Author’s response to reviews

Title: Sentinel node biopsy for breast cancer: is it already a standard of care? A survey of current practice in an italian region

Authors:

Dr Giorgio Zavagno (giorgio.zavagno@unipd.it)
Dr Gianluca De Salvo (gianluca.desalvo@unipd.it)
Dario Casara (dario.casara@unipd.it)
Paola Del Bianco (paola.delbianco@unipd.it)
Domenico Rubello (domenico.rubello@sanita.padova.it)
Fabrizio Meggiolaro (fabrizio.meggiolaro@unipd.it)
Carlo Riccardo Rossi (carlor.rossi@unipd.it)
Mariaelena Pierobon (mariaxagosto@libero.it)
Mario Lise (mario.lise@unipd.it)

Version: 2 Date: 12 Dec 2003

PDF covering letter
SENTINEL NODE BIOPSY FOR BREAST CANCER: IS IT ALREADY A STANDARD OF CARE? A SURVEY OF CURRENT PRACTICE IN AN ITALIAN REGION

Answers to Referees’ comments

GENERAL

1. The aim of this paper was to investigate whether and, if so, how, breast surgeons in our region perform SNB in their practice. It was not our aim to reporting our personal opinions on issues such as whether or not SNB has been validated, or to comment on which responses to our questions are better or worse. Moreover, even we authors do not altogether agree on some specific issues touched in the questionnaire. We simply point out that SNB has already been widely adopted in clinical practice in our region and, as clearly stated in the discussion, that we strongly believe that this technique should be well learnt, well performed and well standardized. Unfortunately, our survey shows that at present this is not the case.

2. We added the questionnaire form as an appendix, as requested.

3. The paper has been reviewed by a mother-tongue English-language expert.

REVIEWER: AS

1. Our aim was to verify whether the practice of SNB was equally distributed among highly specialized academic centres and small community hospitals. We presumed that it was more likely that an innovative technique such as SNB would have been first investigated and then adopted in clinical practice within academic centres rather than in small hospitals. Finally, academic centres and large hospitals usually have the facilities required for performing this procedure (i.e. nuclear medicine services); these are often unavailable in small suburban hospitals. In fact, our comparison demonstrated that the clinical use of SNB is more diffuse in academic centres and in hospitals with high-volume breast surgery.

Revision performed: none.

2. Revision performed: The adverb “however” has been removed twice from the Introduction (pag.3, line 9; pag. 4, line 2).

3. The proposed cut-off of 2 cm for DCIS is indeed arbitrary. The aim was only to establish whether surgeons perform SNB in all cases, in selected cases or in no cases of DCIS. As is known, the indication to SNB in DCIS is still controversial and not only the size but also the grade of the tumour and the histologic subtype should be considered.

Revision performed: a comment on the high frequency of SNB in DCIS has been added to the Discussion (pag. 11, lines 3-6)

4. Revision performed: we have amplified the discussion on the rates of SN identification and false negative results reported in medical literature (pag.9, lines 15-24)

5. We agree with Dr. Spillane, and have had the same personal experience. In fact, it does appear difficult to remove all radioactive nodes in patients under local anaesthetic. However, we think that any consideration of the best anaesthesia to be used is beyond the scope of the paper.

Revision performed: none
6. All the surgeons in Veneto use intradermal/subdermal tracer injection. Therefore, extra-axillary nodes identification is very rare. We asked surgeons what they do in cases of internal mammary nodes identification (questions 27 and 28 of the questionnaire), but this point was not dealt with in the paper because it is so infrequent. 

Revision performed: we added this point to the Results (pag.8, lines 18-21) and to the Discussion (pag.11, lines 21-23).

7. We are too convinced that a superficial approach to SNB is wrong and dangerous. The GIVOM group, that we represent, has already taken some steps: we have informed our regional health authorities of this problem and are urging them to organize institutional courses to teach the technique properly and to start a quality control programme; we have organized a regional meeting of breast surgeons in order to discuss the various issues involved and to form a working group aiming to set out regional guide-lines to improve standardization of the procedure. 

Revision performed: we have now added to the Conclusions a sentence that stresses that a superficial approach to SNB is wrong (pag.12, lines 11-12)

8. Revision performed: A correction has been made (pag.9, line 8)

REVIEWER: HC

1. We do not fully share doctor’s Cody enthusiasm for the widespread adoption of sentinel node biopsy in the clinical practice. We believe that this is a diagnostic procedure with some potential therapeutic consequences, such as the failure of local disease control and lack of adjuvant systemic treatments in some patients with false negative sentinel node. Our group is, in fact, co-ordinating a multicentric randomized trial to further investigate this issue. Sentinel node is still widely debated and the huge amount of published papers on this issue reflects the wide range of different opinions. The Veronesi trial has been criticized in Krag’s Editorial in the same issue of the Journal. The authors themself acknowledge that: “because of the number of patients was small, firm conclusions cannot be drawn”. A letter by us to the Editor explaining our doubts appeared in the latest issue of the Journal (New Eng J Med 2003; 349: 1968-1971).

Revision performed: we have modified part of the Introduction, addressing the question of sentinel node biopsy as a diagnostic test and citing the trial by Veronesi (pag. 3, lines 13-17 and 20-22).

2. In the Results section we already reported reasons given by surgeons for not performing SNB on a routine basis. The reasons were organisational rather than conceptual. The fact that SNB is currently performed in all the large academic centres is not surprising, since for institutional reasons these centres started research on SNB very early and all the required facilities (i.e. nuclear medicine services) are available. This is not the case for some non-academic centres performing more than 60 breast cancer operations per year and, even more so, for small hospitals where breast surgery is performed on an occasional basis (Tab. 1).

Revision performed: the analysis of reasons for not performing SNB in clinical practice is now included also in the Discussion (pag. 9, lines 4-7).

3. Indeed, no surgeon reported routine utilization of SNB for tumours larger than 3 cm. Since tumour diameter and rate of nodal metastases are strictly correlated, the number of false negative sentinel node cases increases in relation to the diameter of primary tumour even if the sensitivity of the method and the false negative rate remain the same. In fact, supposing an average 10% false negative rate, we would expect 2/100 false negative cases with SNB performed only in patients with
T1a-b tumours (frequency of N+ = ~20%), but this would increase to 6/100 if SNB were performed in patients with tumour diameters of 4 cm (frequency of N+ = ~60%). Moreover, the advantage of avoiding axillary dissection because of a negative sentinel node concerns roughly 80/100 patients with tumours <1 cm but only 40/100 patients with primary tumours measuring 4 cm. These considerations are important, since the prognostic impact of a false negative sentinel node is still unclear. Moreover, both the Consensus Conference of Philadelphia (Breast J 2002; 8: 127) and the Italian guidelines (FONCAM) advise to reserve SNB for patients with primary tumours <3 cm. We already made these observations in our discussion (pag. 10, lines 18-25).

Revision performed: we added the quotation of Olson’ paper in the discussion (pag. 10, line 20).

4. We agree with the reviewer regarding the infrequent use of frozen section examination, although the two-step procedure has the advantage of being a quicker operation, usually performed under local anaesthesia with or without sedation and on a day-surgery basis, and can be curative for most patients with small breast cancer. Moreover, the rate of false negative frozen-section examination with current techniques in case of nodal micrometastasis is a central issue, and still is ill defined.

Revision performed: we have added a brief comment on this issue in the Discussion (from pag.11, line 26 to pag.12, lines 1-2).

5. Our review considers many aspects of SNB practice, several of which have not been investigated by American and Canadian surveys. We have added comparisons with these studies regarding some issues in common, such as the problem of learning curve or SNB in DCIS.

Revision performed: We added some comparison with other surveys to the Discussion (pag. 10, lines 14-17; pag. 11, lines 5-6; pag.11, lines 14-15).

6. Even when we consider a cut-off of 20 cases, 65.6% of surgeons interviewed had an insufficient learning phase (pag.7, lines 2-5).

Revision performed: none.

7. See point 4

8. We entirely agree.

Revision performed: We added this point to the Conclusions (pag.12, line 4 and lines 15-17)