Introduction

- Previous comparisons of tamoxifen vs placebo for breast cancer risk reduction suggest tamoxifen reduces risk in under half of women. Measures to predict who benefits would be useful.
- In the IBIS-I trial, only those women with a ≤10% reduction in mammographic density response to tamoxifen experienced a reduction in breast cancer risk but this was significant (63%).
- Estimation of density change depended upon a highly trained radiologist
- In this study we explore the value of other approaches to prediction of change using the IBIS-II data as a baseline

Objectives

The aims of this study were to assess:
- IBIS-2 predictability
- other measures of mammographic density estimation
- whether blood measures predict density change

Methods

Eligibility: premenopausal women aged 33-46 attending a family history clinic and monitored according to NICE guidelines; >17% lifetime risk of breast cancer

Mammographic density:
- 1 year of treatment with tamoxifen

- Table 1: demographic details
  - Parity: Parous 83 (79)
  - Nulliparous 22 (21)
  - BMI ≥ 23 35 (13)
  - 24-25 13 (12)
  - 26-29 30 (29)
  - ≥ 30 26 (25)
  - BC Risk (%) 17-29 26 (25)
  - ≥ 30 79 (75)
  - Age (median) 42.4

- Of those that had their weight recorded during the study (n=104) 12 (11.5%) had >3% weight gain, 29 (27.9%) had >3% weight loss and 60 (60.8%) remained stable.

- IBIS-II reader (WR) who estimated percent density to the nearest 5% and read mammograms independently
- 2/3 consultant radiologists or advanced radiographic practitioners who marked percent density on a Visual Analog Scale (VAS) and read baseline and year 1 mammograms at the same time
- A computer thresholding technique (CUMULUS)
- Automated volumetric methods: Quantra™ and Volpara™

Results

- Table 2: Area based measures (percent density)
  - % point density change* WR (n=100)
  - 20 (242) % RW (n=100) % VAS (n=100) Cumulus (98)
  - 40+ 2 (1) 0 (0) 0 (0) 1 (1)
  - 30+ 14 (6) 5 (5) 0 (0) 3 (3)
  - 20+ 34 (14) 12 (11) 0 (0) 13 (13)
  - 10+ 91 (38) 35 (33) 6 (6) 30 (31)
  - 0+ 97 (40) 47 (81) 77 (17) 44 (44)
  - increase 4 (2) 4 (4) 18 (17) 8 (8)

- Table 3: Volumetric based measures (Volpara™ and Quantra™)
  - % point density change* % reduction in volume %
  - Volpara™ Quantra™ Volpara™ Quantra™
  - 40+ 0 (0) 0 (0) 5 (9) 15 (15)
  - 30+ 0 (0) 0 (0) 15 (15) 14 (14)
  - 20+ 0 (0) 1 (1) 24 (24) 20 (20)
  - 10+ 0 (0) 9 (9) 26 (27) 17 (17)
  - 0+ 71 (72) 63 (64) 11 (11) 16 (16)
  - increase 27 (28) 25 (26) 17 (17) 16 (16)

- Table 2 shows good reproducibility between pre-menopausal women in IBIS-I and the current study (RW and Cumulus). However in-house radiologists saw less reduction.

- Table 3 shows little change in volumetric percent density methods, whereas a greater than 10% reduction in density was seen in 68% of women for Quantra™ and in 72% for Volpara™

- Figure 1: Change in dense volume (cm3) over time

Conclusions

1. Density reduction was reproducible between studies (RW)
2. Detection of change difficult in general radiological practice
3. Absolute measures of dense area and dense volume show greatest changes and may be most useful for clinical practice, however their relationship with the long-term effect of tamoxifen and the prevention of breast cancer needs to be established
4. Serum tamoxifen levels may be a surrogate mark of density change.

References