breast tumors as a consequence of random variations in the measurements of tumor size

Materials and Methods: Unidimensional measurements (largest diameter, RECIST) and bidimensional measurements (product of largest diameter and its perpendicular, WHO) of tumor extent were performed on 159 lesions in breast cancer patients, using mammography, ultrasonography, and MRI. The random variations in these measurements were quantified using an analysis of variance technique, and were used to predict the fraction of false-positive calls for tumor regression and the fraction of false-positive tumor progressions that result from employing the WHO and the RECIST guidelines for monitoring tumor response to neoadjuvant treatment.

Results: Using the WHO criteria, the estimated fraction of false-positive calls for tumor regression is 13% (mammography), 10% (ultrasonography), and 13% (MRI). For tumor progression, the estimated fraction of false-positive calls is 29% (mammography), 26% (ultrasonography), and 28% (MRI). Employing the RECIST criteria results in an estimated fraction of false-positive calls for tumor regression of 13% (mammography), 12% (ultrasonography), and 11% (MRI). For tumor progression, the estimated fraction of false-positive calls is 23% (mammography), 22% (ultrasonography), and 19% (MRI).

Conclusions: Both the WHO and the RECIST guidelines overestimate tumor regression and tumor progression. In particular, tumor progression may be considerably overestimated, although somewhat less by the RECIST than by the WHO guidelines. If a lower fraction of false-positive calls is desired in monitoring the response of solid breast tumors to neoadjuvant treatment, the criteria may need to be refined using quantitative knowledge of the reproducibility in the measurements of tumor extent

128 POSTER

Six-year experience of equivocal (B3) and suspicious (B4) breast core biopsies from screen-detected lesions: correlation with radiology, cytology and final excision

M.S. Gill, M.J. Staunton, J.J. Shrimankar. Royal Victoria Infirmary and Newcastle Breast Unit, University Department of Pathology, Newcastle, UK

Background: To review our experience with equivocal and suspicious results on breast core needle biopsies (CNB) from screen-detected lesions between 01/07/1997 and 30/06/03.

Methods: The data were extracted from the National Health Service Breast Screening Programme (NHSBSP) screening office computer, cytology files and histopathology database. Radiology, Fine Needle Aspiration Cytology (FNAC) and CNB were reported according to the guidelines of the NHSBSP. B3/B4 CNBs were correlated with pre-operative Radiological and FNAC findings and subsequent pathology excision results.

Results: During the study period, 915 CNBs were received from screen-detected lesions. 70 (7.7%) were reported B3 and 40 (4.4%) were reported B4. 109/110 of the B3/B4 CNBs had concurrent FNAC. The radiological risk score was available for all 110 cases. 103/110 (93.6%) had excision biopsy (all histology reports available); the remaining 7 patients have radiological follow-up available for a mean of 45 months (range 12–75). The Positive Predictive Value for malignant histology on excision (PPV) of B4 was 87.5% and the PPV of B3 was 36%.

All B4 cases were excised and the 5 benign B4 CNB were derived from atypical ductal hyperplasia (ADH). The 38 cases with B3 CNB and a benign excision biopsy included ADH (6), radial scar/complex sclerosing lesion (18), atypical lobular hyperplasia (1), granular cell tumour (1), myofibroblastoma (1), Phyllodes tumour (1), papilloma (3), fibrocystic change (3), fibroadenoma (1), sclerosing adenosis (1), pseudoangiomatous stromal hyperplasia (1), and normal breast tissue (1).

During the study period, 2615 FNAC were performed on screen-detected lesions. FNAC statistics of this cohort of FNAC indicate a 59% absolute sensitivity for FNAC with a PPV of 99.8% for C5 cytology and 85.3% for C4 cytology. We had no C5 FNAC among the 25 cancers with B3 CNB. Only 14 of the 35 cancers with B4 CNB had a C5 FNAC.

Conclusions: There have been fears that the B3 category may lead to an increase in the benign biopsy rate, but our data support excision of lesions with B3 at CNB. There are no Mammotome biopsies in this study but this may be a viable second line of investigation. We speculate that cancers with a B3 or B4 CNB may be a sub-group in which it is difficult to obtain a pre-operative diagnosis by any diagnostic modality as the FNAC results in this subset are at variance with our overall cytology results. Excision is mandatory for any case with a B4 diagnosis.

POSTER

Breast duct micro-endoscopy does not diagnose pre-invasive malignancy

D. Kulkarni¹, N. Beechey-Newman¹, A. Kothari¹, C. D'arrigo², G. Culora³,
H. Hamed¹, I. Fentiman¹. ¹Guys and St Thomas Hospital, Breast
Oncology, Department of Academic Oncology, London, UK; ²Guys and
St Thomas Hospital, Breast Pathology, London, UK; ³St Thomas Hospital,
Cyto-Pathology, London, UK

Introduction: We have previously demonstrated the feasibility of breast duct micro-endoscopy. We describe the early results of this technique when used to investigate nipple discharge.

Procedure: Duct endoscopy was carried out using micro endoscopes between 0.5 mm and 1.1 mm external diameter. (Polydiagnost GmbH). For the first time a micro-cytology brush was used to obtain samples in addition to duct aspirates.

Results: 28 patients were investigated, 20 had unilateral single duct discharge (16/20 bloodstained), and 8 unilateral multi-duct discharge (3/8 bloodstained). 12 cases were carried out under local anaesthesia. Good visualisation of the discharging ducts was achieved in 100% of cases to a maximum depth of 7.5 cm, (median depth 5.2 cm). A maximum of 8 duct bifurcations (median 3) were crossed during the examinations. We identified pathology in 15 patients (single papilloma in 6, multiple papilloma in 2, duct adhesions 2, inflammation in 5, obstructed duct in 2, foreign body in 1). 2 patients also had nipple aspirate cytology examined and 1 of these yielded cells. 4 had cytology by micro-brush, and 3 provided sufficient cells for analysis. All cases subsequently underwent excisional surgery. The findings on endoscopy were in agreement with the pathology in 20 cases. Endoscopy failed to diagnose papillomas in 4 cases where the lesions were in adjacent, non-discharging ducts. In 1 case multiple papillomas were seen but histology suggested that these were polypoid granulomas. Cytology (aspirate) showed papillary fragments. Cytology was in agreement with the histology in 3/4 cases. However, DCIS was diagnosed on histology in one case, DCIS/LCIS in one case and ADH in another. None of these 3 cases had visible macroscopic abnormalities within the discharging duct on endoscopy. Cytology was available in 1 of these patients (aspirate and micro-brush) but this provided insufficient cells for diagnosis (C1).

Conclusion: Breast duct micro-endoscopy provides clear pictures of the discharging ducts to a greater depth than would usually removed at surgery. Papillomas in adjacent ducts can be missed but these are probably not contributing to the discharge. In this small series breast duct micro-endoscopy on its own is not sufficient to diagnose pre-invasive malignancy.

130 POSTER

The role of axillary nodal staging during preoperative breast diagnostics

E. Ambrozay¹, G. Cserni², P. Serényi², M. Tarján², M. Lorincz¹, K. Loránd¹. ¹Mamma Rt at the Bács-Kiskun County Teaching Hospit, Department of Mammography, Kecskemét, Hungary 2.Bács-Kiskun County Teaching Hospital, Department of Pathology, Kecskemét, Hungary

The ultrasonographic work-up of the axilla is part of the examination of the breast. This permits an imaging assessment of axillary nodal status and offers guidance for fine needle aspiration (FNA) of visualized lymph nodes (LNs). The presence and demonstration of metastatic LNs obviates the need for sentinel lymph node (SLN) biopsy even in the event of non-palpable axillary LNs.

During a period of 6 months, there were 64 patients who had axillary FNA cytology (FNAC) from enlarged LNs. LNs were categorised either as reactive or pathological by ultrasound (US). LNs were classified as pathological if they had an even or uneven enlargement of the cortical area, had a central area that had become hypoechogenic, or had become rounded. US-guided sampling was done from the cortical area of the LNs.

Of the 37 cases categorised as pathological by US, FNAC was reported as inadequate in 5, and as negative for metastasis in 8. Eleven patients had no axillary surgery either because of primary chemotherapy or because of negative breast imaging findings and FNAC of the axillary LN, whereas 26 patients had either diagnostic excision of the LN, or SLN biopsy or axillary dissection; 21 had metastatic disease in the axilla, 2 had nodal involvement by lymphoma, 1 had tuberculous lymphadenitis, and 2 patients had no relevant nodal pathology. Three inadequate and 3 negative FNAC specimens were found to have metastasis in the axilla; the tuberculous lesion and one of the lymphomas were reported as inadequate and negative, respectively. Of the 27 cases categorized as reactive by US, 8 were reported as inadequate, 1 as metastatic and the remaining as non metastatic by FNAC. Eleven patients had some type of axillary surgery, 8 had metastatic nodal involvement, and 1 had nodal involvement by a lymphoma. The sensitivity and specificity of axillary US to detect metastatic

nodal involvement were 72% and 38%, respectively. The same values for axillary US-guided FNAC were 61% and 89%, respectively, while the combination of the two methods was characterized by a sensitivity of 76% and a specificity of 38%.

We conclude that axillary US and US-guided FNAC are valuable methods for selecting patients who may not need SLN biopsy for staging, but should undergo axillary dissection immediately. It must be kept in mind that the axillary nodes might have pathologic findings even in the absence of nodal metastasis, as demonstrated by 3 lymphoma cases and a tuberculous infection in our series.

131 POSTER

The effectiveness of routine follow-up to detect locoregional recurrences after treatment for early stage invasive breast cancer: a systematic review

<u>G.H. de Bock¹</u>, J. Bonnema², J. van der Hage², J. Kievit^{1,2}, C.J.H. van de Velde². ¹Leiden University Medical Center, Department of Medical Decision Making, Leiden, The Netherlands; ²Leiden University Medical Center, Department of Surgery, Leiden, The Netherlands

Background: Whether routine follow-up after treatment for primary breast cancer has any prognostic benefit is a topic of ongoing debate. The aim of this paper is to review the effectiveness of routine follow-up to detect locoregional recurrences after treatment for early stage invasive breast cancer.

Methods: We performed a systematic review and meta-analysis of studies published in peer-reviewed journals on the effectiveness of routine follow-up to detect isolated locoregional recurrences in patients treated for primary operable breast cancer. As main outcome measure we considered: the proportion of asymptomatic locoregional recurrences diagnosed during routine visits compared to the proportion of symptomatic locoregional recurrences diagnosed during or outside routine visits. Twelve studies that involved a total of 5045 patients and 378 locoregional recurrences were identified.

Results: Pooling data showed an overall estimate of 40% of locoregional recurrences diagnosed during routine consultation before the patient had symptoms (95% C.I.: 35–45); of these 47% (95% C.I.: 39–54) were diagnosed after mastectomy and 36% (95% C.I.: 28–43) were diagnosed after breast conserving therapy. The studies about the follow-up of patients after mastectomy were all published before 1995, whereas all studies, with the exception of one, about breast conserving therapy were published after 1995. There was no information in the literature on treatment or survival benefit, nor on quality of life. Besides differences in therapy, we have not been able to discern subgroups of patients in whom results were different.

Conclusion: An important percentage of isolated locoregional recurrences is diagnosed during routine consultation prior to symptomatic presentation, in patients treated for early stage invasive breast cancer. This systematic review highlights the need for further development of a cost-effective routine for the follow-up of patients after a diagnosis of breast cancer.

132 POSTER

Breast cancer staging and treatment planning according to internal mammary lymph node morphology

A. Petrovsky¹, A. Trigolosov², Y. Vishnevskaya³, B. Polyakov⁴, M. Nechushkin⁵. ¹Moscow Sechenov Medical Academy, Oncology, Moscow, Russian Federation; ²Russian Cancer Research Center, Radiosurgery, Moscow, Russian Federation; ³Russian Cancer Research Center, Pathology, Moscow, Russian Federation; ⁴Moscow Sechenov Medical Academy, Oncology, Moscow, Russian Federation; ⁵Russian Cancer Research Center, Radiosurgery, Moscow, Russian Federation

The rate of the internal mammary lymph nodes (IMN) metastasis in breast cancer patients is in the range between 12 and 55% according to different publications. Unfortunately nowadays there is the lack of the preoperative non-invasive routine methods for the definite detection of the IMN involvement.

During 1998–2003 1088 patients underwent either videothoracoscopic IMN dissection (710 women) or open IMN biopsy (378 women). Very low rate of intra and post-surgical complications connected to videothoracoscopic IMN dissection could be registered in all the patients. No specific complications were detected during or after open IMN biopsy. 210 of all the patients (19.3%) had morphologically verified metastasis in IMN. In 5.3% IMN involvement was detected without axilliary lymph node metastasis. According to our results there is IMN metastasizing rate dependence on the additional involvement of the axilliary lymph nodes, patients age, size and histological structure of primary breast tumor and no statistically significant connections could be found with location, estrogen receptor level and menstruation function of the patients. Only patients

with verified INM metastasis underwent radiation therapy at this zone. No recidives in parasternal region was detected in non-radiated women in 5-year monitoring period. It was shown that patients with IMN metastasis have significantly worth prognosis in comparison with IMN negative. Both techniques could be recommended to the breast cancer patients for correct staging and treatment planning.

133 POSTER

The role of ultrasonography in addition to mammography in the detection of breast cancer

A. Kowalczyk¹, M. Nowaczyk², M. Kanas², A. Legowik-Chmielewska², R. Dziadziuszko¹, E. Solska², J. Jassem¹. ¹Medical University of Gdansk, Department of Oncology and Radiotherapy, Gdansk, Poland; ²Regional Oncology Outpatient Unit, Gdansk, Poland

Background: Mammography is the only proved efficacious screening imaging modality for breast cancer. Additional breast ultrasonography is often performed to assess interminate mammographical findings.

Aim of the study: To evaluate the diagnostic performance of ultrasonography as an adjunct to mammography in the detection of breast cancer and to identify clinical indications.

Material and methods: Records of women referred for breast imaging to the Regional Oncolgy Outpatient Unit in Gdansk from January 2001 to June 2001 were retrospectively analyzed. Results of mammography and ultrasonography were assessed using a 5-point grading scale of increasing suggestion of malignancy. Indications for referral, age, hormonal use and results of clinical examination were evaluated. Median age was 52 years (range 35–78). Median follow-up was 16 months (range 12–28). Detailed data will be provided at the conference.

Results: Out of 4600 consecutive patients in 80 (1.7%) mammography suggested breast cancer. Of the remaining 4520 patients in 830 cases ultrasonography was additionally performed following the suggestion of a radiologist. No additional malignancy was detected and neither were clinical indications for additional ultrasonography defined.

Conclusions: The role of additional ultrasonography performed as an adjunct to mammography in the detection of cancer is negligible. No subgroup of patients who would benefit this procedure was selected.

134 POSTER

Routine mammograms in symptomatic women <50 yrs with normal physical examination: is it justified?

H. Hamed, A. Kothari, S. Ibrahim, N. Beechey-Newman, I. Fentiman. Guy's Hospital, Academic Oncology, London, UK

Introductory Sentence: This unique abstract studies whether routine mammography is justified in "symptomatic" women under the age of 50 yrs who are found to have a normal clinical breast examination. As there is growing pressure to lower the age of entry into breast cancer screening programmes this study assumes significance.

Introduction: In the UK breast cancer screening is offered to all women between the ages of 50 and 69 yrs. There is little doubt that breast cancer screening enhances both early diagnosis and improves survival. It is also well accepted that a vast majority of breast cancers will be diagnosed in "symptomatic" women. This retrospective study looks into whether routine mammograms of "symptomatic" women below the age of 50 yrs with normal physical examination will significantly increase the number of breast cancers diagnosed. In addition we wanted to assess whether the current practice of referring women with unremarkable breast examination for routine mammograms is justified.

Methods: The mammogram results of 754 women below the age of 50 yrs referred on account of varied breast symptoms and found to have normal physical examination were analysed. Women who had any suspected abnormality on physical examination or recalled for further assessment for any reason were excluded. Only patients that the clinician was happy to discharge but arranged for routine mammograms to complete the assessment were included.

Results: The median age of the cohort was 44 years (range 35–50) and 61% were premenopausal. 6/754 (0.79%) of the women were recalled following routine mammograms. 3 of these were discharged after further imaging. The remaining 3 went on to have needle localised excision biopsies. 2 of those were invasive breast cancers and 1 was sclerosing adenosis. Routine mammography of our cohort therefore yielded only 2 breast cancers (2.6 per 1000) which would otherwise have been missed had these women not had routine mammograms.

Discussion: For a breast cancer programme to remain viable it is estimated that a diagnosis of 5 breast cancers per thousand women screened is to be achieved. There is also growing pressure to lower the age of entry into screening to 40 yrs. This study demonstrates that relying on clinical examination alone would be half as effective as in screening programmes. Our data do not support the current practice of carrying out