In addition, following menopause, bone mineral density (BMD) drops rapidly. This predisposes women to risks of osteoporosis and fracture. HRT with estrogen (E) and/or progesterone (P) is effective for this indication. Randomized data have now shown that HRT with combined E and P results in increased cardiac and cerebrovascular events, while E alone does not increase or decrease either cardiac or cerebrovascular events, but may be associated with increased dementia.

Theoretically, HRT is thought to be contraindicated following a diagnosis of breast cancer since either E and/or P might predispose to breast cancer recurrence. The data supporting this point of view are few however. While one relatively small randomized trial (HABITS) suggested that HRT was associated with an increased risk of breast cancer recurrence (HR = 3.3), another small randomized trial suggested no such risk (HR = 0.8).

Evidence-based alternatives to HRT for vasomotor responses can include SSRI-based anti-depressants such as venlafaxine (Effexor), fluoxetine (Prozac), and paxetine (Paxil). In addition, gabapentin (Neurontin) has now been shown to be effective in comparison to placebo and superior to venlafaxine in randomized trials with hot flashes as an endpoint.

Evidence-based alternative treatments for osteoporosis include vitamin D, calcium, and exercise, as well as tamoxifen, raloxifene or oral bisphosphonates such as alendronate (Fosamax) and residronate (Actonel). It is known that these drugs not only reduce osteoporosis, but also reduce the risk of fracture in postmenopausal women. Lipid-lowering drugs such as statins are proven to be effective both in lowering lipids and in reducing cardiac events. Exercise, and weight control are also known to positively affect cardiac health. Exercise and/or weight control may also reduce the risk of developing primary breast cancer and/or recurrence following treatment of primary breast cancer.

242 Proffered Paper Oral

Hormone replacement therapy in relation to the risk of specific histological types of breast cancer: results from the Million Women Study

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Background: Use of hormone replacement therapy (HRT) is associated with an increased risk of breast cancer but relatively little is known about how this risk may vary according to histological type.

Methods: The relative risk of specific histological types of breast cancer in relation to HRT use is examined among women participating in the Million Women Study. Analyses are based on 935,668 postmenopausal women, recruited into the study between 1996 and 2001 aged 50–64, with an average duration of follow-up of approximately 3 years. During the follow-up period, 12,774 breast cancers of known histological type were diagnosed of which 11,235 were invasive including 7729 ductal cancers, 1476 lobular cancers, 473 tubular cancers, 68 medullary cancers and 145 mucinous cancers.

Results: Current use of HRT was associated with a materially greater increase in the risk of lobular and tubular breast cancer than ductal breast cancer but there was no evidence of any increase in the risk of medullary cancer. A comparatively greater risk of lobular and tubular cancer versus ductal cancer was observed for both oestrogen-only and combined HRT but the magnitude of the corresponding relative risks were consistently larger for users of combined compared to oestrogen-only preparations. Similar patterns of risk in relation to current HRT use were observed for in situ disease in that the relative risk of lobular carcinoma in situ was significantly greater than that for ductal carcinoma in situ.

Conclusions: There are substantial and, in some cases, qualitative differences in the effect of HRT use on specific types of breast cancer. Further exploration of these differences, and in particular the extent to which they may be due to differences in hormone receptor status, should lead to a better understanding of the biological mechanisms underlying the development of breast cancer.

243 Proffered Paper Oral

Efficacy of HRT in treating oestrogen deficiency symptoms in women taking concomitant tamoxifen: the UK HRT trial experience

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Introduction: In the UK trial of hormone replacement therapy (HRT) in symptomatic women with early stage breast cancer, participants were randomised to receive HRT or detailed information about non-hormonal, prescription and complementary HRT alternatives for 2 years. When the trial was closed prematurely in July 2004 due to adverse publicity about HRT, 197 women had been recruited. The IBIS-I tamoxifen chemoprevention trial investigators report a lack of HRT efficacy in the presence of tamoxifen; this observation has been tested in the UK HRT trial.

Methods: Participating women completed validated self-administered questionnaires documenting the frequency and impact of oestrogen deficiency symptoms (i.e. hot flushes, night sweats, vaginal dryness) and quality of life (including FACT-ES, endocrine symptoms). Changes in hot flush and night sweat frequency were divided into 4 groups (based on quartiles of the total series) for description and relationship with treatment investigated by Mann-Whitney tests. Change in vaginal dryness was based on a dichotomy, any increase vs. any decrease, and compared by Fisher's exact test. Mean change in impact scores and FACT-ES subscale scores were compared across treatment using Mann-Whitney tests. All analyses are limited to women taking tamoxifen at baseline and questionnaire response to 6 months post randomisation.

Results: At baseline, 132 women were taking tamoxifen; 67 were allocated to receive HRT and 65 were not. HRT reduced the frequency of hot flushes (35% HRT patients in top quartile v 18% no-HRT patients, $p = 0.05$) and night sweats (45% HRT patients in top quartile v 23% no-HRT patients, $p = 0.06$) and the impact of hot flushes and night sweats being perceived as problematic, ($p = 0.002$, $p = 0.05$ respectively), causing distress ($p = 0.006$, $p = 0.03$) and interfering with daily life ($p = 0.004$, $p = 0.30$) compared with those not allocated to receive HRT. There was no significant difference in vaginal dryness by allocated treatment group over 6 months but the number of responders was small (20 patients). HRT use significantly improved FACT-ES scores ($p = 0.005$).

Conclusion: These results show that HRT confers considerable symptomatic and quality of life benefit to symptomatic women with early stage breast cancer even if they are taking concomitant tamoxifen. Further research should continue to identify sub-groups of symptomatic breast cancer survivors who could benefit without being placed at increased risk of disease recurrence.

Thursday, 23 March 2006 14:15–16:00

SCIENTIFIC SESSION

Breast reconstruction

244 Invited

Radiotherapy in patients undergoing breast reconstruction

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Breast reconstruction is currently a common procedure in breast cancer patients undergoing mastectomy. At the same time a proportion of these patients will be candidates for postmastectomy radiotherapy. Most typical clinical situations include breast reconstruction in conjunction with chest wall irradiation as elements of primary breast cancer management, mastectomy with breast reconstruction after the failure of breast-conserving therapy, and radiotherapy following local recurrence within the reconstructed breast. There are many available techniques of breast reconstruction, including implants and autologuous tissues, and their sequencing in relation to radiotherapy varies in particular patients. Thus, physicians are faced with different clinical situations requiring individual approach, and a close cooperation between radiation oncologist and plastic surgeon.

Available data suggest that breast reconstruction has no impact on the risk of locoregional failure or overall prognosis. Immediate reconstruction does not delay nor interfere with the delivery of adjuvant chemotherapy or post-mastectomy radiotherapy, although it usually requires some technical modifications. The presence of prosthesis does not markedly affect the radiation dose distribution; however radiation may induce some alterations to the prostheses. Breast reconstruction does not seem to impact the type and intensity of acute radiation reactions, whereas the type of reconstruction-related late complications depends largely on the surgical technique.

It is generally agreed that the combination of breast reconstruction and radiotherapy is feasible, although at the expense of increased risk of complications and less satisfactory cosmesis. Breast reconstruction using autologuous tissue, although more complex, seems to provide better cosmesis and lower risk of complications and is preferred in these patients. Prosthetic reconstruction is generally not recommended in patients who underwent radiotherapy and in candidates to radiotherapy. Thus, immediate reconstruction should be avoided in patients with a high likelihood of postmastectomy irradiation.