CADTH

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Preoperative Seed Placement for Breast Cancer Surgery: Clinical Effectiveness, Cost-Effectiveness, and Guidelines

Service Line: Rapid Response Service
Version: 1.0
Publication Date: April 01, 2019
Report Length: 12 Pages

CADTH

Authors: Ke Xin Li, Charlene Argáez

Cite As: Preoperative seed Placement for beast cancer surgery: clinical effectiveness, cost-efectiveness, and guidelines. Ottawa: CADTH; 2019 Apr. (CADTH rapid response report: summary of abstracts).

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Research Questions

1. What is the clinical effectiveness of preoperative seed placement for patients undergoing surgery for breast cancer?
2. What is the cost-effectiveness of preoperative seed placement for patients undergoing surgery for breast cancer?
3. What are the evidence-based guidelines regarding methods of preoperative tumor localization for patient undergoing surgery for breast cancer?

Key Findings

Three systematic review and meta-analyses, two randomizd controlled trials, eleven non-randomized studies, and one economic evaluation were identified regarding preoperative seed placement for breast cancer surgery. No relevant evidence-based guidelines 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. For questions #1 and #2, no methodological filters were applied to limit retrieval by study type. A Guidelines filter was applied to question #3 to limit the 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, 2014 and March 20, 2019. 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	Adults undergoing surgery for breast cancer
Intervention	Preoperative placement of radioactive seeds for tumor localization
Comparator	Q1,2: Preoperative placement of wire for tumor localization Q3: No comparator
Outcomes	Q1: Clinical effectiveness (e.g., tumor delineation, outcome margins, quality of specimen removed) Q2: Cost-effectiveness Q3: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized trials, 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.

Three systematic review and meta-analyses, two randomizd controlled trials, eleven non-randomized studies, and one economic evaluation were identified regarding preoperative seed placement for breast cancer surgery. No relevant health technology assessments or evidence-based guidelines were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One systematic review,[1] one systematic review with meta-analyses,[2] and one meta-analysis[3] were identified regarding preoperative seed placement for breast cancer surgery. One systematic review by Gray et al. reported that radioactive seed localization (RSL) was found to lower positive tumour margin rates when compared to wire localization (WL).[1] The systematic review with meta-analyses reported no clear evidence for one localization technique over another.[2] The authors suggested RSL could be offered to as an equally reliable alternative to WL.[2] The focus of the meta-analysis by Pouw et al. was to evaluate the use of RSL with irradicality and re-excision rates as outcomes.[3] No further details regarding outcomes or results were provided in the abstract.[3]

Two randomizd controlled trials and eleven non-randomized studies were identified.[4-16] A wide range of health outcomes were reported and the conclusions were inconsistent.[4-16] Detailed study characteristics are provided in Table 2.

The 2014 economic evaluation by Loving et al. reported that RSL could modestly reduce cost per patient in a bundled payment system when compared to WL.[17] However, RSL could cause a moderate loss of revenue for a fee-for-service system.[17]

No relevant health technology assessments or evidence-based guidelines were identified.

Table 2: Characteristics of Included Literature

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Outcomes	Conclusions
Systematic Reviews and Meta-analyses				
Gray, 2018[1] **US**	106 articles included N = NR Age: NR	Localization techniques (including radioactive seed localization and radioguided occult lesion localization) vs. WL	• Positive margin rates	"Localization techniques such as radioactive seed localization and radioguided occult lesion localization were found potentially to lower positive margin rates as alternatives to WL depending on baseline positive margin rates."[1]
Chan, 2015[2] **UK**	11 RCTs included: 6 RCTs ROLL vs. WGL; 2 RCTs RSL vs. WGL; 1 RCT CAL vs. WGL; 1 RCT IOUS vs. WGL; 1 RCT modified ROLL in combination with methylene dye versus WGL MA performed N = NR Age: NR	RSL vs. WGL	• Successful localization • Successful excision • Positive tumour margins • Re-operation rates • Postoperative complications	"Owing to a lack of trials in certain localization techniques, we could only draw conclusions about ROLL and RSL versus WGL. There is no clear evidence to support one guided technique for surgically excising a non-palpable breast lesion over another. Results from this Cochrane review support the continued use of WGL as a safe and tested technique that allows for flexibility in selected cases when faced with extensive microcalcification. ROLL and RSL could be offered to patients as a comparable replacement for WGL as they are equally reliable."[2]
Pouw, 2015[3] **Netherlands**	Number of included studies NR MA performed N = 3168 Age: NR	RSL Comparators NR	• Irradicality • Re-excision rates	"The clinical adaptation shows growing confidence in RSL and further growth is expected."[3]
Randomized Controlled Trials				
Langhans, 2017[4] **Denmark**	N = 444 n = 409 randomized n = 207 RSL n = 206 WGL Age: NR	RSL vs. WGL	• Positive resection margin rate • Duration of surgical procedure • Weight of surgical specimen • Pain	"RSL offers a major logistic advantage, as localization can be done several days before surgery without any increase in positive resection margins compared with WGL."[4]

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Outcomes	Conclusions
Bloomquist, 2016[5] **US**	N = 135 n = 70 RSL n = 55 WL Age: NR	RSL vs. WL	• Pain • Convenience rating of procedure • Volume of the main specimen • Volume of the first surgery • Rate of positive margins	"RSL resulted in less severe pain and higher convenience compared to WL, with comparable excision volume and positive margin rates. High patient satisfaction with RSL provides another incentive for surgeons to strongly consider RSL as an alternative to WL."[5]
Non-Randomized Studies				
Horwood, 2019[6] **US**	N = NR Age: NR	RSL vs. WL	• Re-excision rate • Margin positivity • Volume of tissue removed • Complication rate	"There was no difference in re-excision rate, margin positivity, volume of tissue removed, and complication rate for RSL vs WL (P = 0.9934, P = 0.9934, P = 0.6645, and P = 0.4716 respectively). The only difference was a longer OR time, RSL = 104.408 minutes vs WL = 82.386 minutes. (P = 0.0163). RSL and WL are comparable techniques for localization of nonpalpable breast lesions."[6]
Milligan, 2018[7] **UK**	N = 200 Age: NR	RSL vs. GWL	• Total specimen excision weight • Surgical resection margins • Invasive carcinoma	"In this study, RSL is shown to be non-inferior to the use of GWL for non-palpable carcinoma in patients undergoing BCS and we suggest that it could be introduced successfully in other breast units. Advances in knowledge: Here we have demonstrated the use of RSL localization results in significant lower weight resection specimens of breast carcinoma when compared with a matched group using GWL, without any significant differences in oncological outcome between the groups."[7]
Parvez, 2018[8] **Canada**	N = 803 Age: NR	RSL vs. WL	• Positive margin rate • Re-operation • Mean specimen volume	"There has been variable adoption of RSL in our city. Despite this, relevant surgical outcomes have been similar across groups."[8]
Stelle, 2018[9] **US**	N = 382 lesions n = 205 RSL n = 155 WL	RSL vs. WL	• Mean specimen size • Re-excision for margin	"The use of RSL is a viable option in the community setting, with several benefits over WL. While operative times were slightly longer with RSL,

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Outcomes	Conclusions
	Age: NR		clearance • Mean operating room time	there was no difference in specimen size or re-excision rate for malignant lesions."[9]
Fung, 2017[10] **Canada**	N = 298 Age: NR	RSL vs. WL	• Recurrence • Median time to recurrence • Positive margins at first surgery and final surgery	"There was no detectable difference in BC recurrence between WL and RSL groups and positive margins at initial or final surgery both predicted for BC recurrence."[10]
In 't Hout, 2016[11] **Netherlands**	N =236 n = 87 IL n = WL	IL vs. WL	• Overall success rate • Radical resection rate • Median operation time • Volume of the specimen	"Localization of non-palpable breast cancer using Iodine-125 seeds is, at least, as good as the standard wire localization procedure."[11]
Rarick, 2016[12] **US**	N = 106 n = 44 RSL n = 62 CWL Age: NR	RSL vs. CWL	• Margin classifications	"This study shows that there were no significant marginal status differences between RSL and CWL lumpectomy specimens with invasive carcinoma. Rather, what was relevant is whether the entire specimen could be classified as having negative/close margins. Significant workflow challenges in surgical pathology laboratories are expected with the adoption of the RSL process."[12]
Luiten, 2015[13] **Netherlands**	N = 169 n = 91 RSL n = 78 WGL Age: NR	RSL vs. WGL	• Risk of extensively involved resection margins	"In patients treated with breast-conserving surgery for non-palpable DCIS, localization with iodine-125 seeds is superior to the WGL technique in reducing the risk of extensively involved resection margins."[13]
Sharek, 2015[14] **US**	N = 232 Age: NR	RSL vs. WL	• Closest surgical margin • Reexcision rate • Reoperation rate • Ratio of the tumor volume to initial surgical specimen volume	"RSL is an acceptable alternative to wire localization and offers significant improvements in workflow."[14]

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Outcomes	Conclusions
			• Ratio of the tumor volume to total volume resected • Clinical or computed cosmesis scores • Scheduled biopsy slot utilization • Time spent scheduling, • Biopsy wait time after rsl institution	
Chiu, 2014[15] **US**	N = 103 n = 49 RSL n = 44 WL Age: NR	RSL vs. WL	• Margin status • Re-excision rate	"RSLE is an effective technique for excision of nonpalpable breast lesions in the community setting. This technique allows for accurate localization and appears to allow for smaller volume of tissue to be excised."[15]
Diego, 2014[16] **US**	N = 324 n = 128 RSL n = 196 WL Age: mean age 54 years	RSL vs. WL	• Operating room time • Upstage rate • Targeted lesions retrieved • Specimen volume	"RSL is comparable to WL for EBB of HRLs with similar OR times and upstage rates. SV is significantly decreased with RSL and may translate into improved cosmetic outcomes without sacrificing the diagnostic accuracy of the EBB."[16]

BC = breast cancer; CAL = cryo-assisted techniques; CI = confidence interval; CWL = conventional wire localization; EBB = excisional breast biopsies; GWL = guidewire-localization; HRL = high-risk lesions; IL = Iodine-125 seeds; IOUS = intraoperative ultrasound-guided lumpectomy; MA = meta-analysis; NR = not reported; OR = operating room; RCT = randamized controlled trial; ROLL = radioguided occult lesion localization; RSL = radioactive iodine ((125)I) seed localization; RSLE = Radioactive seed localized excision; UK = United Kingdom; US = United States; vs. = versus; WGL = wire-guided localization; WL = wire localization.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Gray RJ, Pockaj BA, Garvey E, Blair S. Intraoperative margin management in breast-conserving surgery: a systematic review of the literature. *Ann Surg Oncol*. 2018 Jan;25(1):18-27.
PubMed: PM28058560

2. Chan BK, Wiseberg-Firtell JA, Jois RH, Jensen K, Audisio RA. Localization techniques for guided surgical excision of non-palpable breast lesions. *Cochrane Database Syst Rev*. 2015 Dec 31(12):Cd009206.
PubMed: PM26718728

3. Pouw B, de Wit-van der Veen LJ, Stokkel MP, Loo CE, Vrancken Peeters MJ, Valdes Olmos RA. Heading toward radioactive seed localization in non-palpable breast cancer surgery? A meta-analysis. *J Surg Oncol*. 2015 Feb;111(2):185-191.
PubMed: PM25195916

Randomized Controlled Trials

4. Langhans L, Tvedskov TF, Klausen TL, et al. Radioactive seed localization or wire-guided localization of nonpalpable invasive and in situ breast cancer: a randomized, multicenter, open-label trial. *Ann Surg*. 2017 Jul;266(1):29-35.
PubMed: PM28257326

5. Bloomquist EV, Ajkay N, Patil S, Collett AE, Frazier TG, Barrio AV. A randomized prospective comparison of patient-assessed satisfaction and clinical outcomes with radioactive seed localization versus wire localization. *Breast J*. 2016 Mar-Apr;22(2):151-157.
PubMed: PM26696461

Non-Randomized Studies

6. Horwood CR, Grignol V, Lahey S, et al. Radioactive seed vs wire localization for nonpalpable breast lesions: a single institution review. *Breast J*. 2019 Mar;25(2):282-285.
PubMed: PM30706613

7. Milligan R, Pieri A, Critchley A, et al. Radioactive seed localization compared with wire-guided localization of non-palpable breast carcinoma in breast conservation surgery-the first experience in the United Kingdom. *Br J Radiol*. 2018 Jan;91(1081):20170268.
PubMed: PM29076748

8. Parvez E, Cornacchi SD, Fu E, et al. Adoption and outcomes of radioguided seed localization for non-palpable invasive and in-situ breast cancer at three academic tertiary care centers. *Am J Surg*. 2018 Dec;216(6):1160-1165.
PubMed: PM30005808

9. Stelle L, Schoenheit T, Brubaker A, et al. Radioactive seed localization versus wire localization for nonpalpable breast lesions: a two-year initial experience at a large community hospital. *Ann Surg Oncol*. 2018 Jan;25(1):131-136.
PubMed: PM29134380

10. Fung F, Cornacchi SD, Reedijk M, et al. Breast cancer recurrence following radioguided seed localization and standard wire localization of nonpalpable invasive and in situ breast cancers: 5-Year follow-up from a randomized controlled trial. *Am J Surg*. 2017 Apr;213(4):798-804.
PubMed: PM27810132

11. In 't Hout BA, Schenk KE, van der Linden AN, Roumen RM. Efficacy of localization of non-palpable, invasive breast cancer: Wire localization vs. Iodine-125 seed: a historical comparison. *Breast*. 2016 Oct;29:8-13.
PubMed: PM27376887

12. Rarick J, Kimler BF, Tawfik O. Comparison of margin status and lesional size between radioactive seed localized vs conventional wire localized breast lumpectomy specimens. *Ann Diagn Pathol*. 2016 Apr;21:47-52.
PubMed: PM27040931

13. Luiten JD, Beek MA, Voogd AC, Gobardhan PD, Luiten EJ. Iodine seed- versus wire-guided localization in breast-conserving surgery for non-palpable ductal carcinoma in situ. *Br J Surg*. 2015 Dec;102(13):1665-1669.
PubMed: PM26492349

14. Sharek D, Zuley ML, Zhang JY, Soran A, Ahrendt GM, Ganott MA. Radioactive seed localization versus wire localization for lumpectomies: a comparison of outcomes. *Am J Roentgenol*. 2015 Apr;204(4):872-877.
PubMed: PM25794081

15. Chiu JC, Ajmal S, Zhu X, Griffith E, Encarnacion T, Barr L. Radioactive seed localization of nonpalpable breast lesions in an academic comprehensive cancer program community hospital setting. *Am Surg*. 2014 Jul;80(7):675-679.
PubMed: PM24987899

16. Diego EJ, Soran A, McGuire KP, et al. Localizing high-risk lesions for excisional breast biopsy: a comparison between radioactive seed localization and wire localization. *Ann Surg Oncol*. 2014 Oct;21(10):3268-3272.
PubMed: PM25034818

Economic Evaluations

17. Loving VA, Edwards DB, Roche KT, et al. Monte Carlo simulation to analyze the cost-benefit of radioactive seed localization versus wire localization for breast-conserving surgery in fee-for-service health care systems compared with accountable care organizations. *Am J Roentgenol*. 2014 Jun;202(6):1383-1388.
PubMed: PM24848839

Guidelines and Recommendations

No literature identified

Appendix — Further Information

Previous CADTH Reports

18. Nakhuda H, Jones S. Surgical clips for breast biopsy: comparative clinical effectiveness, cost-effectiveness, and guidelines. Ottawa (ON): CADTH; 2018 May: https://www.cadth.ca/sites/default/files/pdf/htis/2018/RB1227%20Surgical%20Clips%20for%20Breast%20Biopsy%20Final.pdf Accessed 2019 Apr 01.

19. Clark M, Cunningham J, Banks R. Ultrasound-guided wire localizations compared with mammographic stereo localizations prior to surgery of the breast: clinical effectiveness, cost- effectiveness, and guidelines. Ottawa (ON): CADTH; 2009 Dec: https://www.cadth.ca/sites/default/files/pdf/htis-L1/J0348%20US-Guided%20Wire%20Localizations%20of%20the%20Breast%20final.pdf Accessed 2019 Apr 01.

Health Technology Assessments – Methodology Unclear

20. Lessard J. [Use of radioactive seeds for the preoperative localization of non-palpable breast tumours]. Quebec (QC): Institut national d'excellence en santé et en services sociaux (INESSS); 2016: https://www.inesss.qc.ca/nc/en/publications/publications/publication.html?PublicationPluginController%5Bcode%5D=FICHE&PublicationPluginController%5Buid%5D=428&PublicationPluginController%5BbackUrl%5D=%252Fnc%252Fen%252Fpublications%252Fpublications.html%253FPublicationPluginController%25255Bpointer%25255D%253D0&cHash=1bbf19928e0562e3d5072e860a7babca Accessed 2019 Apr 01.

Randomized Controlled Trials – Alternative Outcomes

21. Parvez E, Cornacchi SD, Hodgson N, et al. A cosmesis outcome substudy in a prospective, randomized trial comparing radioguided seed localization with standard wire localization for nonpalpable, invasive, and in situ breast carcinomas. *Am J Surg*. 2014 Nov;208(5):711-718. PubMed: PM25201587

Non-Randomized Studies

Alternative Comparators

22. Rhee D, Pockaj B, Wasif N, et al. Operative outcomes of conventional specimen radiography versus in-operating room specimen radiography in radioactive seed-localized segmental mastectomies. *Am J Surg*. 2018 Jan;215(1):151-154. PubMed: PM28784236

23. Mango V, Ha R, Gomberawalla A, et al. Evaluation of the SAVI SCOUT surgical guidance system for localization and excision of nonpalpable breast lesions: a feasibility study. *Am J Roentgenol*. 2016 Oct;2017(4) . PubMed: PM27304083

Alternative Outcomes

24. Ong JSL, Teh J, Saunders C, et al. Patient satisfaction with Radioguided Occult Lesion Localisation using iodine-125 seeds ('ROLLIS') versus conventional hookwire localisation. *Eur J Surg Oncol*. 2017 Dec;43(12):2261-2269. PubMed: PM29102440

25. Dryden MJ, Dogan BE, Fox P, et al. Imaging factors that influence surgical margins after preoperative 125I radioactive seed localization of breast lesions: comparison with wire localization. *Am J Roentgenol*. 2016 May;206(5):1112-1118. PubMed: PM27007608

Methodology Unclear

26. Da Silva M, Porembka J, Mokdad AA, et al. Bracketed radioactive seed localization vs bracketed wire-localization in breast surgery. *Breast J*. 2018 Mar;24(2):161-166. PubMed: PM28707718

Clinical Practice Guidelines – Methodology Not Specified

27. Association of Breast Surgery. Best practice guidelines for surgeons in breast cancer screening. In: Downey S, Chagla L, Chandran V, et al., eds. London (UK): The Royal College of Surgeons; 2018 Jan: https://associationofbreastsurgery.org.uk/media/64276/final-screening-guidelines-2018.pdf Accessed 2019 Apr 01.
See: Localisation, page 4

28. Canadian Association of Radiologists. CAR practice guidelines and technical standards for breast imaging and intervention. Ottawa (ON): CAR; 2016 Sep (rev): https://car.ca/wp-content/uploads/Breast-Imaging-and-Intervention-2016.pdf.
See: Radioactive Seed Localization, page 31 Accessed 2019 Apr 01.

29. Princess Margaret Cancer Centre. Princess Margaret Cancer Centre clinical practice guidelines: breast cancer - breast site. Toronto (ON): Princess Margaret Cancer Centre, University Hospital Network; 2015 Sep (rev): https://www.uhn.ca/PrincessMargaret/Health_Professionals/Programs_Departments/Breast/Documents/CPG_Breast_BreastCancer.pdf. Accessed 2019 Apr 01.

Review Articles

30. Boughey JC, Alvarado MD, Lancaster RB, et al. Surgical standards for management of the axilla in breast cancer clinical trials with pathological complete response endpoint. *NPJ Breast Cancer*. 2018 Aug 17;4:26. PubMed: PM30131975

31. Woods RW, Camp MS, Durr NJ, Harvey SC. A Review of Options for Localization of Axillary Lymph Nodes in the Treatment of Invasive Breast Cancer. *Acad Radiol*. 2018 Aug 22. PubMed: PM30143401