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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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.

or MRI was used according to recommendations by the radiologist. Only four patients had evidence of skeletal involvement on imaging (X-ray, CT scan, MRI). In this subgroup of patients we modified treatment strategy, but maintained indication for surgical breast conservation in patients with T_1 lesions. No true positive was found among patients with node-negative or grade 1 tumors. Thus, BS detected tumor bone spread in 4 out of the 765 patients studied (0.5%), with a positive predictive value of 10%.

Baseline bone scans had a cost of 240 Euro each (183,600 Euro total). Bone scans that were interpreted as positive or suspicious for metastatic disease on initial presentation resulted in 42 confirmatory studies, including 16 plain films, 18 computed tomography (CT) scans, 8 magnetic resonance imaging (MRI) scans. These additional tests cost another 9600 Euro.

Bone scan in the initial staging of breast cancer is not mandatory. According to START (State of the Art Oncology in Europe), accurate history and general examination, a full blood count, liver function tests and a chest radiograph are standard procedures on a general consensus basis in the preoperative evaluation of all patients with newly detected breast cancer. Bone scan may also be requested by the patient, who needs to be reassured about lack of evidence for tumor dissemination. Most research protocols dealing with adjuvant or neoadjuvant therapy for breast cancer require a baseline bone scan, leading to the consideration of bone scan as a routine examination for staging prior or, in asymptomatic patients, immediately after breast cancer surgery.

A relevant staging is crucial for choosing a proper treatment. In our study the cost-benefit balance of bone scintigraphy in the initial staging of operable (T_{1-2}, N_{0-1}) breast cancer excluded any relevant role of this technique for the early detection of metastatic bone metastases

Medical efforts and financial expenditures devoted to initial breast cancer staging represents a heavy burden on health care resources. We conclude that staging of asymptomatic $T_{1-2}N_0$ breast cancer should not include bone scan as a routine examination.

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