category. The 10-year RFS of a patient with a BMI of 25 kg/m^2 vs. one with a BMI of 35 kg/m^2 was approximately 70% vs. 65%.

Table 1. Relapse Free and Overall Survival by BMI

BMI (kg/m^2)	N	RFS (%)		OS (%)	
		5 year	10 year	5 year	10 year
<25	642	80.9	71.4	87.7	76.9
25.0–29.9	628	75.5	66.5	84.1	70.6
⩾30	636	74.9	65.0	82.7	69.8

Conclusions: We found a modest linear relationship between BMI and outcome in node-positive breast cancer patients receiving chemotherapy. Obesity, an increasing public health concern, is a modifiable factor; additional research is needed to determine the impact of weight loss on breast cancer outcomes.

414 Proffered paper oral

Variations in the Prevalence of Risk Factors for Breast Cancer in Different Ethnic Groups in the Million Women Study

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Background: The Million Women Study is a large prospective study in the United Kingdom (UK), designed to investigate the health of women, with a focus on breast cancer. There are known differences in the incidence of breast cancer in different ethnic groups in the UK, but information about the risk factors for the disease in these ethnic groups is limited. The aim of this study is to describe the distribution of known risk factors for breast cancer by ethnic origin in this cohort.

Materials and Methods: UK women aged 56 years, on average, were recruited into the Million Women Study between 1996 and 2001. Information about risk factors and potential confounders for breast cancer and other diseases were collected using self administered questionnaires. Participants of the study are linked to routinely-collected national databases, such that information on incident cancers and hospital admissions are notified automatically to the study investigators.

Results: Of the 1.1 million women in the study with a recorded ethnicity, almost 8000 women were Asian and almost 5000 women were Black. On average, Black women had 3.1 children, compared to 2.9 children for Asian women and 2.4 children for white women. The prevalence of having ever breastfed amongst parous women was lower for white women (69%) than for Asian (83%) or Black (83%) women. The mean body mass index was higher for Black women (28.1 kg/m^2) compared to Asian (26.0 kg/m^2) and white (26.2 kg/m^2) women. Never use of alcohol was much more common amongst Asian (70%) than Black (38%) or white women (23%). Current HRT use was higher for white women (35%), compared to Black (29%) and Asian (24%) women. 10% of white women had a first degree relative with breast cancer, compared to 8% of Black women and 6% of Asian women. A much higher prevalence of social deprivation was found in Black and Asian women than in white women with 55% of Blacks, 43% of Asians and 19% of whites in the lowest socio-economic quintile. All these differences were highly statistically significant ($P < 0.001$).

Conclusion: The Million Women Study provides a unique opportunity to compare the health of women of different ethnic origins in the UK. These results show substantial and significant differences in the risk factors for breast cancer between middle-aged Black, Asian and white women in the UK. Further analyses will be done comparing differences in the incidence and management of breast cancer in women by ethnic origin, allowing for their large differences in risk factors for the disease.

415 Proffered paper oral

Genetic Variability in Multi Drug Resistance Protein 1 (ABCC1/MRP1) and UDP-Glucuronosyltransferase-2B7 (UGT2B7) Are Highly Correlated with Severe Haematological Toxicity of Adjuvant FEC in Breast Cancer

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Background: We assessed the impact on hematological chemotherapy toxicity of single nucleotide polymorphisms (SNP) in germline DNA in a panel of potential genes of interest through high throughput sequencing. First aim was to validate the predictive value of certain SNP that have previously been shown to correlate with toxicity/outcome in small patient groups receiving at least one of the FEC compounds (ABCBI/MDRI, ABCC1/MRP1, ABCC2/MRP2, ABCG2, ALDH3A1, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP3A5, DPYD, GSTP1, MTHFR, NQ01, TYMS, XPD/ERCC2, XRCC1). Secondly we investigated previously not studied genes known to be involved in epirubicin metabolisation (UGT1A1, UGT1A6, UGT2B7).

Material and Methods: We identified 1089 breast cancer patients treated in a single centre with 3 to 6 cycles of (neo-)adjuvant FEC (fluorouracil 500, epirubicin 100, cyclophosphamide 500 mg/m^2) from 2000–2010 for whom germline DNA is available. All patients were retrospectively evaluated through electronic chart review for febrile neutropenia (primary endpoint), febrile neutropenia first cycle, prolonged grade 4 or deep (<100/μl) neutropenia, anemia grade 3−4 and thrombocytopenia grade 3-4. For statistical evaluation, correction was made for number of planned cycles, primary growth factor use, age and body mass index. Because of multiple testing the false discovery rate (FDR) was calculated.

Results: Variant genotypes for rs45511401 (GT/TT, 12%) in the Multi Drug Resistance Protein 1 gene (MRP1/ABCC1), compared to the wild-type (GG, 88%) were associated with febrile neutropenia, febrile neutropenia in first cycle and thrombocytopenia (respectively 26.5 vs 15.8%, 17.1 vs 9.7% and 3.4 vs 0.3%; p-value 0.007, 0.027 and 0.005, FDR 0.3, 0.79 and 0.19). Variant genotypes for rs7668282 (CC/CT, 1.5%) in the UDP-Glucuronosyltransferase 2B7 gene (UGT2B7) compared to the wild-type (TT, 98.5%) genotype were associated with febrile neutropenia and prolonged or deep neutropenia (respectively 6.7 vs 17.2% and 6.7 vs 35.3%, p value 0.024 and 0.001, FDR 0.53 and 0.04). More details on other endpoints and other SNP will be presented, although in general no important association was found for other SNP mentioned.

Conclusions: Genetic variation in the MRP1 and UGT2B7 gene was highly associated with severe haematologic toxicity of FEC, while other previously described SNP were not validated. This is by far the largest breast cancer cohort in which the impact of genetic variability on toxicity was investigated.

416 Proffered paper oral

An Investigation of Interactions Between Genetic Variants and Established Risk Factors for Breast Cancer in the NCI Breast and Prostate Cancer Cohort Consortium (BPC3)

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Background: Recently various breast cancer susceptibility loci have been identified by genome wide association studies (GWAS). Relatively little is known about the possible interplay between these loci and established risk factors for breast cancer risk. Prospectively collected data from large populations are needed to test reliably for such gene-environment interactions.

Methods: We studied 8,576 women with breast cancer and 11,892 controls from the NCI Breast and Prostate Cancer Cohort Consortium (BPC3). We assessed whether 17 single nucleotide polymorphisms (SNPs) previously associated with breast cancer risk,
(*FGFR2*-rs2981582, *FGFR2*-rs3750817, *TNRC9*-rs3803662, 2q35-rs13387042, *MAP3K1*-rs889312, 8q24-rs13281615, *CASP8*-rs1045485, *LSP1*-rs3817189, *COL1A1*-rs2075555, *COX11*-rs6504950, *RNF146*-rs2180341, 6q25-rs2046210, *SLC4A7*-rs4973768, *NOTCH2*-rs11249433, 5p12-rs4415084, 5p12-rs10941679, *RAD51L1*-rs999737),
modified the odds ratios for established risk factors (age at menarche, parity, age at menopause, use of hormone replacement therapy, family history, height, body mass index, smoking status, and alcohol consumption). We also studied the possible differential effect of the polymorphisms by subgroups of tumor stage, estrogen receptor, progesterone receptor status and age at diagnosis.

Results: We confirmed the association of all but three SNPs (in *LSP1*, *COL1A1* and *RNF146*) with breast cancer risk. After correction for multiple testing, we did not find any significant interactions between SNPs and the established risk factors. We confirmed previously reported reports of differential effects of SNPs in *FGFR2* and *TNRC9* with estrogen and progesterone receptor status.

Conclusions: Our study provides evidence against the hypothesis that known common breast cancer loci strongly modify the associations

between established risk factors and breast cancer risk. These findings are important given the size, prospective design, and comprehensive approach of our study.

Friday, 23 March 2012 10:30–11:30

PROFFERED PAPER

Imaging

417 Proffered paper oral

3-Tesla MRI is More Efficient for the Evaluation of Tumor Extent of Breast Cancer: a Comparative Study with Conventional 1.5-Tesla MRI

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Background: High quality of space and temporal resolution is demanded from the diagnosis for intraductal spreading area of breast cancer. In our hospital, from April 2007, 3-Tesra (T) MRI was transduced and high resolution dynamic studies for bilateral mammary have been performed. However, superiority of 3-T MRI to 1.5-T MRI remains almost unproven in the evaluation of intraductal spreading area of breast cancer.

Objective: Our goal is to determine the accuracy of 3-T MRI in the evaluation of breast cancer tumor extent, compared with conventional 1.5-T MRI, by reviewing pre-operative MRI report and pathological diagnosis of resected specimen.

Methods: We assessed 342 patients with primary breast cancer who underwent the 3-T or 1.5-T breast MRI as pre-operative examination between April, 2007 and March, 2011. Concerning the diagnosis of intraductal spreading area of breast cancer, we weighed 3-T MRI against conventional 1.5-T MRI. Using 1.5-T or 3-T MRI (Achieva, Philips), we injected contrast medium and photographed five aspects before injection and after injection for every 90 seconds. We obtained fat-sat T1-weighted magnetic resonance image (T1WI), multi-planar reconstruction (MPR) image and standard maximum intensity projection (MIP) image based on T1WI by coronal section, and furthermore slab MIP image with Aquerius net, and we evaluated the enhanced area.

Results: 138 cases were examined with 1.5-T MRI, and 204 cases with 3-T MRI. In 1.5-T group, 40 cases (30%) were underestimated, additional resection were required intra-operatively with cancer-cells positive surgical margin in 18 cases (13%), and surgical margin was positive with carcinoma cells by final pathological findings in 12 cases (9%). In two patients we were forced to changes from breast-conserving surgery to mastectomy, and two cases underwent reoperation (mastectomy) with the diagnosis of widely positive surgical margin. In comparison with 1.5-T MRI group, 28 cases (14%) were underestimated in 3-T MRI group, intraoperative addition resection in 12 cases (6%), and surgical margin positive by the final pathological findings in 18 cases (9%), respectively.

Conclusion: The concern to enhance an artifact is known on 3-T MRI because it has high resolution. However, it may be more efficient rather than1.5-T MRI to evaluate the intraductal spreading area of breast cancer and to determine the appropriate extent of surgical resection.

418 Proffered paper oral

Analysis of the Impact of Intraoperative Margin Assessment with Adjunctive Use of MARGINPROBE® Vs. Standard of Care on Margin Status with Different Definitions of Positive Margin Depth, Results From a Randomized Prospective Multi Center Study

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Background: The current practice of breast conserving surgery (BCS) involves intraoperative margin assessment according to the surgeon's gross assessment and judgment. This intraoperative assessment has been associated with a 20% to 40% reoperation rate to assure negative margins. MarginProbe (Dune Medical Devices, Framingham, MA) was developed to provide real-time assessment of lumpectomy specimens to evaluate for the presence of disease at the surgical margins. A 21-center international pivotal study was conducted to determine if adjunctive use of MarginProbe can enable surgeons to identify positive margins intraoperatively, resulting in fewer patients who are candidates for re-excision procedures. Results for a 1 mm definition of positive margins have been reported previously. We sought to understand the benefit of device use at alternative thresholds.

Methods: 664 women with non-palpable lesions undergoing lumpectomy for DCIS and invasive cancer were enrolled and 596 randomized (1:1) in the operating room following standard of care (SOC) lumpectomy. In the device arm, MarginProbe was used to assess all surfaces of the lumpectomy specimen and positive readings required additional resections. The device was not used on additional resections. All specimens were examined to verify excision of the target lesion intraoperatively. Pathologists were blinded to study arm. Additional surgeries to re-excise involved margins were performed per each individual site criteria. Patients were followed for 2 months following surgery; additional procedures were documented. Distance from tumor to each margin face was recorded for each patient.

Results: Following lumpectomy, the number of patients having positive margins due to failed intraoperative assessment was significantly reduced in the device arm at each potential definition of positive margins (see Table 1).

Conclusions: It has been shown previously that adjunctive use of MarginProbe significantly reduced the number of candidates for re-excision at a 1 mm definition of positive margins. Based on this analysis, surgeons can expect a substantial reduction in the number of patients with positive margins at definitions from tumor on ink to 5 mm.

Table 1. Patients with positive margins after 1st surgery

Depth	Device (%), N = 298	Control (%), N = 298	p-value
0 mm	6.4	13.4	0.0057
1 mm	15.4	38.3	<0.0001
2 mm	22.5	49.7	<0.0001
3 mm	30.9	57.0	<0.0001
4 mm	36.6	61.7	<0.0001
5 mm	39.9	66.4	<0.0001

*Excludes positive margins on shavings, as device was only used on the main specimen.

419 Proffered paper oral

The Impact of Preoperative Real-Time Virtual Sonography (RVS) on Surgical Treatment of Breast Cancer

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Background: We recently have developed a real-time virtual sonography (RVS) system which can synchronize a sonography image and the MRI image with multi-planar reconstruction of the same section in real time. The aim of this study was to evaluate the utility of RVS as a diagnostic tool to determine the surgical management of breast cancer.

Material and Methods: In a retrospective study, we reviewed 210 consecutive women who underwent radical surgery for breast cancer at Aichi Medical University Hospital between 2009 and 2010. On the basis of mammographic findings and sonographic findings, 102 women with 103 breasts were identified as candidates for breast-conserving therapy (BCT) and underwent contrast-enhanced MRI if not contraindicated. MRI images were obtained with the patient lying supine by the use of flexible body surface coil. Of the breast in which the additional lesion was detected by MRI, we determined the extent of resection after we re-assessed the lesion with RVS system and confirmed the histological diagnosis of them by RVS-guided needle biopsy if necessary. Comparing pathological findings on the excised specimens with preoperative imaging findings, we examined the accuracy of the extent of resection which was determined by using RVS.

Results: Of 99 women with 100 breasts who underwent MRI, in 30 breasts, additional lesions were detected by both MRI and RVS. In 2 breasts of them, additional lesions were diagnosed as benign by RVS-guided needle biopsy. In the remaining of 28 breasts, we broadened the extent of resection based on the RVS finding. In 9 breasts of them which were treated by mastectomy, the wide extent of ductal carcinoma in situ (DCIS) was confirmed pathologically. From specimens of 19 breasts treated by BCT with wider margins than anticipated, the additional lesions were diagnosed as the wide extent of DCIS, multicentric breast cancer and sclerosing adenosis in 16, 2 and 1 respectively. In 20 of the 28 breasts, complete resection was achieved. In a total of 94 breasts treated by BCT, the rates of incomplete resection of non-invasive disease and invasive disease were 19% and 3%.

Conclusions: The use of RVS made it possible for us to project MRI information onto a body surface and to determine the extent of resection more precisely and easily. Our results suggest that using preoperative RVS in combination with conventional imaging modality can reduce the rate of incomplete resection of invasive diseases after BCT for breast cancers.