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Predictive markers for breast cancers of limited extent

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Background: Magnetic Resonance Imaging (MRI) is more often considered to plan and guide minimally invasive treatment or partial breast irradiation (PBI) in patients with localized breast cancer. Although MRI has shown superior ability to visualize invasive breast cancer, microscopic disease extensions are underestimated in 50% of tumours at distances $\geqslant$10 mm from the MRI-visible lesion [1]. The purpose of this study was to find preoperative markers predictive of breast cancers of limited extent (i.e, small components of disease) and extended breast cancers (extensive components of disease) around the MRI-visible lesion.

Materials and Methods: Seventy-eight breast-cancer patients (80 breasts) eligible for breast-conserving therapy on the basis of conventional imaging and MRI were included. The wide-local excision specimens were processed using complete embedding, reconstruction and correlation with MRI.

Tumors were stratified by the absence (limited breast cancer) or presence (extensive breast cancer) of occult microscopic disease beyond 10 mm from the edge of the MRI-visible lesion. Imaging features at mammography, ultrasonography, contrast-enhanced MRI as well as at histology were evaluated for their ability to discriminate between limited and extensive breast cancers. Binary logistic regression with feature selection by double cross-validation was employed to create a prediction model that identifies breast cancers of limited extent.

Results: Of the 80 tumors, 77 were visible at MRI. Thirty-nine (51%) tumors were of limited extent. At multivariate analysis, four tumor characteristics were significantly correlated with differences between limited and extensive breast cancers: washout kinetics at MRI, estrogen and progesterone receptor status, and DCIS in the index tumor (area under ROC curve=0.85). The multivariate prediction model correctly identified one-third (14/39) of the breast cancers of limited extent at negligible error rate (5%).

Conclusions: Cancers with limited disease load around the MRI-visible lesion are associated with absence of washout kinetics at MRI, positive estrogen receptor status, negative progesterone receptor status and low quantity of DCIS in the index tumor. Preoperative knowledge of these properties from MRI and core biopsies may help to identify tumors suitable for minimally invasive therapies or PBI.

References

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Analysis of atypical hyperplasia and carcinoma in situ in nonpalpable breast lesions: final outcome and underestimation rates

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Background: The diagnosis of high risk and preinvasive lesions increases with breast cancer screening. Their significance and management is related to the type of biopsy sampling. We reviewed all consecutive high risk and in situ lesions diagnosed in a prospective cohort.

Material and Methods: From 2001 to 2007, 2708 nonpalpable breast lesions BI-RADS 3 to 5 were prospectively reviewed by a multidisciplinary staff in a breast disease unit (Saint Louis Hospital, Paris) and were reclassified according to the BI-RADS categories. On the 2708 lesions, 309 core needle biopsies, 807 vacuum assisted biopsies, and 521 open breast biopsies were performed. The median follow up was 36.9 months.

Results: A total of 371 high risk and in situ lesions was diagnosed (13.7%). Biopsy showed atypical ductal hyperplasia (ADH) in 78 cases, atypical lobular hyperplasia (ALH) in 50 cases, lobular carcinoma in situ (LCIS) in 24 cases, and ductal carcinoma in situ (DCIS) in 219 cases. In 78 ADH lesions, surgery was performed in 67 cases (86%), and carcinoma was diagnosed in 10 cases (12.8%). In 50 ALH lesions, surgery was performed in 39 cases (78%); seven carcinomas were diagnosed (14%). All 24 lesions yielding LCIS were excised, one single lesion was upgraded to lobular infiltrating carcinoma (4.2%). On 219 biopsies yielding DCIS, surgery performed in 211 (97%) revealed malignant invasive lesions in 34 cases (15.5%).

We performed an analysis excluding high risk or in situ lesions diagnosed on open breast biopsy, as their significance differs compared to when diagnosis is made on a core needle or a vacuum assisted biopsy. For ADH and ALH, the underestimation rate of malignancy was 22% and 18.8% respectively, and for LCIS and DCIS, the underestimation rate of invasive disease was 8.3% and 25.2% respectively.

Conclusion: Both atypical hyperplasia and in situ carcinoma are associated with an underestimation of malignancy. Future research needs to focus on accurately identifying clinical, radiologic, and histologic predictors of invasion in patients with DCIS diagnosed on biopsy, and select the most appropriate candidates for sentinel lymph node biopsy in front of high risk or in situ lesions.

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Contra-lateral breast cancer in patients with previous breast cancer − a twelve year experience

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Background: Current practice in the UK for evaluating contra-lateral disease in women with a recent diagnosis of breast cancer is to perform clinical examination and mammography. In the ACRIN trial, 969 women diagnosed with recent breast cancer, MRI detected biopsy proved contra-lateral tumours in 30 of 969 women after negative mammographic and clinical examination. This was a yield of 3.1%. However the positive predictive value of a positive MRI was only 21%.

Aims: Aim of the study is to identify the incidence of contra-lateral breast cancer in previous breast cancer patients and the role of MRI in follow up.

Methods: Details of patients diagnosed with breast cancer over a period of 12 years were obtained from the Cancer Registry. The database was then scrutinized to establish the number of bilateral/contra-lateral cancers. Time to diagnosis of the contra-lateral cancer was identified, mammography of these identified patients were reviewed retrospectively to identify whether it was a missed diagnosis.

Results: Over a twelve year period (1995–2006), 2051 cancers were diagnosed in 2005 women. 23 out of 2005 were bilateral cancers at initial assessment (1.5%). Fifteen developed contra-lateral cancers at a later date (0.75%). Contra lateral cancers were seen over a period from 15 months to 84 months. 73% of contra lateral cancers were seen in the first 5 years.

Four contra lateral cancers were seen within the first two years, seven were seen between 2−5 years and the remainder was seen between 5−8 years. The seven patients diagnosed with contra lateral cancers in the first three years could have been identified early with addition of an MRI. In order to pick up this small group, all patients (n = 2005) should had regular MRI instead of mammograms, that would be 7 out of 2005 suggesting a pick up rate of 0.35%. If infiltrating contra-lateral cancers were considered then it would be 3 patients (0.15%). All of the contra lateral disease was diagnosed at routine follow up surveillance examinations.

Conclusions: Overall rate of contra-lateral breast cancer was 2.25%, of which 1.5% was diagnosed at the time of the initial breast cancer detection. Addition of an MRI in surveillance would have prevented three patients out of 2005 patients developing contra lateral infiltrating cancer. To conclude the incidence of contra lateral cancers is low and routine use of MRI for contra lateral breast surveillance is not feasible and cost effective.

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Actual role of mammographic wire-guided biopsies

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Background: For years, mammographic wire-guided biopsy (MWGB) has been the standard procedure for diagnosing not palpable breast lesions. Nowadays, sterotactic core biopsy in mammographically detected lesions, or sonographic guided core biopsy, permit histological confirmation previous to surgery, making possible to add in the same definitive surgery sentinel node biopsy in invasive carcinomas. We evaluated our MWGB in

order to know the actual role of this procedure in diagnosis and treatment of non palpable breast lesions.

Material and Methods: We retrospectively analysed 745 consecutive MWGB (years 2003–2008) at the Gynaecology Department of the Universitary Hospital "12 de Octubre" in Madrid.

Results: 18.5% of MWGB had previous core biopsy diagnosis, 81.5% had diagnostic intention (without previous core-biopsy), 2.4% confirmation of previous stereotactic diagnosis (8.7% benign, 8.7% atypical hyperplasia (AH), 1.4% in situ lobular carcinoma (ISLC)) and 16.1% excised carcinomas previously diagnosed by previous core biopsy.

39.5% of MWGB were invasive carcinomas, 13.6% in situ ductal carcinomas (ISDC), 1.2% microinvasive carcinomas, 2.3% ISLC, 7.5% AH and 35.6% had benign histology.

Of our MWGB we had 44.6% during years 2003–2004, 33.3% in 2005–2006 and 26.1% in 2007–2008 of benign results ($p = 0.0001$). Inversely, diagnosis of malignancy increased (benign lesions not excised with MWGB after diagnostic core biopsy): 2003–2004: 44.6%, 2005–2006: 54.6%, 2007–2008: 65.9%.

Without previous core biopsy in carcinomas (ISDC or invasive carcinomas) we found 51.9% affected margins, with previous core biopsy 19.5% ($p = 0.0001$). In 2003–2004 (no core biopsias yet) 53.6% of margins in carcinomas were affected; in 2005–2006 (beginning of core biopsies) 51.7%, and in 2007–2008 (progressive implantation of core biopsies) 28.8% ($p = 0.001$). Because of this, se ampliaron un 66.4% of biopsies had to be re-excised in 2003–2004, 58.35% in 2005–2006, and only 32.7% in 2007–2008 ($p = 0.0001$).

Conclusions: MWGB is an efficient management of non palpable breast lesions preferably after histological confirmation of malignant or premalignant breast disease. During last years diagnosis of non palpable lesions has been optimized. Core biopsies has permitted the avoidance of unnecessary surgeries (benign histologies) and the necessity of re-excisions for affected margins or planning a second surgery for sentinel node in case of invasive carcinomas.

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Comparisons between core needle biopsy and definite surgery in estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 expressions in breast carcinoma

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Background: To evaluate immunohistochemical detection of estrogen receptor (ER), progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER2) expressions in core needle biopsy and definite surgery in breast carcinoma

Material and Methods: This series is a retrospective review of 310 invasive breast cancer patients who have received core needle biopsy and definite sugery at Chnaghua Christian Hospital between January 2006 and October 2007. We compare immunohistochemical detection of ER, PR and HER2 expressions in breast carcinoma using formalin fixed resection tissue. ER, PR and HER2 expressions were scored 0, 1+, 2+, and 3+ by immunohistochemical detection. The consistency of core needle biopsy and definite surgery were compared by stratifying pathology results with the Wilcoxon Signed Ranks test.

Results: The nonparametric test (2-tailed) for comparison of core needle biopsy and definite surgery in ER, PR and HER2 expressions showed no statistically difference ($p = 0.572$, 0.246, 0.198). However, discrepancies of core needle biopsy and definite surgery in ER expression 0, 1+, 3+, PR expression 0, 1+, 2+, 3+ and HER2 expression 0, 2+, 3+ were shown in stratifying pathology results by the Wilcoxon Signed Ranks test ($p < 0.001$). HER2 expression 1+ and ER expression 2+ in core needle biopsy is consistent to definite surgery ($p = 0.994$, 0.808 respectively).

Conclusions: Immunohistochemical detection of estrogen receptor (ER), progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER2) expressions in core needle biopsy is not strongly concordant with definite surgery in breast carcinoma.

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Safety and accuracy of MR-guided vacuum biopsy of breast lesions visible by breast MRI alone

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Background: To investigate the diagnostic accuracy and safety of MR-guided vacuum biopsy in routine clinical practice.

Material and Methods: Over a 3-year-period (07–2006 through 07–2009) MR-guided vacuum assisted biopsy (VAB) was performed according to a standardized clinical protocol. The interventions were done on a 1.5 T closed bore magnet using an ATEC-system (Suros) with 9G needles. Validation of VAB results of each lesion was obtained by a careful radiological-pathological correlation; in addition, VAB histology results categorized as B3−5 underwent subsequent surgical resection, and VAB results categorized as B2 underwent follow-up MRI after 6 months. In cases of uncertain radiological-pathological concordance control MRI was done within one week after VAB. All patients were followed clinically to document local complications.

Results: 491 MR-guided vacuum biopsies were performed in 321 patients, with 170 women undergoing VAB of more than one target lesion uni- or bilaterally within one session. Age range of patients was 30−77 years (mean 53/±11). VAB histology was malignant in 185/491 (38%) cases: 55/185 invasive cancers (29.7%), 93/185 pure DCIS (50.3%), 33/185 both invasive cancer and DCIS (17.8%) and 4/185 LCIS (2.2%). In 307/491 cases (62%) benign changes were found including radial scar and ADH. Average size of target lesion was 10.4 mm with a minimal size of 3 mm. Over the entire study no false-negative VAB results were observed, i.e. no malignant lesion identified at follow up after benign VAB. In patients undergoing surgical biopsy or treatment after MR-guided VAB, the final surgical pathology result was concordant with the VAB histology in all cases. One patient (0.3%) developed a hematoma requiring surgical evacuation, no other serious adverse events were observed.

Conclusions: MR-guided VAB is an extremely accurate and safe method to biopsy even very small breast lesions visible by MRI alone. The accuracy and reliability of target tissue sampling offered by MR-guided VAB appears to be higher than that achieved by MR-guided needle localization and surgical biopsy. Accordingly, MR-guided VAB can safely replace open biopsy, thereby avoiding unnecessary surgery. This is especially important for women in BIRADS 6 situation, who require histological verification of additional lesions identified at pre-operative MRI.

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New approach for histological diagnosis of additional breast lesions using ultrasound with magnetic resonance volume navigation and fusion imaging as reference: initial results

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Background: High percentage of benignancy of incidental and additional lesions at breast magnetic resonance (MR) guided biopsy are widely reported as well as low cost-effectiveness compared to ultrasound guided (US). Second look US seems to solve this clinical problem only in one-third of cases. Nowadays is possible to use MR volume for navigation and fusion during US exam (VNav). Purpose of this study was to evaluate this new approach to obtain lesion correlation and histology.

Materials and Methods: Fifteen consecutive patients (53±14 years, range 35−75) with additional only MR-detected lesions underwent bilateral contrast-enhanced breast MR in supine position using flexible surface body coil. Three vitamin E pills and the corresponding drawing pen signs were used as skin reference for final alignment. Breast US and MR co-registration was manually obtained and maintained by means of a dual electromagnetic systems consisting of a magnetic transmitter positioned close to the patient and two small magnetic receivers positioned on a linear probe's bracket. Large core US guided biopsy with VNav was used for lesion sampling and carbon clip positioning. Clip-to-lesion distance at surgical pathologic examination was used as standard of reference.

Results: All twenty-two additional lesions had a correlation during US with VNav. No additional MR-guided biopsy was needed. At pathologic examination clip position distance from the lesion was reported 0.7±0.4 cm (mean±SD). Seventy-three percent of lesions (16/22) were malignant and 26% (6/22) were benign. Three out of 6 benign lesions were classified as high-risk lesions.

Conclusions: Breast US guided biopsy with VNav for only MR-detected lesions is feasible and seems to allow an accurate tool for sampling breast lesions with a strong reduction of MR guided procedures.

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A prospective study of breast trauma presenting to a rapid-access clinic

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Background: Approximately 1% of all patients present to our rapid-access breast clinic with a history of trauma and a palpable lump. The aim of this study was to determine the frequency with which the lump was directly related to trauma or was an incidental finding by the patients examining themselves post-injury.