by the Association of Breast Surgeons.⁹

No summary could be provided on the comparative cost-effectiveness of breast biopsy with and without surgical clips and the comparative cost-effectiveness of surgical clips in patients undergoing breast biopsy for suspected breast cancer or undergoing breast cancer treatment.

Table 2: Summary of Included Non-Randomized Studies on the Clinical Effectiveness of the Use of Surgical Clips for Breast Biopsy

First Author, Year	Study Characteristics and Population	Intervention	Comparator	Results and Author Conclusions
Non-Randomized Studies				
Ebner, 2017 ³	<ul style="list-style-type: none"> Retrospective descriptive study Post-surgical patients who underwent breast-conserving treatment in early breast cancer N = 110 	<ul style="list-style-type: none"> GMI and NTI for electron boost with surgical clips 	<ul style="list-style-type: none"> GMI and NTI for electron boost without surgical clips 	<ul style="list-style-type: none"> Use of intra-surgically placed clips reduced GMI and NTI Authors concluded that surgical clips use allows for more at-risk tissue to be included in the radiotherapy field, and normal tissue receives less radiotherapy
Gentile, 2016 ⁴	<ul style="list-style-type: none"> Retrospective chart review Patients who underwent segmental mastectomy or excisional breast biopsy N = 220 	<ul style="list-style-type: none"> Intraoperative ultrasound-guided excision using hydrogel-encapsulated (HydroMARK) biopsy clips (N = 107) 	<ul style="list-style-type: none"> Traditional preoperative wire localization (N = 113) 	<ul style="list-style-type: none"> No difference in re-excision rates for positive margins between intervention and comparator Intraoperative ultrasound-guided excision using HydroMARK biopsy clips is a feasible and safe alternative to traditional preoperative wire localized excision for non-palpable breast lesions
Corsi, 2015 ⁵	<ul style="list-style-type: none"> Retrospective review Non-palpable breast cancer patients treated with lumpectomy N = 209 	<ul style="list-style-type: none"> Preoperative localization using sonographically visible clips N = 150 	<ul style="list-style-type: none"> Preoperative localization using radiopaque clips (N = 59) 	<p>Clear margins:</p> <ul style="list-style-type: none"> Radiopaque: 57.6% Sonographically visible: 89.3% ($P < 0.0001$; odds ratio, 7.6; 95% CI, 3.4 to 17.2) <p>Re-excision rate:</p> <ul style="list-style-type: none"> Sonographically visible: decrease from 42.4% to 10.7% ($P < 0.0001$), and 5.08 resection ratio compared to 3.54 for radiopaque ($P = 0.03$)

First Author, Year	Study Characteristics and Population	Intervention	Comparator	Results and Author Conclusions
Guo, 2015 ⁶	<ul style="list-style-type: none"> Comparative study Patients with SCS 3~5 and ≥ 5 surgical clips undergoing EB-PBI treatment plan using four dimensional computed tomographys cans N = 20 	<ul style="list-style-type: none"> EB-PBIC+S plan 	<ul style="list-style-type: none"> EB-PBIC plan EB-PBIS plan 	<ul style="list-style-type: none"> IGTV+S volume was significantly larger than that of IGTVS and IGTV PTVC+S volume was larger than that of PTVS and PTVC EB-PBIC+S PTV coverage similar to EB-PBIC and EB-PBIS EB-PBIS had lowest ipsilateral lung doses and ipsilateral normal breast compared with EB-PBIC+S and EB-PBIC plans
Blumencranz, 2014 ⁷	<ul style="list-style-type: none"> Retrospective chart review Female patients undergoing partial mastectomies after percutaneous biopsies N = 691 	<ul style="list-style-type: none"> Stereotactic and ultrasound biopsy with hydrogel biopsy tissue markers (HydroMARK) 	<ul style="list-style-type: none"> Stereotactic and ultrasound biopsy with standard (other) markers 	<p>Stereotactic biopsy:</p> <ul style="list-style-type: none"> 75.8% of standard markers required WL versus 17.1% for HydroMARK ($P < 0.0001$) <p>Ultrasound biopsy:</p> <ul style="list-style-type: none"> 22.6% of standard marker required WL versus 4.3% for HydroMARK ($P < 0.0001$)
Harris, 2014 ⁸	<ul style="list-style-type: none"> Multi-centre observational study embedded within a randomized controlled trial Patients receiving breast radiotherapy within IMPORT-HIGH N = 218 	<ul style="list-style-type: none"> Patient set-up using clip-based IGRT 	<ul style="list-style-type: none"> Patient set-up using standard imaging 	<p>Safety margins:</p> <ul style="list-style-type: none"> Clip-based IGRT: < 5 mm Standard imaging: < 8 mm <p>Median tissue volume irradiation</p> <ul style="list-style-type: none"> 29 cm³ (range 11 to 193 cm³) decrease in clip-based IGRT compared to standard imaging

GMI = Geographic Mass Index; NTI = Normal Tissue Index; SCS = Seroma Clarity Score; EB-PBI = External-Beam Partial Breast Irradiation; C+S = Clips and Seroma; C = Clips; S = Seroma; IGTV = Internal Gross Target Volume; PTV = Planning Target Volume; WL = Wire Localization; IMPORT HIGH = Intensity Modulated and Partial Organ Radiotherapy – HIGHer-risk patient group; IGRT = Image-Guided Radiotherapy

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

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[PubMed: PM23115016](#)
2. Yang TJ, Tao R, Elkhuzen PH, van Milet-Vroegindewij C, Li G, Powell SN. Tumor bed delineation for external beam accelerated partial breast irradiation: a systematic review. *Radiother Oncol*. 2013 Aug;108(2):181-9.
[PubMed: PM23806188](#)

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

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4. Gentile LF, Himmeler A, Shaw CM, Bouton A, Vorhis E, Marshall J, et al. Ultrasound-Guided Segmental Mastectomy and Excisional Biopsy Using Hydrogel-Encapsulated Clip Localization as an Alternative to Wire Localization. *Ann Surg Oncol.* 2016 Oct;23(10):3284-9.
[PubMed: PM27338745](#)
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[PubMed: PM26885108](#)
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[PubMed: PM25034819](#)
8. Harris EJ, Mukesh M, Jena R, Baker A, Bartelink H, Brooks C, et al. A multicentre observational study evaluating image-guided radiotherapy for more accurate partial-breast intensity-modulated radiotherapy: comparison with standard imaging technique. Southampton (UK): NIHR Journals Library; 2014 Nov. (Efficacy and Mechanism Evaluation). [cited 2018 May 25]. Available from <https://www.ncbi.nlm.nih.gov/books/NBK263513/>

Economic Evaluations

No literature identified.

Guidelines and Recommendations

9. Multiple technology appraisal (MTA) Breast cancer (early) - Intrabeam IORT [ID618] [Internet]. London (GB): National Institute for Health and Technology Excellence; 2018 Jan 31. [cited 2018 May 25]. Available from: <https://www.nice.org.uk/guidance/ta501/documents/committee-papers>
See: Evidence, Committee Papers, Appraisal consultation: 2, page 30

Appendix — Further Information

Clinical Practice Guidelines – Non-Systematic Methodology

10. Bossuyt V, Provenzano E, Symmans WF, Boughey JC, Coles C, Curigliano G, et al. Recommendations for standardized pathological characterization of residual disease for neoadjuvant clinical trials of breast cancer by the BIG-NABCG collaboration. *Ann Oncol*. 2015 Jul;26(7):1280-91. [cited 2018 May 25]. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4804123>
PubMed: [PM26019189](https://pubmed.ncbi.nlm.nih.gov/26019189/)

Non-Randomized Studies – Alternative Outcome

11. Yen P, Dumas S, Albert A, Gordon P. Post-Vacuum-Assisted Stereotactic Core Biopsy Clip Displacement: A Comparison Between Commercially Available Clips and Surgical Clip. *Can Assoc Radiol J*. 2018 Feb;69(1):10-5.
PubMed: [PM29458952](https://pubmed.ncbi.nlm.nih.gov/29458952/)
12. Pinkney DM, Mychajlowycz M, Shah BA. A prospective comparative study to evaluate the displacement of four commercially available breast biopsy markers. *Br J Radiol*. 2016 Sep;89(1065):20160149. [cited 2018 May 25]. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5124921>
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Economic Study – Direct Cost Comparison

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PubMed: [PM26745082](https://pubmed.ncbi.nlm.nih.gov/26745082/)

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