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**HONG KONG BREAST CANCER FOUNDATION
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Summary of Session 2

Update in Treatment of Axilla in Breast Cancer

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Evolution of axillary surgery in breast cancer management

Where were we?

The landmark study NSABP B-32 trial, which compared sentinel lymph node biopsy with conventional axillary dissection in clinically node-negative patients with early breast cancer, established the role of sentinel lymph node in de-escalating axillary surgery.¹ With similar disease-free survival and loco-regional control, it is concluded that when the sentinel lymph node is negative, sentinel lymph node surgery alone with no further axillary dissection is an appropriate, safe and effective treatment for these early breast cancer patients, leaving axillary dissection to only clinically or pathologically node-positive patients.

Where are we?

The American College of Surgeons Oncology Group (ACOSOG) Z0011 enrolled women with clinically node-negative early breast cancer (T1 or T2) undergoing breast conserving therapy (BCT), with 1 or 2 positive axillary sentinel lymph nodes and randomised them into the gold standard of axillary dissection versus no axillary dissection (no further surgery after sentinel lymph node biopsy).² There was no difference in overall survival (83.6% vs 86.3%), disease-free survival (78.2% vs 80.2%) as well as loco-regional control between the two groups, concluding that routine use of axillary dissection for all patients with positive sentinel nodes is no longer justified based on these 10-year outcomes. Omission of axillary dissection in sentinel node-positive patients with low disease burden as standard clinical practice is recommended in this selected group of patients (undergoing BCT, whole breast irradiation and systemic adjuvant therapy). However, Z0011 was criticized as the unexpectedly low event rates may be due to selection of a favorable subset of patients, systemic therapy effects and incidental radiation to lower axillary lymph nodes, and thus the study population was not representative of breast cancer patients as a whole.

The AMAROS (After Mapping of the Axilla: Radiotherapy Or Surgery) non-inferiority trial compared axillary dissection with axillary radiotherapy in sentinel node-positive patients undergoing BCT or mastectomy.³ The 10-year cumulative incidence rates of axillary lymph node recurrence were found to be very low in both arms (0.93% vs 1.82%). The results showed that both axillary dissection and axillary radiotherapy provided an excellent and comparable loco-regional control in sentinel node-positive patients with no difference in overall survival (84.6% vs 81.4%), distant metastasis-free survival (81.7% vs 78.2%) and loco-regional recurrence (3.59% vs 4.07%). It was also demonstrated

that the occurrence of lymphoedema was significantly less after axillary radiotherapy compared with axillary dissection (14.6% vs 29.4%). It is concluded that, axillary radiotherapy is a reasonable alternative to axillary dissection after a positive sentinel lymph node, and with less upper limb morbidity.

Where shall we be? The ACOSOG Z0011 and AMAROS trials have proven that finding of a single positive node is no longer enough to justify the routine use of axillary dissection. As a result, the role of intraoperative frozen section of sentinel lymph node as an instant guidance on immediate axillary dissection should be seriously reconsidered. In addition, two studies from the Memorial Sloan Kettering Cancer Center (MSKCC) had suggested that screening USG and needle biopsy of axillary lymph nodes in clinically node-negative patients with early breast cancer may represent unnecessary procedures that do not change the treatment plan but increase the cost of care by committing to an upfront axillary dissection, which may not be mandatory.⁴⁻⁵

On the other hand, SENTINA and ACOSOG Z1071 evaluated the use of sentinel lymph node in restaging the axilla after neoadjuvant therapy for patients who presented with clinically node-positive disease, while they used to have no choice but axillary dissection.⁷⁻⁸ International guidelines now agree that sentinel lymph node biopsy is considered appropriate in selected patients who convert from positive to negative axillary status after neoadjuvant treatment.

Where may we be?

Sentinel lymph node biopsy reduces the potential risk of upper limb morbidities, but does not completely eliminate them. The ongoing SOUND (Sentinel node vs Observation after axillary Ultra-SouND) trial recruits patients with negative finding on preoperative axillary USG and randomized them into having sentinel node biopsy or observation.⁶ The trial aims to determine whether no axillary staging is not inferior to sentinel lymph node surgery, with distant disease-free survival as the primary end-point. In the future, surgical staging with sentinel lymph node biopsy may be replaced by preoperative axillary staging with imaging.

Case study from *Dr Ling Yeuk Hei, Ida*

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In Hong Kong East Cluster, with the routine use of pre-op USG of the axilla, there is a significant decrease in cases with nodal metastasis in sentinel lymph node biopsy (2002: 40%; 2016: 16%). For positive sentinel lymph node biopsy cases, most of them are microscopic disease, without heavy treatment burden. From 2014-2016, there were about 90 cases of breast cancer with sentinel lymph node frozen section per year. The median number of sentinel lymph nodes were 3-4, and the total turn-around time was about 1 hour (15 minute transport time, and 30-15 minute lab processing & reporting time). Sixteen percent of cases had metastasis (9% macro and 7% micro), in which 2% had 3 or more positive lymph nodes. False negative at frozen section was found in 6% of the cases, most of which were of isolated tumour cells and micrometastases only. It was found that frozen section for sentinel lymph node was limited by the lower quality nature of frozen section slides, sampling

error and tissue loss. The frozen section is prepared within 10 minutes compared with overnight processing for tissue block for paraffin section. For the sampling error, for tumour of very small size, if the frozen section does not cut into it, the tumour will be missed. The two cases shown by Dr Ling, demonstrate that it is very difficult to spot the tumour in a frozen section, whereas high power paraffin section is sometimes needed in order to locate the cancer cells.

In the face of change, with the routine use of preoperative evaluation of axillary lymph nodes, a lot of cases are of not very heavy tumour burden. As findings of Z0011 and AMAROS suggest a more conservative approach to treating the axilla, the need of change of practice was discussed in HKEC. Overseas experience suggested that after Z0011, axillary lymph node dissection after positive sentinel lymph node was decreasing. The number of patients requesting intra-operative section was also decreasing. In the UK, most centres do not send sentinel lymph node for intra-operative assessment. In HKEC, without frozen section, decreased OT time was observed. Paraffin section also saves frozen section service and allows better pathology assessment due to high quality of the slides. However, without frozen section, there will be some cases that need further operation. Ruttonjee Hospital started to adopt UK approaches of not sending any frozen sections since January 2017, and the overall rate of axillary dissection after sentinel lymph node biopsy is 8%.

A 52-year woman with past history of depression and rectal prolapse with anterior resection and rectopexy in 2004 presented with right breast lump of 2.5cm at 10 o'clock position, with no palpable axillary lymph node. Mammogram showed a 16-mm spiculated mass at the right breast with no abnormal axillary lymph node. Core biopsy found it was invasive ductal carcinoma which was ER+, PR+ and HER2-. Wide local excision and sentinel lymph node biopsy were performed. Final pathology found that there was 1 sentinel lymph node involved by isolated tumor cells. The case was discussed in a multidisciplinary team meeting. Genetic test was offered but declined by the patient due to financial reason. No axillary dissection was performed as it only involved isolated tumor cells. The patient eventually received chemotherapy, whole-breast irradiation and hormonal therapy.

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