



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Directorate F - Health, Consumers & Reference Materials (Ispra)
Health in Society

European Commission Initiative on Breast Cancer (ECIBC): European guidelines on breast cancer screening and diagnosis Evidence profile

Healthcare question	Should clip-marking vs no clip-marking after needle core biopsy (NCB)/vacuum assisted needle core biopsy (VANCb) be used for surgical therapy planning in patients with breast cancer lesions?
Date	July 2017
Authors	ECIBC Guidelines Development Group (GDG): Mariangela Autelitano, Bettina Borisch, Mireille Broeders, Xavier Castells, Edoardo Colzani, Jan Daneš, Stephen Duffy, Patricia Fitzpatrick, Markus Follmann, Livia Giordano, Paolo Giorgi Rossi, Axel Gräwingholt, Solveig Hofvind, Lydia Ioannidou-Mouzaka, Susan Knox, Miranda Langendam, Annette Lebeau, Helen McGarrigle, Lennarth Nyström, Elsa Pérez Gómez, Cecily Quinn, Peter Rabe, Holger Schünemann, Alberto Torresin, Ruben Van Engen, Cary Van Landsveld-Verhoeven, Sue Warman, Kenneth Young Systematic Review team: Ena Niño de Guzmán, Carlos Canelo-Aybar, Margarita Posso, Iván Solà, David Rigau Comas, Pablo Alonso-Coello. JRC Healthcare Quality team: Asli Uluturk, Elena Parmelli, Zuleika Saz-Parkinson, Donata Lerda
Abbreviations	CI: Confidence interval RR: Risk ratio HR: Hazard Ratio

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clip-marking	No clip-marking after needle core biopsy (NCB)/vacuum assisted needle core biopsy (VANCb)	Relative (95% CI)	Absolute (95% CI)		
Number of patients with Close/Positive margins ^a												
1 ¹	observational studies	serious ^b	not serious	not serious ^c	serious ^d	none	16/145 (11.0%)	35/228 (15.4%)	RR 0.72 (0.41 to 1.25)	43 fewer per 1,000 (from 91 fewer to 38 more)	⊕○○○ VERY LOW	CRITICAL
Local breast recurrence (overall) (follow up: median 49 months)												
1 ¹	observational studies	serious ^b	not serious	not serious ^c	serious ^e	none	2/145 (1.4%)	19/228 (8.3%)	RR 0.17 (0.04 to 0.70) ^f	69 fewer per 1,000 (from 80 fewer to 25 fewer)	⊕○○○ VERY LOW	CRITICAL
Risk of recurrence (follow up: median 49 months; assessed with: Cox hazard multivariate model) ^f												
1 ¹	observational studies	not serious	not serious	not serious ^c	serious ^d	none	2/145 (1.4%)	19/228 (8.3%)	HR 0.27 (0.06 to 1.16)	60 fewer per 1,000 (from 78 fewer to 13 more)	⊕○○○ VERY LOW	CRITICAL
Mortality ^g												
1 ¹	observational studies	serious ^b	not serious	not serious ^c	serious ^e	none	5/145 (3.4%)	35/228 (15.4%)	RR 0.22 (0.09 to 0.56)	120 fewer per 1,000 (from 140 fewer to 68 fewer)	⊕○○○ VERY LOW	CRITICAL
Adverse events												
0							The study did not report this outcome.				-	

Explanations

- a. This is an operational definition of "final margin status". The status "close" means that the post-surgical specimen had less than 2 mm. of free cancer cells margin. Twelve (8.3%) and four (2.7%) women had close or positive margins respectively in the clip group whereas 23 (10.1%) and 12 (5.3%) of women had close and positive margins respectively in the group without clip.
- b. There is a serious risk of bias due to confounding factors; women without a clip had a more advanced nodal disease (24.5%) than women with a clip (13%). The neoadjuvant chemotherapy was not the same for everyone, only 53% received an additional taxane cycle. The reasons for not deployment of a clip in the control group were not clear. There were missing data regarding lymphovascular invasion status, it was unknown in 13% of the total population, it represented 18% of women with clip and 9% in women without a clip.
- c. Since Oh 2007 included women with palpable lesions, for women with non-palpable lesions, the confidence should be downgraded due to indirectness.
- d. The margins of confidence intervals are wide, so there is not enough certainty about the real impact of the intervention.
- e. The number of events was small. This fact may affect the robustness of estimations.
- f. This outcome is a supplementary measure for local breast recurrence. None of the 57 women with residual disease (RD) with a clip inserted presented local recurrence; compared with 11 of the 113 (9.7%) women with RD but without clip placement RR 0.09 (95%CI, 0.01-1.42). In women with pathological complete response (pCR) or near pCR there were no differences in local recurrences between clip and no-clip groups (, 2.47% and 6.48% respectively, RR 0.38 (95% CI 0.08-1.8). Other three factors were independently associated with an increased hazard for local recurrence: T3-T4 clinical tumour size versus clinical stage 1-2 HR 2.66 (95% CI 1.03-6.86), Close or positive margins versus negative margins HR 3.37 (95% CI 1.13-10.07) and Modified Black Nuclear grade (MBNG) 3 versus MBNG 1 or 2 HR 3.86 (95% CI 1.13-13.22).
- g. Mortality rate was selected instead of overall survival, due to incomplete data reporting.

References

- h. Oh JL, Nguyen G, Whitman GJ, Hunt KK, Yu TK, Woodward WA, et al.. Placement of radiopaque clips for tumor localization in patients undergoing neoadjuvant chemotherapy and breast conservation therapy. Cancer; 2007.