Letters to the editor

Will the sentinel lymph node (SLN) stand a second time – SLN biopsy in breast cancer patients with isolated local recurrence following breast conserving therapy and previous SLN procedure

The axillary lymph node status remains one of the most important independent prognostic factors providing significant information for accurate staging and determination of adjuvant therapy. To avoid axillary lymph node dissection (ALND) in clinically node negative patients, sentinel lymph node (SLN) biopsy was proposed as an alternative to ALND, thus minimizing possible post-operative complication (e.g., lymphedema, dysaesthesia, etc).

As a consequence of the frequent application of SLN biopsy, especially when it becomes adopted as standard treatment, a new group of breast cancer patients will emerge in the near future. Characteristics of these patients are that they were treated conservatively, had a SLN biopsy, and on finding an uninvolved sentinel node, ALND was consequently omitted.

In the case of an isolated local recurrence in these patients the question arises whether a re-staging of the axillary lymph node status – especially if the axilla is clinically unsuspicious – is of importance and how it should be performed.

Data from previous studies showed that, depending on the stage of the disease and the treatment given, between 10% and 35% of patients experience an isolated locoregional recurrence (LRR) [1–3]. About 80% of these recurrences happen during the first two years after primary treatment [4]. For the above characterized group the estimated risk will be about 15%–20%.

For patients who had Breast Conserving Treatment (BCT) before the SLN era, treatment options for an isolated local recurrence (e.g., no overt evidence of distant metastases) encompasses local excision or simple mastectomy only, because the axillary lymph nodes were already dissected at the time of the first operation.

For this new group of patients in whom axillary lymph nodes were not dissected the situation is quite different. Clinically involved axillary lymph nodes are a clear indication to perform ALND.

Until now, there are no guidelines on how to proceed in a clinically unsuspicious axilla. One of the options could be to perform ALND routinely, mainly for re-staging reasons.

In this context the question arises whether a SLN biopsy is feasible a second time and, moreover, whether it is reliable in predicting the axillary lymph node status.

We would suggest that the issues above should be investigated in the frame of a properly conducted clinical trial for the following reasons:

First, there is logical concern that the first SLN biopsy and eventually radiotherapy to the breast including skin, etc., might impair the sentinel lymph node mapping. However, if the SLN is defined as a first lymph node draining from the tumor-bearing area it is to be expected that in most patients an identification as well as the consecutive removal of this 'second' SLN should be possible.

Furthermore, the predictive value of the axillary lymph node status of this 'second' SLN should be examined.

Finally, the subgroup of patients in which a second SLN biopsy procedure might be beneficial should be defined.

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References

1. Veronesi U, Luini A, Del Vecchio M et al. Radiotherapy after breast-preserving surgery in women with localized cancer of the breast. N Engl J Med 1993, 328: 1587–91.
2. Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and surgery in early breast cancer. N Engl J Med 1995; 333: 1444–55.
3. Fisher B, Anderson S, Redmond CK et al Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 1995; 333: 1456–61.
4 Recht A, Come SE, Troyan S et al. Local-regional recurrence after masttectomy or breast-concerving therapy. In Harris JR, Lippman M, Morrow M et al. (eds): Diseases of the Breast, second edition Philadelphia: Lippincott-Raven 1999

Coronary spasm induced by capecitabine

We would like to report a case of coronary vasospasm most likely following oral capecitabine administration.

A 63-year-old female with a history of moderate arterial hypertension was diagnosed in June 2000 with breast carcinoma. A tumorectomy with axillary lymphnode dissection was performed. Although 5 out of 10 lymph nodes were metastatic and the tumor cells failed to express steroid receptors, she declined adjuvant chemotherapy and was treated by radiotherapy. Four months after the diagnosis, she developed bone and liver metastases which prompted the administration of vinorelbine (25 mg/m^2) and capecitabine (1500 mg/m^2). Forty-eight hours after the introduction of chemotherapy, the patient developed typical angina pectoris at rest. The ECG showed ST-segment elevation in leads DI, aVL, V5 and V6. There was no pericardial friction rub. Echocardiography was normal.

Initially, chest pain and ECG changes responded to intravenous nitrates. However, recurrent angina required the addition of intravenous heparin, acetylsalicylic acid and betablockers. Troponin levels remained in the normal range. The persistence of clinical and electrocardiographic signs of angina, justified a coronary angiogram which revealed normal coronary arteries

and an adequate left ventricular function. A coronary spasm secondary to capecitabin was suspected. The last dose of the drug was given the morning of the coronary angiogram. The patient presented a new chest pain episode a few hours after the coronary angiogram. Betablockers were stopped and calcium-blockers were introduced. Since then, the patient has not presented any chest pain.

Cardiotoxicity is a recognized side effect of 5-fluorouracil (5-FU), a related fluorinated pyrimidine antagonist, and can manifests as angina pectoris, myocardial infarction, cardiogenic shock, arrythmias and death [1]. Clinical evidence of 5-FU cardiotoxicity is generally considered to occur in about 2% of treated patients, probably more often in those with known coronary disease and previous radiotherapy. Patients have been reported to develop typical clinical and electrographic manifestations within a few hours of initiating the infusion to up to 18 hours after its completion. Symptoms and ECG signs are known to subside at drug cessation, while continuation of the drug has been associated with myocardial infarction, pulmonary oedema and even death. Recurrence of typical chest pain was observed with 5-FU rechallenge. Coronary spasm is postulated to account for this cardiotoxicity [1, 2] though other mechanisms have been proposed [2].

Capecitabine is a fluoropyrimidine which after oral administration is metabolized into 5-FU by thymidine phosphorylase. Since the metabolizing enzyme appears to be preferentially expressed by tumor cells, capecitabine is considered to exert a selective antitumoral action.

A recent randomized phase II study performed in 109 colorectal cancer patients reported 5 cases (4.5%) of probable cardiac toxicity, including 4 patients with chest pain [3]. The pain began four to eight days after initiation of treatment and resolved with interruption of therapy. In two cases, rechallenge with the drug was associated with pain relapse. ECG changes were not reported in the article and no coronary angiogram was performed. In the same article [3] preliminary data from 2 pooled randomized phase III studies performed in 596 patients are mentioned (Van Cutsem E et al., manuscript in preparation): 2% cardiac events were observed in the capecitabin arm *versus* 1.3% in the 5-FU–leucovorin arm.

To our knowledge, no coronary spasm documented by coronary angiogram and secondary to capecitabin has yet been reported. We believe that our clinical observation should remind physicians about the potential coronary toxicity of capecitabine. Clinical and ECG manifestations of angina should prompt drug discontinuation.

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References

1 Anand AJ. Fluorouracil cardiotoxicity. Ann Pharmacother 1994; 28: 374–8.

2. Luwaert RJ, Descamps O, Majois F et al. Coronary artery spasm induced by 5-fluorouracil. Eur Heart J 1991; 12: 468–70.

3 Van Cutsem E, Findlay M, Osterwalder B et al. Capecitabine, an oral fluoropyrimidine carbamate with substantial activity in advanced colorectal cancer: Results of a randomized phase II study. J Clin Oncol 2000; 18: 1337–45.

Bone scan had no role in the staging of 765 consecutive operable $T_{1-2}N_{0-1}$ breast cancer patients without skeletal symptoms

Bone scanning (BS) is considered a sensitive test for the detection of metastatic breast cancer [1–3], but not all abnormal findings on bone scan are diagnostic of skeletal metastasis. For this reason, the role of BS in the staging of breast cancer has been widely questioned in recent years [4–7]. Recent studies have found a relatively low rate (less than or equal to 5%) of abnormal scans in patients with stage I and II breast cancers, and only half of those with positive scans subsequently had documented bony metastasis [2]. Despite these data bone scan continues to be prescribed during staging, and there was never an intention to question the role of 'staging' bone scan immediately after diagnosis and operation. The aim of this report was to ascertain the relevance of bone scan (BS) in detecting asymptomatic bone metastases in the preoperative staging of disease in a group of patients studied by the same team of physicians in a very short recruitment time. No previous study reported our number of patients studied by the same team in so short a recruitment time.

A retrospective review of 765 consecutive patients with operable breast cancer staged according to the TNM staging system as T_{1-2}, N_{0-1} and all referred to the European Institute of Oncology (EIO) between April 1997 and January 2000, was performed. No selection criteria have been used in our cohort.

Patients had a histologically proven breast cancer and had definitive breast surgery and staging preoperative bone scan at the EIO. All bone scans were performed and evaluated by the same team of physicians at the Division of Nuclear Medicine. Whole body scintigraphy was obtained three hours after injection of 740 MBq of Technetium 99m-labeled methylene diphosphonate in anterior and posterior projections by use of a large-field gamma camera (GE MAXXUS) equipped with a HR low energy collimator. Stage of disease was defined by standard pathological examination techniques.

All patients were asymptomatic at the time of BS. Patient characteristics are displayed in Table 1. Increased uptake of uncertain dignity was observed in 40 (5%) patients and attributed, in differential diagnosis, to degenerative bone abnormalities or compression fractures of vertebrae. Detected 'hot spots' were investigated with the same type of radiologic examination. An algorithm that provided X-ray and CT scan

Table 1 Major patient characteristics

	Number of patients	True positive (%)
Total	765	4 (0.5)
T_1N_0	261	–
T_1N_1	237	1 (0.4)
T_2N_0	109	–
T_2N_1	158	3 (2)
ER/PgR positive[a]	652	3 (0.4)
Grade 1	126	–
Grade 2	354	3 (0.8)
Grade 3	274	1 (0.3)
Grade nd	11	–

[a] ER and/or PgR $\geq$ 10% of the cells or 10 fmoles.