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Radioguided Surgery of Occult Breast Lesions

A. Luini,[1] S. Zurrida,[1] V. Galimberti[1] and G. Paganelli[2]

[1]Division of Senology; and [2]Division of Nuclear Medicine, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy

THE EXTENSIVE use of mammography and ultrasonography in clinical practice and for early diagnosis has resulted in a major increase in the detection of occult breast lesions [1, 2]. Clusters of microcalcifications or small opacities of irregular outline may be early signs of a malignancy which is generally well-suited to treatment by breast-conserving surgery. However, surgery must be preceded by precise localisation since the lesion is not palpable. Several localisation techniques are used [3], the most common being to introduce a hooked wire [4, 5] or to inject a path of sterile carbon particles to the lesion, and while each method has its advantages none can be considered ideal [6, 7].

At the European Institute of Oncology, Milan, we have developed a new localisation technique called ROLL (radioguided occult lesion localisation). This involves the inoculation of particles of colloidal human serum albumin, 10–150 μm in diameter (Macrotec, Sorin Biomedica, Saluggia, Italy), labelled with approximately 3.7 MBq of radioactive technetiun (^{99m}Tc), directly into the lesion during mammography or ultrasonography.

Correspondence to A. Luini.
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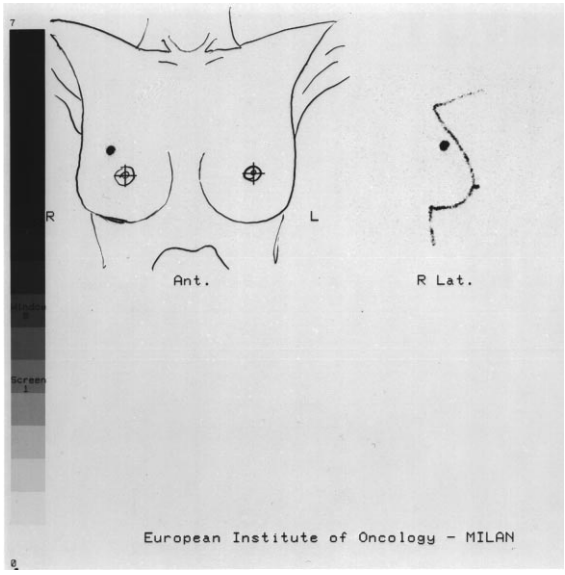

Figure 1. Anterior and lateral projections of the location of the lesion on scintigraphy.

Correct inoculation is verified by superimposing the mammographic image over a scintigraphy scan of the breast. The scintigraphic image is available in the operating room to assist the surgeon in locating the lesion (Figure 1); comparison reveals the presence of any mismatch between the radiological lesion and the point of radioactivity injection.

A gamma detecting probe is then used to locate the lesion as a hot spot. By means of this probe, the surgeon can locate the skin projection of the lesion with precision and hence decide on the most appropriate incision. More importantly, however, the probe is used as often as necessary during surgery to check the position of the lesion. In this way a portion of breast tissue containing the lesion at its centre can be removed, guaranteeing oncological radicality (if the lesion turns out to be malignant) but at the same time avoiding excessive mutilation. This possibility of verifying at any time distinguishes the technique from more conventional methods, and also makes the operation quicker and easier.

There is negligible radiation risk for the patient and health staff. Dose levels are of the order of 0.1 mCi, equivalent to 0.01 of the dose received during bone scintigraphy, or more simply, less than the radiation received during a flight from Rome to New York!

Analysis of the 196 patients with clinically occult breast lesions operated on from March 1996 to April 1997 has shown the technique to be highly satisfactory and reliable, so that it is now in routine use at our institute.

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Chemical Pleurodesis with Mitoxantrone in the Management of Malignant Effusions

A.F. van Belle, G.P.M. ten Velde and E.F.M. Wouters

Department of Pulmonology, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands

METASTATIC DISEASE of the pleura is a frequent cause of exudative pleural effusions. The epidemic of lung cancer today and the increase of most forms of cancer make malignant effusion a common pathology in pulmonary practice. Optimal treatment for these patients with often limited life expectancy has to be effective, as assessed by a low recurrence rate of pleural fluid. Furthermore, the treatment should be inexpensive and should have minor morbidity. None of the various reported methods fulfil all these demands [1].

The standard treatment for controlling malignant pleural effusions is tube thoracostomy with instillation of a sclerosing or cytotoxic drug. Most commonly employed sclerosing agents include talc, tetracycline and tetracycline analogues such as doxycycline and minocycline. Bleomycin is frequently proposed as an important cytotoxic agent for pleurodesis of malignant pleural effusions [2]. Mitoxantrone, an anthracycline derivative, has recently been demonstrated to be effective in the treatment of peritoneal and pleural effusion. Mitoxantrone with its high molecular weight and high polarity exhibits a decreased pleural clearance with prolonged high peak concentrations intrapleurally, favourable factors for local intrapleural treatment. The mechanism of intrapleural action of mitoxantrone has not yet been established. Both the inflammatory and antineoplastic activity of mitoxantrone intrapleurally have been described [3, 4]. There are only limited data about the efficacy of mitoxantrone in the treatment of malignant pleural effusions. In a prospective study in 18 patients, Musch and associates [5] reported a success rate of 75%. A comparative study including bleomycin and mitoxantrone showed almost an equal response rate of 64% and 67%, respectively [6].

Table 1. *Total response (CR + PR) according to primary malignancy*

	No. (%)
Breast cancer	10/11 (91%)
Lung cancer	4/8 (50%)
Mesothelioma	4/5 (80%)
Cancer of unknown origin	7/12 (58%)
Ovarian cancer	2/3 (67%)
Sarcoma	1/1 (100%)

We studied 40 patients with cytologically proven malignant pleural effusion. Patients were treated following standard procedures. In all patients thoracostomy and tube drainage were performed. After adequate drainage and expansion of the lung, 30 mg of mitoxantrone was instilled through the chest tube. In patients with persistent pleural fluid production of more than 200 ml/24 h after the first instillation of mitoxantrone, a second dose of mitoxantrone (30 mg) was administered. Four weeks after pleurodesis, the response rate was assessed radiographically (chest X-ray). The criteria for complete or partial response were defined according to Paladine and associates [2]. A complete response (CR) was obtained in 18 patients (45%) and a partial response (PR) in 12 patients (30%), resulting in an overall response rate (CR + PR) of 75%. 7 patients showed sustained pleural fluid production after the first mitoxantrone instillation, and needed a second instillation of mitoxantrone. In this latter group of 7 patients, a failure rate of 57% was found. The highest success rate was found in patients with breast cancer (Table 1). Remarkably, pleural effusion in mesothelioma patients seemed to respond well, although the patient number was limited. The procedure was well tolerated and side-effects of the intrapleural instillation of mitoxantrone were rare. Importantly, no complaints of pain were noted during and after instillation. The present study confirms previous data that prolonged excessive production of pleural fluid with sustained pleural drainage, after initial treatment with a sclerosing agent, is an unfavourable prognostic factor for successful pleurodesis. The results in our study confirmed the high effectiveness of mitoxantrone for pleurodesis in the absence of significant morbidity. Our reported data justify further longitudinal and biochemical studies in a controlled setting to elucidate the biological action and prognostic relevance of mitoxantrone in the treatment of malignant pleural effusions, and to compare this agent with other treatment procedures for malignant effusions.

Correspondence to A.F. van Belle.
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