350 Poster

Overall Size of Metastases (OSM) in the Sentinel Lymph Nodes; Can It Predict the Probability of Further Axillary Nodal Metastases After Positive Sentinel Lymph Node Biopsy?

R. Nadeem[1], Z. Saidan[1], L. Gudur[1]. [1]*East Lancashire Trust Hospitals, Surgery, Manchester, United Kingdom*

Background: Axillary lymph node dissection (ALND) is currently the recommended procedure in patients with metastatic sentinel lymph node (SLN) biopsy (SLNB). A significant proportion of patients with positive SLNs will not have any additional metastases in non-sentinel lymph nodes (NSLNs). Various nomograms to predict the probability of further axillary nodal metastases after positive sentinel lymph have been introduced. These nomograms have used variables related to tumour characteristics and factors related to the axillary nodes with variable success. The aim of this study is to identify the factors predictive of additional metastases in non-SLNS and to study the clinical utility and accuracy of currently available seven nomograms.

Methods: 138 patients with positive SLNs who underwent completion ALND were identified. Multiple pathological tumour and nodal-related variables including the overall metastases size (OSM) in the SLNs were analysed.

Factors predictive of further metastases in non-SLNs after positive SLNB were evaluated by logistic regression analysis.

Data was then used to calculate the probability of further metastases in non-SLNs predicted by the seven nomograms that are currently in use: MSKCC, Cambridge, Turkish, Stanford, MDACC, Tenon and MOU models.

The area under the receiver-operator characteristic (ROC) curve (AUC were calculated for each nomogram. AUC value $\geqslant$0.80 has an excellent discriminative power.

Results: 54 of 138 patients (41 per cent) had additional metastasis in non-SLNs.

The OSM, multifocality, LVI remained significant after multivariate analysis. In the bootstrap analysis OSM was consistently the single most important variable in predicting non-SLN metastases.

In the following table we divide the nomograms into 3 groups: those that included OSM, models that only used micro versus macrometastases as a variable, and models that did not include metastatic size as a variable and compare their AUC values, clinical utility and false negative rates.

Pathological variables	Nomograms using OSM			Nomograms using micro/ macrometastases		Nomograms with neither micro/macrometastases nor OSM	
Nomograms	Cambridge	Turkish	MOU	Tenon	Stanford	MDACC	MSKCC
AUC values	0.68	0.70	0.74	0.63	0.69	0.56	0.68
95% CI	0.58–0.77	0.61–0.79	0.65–0.82	0.54–0.72	0.60–0.78	0.43–0.69	0.59–0.78
False −ive rate for $\leqslant$10% Probability (P)	2/8 (25%)	9/47 (19%)	0/12 (0%)	2/25 (8%)	1/5 (20%)	2/4 (50%)	0/3 (0%)

Conclusion: The size of metastases in the SLN (OSM) is an important and significant predictor of further metastases in non-SLNs. Predictive tools using OSM showed better AUC values, clinical utility and false −ive rate. This feature is not routinely measured in many breast units. We suggest that it should become a routiune part of the histological analysis and should be routinely documented in the pathological databases.

351 Poster

Fully Automatic Estimation of Film-based Breast Percentage Density Separate Out Postmenopausal Hormone Replacement Treatment Effects as Well as Expert's Estimation

K. Petersen[1], K. Chernoff[1], G. Karemore[1], C. Christiansen[2], M. Nielsen[2]. [1]*BiomedIQ A/S, Imaging, Copenhagen, Denmark;* [2]*Nordic Bioscience A/S, Herlev, Copenhagen, Denmark*

Background: Breast density relate to breast cancer risk and has been shown to increase by hormone replacement treatment. Density estimation is based on expert's intensity thresholding in Cumulus scoring of percentage breast density. We examine if fully automated computer method can separate out the effect of treatment to the same degree.

Material and Methods: Low-dose oral estrogen (1 mg) continuously combined with drospirenone (2 mg) was administered to postmenopausal women for up to 2 years in a randomized, placebo-controlled trial. This post hoc analysis assessed the differences in breast density between treatment (T) and placebo arm (P) at follow up measured from digitized images by two radiologist-based approaches; the categorical BI-RADS scoring (B) and Cumulus-like percentage density scoring (D); and two computer automatic approaches; one using an individual assessment of all pixels in the breast regions (CP), and one being consistent with the radiologists methodology by estimating an optimal density threshold and recording the percentage density (CD).

In the automatic systems, a novel machine learning methd predicting dense breast tissue based on a set of mammograms with the pixelwise density labels as obtained from experts thresholding was used. First it was trained in an unsupervised way to learn a multiscale patch dictionary for the mammograms, before it is fine tuned in a supervised way. In contrast to previous work, this model combined a semi-supervised feature learning approach with a multiscale input and sparsity constraints. In addition to the classifier output (CP), we computed the image intensity threshold which compares best to the computer's pixelwise output (CD).

All computer scorings were performed in a leave-one-out fashion to avoid bias.

Results: The four methods scored the percentage density as in the table (mean$\pm$std, t-test, Area Under the ROC, and Pearson's R).

Methods	B	D	CP	CD
P	2.02$\pm$0.61	19.7$\pm$12.7	27.9$\pm$11.2	24.9$\pm$13.9
T	2.18$\pm$0.59	24.8$\pm$12.2	35.4$\pm$11.4	34.3$\pm$15.4
p-val T vs P	0.24	0.05	0.004	0.005
AUC	0.56	0.62	0.68	0.67
R to B	1	0.86	0.70	0.70
R to D	0.86	1	0.86	0.87

Conclusion: In this study, both automated methods correlate to manual continuous density scoring as well as manual to manual earlier reported in literature and separate out treatment effect better manual scoring (AUC >0.67 compared to 0.62) even though it was rained to mimic manual scoring.

352 Poster

Evaluation of EGFR, VEGFR2, IGF-1R and HIF-1a Expression and Their Prognostic Value in Iranian Triple-negative Breast Cancer Patients

R. Mehdizadeh[1], S. Najafi[2], I. Jahanzad[3]. [1]*University Of Tehran Iranian Center For Breast Cancer (Icbc), Department Of Cell And Molecular Biology, Tehran, Iran;* [2]*Iranian Center For Breast Cancer (Icbc) Academic Center For Education Culture And Research (Acecr), Department Of Medical Oncology, Tehran, Iran;* [3]*Cancer Institute Of I.r. Iran Tehran University Of Medical Sciences, Department Of Pathology, Tehran, Iran*

Background: Triple negative breast cancer (TNBC) carries a poor prognosis and therapeutic options are limited to date. Often, these tumors are defined as estrogen receptor (ER) negative/progesterone receptor (PR) negative/human epidermal growth factor receptor 2 (HER-2) negative (triple negative) by immunohistochemistry (IHC). The aim of this study was to investigate to what extent epidermal receptor growth factor (EGFR), vascular endothelial growth factor receptor 2 (VEGFR2), hypoxia inducible factor-1α (HIF-1α) and insulin-like growth factor receptor1-R (IGF1-R) express in TNBC and do these expressions have prognostic value.

Material and Methods: From 1132 breast cancer patient who were treated and followed in our center (ICBC) from 2006 to 2010, one hundred and three of them were TNBC in which at first triple negativity was confirmed and then Expression of EGFR, VEGFR2, HIF-1α and IGF1-R was studied by IHC in them.

Fixed in formalin blocks were used and IHC analyses were performed on Tissue Microarray (TMA) blocks with antibodies for EGFR, VEGFR2, HIF-1α and IGF1-R.

Results: Age at diagnosis (Means $\pm$11.7) was 49.5, most of the tumors was IDC (101, 98%). Eighteen (17.5%) patients came in very early stage (I) but the rest in later stages (stage II 46.6%, stage III 30.1%, metastatic 5.8%). Just one of them had histological grade I at presentation but most have II or III (49.5%, 49.5%). After about thirty months of follow up (29.4$\pm$14.1) local recurrence appeared in 8 (7.8%), secondary metastasis in 16 (15.5%) and death in 18 (17.5%) patients.

We analyzed tumor samples from 103 patients with primary classic IDC, EGFR expressed in 23 (23.3%), VEGFR2 in 96 (93.2%), IGF-1R in 99 (96.1%) and HIF-1α in 67 (65%) samples.

Conclusions: EGFR, VEGFR2, HIF-1α and IGF-1R did not correlate with either tumor stage or event free survival and OS. This IHC-based molecular classification does show a distinct clinical outcome and no one shows any relation to prognosis.