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# Sonography Versus Palpation in the Detection of Regional Lymph-Node Metastases in Patients with Malignant Melanoma

**Lucas Prayer, Hedy Winkelbauer, Norbert Gritzmann, Fritz Winkelbauer, Michael Helmer and Hubert Pehamberger**

**High-resolution real-time sonography was done in 217 patients with malignant melanoma to compare its value in detecting regional lymph-node metastases with that of palpation. Lymph-node metastases were found in 29 patients by ultrasound whereas, by palpation, metastases were detected in 15 patients only. The presence of metastases was proven by histopathology after surgical lymphadenectomy in these ultrasound positive cases. Thus sonography was superior to palpation, and in addition permitted distinction between metastatic changes and inflammatory lymph-node enlargement. Ultrasound is recommended for preoperative staging as well as in postoperative monitoring of patients with malignant melanoma.**
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## INTRODUCTION

ALTHOUGH THE incidence of malignant melanoma is increasing worldwide [1–3], prognosis and survival rates are improving [1] primarily because the tumour is being recognized in earlier phases. The presence of lymph-node metastases correlates with the depth of invasion of the primary tumour; these factors are the most important prognostically. Thus early detection of lymph-node metastases is critical in the management of melanoma patients [4–6]. Palpation of regional lymph nodes has a high rate of error, with a reported frequency of false negative findings of up to 39% [7]. Our aim was to evaluate the use of high-resolution real-time sonography in the detection of regional lymph-node metastases, to compare sonography with palpation and to determine whether sonograms in preoperative staging and postoperative care of melanoma patients are routinely indicated.

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## PATIENTS AND METHODS

We studied 217 patients with primary malignant melanoma (Table 1). Primary lymph nodes, dependent on tumour localisation, were examined by palpation and by high-resolution real-time sonography. Lymph nodes were investigated either before or after removal of the primary melanoma in postoperative follow-up.

Sonography was done with an ATL 'Ultramark 8' with a 7.5 MHz anular array; a detachable elastomere (hydrated polyacrylamide-agar) was used to reduce artefacts. The visible lymph nodes were documented in longitudinal and cross sections. Circular and oval masses with poor echo were regarded as indicative of metastatic changes; on the other hand, longitudinally configurated lymph nodes, the hilum of which appeared

*Table 1. Details of patients with primary melanoma*

| | No. |
|---|---|
| M/F | 104/113 |
| Mean age (range) | 56 (25–82) |
| Localization | |
| Head/neck | 42 |
| Arm | 61 |
| Shoulder | 23 |
| Leg | 91 |
| Type | |
| Superficial spreading | 139 |
| Nodular | 64 |
| Acral lentiginous | 8 |
| Lentigo maligna | 6 |
| Microstaging | |
| Clark's level of invasion | |
| I | 0 |
| II | 93 |
| III | 89 |
| IV | 33 |
| V | 2 |
| Breslow's tumour thickness (mm) | |
| > 0.75 | 25 |
| 0.75–1.5 | 96 |
| 1.5–3 | 79 |
| > 3 | 17 |

as an echogenic eccentric area, were regarded as "enlarged reactively". Sonography was done by a radiologist whereas the palpations were done by dermatologists. Firm resistance was graded as a sign of metastatic enlargement. Sonography and palpation were done independently within one week. Sonographically suspicious lymph nodes were removed surgically and evaluated histopathologically. Patients with lymph nodes that were classified by sonography to be inflammatory and reactively enlarged and patients with normal findings were seen again every 2 months for 6 months.

## RESULTS

In 29 (13%) of the patients, histopathologically verified regional lymph-node metastases were found (Table 1). Sonography revealed regional lymph-node metastases in all 29 patients. There were no false-negative sonographic results—i.e. melanoma metastases did not occur within the following 6 months in any of the patients classified as having no suspect regional lymph nodes.

*Table 2. Sonography compared with palpation in detection of regional lymph-node metastases in 217 melanoma patients*

| | Metastases | |
|---|---|---|
| Test | Present | Not present |
| Sonography | | |
| Positive | 29 | 6 |
| Negative | 0 | 182 |
| Palpation | | |
| Positive | 15 | 17 |
| Negative | 14 | 171 |

*Table 3. Sonography compared with palpation by lymph-node region*

| | Metastases | |
|---|---|---|
| Region | Present | Not present |
| Cervical | | |
| Sonography | | |
| Positive | 7 | 1 |
| Negative | 0 | 34 |
| Palpation | | |
| Positive | 5 | 4 |
| Negative | 2 | 31 |
| Axillary | | |
| Sonography | | |
| Positive | 10 | 1 |
| Negative | 0 | 73 |
| Palpation | | |
| Positive | 4 | 5 |
| Negative | 6 | 69 |
| Inguinal | | |
| Sonography | | |
| Positive | 12 | 4 |
| Negative | 0 | 75 |
| Palpation | | |
| Positive | 6 | 8 |
| Negative | 6 | 71 |

Ultrasound gave a false-positive in 6 subjects in whom, despite careful histological evaluation, no metastatic changes in the surgically removed lymph nodes (which were oval) were seen. In another 6 cases sonography showed small lymphoceles after a previous operation.

Palpation revealed lymph-node metastases in 15 patients. In 17 patients clinical examination was false-positive—i.e. sonographically no suspicious lymph nodes were detected. In 14 patients palpation revealed false-negative results in that lymph-node metastases were detected by subsequent sonography (Table 2).

When these data were analysed according to lymph-node regions we found the results to be more correct in the cervical than in the axillary regions (Table 3). Reactive lymph nodes were more frequently seen in inguinal and cervical regions, whereas in axillary lymph nodes predominantly metastatic changes were observed.

The smallest palpable metastasis was 16 mm, whereas the smallest metastasis detected by ultrasound was 11 mm in diameter.

The sensitivity specificity and accuracy of the two techniques are shown in Table 4.

*Table 4. Sensitivity and specificity*

| | Sonography | Palpation |
|---|---|---|
| Sensitivity | 100%* | 52% |
| Specificity | 97% | 91% |
| Accuracy† | 97% | 86% |

*Sensitivity was 100% because only these patients had histopathological examination.

†$\text{Accuracy} = \frac{\text{true positive} + \text{true negative reports}}{\text{no. of all patients examined}}$.

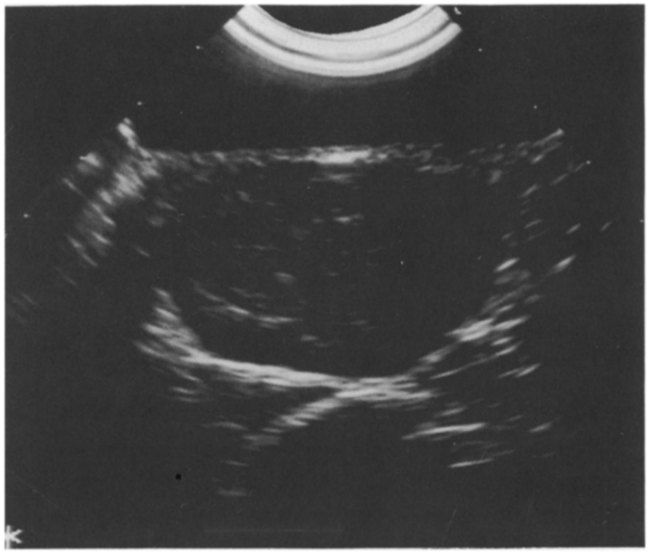

**Fig. 1. Patient aged 46. Nodular melanoma in right thigh had been excised 4 years ago (Clark stage III, Breslow 3.2 mm). Longitudinal section through right inguinal lymph-node metastasis, measuring about 3.5 cm in diameter. Circular mass has typically poor echogenicity.**

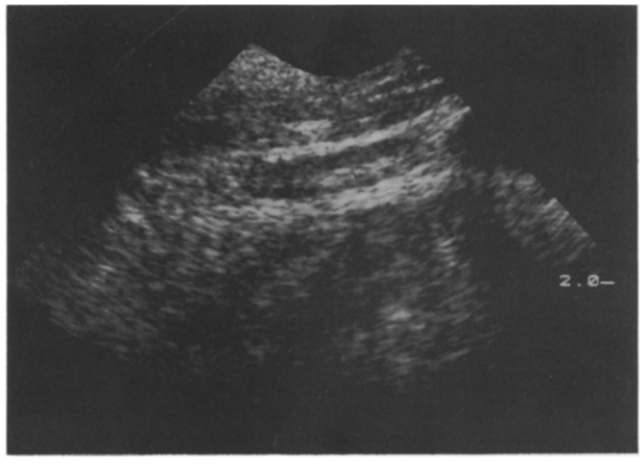


**Fig. 2. Patient aged 37. Superficial spreading melanoma in left temple had been excised 2 years ago (Clark stage II, Breslow 0.72 mm). Longitudinal section through left cervical reactive inflamed lymph node, measuring about 2 cm in diameter. Longitudinally configured lymph node with eccentric, echogenic hilum.**

## DISCUSSION

Immediate radical excision of the primary tumour is the treatment of choice in malignant melanoma. Controversy exists, however, about the management of regional lymph nodes, the most common site of metastases in melanoma [1–3, 5, 6, 8]. Whilst the therapeutic excision of involved lymph nodes is generally accepted, the value of elective lymph-node dissection is debated. Some groups prefer to excise palpable metastatic nodes only whereas others excise the nodes even when they appear normal because of the risk of occult metastases [5–8]. However, comparative studies reveal the 5-year survival rate after lymph-node excision to be significantly higher in those patients in whom metastases were already palpable [1, 2]. Furthermore, prophylactic lymph-node dissection might lead to an unfavourable "immunodeficiency" [9, 10]. Thus early recognition of clinically innocent but microscopically involved lymph nodes is important in the decision about therapeutic strategies in malignant melanoma and techniques are needed to answer this question.

In our study of ultrasound techniques in the detection of early, clinically undetectable, regional lymph-node metastases in malignant melanoma, we found sonography to be superior to palpation.

Sonography permitted a clear presentation of the lymph-node regions examined and an exact ascertainment of location, size, and relation of the metastases to the surrounding structures. In cases with unsharp borders of visible masses, indicating rupture of the capsule, sonography plus palpation was done. An invasive growth could be excluded when mobility was free [11–14]. Even in cases of clinically evident lymph-node metastases, sonograms provided essential and relevant preoperative information. In 6 out of 15 patients with clinically positive lymph nodes, sonograms revealed metastases additional to those diagnosed conclusively by palpation. However, incipient or partial lymph-node involvement could not be located, indicating that sonography cannot identify micrometastases. In addition, postoperative cystic or multiseptate formations caused diagnostic problems: the differentiation of lymphoceles from necrotic metastases was difficult.

Because of their distinct morphology we were able to differentiate between reactive lymph nodes and melanoma metastases. Metastases were typically identifiable as oval or circular masses with poor or no echo at all (Fig. 1). In contrast, inflamed and enlarged lymph nodes had a longitudinal shape and an eccentric and highly echogenic hilum (Fig. 2). This differentiation proved to be valuable, with a "grey zone" of only about 5% [11, 13, 14]; in our series, 17 patients with palpable but sonographically negative lymph nodes were saved from invasive surgical intervention. All of these patients were, of course, followed up clinically and sonographically every 2 months, and none of them developed metastases.

Although sonography was more sensitive and specific than palpation in detecting lymph-node metastases, verification of our findings would require surgical exploration and histopathological examination of all lymph nodes investigated by non-invasive techniques. We did not do this for ethical and medical reasons, since the elective prophylactic excision of clinically and/or sonographically innocent lymph nodes in melanoma patients has no influence on disease-free interval or survival [4, 7, 9].

Our data indicate that in view of its high diagnostic efficacy and accuracy as well as clinical relevance, sonography of regional lymph nodes is indispensable in the management of melanoma patients [15, 16]. Sonograms are mandatory in preoperative staging as well as in postoperative care and might help to improve and increase survival.

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# Cigarette Smoking and Risk of Breast Cancer: a Prospective Study of 24 329 Norwegian Women

**Lars J. Vatten and Stener Kvinnsland**

**The association between cigarette smoking and incidence of breast cancer has been analyzed in 242 cases of breast cancer that developed among 24 329 Norwegian women over 11–14 years of follow-up. At baseline they were aged 35–51. There was no overall association between cigarette smoking and the risk of breast cancer. The age-adjusted incidence rate ratio (IRR) was unity (IRR=1.04, 95% CI 0.76–1.42) for regular smokers (10 or more cigarettes daily) compared with non-smoking women. In women who reported smoking between 1 and 9 cigarettes per day there was an age-adjusted IRR of 1.28 (95% CI 0.95–1.73). The lack of association with cigarette smoking was replicated in subgroup analyses of women diagnosed before age 51 ("premenopausal") and among women diagnosed after this age ("postmenopausal"). However, there was a significant interaction between cigarette smoking, body mass index and age at diagnosis ($P = 0.01$), which might indicate that an interaction between cigarette smoking and body mass exerts differential effects on breast cancer risk in premenopausal and postmenopausal women.**
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## INTRODUCTION

THE HYPOTHESIS that cigarette smoking may reduce the risk of breast cancer [1–3], possibly due to an anti-oestrogenic effect, has not been confirmed in most epidemiological studies. One cohort study [4] showed a decreased risk in smokers, whereas another [5] yielded opposite results. Some case-control studies have also demonstrated a reduced risk [6, 7] of breast cancer in smokers, but most studies show no effect [8–15].

Although the overall association between smoking cigarettes and breast cancer incidence may approximate unity, characteristics within subgroups may modify the effect. Overweight may be inversely related to breast cancer risk among premenopausal women [16–18], in contrast to the positive association with body mass among postmenopausal women [19]. A relation with oestrogen (and possibly progestagen) metabolism has been suggested [20]. Combined with the evidence that cigarette smoking affects the metabolism of oestradiol [3], an interaction effect on breast cancer risk may exist between cigarette smoking and body mass. Such an interaction should also depend on menopausal status.

In this prospective study we explored the overall relation between cigarette smoking and risk of breast cancer. We then examined whether the effect of smoking might vary between women diagnosed before age 51 ("premenopausal") compared with women diagnosed after this age ("postmenopausal"), before we tested the possible interaction between cigarette smoking, age at diagnosis and body mass index (BMI) in relation to the risk of developing breast cancer.

## METHODS

*The cohort*

Between 1974 and 1978 all men and women aged 35–51 and living in three separate counties in Norway were invited to participate in a health screen organized by the National Health Screening Service. The screen included a questionnaire, and standardized measurements of height, weight and blood pressure [21, 22].

26 252 women were invited; 24 617 (93.8%) attended. To reduce a potential bias due to preclinical changes in smoking habits, all cancer cases (including breast cancer) that had

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