Editorial Article

How to avoid the uncertainties of intraoperative examination of the sentinel lymph node in breast cancer?

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Summary

Numerous researchers have confirmed the diagnostic relevance of the sentinel lymph node (SLN) examination in breast carcinoma. Many technical problems are analyzed which are correlated with the intraoperative examination of the SLN and its sensitivity and specificity. In order to avoid the incidence of false positive or false negative intraoperative diagnoses, the authors propose the examination of SLN under local anesthesia, awaiting its definitive analysis before carrying out tumorectomy and/or axillary lymphadenectomy.

*Key words:*Sentinel lymph node; Breast cancer; Intraoperative examination; Tumorectomy.

The idea of a sentinel lymph node (SLN) in breast carcinoma was first suggested by Giuliano *et al.* in 1994 [1]. Since then numerous researchers have confirmed the relevance of this technique and for many it has become the reference method for axillary evaluation [2-4] in the early stage of breast cancer. The classical technique consists of finding and excising the SLN(s) under general anaesthesia during tumorectomy. Intraoperative examination of the SLN serves as the basis in deciding whether or not complete axillary lymphadenectomy is necessary. Intraoperative examination of the SLN (IESLN) is therefore the deciding factor for the remainder of the intervention: if positive, complete lymphadenectomy is carried out during the operation, while if it is negative, lymphadenectomy is not performed. IESLN sensitivity and specificity must be optimal since, in the case of a false positive, the surgeon would perform lymphadenectomy unnecessarily, while a false negative would mean that the patient would have to be re-operated for lymphadenectomy once the definitive results became available.

Two major types of technique have been proposed for evaluating the SLN, namely frozen section analysis and imprint cytology. It is difficult to judge which technique is better than the other. Two authors compared the two methods and came up with entirely conflicting results: according to Van Diest *et al.* [5], frozen section analysis is better, while Motomura *et al.* found that imprint cytology is superior [6]. Nor do data given in the literature (Table 1) provide any reason for preferring one technique rather than the other. Most authors compared the results from the IESLN with a definitive examination based on hematoxylin eosin (HE) and immunohistochemistry (IHC). However, some authors only used HE [7-11] and therefore probably underestimated an appreciable level of micrometastases that can only be detected by IHC. Hence, it is likely that such authors overestimated the sensitivity of IESLN. In fact, Turner showed that IESLN sensitivity fell from 91.6% to 74.2%, depending on whether HE or IHC was used [12]. This means that IESLN performance is lowered even further in the presence of lymph node micrometastases which are conventionally defined as metastases under 2 mm. Authors who delved into this problem showed that while sensitivity was acceptable in the case of macrometastases, it became very poor (< 30%), in the case of micrometastases [5, 13]. Another problem linked to IESLN concerns the existence of rare false positives reported by certain authors [6, 7, 10, 11, 14, 15]; this situation is highly problematic since it can lead to complete axillary lymphadenectomy being performed in patients who do not need it. Finally, the work of Veronesi et al. and Zurrida *et al.* [16, 17] should be pointed out. They achieved a good sensitivity of 95.8% [16], but at the expense of considerably lengthening the IESLN by a response time of 40 minutes!

For all these reasons, we are not really satisfied with IESLN and have devised a strategy designed to avoid it, i.e., detection of the SLN under local anaesthesia (SLNLA) and awaiting its definitive analysis by means of HE and IHC before carrying out tumorectomy on the patient and axillary lymphadenectomy if necessary. This avoids:

– any second operation for axillary lymphadenectomy;

– wrongful lymphadenectomy if the IESLN gives a false positive.

It also allows pathologists to work under improved conditions. When they know they only have to carry out one definitive examination on the SLNs, they can treat them in a more satisfactory manner, avoiding the damage caused by intraoperative analysis, particularly when small lymph nodes are involved.

This strategy has led us to manage our breast cancer patients differently. Before operating on them, we now have the vast majority of prognostic factors which affect treatment: tumor size evaluated by imaging; histological type, histologic grade, presence of hormone receptors evaluated from the tumor biopsy, and the status of the axillary lymph node assessed from a sample of the SLNLA. We have demonstrated that it is perfectly feasible to carry out excision of the SLNLA in an unselected population (publication in press), with the same rates of detection as those achieved with general anaesthesia (a single failure out of 80 patients). We now use this first-line strategy for all our patients T0, T1 or T2 < 3 cm and N0, M0. Lastly, excision of the SLNLA means that tumorectomy under local anaesthesia can then be performed for tumors < 1 cm on a dedicated stereotactic table (ABBI®). In this way, we have been able to treat a few of our patients entirely under local anaesthesia. We feel that this approach constitutes an extremely interesting procedure in terms of minimally invasive breast surgery.

Hence, we consider that the best way to avoid the uncertainties of an intraoperative examination of the SLN is… not to carry out intraoperative examinations!

Table 1. — *Case series in the literature evaluating the performance of intraoperative examination of the SLN by comparison with the definitive anatomical and histopathological examination.*

Author (Year) (Ref.)	N	Intraoperative technique	Control	Sensitivity	Specificity	NPV[1]	PPV[2]
Shiver (2002) [13]	133	Imprint cytology	HE[3] and IHC[4]	56%	100%	88%	100%
				macro: 87% micro: 22%			
Creager (2002) [14]	678	Imprint cytology	HE and IHC	53%	98%	82%	94%
Henry-Tillman (2002) [7]	68	Touch preparation	HE	94.2%	99.8%		
	165	Frozen section	HE	85.7%	98.6%		
Baitchev (2002) [18]	128	Imprint cytology	HE and IHC	83.3%	100%	92.5%	100%
Lee (2002) [8]	65	Touch imprint	HE	65%	100%	88%	100%
Smidt (2002) [15]	148	Scrape cytology	HE and IHC	67%	98%	81%	95%
Llatjos (2002) [19]	76	Imprint cytology	HE and IHC	67.7%	100%	81.8%	100%
Van der Loo (2001) [9]	275	Frozen section	HE	83.1%	100%	93.8%	100%
Chao (2001) [10]	203	Frozen section	HE	68%	99.3%	89.8%	97.3%
Gulec (2001) [20]	157	Frozen section	HE and IHC	43.9%	100%	83.5%	100%
Tanis (2001) [11]	262	Frozen section	HE	74%	99%		
Veronesi (2001) [16]	295	HE: 40 min.	HE and IHC	95.8%		95.4%	
Kane (2001) [21]	150	Gross examination and touch prep analysis		54%	100%		100%
Motomura (2000) [6]	101	Frozen section	HE and IHC	52%	100%		100%
		Imprint cytology		90.9%	98.5%		
Weiser (2000) [22]	890	Frozen section	HE and ICH	macro: 92% micro: 17%			
Viale (1999) [23]	155	Frozen section	HE and IHC			94.1%	
Turner (1999) [12]	278	Frozen section	HE	91.6%	100%		100%
		Imprint cytology		macro: 98% micro: 28%			
			IHC	74.2%			
Van Diest (1999) [5]	74	Frozen section	HE and IHC	87% (91%)	100%		
	54	Imprint cytology		62% (63%)	100%		

[1]Negative predictive value; [2]Positive predictive value; [3]Hematoxylin eosin; [4]Immunohistochemistry.

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