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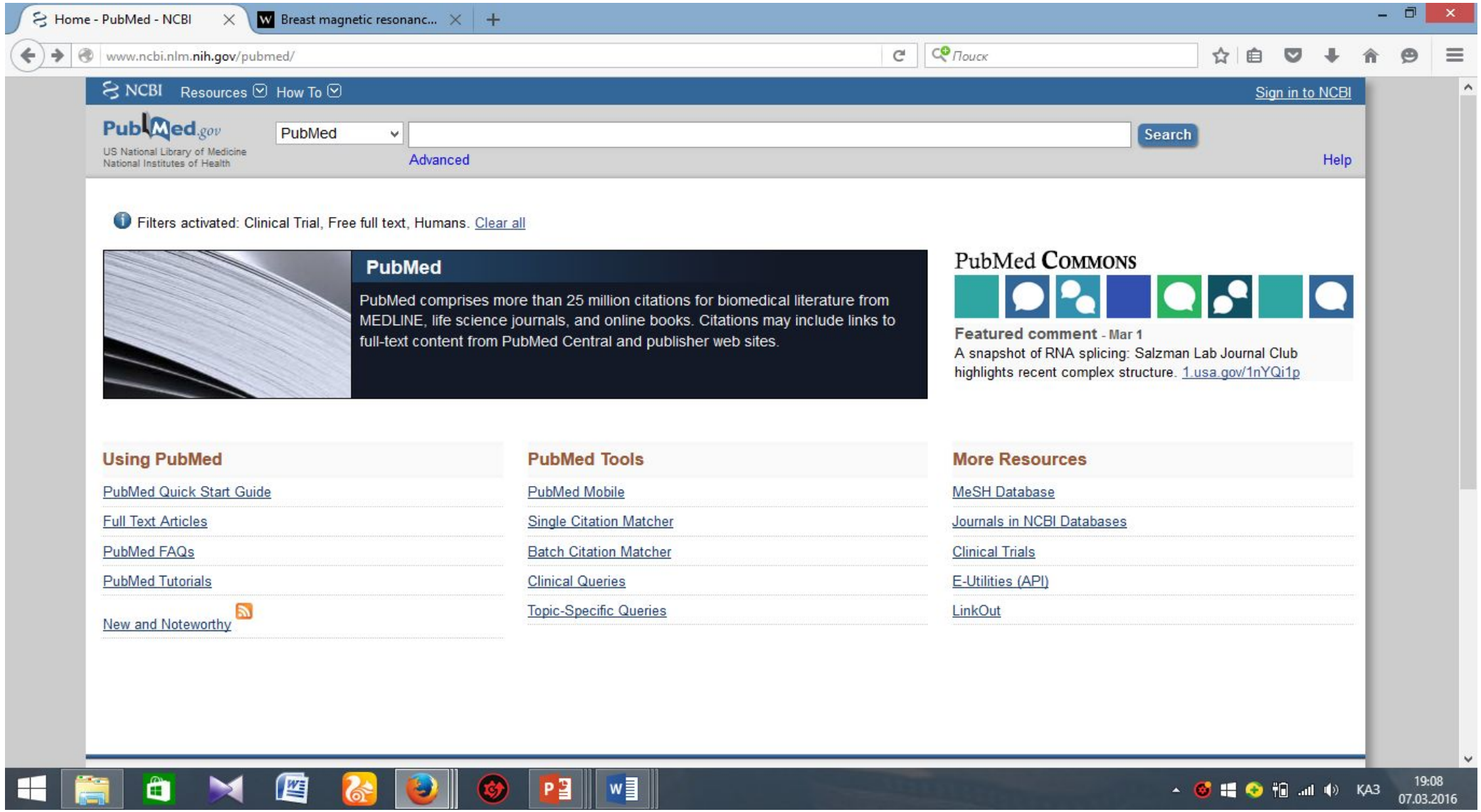
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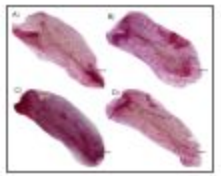
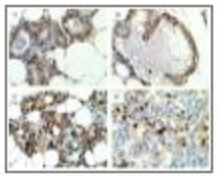
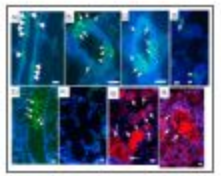


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Abstract

BACKGROUND

Intensive screening is an alternative to prophylactic mastectomy in women at high risk for developing breast carcinoma. The current article reports preliminary results from a screening protocol using high-quality magnetic resonance imaging (MRI), ductal lavage (DL), clinical breast examination, and mammography to identify early malignancy and high-risk lesions in women at increased genetic risk of breast carcinoma.

METHODS

Women with inherited *BRCA1* or *BRCA2* mutations or women with a > 10% risk of developing breast carcinoma at 10 years, as estimated by the Claus model, were eligible. Patients were accrued from September 2001 to May 2003. Enrolled patients underwent biannual clinical breast examinations and annual mammography, breast MRI, and DL.

RESULTS

Forty-one women underwent an initial screen. Fifteen of 41 enrolled women (36.6%) either had undergone previous bilateral oophorectomy and/or were on tamoxifen at the time of the initial screen. One patient who was a *BRCA1* carrier had high-grade ductal carcinoma in situ (DCIS) that was screen detected by MRI but that was missed on mammography. High-risk lesions that were screen detected by MRI in three women included radial scars and atypical lobular hyperplasia. DL detected seven women with cellular atypia,

CONCLUSIONS

Breast MRI identified high-grade DCIS and high-risk lesions that were missed by mammography. DL detected cytologic atypia in a high-risk cohort. A larger screening trial is needed to determine which subgroups of high-risk women will benefit and whether the identification of malignant and high-risk lesions at an early stage will impact breast carcinoma incidence and mortality. Cancer 2004. © 2004 American Cancer Society.

Between 9000 and 18,000 new diagnoses of breast carcinoma per year in the United States are associated with a genetically defined predisposition.[1, 2] Mutations in *BRCA1* and *BRCA2* account for > 60% of inherited breast carcinoma. By age 50 years, 50% of mutation carriers will develop breast carcinoma. This observation emphasizes the need for sensitive screening strategies that begin at an early age. The only known effective intervention for preventing breast carcinoma in high-risk women is prophylactic mastectomy,[3, 4] although tamoxifen may benefit some women with inherited *BRCA* mutations.[5] Intensive screening with conventional mammography and clinical examination is recommended as an alternative to prophylactic surgery and as a complement to tamoxifen, despite concerns that this strategy may not have sufficient sensitivity to reduce breast carcinoma mortality and that ionizing radiation from mammography may promote *BRCA*-related breast carcinogenesis.[6, 7] These issues are particularly relevant to women age < 50 years, in whom it has been estimated that the sensitivity of mammography is lower compared with the sensitivity in women ages 50–64 years. Furthermore, as more women age < 30 years are identified with deleterious mutations in susceptibility genes, the concern of yearly exposure to ionizing radiation from 4-view mammography becomes greater.

Screening mammography is recommended for women age > 50 years who are at average risk based on the mortality reduction demonstrated from 8 randomized, controlled trials that evaluated the ability of mammography to reduce breast carcinoma mortality, but this is not recommended not for women age < 50 years.[8] Estimates of the sensitivity of mammography from these published trials, which included women of all ages, have ranged from 39% to 89%. After the exclusion of women age > 50 years, the sensitivity of mammography ranges from 39–66%. Many published studies have confirmed that the sensitivity of mammography increases with age.[9, 10] The sensitivity of mammography may be decreased further in women who carry a deleterious mutation in *BRCA1* or *BRCA2*; pilot studies evaluating mammography in *BRCA1* and *BRCA2* carriers have found a high rate of false-negative results.[6, 11, 12] This may be attributable both to increased breast density in young women and to tumor phenotype, including features such as pushing margins, which may contribute to a smooth appearance rather than a spiculated appearance of a mass on mammography.[13] The data do not support reliance on annual mammography as the sole mode for the detection of early breast carcinoma in *BRCA1* and *BRCA2* mutation carriers.

Contrast-enhanced magnetic resonance imaging (MRI) has demonstrated high sensitivity as a diagnostic tool for the detection of invasive breast carcinoma but reportedly has a specificity ranging from 37% to 97%.[14–17] Breast lesions on contrast-enhanced MRI are assessed for malignancy based on morphologic and pharmacokinetic patterns of enhancement. Morphologic features of malignancy

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Breast magnetic resonance image screening and ductal lavage in women at high genetic risk for breast carcinoma.

Hartman AR[1], Daniel BL, Kurian AW, Mills MA, Nowels KW, Dirbas FM, Kingham KE, Chun NM, Herfkens RJ, Ford JM, Plevritis SK.

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Abstract

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CONCLUSIONS: Breast MRI identified high-grade DCIS and high-risk lesions that were missed by mammography. DL detected cytologic atypia in a high-risk cohort. A larger screening trial is needed to determine which subgroups of high-risk women will benefit and whether the identification of malignant and high-risk lesions at an early stage will impact breast carcinoma incidence and mortality.

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