Impact of sentinel node biopsy on long-term quality of life in breast cancer patients

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Background: The aim of this study was to assess long-term quality of life (QoL) over a period of 6 years in women with breast cancer (BC) who underwent sentinel lymph node biopsy (SLNB), axillary lymph node dissection (ALND), or SLNB followed by complementary ALND.

Methods: The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ)-C30 and the EORTC-QLQ-BR-23 questionnaires were used to assess QoL before surgery, just after surgery, 6, 12 and 72 months later. The longitudinal effect of surgical modalities on QoL was assessed with a mixed model analysis of variance for repeated measurements.

Results: Five hundred and eighteen BC patients were initially included. The median follow-up was 6 years. During the follow-up, 61 patients died. None of the patients of the SLNB group developed lymphedema during follow-up and the relapse rate was similar in the different groups (P = 0.62). Before surgery, global health status (P = 0.52) and arm symptoms (BRAS) (P = 0.99) QoL scores were similar whatever the surgical procedure. The BRAS score (P = 0.0001) was better in the SLNB group 72 months after surgery. Moreover, during follow-up, patients treated with SLNB had lower arm symptoms scores than ALND patients and there was no difference for arm symptoms between patients treated with ALND and those treated with SLNB followed by complementary ALND.

Conclusion: Long-term follow-up showed that SLNB was associated with less morbidity than ALND.
Surgical procedures for BC have improved according to the results of randomised trials testing new procedures (Lacour et al., 1983; Maddox et al., 1983; Jacobson et al., 1995; Fisher et al., 2002; McCreary et al., 2005). Breast-conserving treatment is now regarded as a standard treatment for early BC and sentinel lymph node biopsy (SLNB) became an alternative to axillary lymph node dissection (ALND) in the 1990s (McCreary et al., 2005). Sentinel lymph node biopsy is a proven safe surgical method and causes less morbidity than ALND (Krag et al., 1993; Burak et al., 2002) with a smaller impact on QoL (Veronesi et al., 2011). Moreover, ALND may result in significant arm morbidity (Kuehn et al., 2000), including wound infections, seroma formation, damage to sensory and motor nerves, pain, loss of strength, impaired range of shoulder motion (Kissin et al., 1986), and lymphedema, which is of particular concern for women undergoing axillary surgery. Lymphedema is the most common long-term morbidity following axillary surgery and it may be associated with decreased limb mobility and functional problems, pain, sleep disturbance, anxiety, depression, poor wound healing and increased risk of infection (Erickson et al., 2001). To our knowledge, no prospective study has assessed QoL after axillary surgery for BC with a long follow-up.

The aim of this study was to assess long-term QoL over a period of 6 years in women with BC who underwent ALND, SLNB or SLNB followed by ALND.

**PATIENTS AND METHODS**

**Patients.** The design of this study has been described elsewhere (Dabakuyo et al., 2009). Briefly, it was a prospective multicentre study that include all women operated on for BC as the primary treatment in five hospitals of the Côte d’Or and Saône et Loire (French counties). Cases were registered from January 2005 to January 2006. Since the American Society of Clinical Oncology (ASCO) published recommendations for sentinel lymph node biopsy in early-stage BC in 2005 (Lyman et al., 2005), it was therefore impossible to conduct a randomised trial. The study was thus designed to assess routine surgical procedures, and the choice between ALND and SLNB was made by surgeons according to ASCO recommendations and according to their usual practice in their centre. A third group was defined for patients who underwent SLNB with additional lymphadenectomy.

Written informed consent was obtained from every participant in accordance with a protocol approved by local ethics committees (‘Comité de Protection des Personnes’ de Bourgogne).

**Studied variables and end points.** QoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ)-C30 and the EORTC-QLQ-BR23 (Aaronson et al., 1993). QoL scores vary from 0 (worst) to 100 (best) for the functional and global health status (GHS) parameters and from 0 (best) to 100 (worst) for symptoms parameters. A five-point difference in QoL scores is considered the minimum clinically significant difference (Osoba et al., 1998). The GHS, the arm (BRAS) and breast (BRBS) symptoms scores were targeted for analyses.

**Follow-up.** The QoL was assessed by the patients according to a time-driven design: before surgery, just after surgery and 6 and 12 months later. In addition, a final assessment of QoL was done in summer 2011 (about 6 years after the surgery).

Clinical variables such as age, administration and duration of the hormone replacement therapy, tumour size (category into three classes: \( \leq 10 \text{ mm} \) (T1mic, T1a and T1b), \( 11–20 \text{ mm} \) (T1c), \( >20 \text{ mm} \)(T2)), tumour histology, c-erb-2 status, the Scarff Bloom and Richardson (SBR) grade and hormone receptor status (either oestrogen or progesterone) were recorded at the time of surgery. At the time the QoL data were updated, information about treatments (chemotherapy, radiotherapy and hormone therapy), the occurrence of lymphedema or breast tumour recurrence, the type of recurrence, as well as the type of surveillance since the diagnosis (regular with one consultation with a mammogram every year or irregular, with less than one consultation with a mammogram every year) were also retrospectively collected.

**RESULTS**

**Population.** A pragmatic prospective multicentre study was conducted in five hospitals of the Côte d’Or and Saône et Loire (French counties). All of the women undergoing breast surgery as...
Table 1. Clinical and pathological features according to surgery modalities

| Variables                  | ALND | SLNB | SLNB + ALND* |
|----------------------------|------|------|--------------|
| **Hospital**               |      |      |              |
| CGFL                       | 143  | 103  | 37           |
| Private hospital of Dijon  | 17   | 24   | 5            |
| Le Creusot                 | 0    | 17   | 0            |
| Chalon sur Saône           | 4    | 14   | 1            |
| Macon                      | 1    | 15   | 0            |
| **Hospital status**        |      |      |              |
| Premenopausal              | 43   | 26   | 9            |
| Postmenopausal             | 122  | 146  | 34           |
| Unknown                    | 0    | 1    | 0            |
| **HRT**                    |      |      |              |
| Yes                        | 34   | 45   | 6            |
| No                         | 106  | 96   | 33           |
| Unknown                    | 25   | 32   | 4            |
| **Tumour histology**       |      |      |              |
| Invasive ductal            | 134  | 133  | 37           |
| Invasive lobular           | 17   | 9    | 3            |
| In situ                    | 6    | 23   | 0            |
| Medullary cancer           | 1    | 0    | 1            |
| micro-invasive cancer      | 1    | 1    | 1            |
| Unknown                    | 6    | 7    | 1            |
| **SBR Grade**              |      |      |              |
| 1                          | 32   | 69   | 10           |
| 2                          | 64   | 56   | 21           |
| 3                          | 52   | 19   | 10           |
| Unknown                    | 17   | 29   | 2            |
| **C-erb-2 status**         |      |      |              |
| Positive                   | 25   | 14   | 4            |
| Negative                   | 121  | 104  | 36           |
| Unknown                    | 19   | 55   | 3            |
| **Hormone receptor status**|      |      |              |
| Positive                   | 120  | 113  | 33           |
| Negative                   | 25   | 22   | 6            |
| Unknown                    | 20   | 38   | 4            |
| **Treatments**             |      |      |              |
| Surgery                    |      |      |              |
| Lumpectomy                 | 88   | 155  | 42           |
| Mastectomy                 | 77   | 17   | 1            |
| Unknown                    | 0    | 1    | 0            |
| **Adjuvant chemotherapy**  |      |      |              |
| Yes                        | 111  | 28   | 28           |
| No                         | 54   | 141  | 15           |
| Unknown                    | 0    | 4    | 0            |
| **Radiotherapy**           |      |      |              |
| Yes                        | 139  | 149  | 41           |
| No                         | 26   | 23   | 2            |
| Unknown                    | 0    | 1    | 0            |

*P-value*
the primary treatment were eligible. Patients with synchronous bilateral BC were excluded. Cases were registered from January 2005 to January 2006. From 1 January 2005 to 1 January 2006, 518 BC patients were initially included. In July 2011, when the QoL data were updated, 61 (11.8%) patients had died, 9 (1.7%) were lost to follow-up. For patients who had died, 44 (72.1%), 8 (13.1%) and 9 (14.8%) had been treated by ALND, SLNB and SLNB + ALND, respectively.

QoL questionnaires were sent to 448 patients. Of these, 381 (85%) answered and were thus retained for the analyses. For this population, the median follow-up was 6 years (1.7; 6.6), 365 patients (95.8%) had small tumours (≤ 50 mm), 6 patients had tumours larger than 50 mm (1.6%) and for 10 patients (2.6%) the information about the tumour size was missing. The mean tumour size (P < 0.0001) was: 21 mm (s.d. = 14), 11 mm (s.d. = 10) and 15 mm (s.d. = 6) for the ALND, SLNB and SLNB + ALND groups, respectively, while the mean age at diagnosis (P = 0.18) was 58 (s.d. = 12), 60 (s.d. = 11) and 59 (s.d. = 11), respectively. Among the study population, 165 patients (43%) underwent ALND, 173 patients (45%) had SLNB and 43 (11%) patients had SLNB + ALND. For 40 (93%) of these 43 patients, SLNB was followed by immediate complementary ALND. The clinical and pathological features of the three groups of patients are presented in Table 1. Sentinel lymph node biopsy was more often performed in patients with small tumours, and none of the patients of the SLNB group had lymphedema. Patients who underwent SLNB were also more often treated with conservative surgery (P < 0.0001), without adjuvant chemotherapy (P < 0.0001) and without adjuvant hormone therapy (P < 0.0001).

Comparison of the features of the patients who completed and those who did not complete the questionnaire at 72 months. The responders and the non-responders were different only for the hospital (P = 0.007). All other characteristics were similar: type of axillary surgery (ALND, SLNB, SLNB + ALND) (P = 0.579), the occurrence of lymphedema (P = 0.41), breast reconstruction (P = 0.18), the type of surveillance (P = 0.81), the tumour recurrence (P = 0.08), age (P = 0.93), the treatments: surgery (lumpectomy, mastectomy) (P = 0.95), adjuvant chemotherapy (P = 0.27), radiotherapy (P = 0.31), hormone therapy (P = 0.65). In addition, the QoL scores before, after, at 6 and 12 months after the surgery in the two groups were comparable.

QoL scores according to the surgical procedure. Patients’ missing-score profiles were not different according to the surgical procedure. Indeed, there was no difference between the types of surgery for the proportions of patients without missing scores, with drop-out scores, with intermittent missing scores, with all scores

| Variables                  | ALND | %  | SLNB | %  | SLNB + ALND* | %  | P-value |
|----------------------------|------|----|------|----|--------------|----|---------|
| Hormone therapy            |      |    |      |    |              |    |         |
| Yes                        | 135  | 81.8| 108  | 62.4| 34           | 79.1| <0.0001 |
| No                         | 29   | 17.6| 65   | 37.6| 8            | 18.6|         |
| Unknown                    | 1    | 0.6 | 0    | 0.0 | 1            | 2.3 |         |
| Breast reconstruction      |      |    |      |    |              |    | 0.07    |
| Yes                        | 22   | 13.3| 12   | 6.9 | 2            | 4.7 |         |
| No                         | 140  | 84.8| 158  | 91.3| 40           | 93.0|         |
| Unknown                    | 3    | 1.8 | 3    | 1.7 | 1            | 2.3 |         |
| Lymphedema                 |      |    |      |    |              |    | <0.0001 |
| Yes                        | 17   | 10.3| 0    | 0.0 | 3            | 7.0 |         |
| No                         | 143  | 86.7| 170  | 98.3| 39           | 90.7|         |
| Unknown                    | 5    | 3.0 | 3    | 1.7 | 1            | 2.3 |         |
| Type of monitoring         |      |    |      |    |              |    | 0.91    |
| Regular                    | 154  | 93.3| 160  | 92.5| 41           | 95.3|         |
| Irregular                  | 8    | 4.8 | 10   | 5.8 | 2            | 4.7 |         |
| Unknown                    | 3    | 1.8 | 3    | 1.7 | 0            | 0.0 |         |
| Recurrence                 |      |    |      |    |              |    | 0.62    |
| Yes                        | 10   | 6.1 | 9    | 5.2 | 4            | 9.3 |         |
| No                         | 150  | 90.9| 161  | 93.1| 39           | 90.7|         |
| Unknown                    | 5    | 3.0 | 3    | 1.7 | 0            | 0.0 |         |
| Tumour size (mm)           |      |    |      |    |              |    | 0.0001  |
| ≤ 10 mm                    | 35   | 21.2| 91   | 52.6| 10           | 23.3|         |
| 10–20 mm                   | 54   | 32.7| 71   | 41.0| 28           | 65.1|         |
| > 10 mm                    | 72   | 43.6| 5    | 2.9 | 5            | 11.6|         |
| Unknown                    | 4    | 2.4 | 6    | 3.5 | 0            | 0.0 |         |

Abbreviations: ALND = axillary lymph node dissection; CGFL = Centre Georges François Leclerc; HRT = hormone replacement therapy; SBR = Scarff Bloom and Richardson; SLNB = sentinel lymph node biopsy. Kruskal–Wallis test was used to test the homogeneity of the different groups for quantitative variables; Pearson’s χ²-test was used to test the homogeneity of the different groups for qualitative variables.

Forty patients had SLNB + ALND at the same time.
missing for GHS \((P = 0.8)\), BRAS \((P = 0.81)\) and BRBS \((P = 0.51)\) scores (Table 2).

Before surgery, GHS \((P = 0.52)\) and BRAS \((P = 0.99)\) QoL scores were similar whatever the surgical procedure (Table 3). There were no differences for GHS and BRBS according to the surgical procedure just after surgery, 6 months later, 12 months later or 72 months later (Table 3, Figures 1a and c). However, BRAS scores were better in the SLNB group after the surgery \((P = 0.004)\), 6 months later \((P = 0.001)\), 12 months later \((0.0001)\) and 72 months later \((P = 0.0001)\) (Figure 1b). Two-by-two comparison with the Bonferroni correction (statistical significance level \(P < 0.02\)) showed significantly better BRAS scores in the SLNB group than in the ALND and SLNB + ALND groups at 6 months \((P = 0.0003\) and \(P = 0.01\), respectively) and 12 months \((P = 0.0001\) and \(P = 0.002\), respectively). After the surgery \((P = 0.0006)\) and at 72 months \((P < 0.0001)\), BRAS scores were significantly different only between the SLNB and ALND groups.

At 72 months, the body image (BRBI) score was different according to the surgical procedure \((P = 0.0005)\). Two-by-two comparison with the Bonferroni correction confirmed that the BRBI score was better in the SLNB group than in the ALND group \((P = 0.0001)\). Moreover, at 72 months, two-by-two comparison with the Bonferroni correction showed that the future perspectives \((P = 0.0006)\), the systemic therapy side effects \((P = 0.0097)\) and upset by hair loss \((P = 0.0008)\) QoL scores were better in the SLNB group than in the ALND group.

Of the studied population, 258 (68\%) had the most favourable prognostic characteristics (tumour size smaller than 50 mm \((T1–T2)\) and positive hormone receptor status). Comparisons of QoL scores in these patients according to the surgical procedure showed similar results to those obtained in the whole population. Indeed, BRAS scores were also better in the SLNB group after the surgery \((P = 0.006)\), 12 \((P = 0.007)\) and 72 months later \((P = 0.0001)\). Scores for body image \((P = 0.002)\) and upset by hair loss \((P = 0.002)\) were also better in SLNB group 72 months after surgery.

### Longitudinal GHS QoL scores.

There was no significant effect of the patients’ profiles \((P = 0.15)\) on the GHS scores and there was no interaction between the follow-up and the type of surgery \((P = 0.22)\). In addition, the hospital \((P = 0.92)\), the hormone status \((P = 0.75)\), the SBR grade \((P = 0.28)\), the treatments: type of surgery \((\)lumpectomy, mastectomy\() \((P = 0.26)\), adjuvant chemotherapy \((P = 0.36)\), hormone therapy \((P = 0.20)\), the occurrence of lymphedema \((P = 0.55)\), which were different depending on the type of axillary surgery, had no independent effect on the GHS scores. Only the tumour size \((P = 0.04)\) affected GHS scores. Indeed, women with tumour smaller than 10 mm had higher GHS scores \((MD = 7.2)\) than did women with tumours larger than 20 mm \((P = 0.01)\).

Whatever the surgical procedure, GHS scores decreased after surgery, started increasing 6 months later until 12 months but decreased again 72 months later. Whatever the follow-up, the surgical procedure had no impact on GHS scores \((P = 0.0726)\) (Table 4).

### Longitudinal BRAS QoL scores.

There was no significant effect of the patients’ profiles \((P = 0.16)\) on the BRAS scores. In addition, the hospital \((P = 0.92)\), the hormone status \((P = 0.32)\), the SBR grade \((P = 0.38)\), the treatments: type of surgery \((\)lumpectomy, mastectomy\() \((P = 0.55)\), adjuvant chemotherapy \((P = 0.35)\), the tumour size \((P = 0.81)\), which were different depending on the type of axillary surgery, had no independent effect on the BRAS scores. Patients treated without hormone therapy had lower scores for arms symptoms than those treated with hormone therapy \(MD = -3.91(P = 0.049)\). The occurrence of lymphedema \((P < 0.0001)\) also affected BRAS scores. Indeed, in women without lymphedema during follow-up, arms symptoms scores were lower \((MD = -13.4, P < 0.0001)\).

Whatever the surgical procedure, BRAS scores increased after the surgery \((MD = 12.6, s.d. = 2.2, P < 0.0001)\), 6 months later \((MD = 12.6, s.d. = 2.1, P < 0.0001)\), 12 months later \((MD = 13.2, s.d. = 2.1, P < 0.0001)\) and 72 months later \((MD = 15.5, s.d. = 2.1, P < 0.0001)\).
A quantitative interaction was seen between the follow-up and the type of surgery ($P = 0.04$). In fact, patients treated with SLNB had lower symptoms scores during the follow-up than patients treated with ALND. BRAS scores were lower in the SLNB group than in the ALND group after the surgery ($MD = 7.6$, s.d. $= 3.1$, $P = 0.01$), 6 months later ($MD = 6.1$, s.d. $= 3$, $P = 0.04$), 12 months later ($MD = 9$, s.d. $= 3$, $P = 0.003$) and 72 months later ($MD = 10.8$, s.d. $= 2.9$, $P = 0.0002$). However, BRAS scores were not significantly different between ALND and SLNB + ALND whatever the follow-up time (Table 5).

**Longitudinal BRBS QoL scores.** There was no significant effect of the patients’ profiles ($P = 0.51$) on the BRBS scores and there was no interaction between the follow-up and the type of surgery ($P = 0.2$). In addition, the hospital ($P = 0.86$), the SBR grade ($P = 0.75$), the treatments: type of surgery (lumpectomy, mastectomy) ($P = 0.78$), adjuvant chemotherapy ($P = 0.51$), hormone therapy ($P = 0.54$), the occurrence of lymphedema ($P = 0.56$), the tumour size ($P = 0.45$) had no independent effect on the GHS scores. Only the hormone status ($P = 0.03$) affected BRBS scores.
Quality of life after sentinel node biopsy

Whatever the surgical procedure, BRBS scores were higher 6 months than immediately after the surgery ($P = 0.001$). However, BRBS scores 12 months after surgery ($P = 0.52$) and 72 months after surgery ($P = 0.41$) were not different to post-surgery scores (Table 4).

Whatever the follow-up, the axillary surgical procedure had no impact on BRBS QoL scores ($P = 0.84$) (Table 4), and premenopausal women were more likely than postmenopausal women to have high breast symptoms scores (MD = 4.4, $P = 0.03$).

The results of previous studies suggest that SLNB is associated with less morbidity than ALND (Kissin et al, 1986; Kuehn et al, 2000; Erickson et al, 2001; Burak et al, 2002; Veronesi U et al, 2003; Purushotham et al, 2005; Mansel et al, 2006; Del Bianco et al, 2008; Dabakuyo et al, 2009; Gill, 2009; Wang et al, 2011), but the comparative effects of these two approaches on tumour recurrence, patient survival and QoL with long follow-up data are still unclear. To our knowledge, no prospective study has assessed QoL after axillary surgery for BC with a long follow-up. Published studies with long-term follow-up stopped monitoring patients 3 years after surgery (Kootstra et al, 2008; Kootstra et al, 2010; Land et al, 2010).

The aim of this pragmatic prospective multicentre study was to assess long-term QoL over a period of 6 years in women with BC who underwent ALND, SLNB or SLNB followed by ALND. To our knowledge, no prospective study has assessed QoL after axillary surgery for BC with a long follow-up. Published studies with long-term follow-up stopped monitoring patients 3 years after surgery (Kootstra et al, 2008; Kootstra et al, 2010; Land et al, 2010).

The higher mortality in the ALND group may be related to the larger tumour size seen in this group at baseline. It is well known that tumour size is an important prognostic factor in BC. The higher mortality in the ALND group may be related to the larger tumour size seen in this group at baseline. It is well known that tumour size is an important prognostic factor in BC.

### DISCUSSION

The results of previous studies suggest that SLNB is associated with less morbidity than ALND (Kissin et al, 1986; Kuehn et al, 2000; Erickson et al, 2001; Burak et al, 2002; Veronesi U et al, 2003; Purushotham et al, 2005; Mansel et al, 2006; Del Bianco et al, 2008; Dabakuyo et al, 2009; Gill, 2009; Wang et al, 2011), but the comparative effects of these two approaches on tumour recurrence, patient survival and QoL with long follow-up data are still unclear. To our knowledge, no prospective study has assessed QoL after axillary surgery for BC with a long follow-up. Published studies with long-term follow-up stopped monitoring patients 3 years after surgery (Kootstra et al, 2008; Kootstra et al, 2010; Land et al, 2010).

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As regards the treatments, the frequencies of radiotherapy and breast reconstruction were not statistically different whatever the surgical treatment groups. However, patients who underwent SLNB were more often treated with conservative surgery, without adjuvant chemotherapy and without adjuvant hormone therapy. Differences between treatments may also be due to the difference in tumour size seen between treatment groups at baseline. Moreover, whatever the surgical procedure, patients with tumour smaller than 10 mm had better global health than those with tumours larger than 20 mm. Taking into account Osoba et al’s (1998) conclusion about clinical difference, namely that a five-point difference in QoL scores is considered the minimum clinically important difference, this statistical difference (MD = 7) should have clinical repercussions. Patients with larger tumours were probably treated more aggressively than those with smaller tumours and this can have a negative effect on their overall health.

The results of this study also showed that, whatever the surgical procedure, premenopausal patients had higher breast symptoms scores than postmenopausal women (MD = 4) and patients treated without hormone therapy had lower arm symptoms scores than those treated with hormone therapy (MD = − 3.9). However, these differences were too small to have a significant clinical impact (Osoba et al, 1998). One striking finding was the beneficial effects of SLNB in comparison with ALND for arm symptoms in patients with BC 5 to 6 years after diagnosis. Moreover, compared with ALND patients, SLNB patients gradually had less pain as time passed. Although the beneficial effect of SLNB in reducing arm morbidity after surgery is well known, this is the first study to report the outcomes after SLNB or ALND with such a long follow-up. These results also confirmed our previous findings (Dabakuyo et al, 2009) that there was no difference for arm symptoms, between patients treated with ALND and those treated with SLNB followed by complementary ALND. This result remained 5 to 6 years after diagnosis.

In this study, the occurrence of lymphedema was responsible for arm morbidity, which affected the arm dimension of QoL. Indeed, patients with lymphedema had very high scores for arm symptoms in comparison with those without lymphedema. None of the patients of the SLNB group developed lymphedema during follow-up. In comparison, 10.3% of the ALND group and 7% of the ALND + SLNB group developed lymphedema. This could explain the better QoL in the SLNB group for arm symptoms.

Another finding was that body image was better 5 to 6 years after diagnosis in patients treated with SLNB. One explanation could be that, in this study, patients who underwent SLNB were more often treated with conservative surgery due to the smaller tumour size in this group than were patients in the ALND and SLNB + ALND groups. Systemic therapy side effects and upset by hair loss QoL dimensions were also better in patients in the SLNB group, who were less often treated with adjuvant chemotherapy and with adjuvant hormone therapy, which may cause side effects and hair loss. Finally, the smaller tumour size and the less aggressive treatment led to better future perspectives in the SLNB group.

The relapse rate in the different surgical groups was similar 5 to 6 years after surgery. As pointed out by Wang et al (2011) in a recent meta-analysis of randomised controlled trials that compared the effectiveness and safety of SLNB with ALND, there was no significant difference between the SLNB and ALND groups for regional recurrence whether the SLNB was positive or negative. Therefore, SLNB can thus be recommended as a safe and acceptable method for the accurate identification of early-stage BC without involvement of the axillary lymph nodes.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### REFERENCES

Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC et al. (1993) The European Organisation for Research and Treatment of Cancer QLQ-C30:

Table 5. Long-term effect of surgical procedure and factors affecting arm symptoms in breast cancer patients

| Arm symptoms                      | Beta (s.e.) | P     |
|-----------------------------------|------------|-------|
| Constant                          | 19.8 (6)   | 0.0011|
| Follow-up                         |            | <0.0001|
| Before surgery                    | Reference  |       |
| After surgery                     | 12.6 (2.2) | <0.0001|
| 6 Months after surgery            | 12.6 (2.1) | <0.0001|
| 12 Months after surgery           | 13.2 (2.1) | <0.0001|
| 72 Months after surgery           | 15.5 (2.1) | <0.0001|
| **Axillary dissection type**      |            |       |
| ALND                              | Reference  |       |
| SLNB                              | 3.1 (3.1)  | 0.32  |
| SLNB + ALND                       | 2.4 (4.2)  | 0.56  |
| **Interaction follow-up time and surgical procedure** | 0.04* |
| After surgery and SLNB            | −7.6 (3.1) | 0.01  |
| After surgery and (SLNB + ALND)   | −5.1 (4.9) | 0.29  |
| After surgery and ALND            | Reference  |       |
| 6 Months after surgery and SLNB   | −6.1 (3)   | 0.04  |
| 6 Months after surgery and (SLNB + ALND) | −2.2 (4.6) | 0.63  |
| 12 Months after surgery and ALND  | Reference  |       |
| 12 Months after surgery and SLNB  | −9 (3)     | 0.003 |
| 12 Months after surgery and (SLNB + ALND) | −0.7 (4.6) | 0.88  |
| 72 Months after surgery and ALND  | Reference  |       |
| 72 Months after surgery and (SLNB + ALND) | −5.3 (4.5) | 0.24  |
| **Lymphedema**                    |            |       |
| Yes                               | Reference  |       |
| No                                | −13.4 (3.2)| <0.0001|
| **Hormone therapy**               |            |       |
| Yes                               | Reference  |       |
| No                                | −3.9 (2)   | 0.049 |

Abbreviations: ALND = axillary lymph node dissection; SLNB = sentinel lymph node biopsy.

NB: Multivariable analyses were adjusted for hospitals, hormone status, the Scarff Bloom and Richardson grade, treatments (the type of surgery, adjuvant chemotherapy, hormone therapy), the occurrence of lymphedema and tumour size.

*Overall effect.
a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 85: 365–376.

Akaiki Hirotugu (1974) A new look at the statistical model identification. IEEE Trans Auto Control 19(6): 716–723.

Burke WE, Hollenbeck ST, Zervos EE, Hock KL, Kemp LC, Young DC (2002) Sentinel lymph node biopsy results in less postoperative morbidity compared with axillary lymph node dissection for breast cancer. Am J Surg 183(1): 23–27.

Dabakuyo TS, Fraisse J, Causseret S, Gouy S, Padaneau MM, Loustalot C, Cuisener J, Sauzedde JM, Smal M, Combier JP, Chevillote P, Rosbacher C, Boulet S, Arveux P, Bonnetaï F (2009) A multicenter cohort study to compare quality of life in breast cancer patients according to sentinel lymph node biopsy or axillary lymph node dissection. Ann Oncol 20: 1352–1361.

Del Bianco P, Zavagno G, Burelli P, Burelli P, Scalco G, Barutta L, Carraro P, Pietrarota P, Meneghini G, Morbin T, Tacchetti G, Pecoraro P, Belardinelli V, De Salvo GL. GIVOM (2008) Morbidity comparison of sentinel lymph node biopsy versus conventional axillary lymph node dissection for breast cancer patients: results of the sentinella-GIVOM Italian randomized clinical trial. Eur J Surg Oncol 34(5): 508–513.

Erickson VS, Pearson ML, Ganz PA, Adams J, Kahn KL (2001) Arm edema in breast cancer patients. J Natl Cancer Inst 93(2): 96–111.

Ferlay J, Autier P, Boniol M, Haenssle H, Colombet M, Boyle P (2007) Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol 18(3): 581–592.

Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, Jeong JH, Wolmark N (2002) Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 347: 1233–1241.

Gill G (2009) Sentinel-lymph-node-based management or routine axillary clearance? One-year outcomes of sentinel node biopsy versus axillary clearance (SNAC): a randomized controlled surgical trial. Ann Surg Oncol 16(2): 266–275.

Jacobson JA, Danforth DN, Cowan KH, d’Angelo T, Chevillote P, Roscher C, Boulet S, Arveux P, Bonnetain F (2009) A multicenter cohort study to compare quality of life in breast cancer patients according to sentinel lymph node biopsy or axillary lymph node dissection. Ann Oncol 20: 1352–1361.

Krag DN, Weaver DL, Alex JC, Fairbank JT (1993) Surgical resection and radiolocalization of the sentinel lymph node in breast cancer using a gamma probe. Surg Oncol 2(6): 335–339.

Kuehn T, Klaus W, Darsow M, Regele S, Flock F, Maiterth C, Dahbender R, Wendt I, Kreienberg R (2000) Long-term morbidity following axillary dissection in breast cancer patients–clinical assessment, significance for quality of life and the impact of demographic, oncologic and therapeutic factors. Breast Cancer Res Treat 64(3): 275–286.

Lacour J, Le M, Caceres E, Koszarowski T, Veronesi U, Hill C (1983) Radical mastectomy versus radical mastectomy plus internal mammary dissection. Ten year results of an international cooperative trial in breast cancer. Cancer 51: 1941–1943.

Land SR, Kopea JA, Julian TB, Brown AM, Anderson SJ, Krag DN, Christian NJ, Costantino JP, Wolmark N, Ganz PA (2010) Patient-reported outcomes in sentinel node-negative adjuvant breast cancer patients receiving sentinel-node biopsy or axillary dissection: national surgical adjuvant breast and bowel project phase III protocol B-32. J Clin Oncol 28(25): 3929–3936.

Lyman GH, Giuliano AE, Somerfield MR, Benson 3rd AB, Bodurka DC, Burstein HJ, Cochran AJ, Cody 3rd HS, Edge SB, Galper S, Hayman JA, Kim TY, Perkins CL, Podoloff DA, Sivasubramaniam VH, Turner RR, Wahl R, Weaver DL, Wolff AC, Winer EP. American Society of Clinical Oncology (2005) American Society of Clinical Oncology Guideline Recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 23(30): 7703–7720.

Maddox WA, Carpenter Jr JT, Laws HL, Soong SJ, Cloud G, Urist MM, Balch CM (1983) A randomized prospective trial of radical (Halsted) mastectomy versus modified radical mastectomy in 311 breast cancer patients. Ann Surg 198: 207–212.

Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, Yioung C, Horgan K, Bundre N, Monypenny I, England D, Sibbering M, Abdullah T, Barr L, Chetty U, Sinnett DH, Fleissig A, Clarke D, El PJ (2006) Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst 98(9): 599–609.

McCready D, Holloway C, Shelley W, Down N, Robinson P, Sinclair S, Miskry D. Breast Cancer Disease Site Group of Cancer Care; Ontario's Program in Evidence-Based Care (2005) Surgical management of early stage invasive breast cancer: a practice guideline. Can J Surg 48: 185–194.

Osoba D, Rodrigues G, Myles J, Zee B, Pater J (1998) Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 16(1): 139–144.

Purushotham AD, Upponi S, Klevesath MB, Bobrow L, Millar K, Myles JP, Duffy SW (2005) Morbidity after sentinel lymph node biopsy in primary breast cancer: results from a randomized controlled trial. J Clin Oncol 23(19): 4312–4321.

Sant M, Alleman C, Sautanilis M, Knijn A, Marchesi F, Capocaccia R, EUROCare Working Group EUROCare-4 (2009) Survival of cancer patients diagnosed in 1995–1999. Results and commentary. Eur J Cancer 45: 931–991.

Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, Intra M, Veronesi P, Robertson C, Maisonneuve P, Renne G, De Cicco C, De Lucia F, Gennari R (2003) A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med 349(6): 546–553.

Vervoort MM, Daisma G, Fracheboud J, de Koning HJ, van den Poll-Franse LV, de Koning HJ (2004) Trends in the usage of adjuvant systemic therapy for breast cancer in the Netherlands and its effect on mortality. Br J Cancer 91(2): 242–247.

Wang Z, Wu LC, Chen QJ (2011) Sentinel lymph node biopsy compared with axillary lymph node dissection in early breast cancer: a meta-analysis. Breast Cancer Res Treat 129: 675–689.

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