Surveillance of "high-risk" women with proven or suspected familial (hereditary) breast cancer: First mid-term results of a multi-modality clinical screening trial

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Background
- Hereditary breast cancer is associated with a high lifetime risk of developing breast cancer and a relatively early age of onset. As a result, early and intensive surveillance is typically recommended starting at age 30 years or at least 5 years prior to the age of onset of disease in the family. The identification of BRCA genetic mutations in this population establishes a hereditary etiology with associated prognostic value. Unfortunately, it has not been clear which imaging modality best serves this high-risk population. The purpose of this prospective clinical study was to determine the optimal imaging modality for surveillance of these women taking into account the high individual risks, young average age, and possible radiosensitivity of breast parenchyma to lesion detection in BRCA mutation carriers.

Materials and Methods
- Single center multidepartmental cooperative group of gynecologic oncologists, geneticists, radiologists
- 750 females (from 338 families) belonging to "high-risk" clinic for women with personal or family history of breast cancer dx at age under 30 years
- 462 women enrolled
- Median age = 38 years
- Prevalence screening rate = 29% Incidence screening rate = 71%
- Pts classified as definite or possible BRCA mutation carriers after genetic testing/pedigree analysis with appropriate psychosocial counseling
- Biannual clinical exam and high-frequency bilateral breast ultrasounds
- Annual 2-view bilateral mammography and breast MRIs
- Independent analysis of images by radiologists From 1996-2001:
  - 1,352 ultrasounds, 674 mammograms and 1,286 MRIs
  - 583 screening rounds, ie: all 3 imaging modalities performed on same visit and validated by histology on biopsy specimen

Results
- Out of 462 women, 51 breast cancers were detected in 47 women.
- Two women were diagnosed with synchronous bilateral breast cancers and two others had second primary cancers.
- MRI had significantly higher sensitivity of 95%, compared to 34% and 42% for mammography and ultrasound, respectively
- Specificity did not differ significantly among the 3 modalities
- Positive predictive value of MRI was 54% versus only 26% and 16% for mammography and ultrasound respectively.
- Only two false negatives with MRI: one pt with DCIS and the second with lymphangitic spread of disease.
- Of the 51 detected cancers, 15 women were symptomatic (palpable lesion, nipple discharge) and 36 were asymptomatic at time of diagnosis.
- Smaller primary lesion size and relative percentage of node-negative tumors in asymptomatic group.
Of the 51 detected cancers, 20 were multicentric lesions. MRI identified all 20, whereas US and mammogram detected only 3 of the 20.

**Author’s Conclusions**
- MRI surveillance identifies invasive and in situ breast cancer in high-risk women with 95% sensitivity.
- There were 2 breast cancers that were not detectable on any of the imaging modalities.
- Of the few cancers missed by MRI, they were also missed by ultrasound and mammography.

**Clinical/Scientific Implications**
- Magnetic resonance imaging offers the highest sensitivity for cancer detection in young, high-risk women undergoing breast cancer screening, compared to both ultrasound and mammography. This increased detection did not appear to compromise either specificity or positive predictive value. In light of the data collected here over a 5-year period, the authors recommend the use of MRI as a replacement for mammography in screening BRCA mutation carriers. The economic, therapeutic and survival outcome implications of such a strategy, however, are still unknown.

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