Conclusion:

The unequivocal findings of this multifaceted investigation are:

1. In HBC patients, polymorphism in C-band (size and localization) region were observed in 100% of the HBC patients. Mean values of spontaneous CA and SCE were observed as 0.13 and 11.01, respectively. Mean value of BLM-induced CA was found as 0.53. In cultured primary tumor tissues and PBL of HBC patients, chromosomes #1, #8, #13, #17 #18 and #20 were very frequently involved in numerical aberrations. Similarly, structural abnormalities in 3p14 were observed in 8/9 families followed by 16q23 in 7/9 families, in both, tumor tissues as well as PBL of the HBC patients.

2. Among HBR, polymorphisms in C-band (size and localization) were seen in 92% of individuals. Mean values of spontaneous CA and SCE were observed as 0.09 and 9.69. Moreover, value of BLM-induced aberration was found as 0.37 CA/cell. Numerical abnormalities of chromosomes #1, #8, #13, #17, #18 and #20 were predominant in PBL. Structural abnormalities in 3p14 were found in 7/9 families followed by 16q23 in 5/9 families.

3. In control group, 27% of women showed polymorphisms in C-band (size and localization). Mean values of spontaneous CA and SCE were observed as 0.06 and 7.67, respectively. The BLM-induced aberration was observed as 0.28 CA/cell. Numerical and structural abnormalities were not observed in this group.

The most interesting finding of the present work is the presence of close patterns of all five cytogenetic markers in FBR with HBC patients.
Particularly in FBR, inability of cells to repair the damage induced by BLM, may be characteristic of germline mutations in regulatory genes that influence the activity of several downstream genes. The downstream genes involved in the detection and/or processing of DNA damage may be induced by either endogenous or exogenous mutagenic stress leading to chromosomal aberrations. Moreover, sprouting of the clones of monosomic and trisomic cells and rearrangement of chromosomes in PBL culture indicate that cells of FBR are more prone for such abnormalities when they get mitogenic stimulus. Therefore, FBR having common chromosomal abnormalities to the HBC patients, might be predisposed for developing the similar cancer. This is an important finding.

Establishment of inherited or acquired susceptibility factors with the help of simple cytogenetic end-points are of prime importance in recognizing individuals at a higher risk to develop breast cancer, so that they may be benefitted by preventive program. Taken together, these are few explanation why the FBR of HBC patients have higher incidence of similar cancer. Attention is now focussed upon high-risk FBR by participation in highly organ-targeted surveillance and management strategies.

Further plans:

We have reported significant correlation in broad statistical cytogenetic profiles averaged over samples associated with HBC patients and their FBR. It is our impression that the cytogenetic markers assessed here may be highly predictive of high-risk group for the development of same cancer. The study of inherited predisposition to cancer is of clinical relevance because family members who are at high-risk may be helped
by screening or by advice about prevention. This is also of biological interest because the families offer a means to identify cytogenetic markers which can predispose to malignancy.

A major breast cancer susceptibility gene, BRCA1, has recently been mapped to a region on chromosome 17q through linkage studies of HBC and hereditary ovarian cancer syndrome and subsequently cloned. BRCA2 has more recently been mapped to the 13q12-13 region. BRCA2 confers only a moderately increased risk of ovarian cancer and is linked to most families with male HBC-affected members. We would like to investigate BRCA1 and BRCA2 in the members of the HBC families using confocal imaging system.