

3 HISTOPATHOLOGICAL GROWTH PATTERNS AS A GUIDE FOR ADJUVANT SYSTEMIC CHEMOTHERAPY IN PATIENTS WITH RESECTED COLORECTAL LIVER METASTASES

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Background. Despite negative trials adjuvant systemic chemotherapy is widely administered in patients with colorectal liver metastases (CRLM). Histopathological growth patterns (HGP) are an independent prognostic factor in patients with CRLM. This study evaluates whether HGP can predict the effectiveness of adjuvant systemic chemotherapy in patients with resected CRLM.

Material and methods. A multicenter cohort study, including patients from two centers, was conducted. Growth patterns were assessed according to the international consensus guidelines.

Results. In total, 816 consecutive patients were included in the study. Adjuvant systemic chemotherapy was administered in 173 patients (21%). Desmoplastic type HGP (dHGP) was associated with a superior overall survival (OS) of 87 months compared to 51 months in patients with non-desmoplastic type HGP (non-dHGP), $p < 0.001$. Adjuvant systemic chemotherapy was associated with a superior median OS of 79 months (95%CI 61–97 months) compared to 56 months for patients who did not receive adjuvant systemic chemotherapy ($p = 0.02$). In patients with dHGP, adjuvant systemic chemotherapy was not associated with an improved OS (HR 0.83, $p = 0.60$). Among patients with non-dHGP, adjuvant systemic chemotherapy was associated with an improved OS (adjusted HR 0.66, $p = 0.004$). In subgroup analysis, superior OS was observed only for patients with non-dHGP that did not receive preoperative chemotherapy (HR 0.51, $p < 0.001$). No significant effect of adjuvant systemic chemotherapy was observed in patients after preoperative chemotherapy with either dHGP (HR 0.93, $p = 0.84$) or non-dHGP (HR 0.93, $p = 0.68$), or in patients with dHGP that were not pretreated (HR 2.50, $p = 0.07$).

Conclusion. After complete resection of CRLM, adjuvant systemic chemotherapy is associated with improved OS in patients with non-dHGP tumors but not in patients with dHGP tumors.

Conflict of interest: No conflict of interest.

Scientific Symposium

Risk Reducing Mastectomy and Management of Familial Breast Cancer

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THREE-DIMENSIONAL ULTRASONOGRAPHY OF THE BREAST; AN ADEQUATE REPLACEMENT FOR MRI IN NEOADJUVANT CHEMOTHERAPY TUMOUR RESPONSE EVALUATION? – RESPONDER TRIAL

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Background. Accurate measurement of tumour response during and after neoadjuvant chemotherapy (NAC) is important and may influence treatment decisions in invasive breast cancer patients. Breast MRI forms the gold standard but is more burdensome, time consuming and costly. In this study response measurement was done with 3-D ultrasound by Automated Breast Volume Scanner (ABVS) and compared to breast MRI. Moreover, patient satisfaction with both techniques was compared.

Methods and materials. A single-institution, prospective observational pilot study evaluating tumour response by ABVS in addition to breast MRI

(standard care) was performed in 25 invasive breast cancer patients receiving NAC. Tumour response was evaluated comparing longest tumour diameters as well as tumour volumes at predefined time points using Bland-Altman analysis. Volume measurements for breast MRI were obtained using a fully immersive virtual reality system (a Barco I-Space) and V-Scope software. Same software was used to obtain ABVS volume measurements using an in-house developed desktop VR system. Inter- and intra-observer agreement was evaluated by Intraclass Correlation Coefficient (ICC).

Results. Twenty-five patients were eligible for baseline measurement, 20 for a mid-NAC response evaluation, and five for a post-NAC response evaluation. MRI and ABVS showed absolute concordance in 73% of patients for the mid-NAC evaluation, with a 'good' correlation for the difference in longest diameter measurement (ICC 0.73, $p < 0.01$) as compared to baseline assessment. Concerning difference in volume measurement in the mid-NAC response evaluation showed a 'fair' correlation (ICC 0.52, $p < 0.01$) and in the post-NAC response evaluation an 'excellent' correlation (ICC 0.98, $p < 0.01$). 'Excellent' inter- and intra-observer agreement was found (ICC 0.88, $p < 0.01$) with comparable limits of agreement (LOA) for observer 1 and 2 in both diameter and volume measurement. Patient satisfaction was higher for ABVS compared to breast MRI, 93% versus 12% respectively.

Conclusion. ABVS showed 'good' correlation with MRI tumour response evaluation in breast cancer patients during NAC with 'excellent' inter- and intra-observer agreement. ABVS has patients' preference over breast MRI and could be considered as alternative to breast MRI, in case results on an on-going prospective trial confirm these results (NTR6799).

Conflict of interest: No conflict of interest.

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PLEOMORPHIC LCIS WHAT DO WE KNOW? A UK MULTICENTER AUDIT OF PLEOMORPHIC LOBULAR CARCINOMA IN SITU

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Background: Pleomorphic lobular carcinoma in situ (PLCIS) is a relatively newly described pathological lesion that is distinguished from classical LCIS (cLCIS) by its large pleomorphic nuclei. The lesion is uncommon and its appropriate management has been debated. The aim of this study is to review data from a large series of PLCIS to examine its natural history in order to guide management plans.

Materials and Methods: Comprehensive pathology data were collected from two cohorts; one from a UK multicentre audit and the other a series of PLCIS cases identified from within the GLACIER study cohort. 179 cases were identified of whom 176 had enough data for analysis making this the largest cohort in the literature.

Results: The mean age of all the 176 cases was 53 (34–94) years. When excluding the GLACIER patients because of the age limits for recruitment (all below 60 years), the mean age increased to 60. Of the 176 cases that had surgery, 133 had unifocal disease while 43 had evidence of multifocality. Pure non-invasive disease was seen in 47 patients. 14 patients had pure PLCIS, 20 had a mixture of PLCIS and cLCIS while concurrent PLCIS and DCIS was seen in 13. Invasive disease was seen in 130 patients, whilst 2 had microinvasive disease (<1mm).

Out of the 130 that had invasive disease 117 (90.0%) had a subtype of invasive lobular malignancy, either as the only invasive component or admixed with other types. 43 (33.1%) classical invasive lobular carcinoma

(ILC), 36 (27.7%) invasive pleomorphic lobular carcinoma (IPLC) and 12 (9.2%) showing a mixture of both. Only 11 (8.5%) had pure invasive ductal/no special type carcinoma (IDC). In 36 patients (27.7%) there was either mixed or multifocal/multicentric tumours, the commonest being mixed ILC and IPLC (12 cases), mixed ILC with IDC (10 cases) or IPLC and IDC 10 cases. A high incidence of histological grade 2 (71.1%) and grade 3 (24.5%) invasive cancers was noted with a predominance of ER positive (92%) and HER-2 negative (92.3%) malignancy.

The preoperative diagnosis was known in 87 patients; of these, 22 had pure PLICIS diagnosed preoperatively. On excision 7 of these 22 had evidence of invasive disease (31.8%) and one (4.5%) had associated DCIS. So when PLICIS was the most significant finding on diagnostic biopsy the upgrade to invasive disease on excision was 31.8%, which is higher than pooled data for classical LCIS and DCIS.

Conclusion: The older age at presentation, high rate of upgrade to invasive cancer, common association with higher grade tumours suggest that PLICIS is an aggressive form of *in situ* disease. These findings support the view that PLICIS is a more aggressive form of lobular in situ neoplasia and supports the tendency to treat akin to DCIS.

Conflict of interest: No conflict of interest.

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INDIVIDUAL ARM LYMPHATIC FLOW PATTERN MAY EXPLAIN SUSCEPTIBILITY TO ARM LYMPHEDEMA AFTER ALND (AXILLARY LYMPHNODE DISSECTION) IN BREAST CANCER SURGERY - AN ANALYSIS BY USING LINF (LYMPHATIC IMAGING WITH NON RADIOACTIVE FLUORESCENT TRACER)

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Background: Although there are many reports which describe risk factors for ALE (arm lymphedema) after breast cancer surgery, none of them answers a question why some of patients who have the same risk factor, for example ALND, do develop ALE and some do not. We hypothesized that there should be anatomical difference in ALF (arm lymphatic flow) among each individual and the difference could account for susceptibility to ALE after ALND in breast cancer surgery.

Material and methods: LINF (Lymphatic Imaging with Non radioactive Fluorescent tracer) was used for observation of ALF. A fluorescent tracer, ICG (indocyanine green) was injected intradermally in the wrists. ICG got into the lymphatics rapidly and the fluorescent image was obtained by Photo Dynamic Eye (Hamamatsu photonics, Japan). Twenty one post-operative breast cancer patients with ALND were subject to LINF and bilateral (operation side and non-operation side) ALFs of each patient were analyzed. Since bilateral ALF patterns are usually almost identical, the flow pattern of non-operation side arm was regarded as preoperative image of operation side arm. Lymphedema was graded into three categories according to the characteristic LINF images. Those are LS (lymphatic spider), LSW (lymphatic spider web), and DP (diffuse pattern). LS is a very early sign of lymphatic stagnation without symptom. As lymphedema progresses LINF image changes into LSW (slightly symptomatic) and then DP (symptomatic).

Results: LINF of non-operation side arm showed none of these abnormal images but smooth linear normal lymphatic flow toward axilla. By counting the axilla-bound flow, the ALF pattern was categorized into two types, namely, single flow type (n=6) in which just one single lymphatic flow drained into axilla and multiple flow type (n=15) in which multiple lymphatic flows drained into axilla. The background of patients of each type was not significantly different. In the single flow type patients, 33% of the contralateral operation side arm showed DP, 50% showed LS or LSW and 17% showed normal linear lymphatic flow. In the multiple flow type patients, 53% showed normal flow, 47% showed LS or LSW and there was no patient who showed DP. There was a statistical difference (p=0.0241) between the two types when Cochran-Armitage trend test was applied. In other words, patients with just a single axilla-bound flow are more susceptible to arm lymphedema after ALND.

Conclusions; Susceptibility to ALE after ALND was discussed from an anatomical point of view with the aid of LINF. By analyzing individual ALF

pattern, it may be possible to distinguish high risk group for lymphedema to whom some lymphedema preventive procedure such as axillary reverse mapping should be considered.

This study was approved by the hospital ethics committee and the informed consent was appropriately obtained from each patient.

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Scientific Symposium

Patient Reported Outcomes

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VALUE BASED LOCOREGIONAL CANCER TREATMENT: THE ECCO VBHC PROJECT

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The past decade has witnessed the accelerated emergence of innovative therapeutic strategies for treating patients with cancer. However - given the exponential increase in costs of these new treatment options, together with the significant strain on national budgets to meet growing demands on health care services - the cost of oncological treatments requires careful consideration.

Estimating which extra clinical benefits might be gained from higher costs incurred (economic evaluation) has hitherto been the standard to assess the value for money of new interventions. However, the perceived primary focus on cost-shifting and cost-reduction has not necessarily reflected what matters most to patients.

A much more patient-orientated, value-based approach considers benefit derived from new treatments which focus on the best patient outcomes achieved per monetary unit spent.

This requires a comprehensive appraisal of the impact of new interventions on a whole spectrum of outcomes as valued by the patient which, in addition to survival, toxicity and quality of life, also takes into account the time and sustainability of health recovery (including social endpoints such as return to employment), while considering the costs across the entire cycle of care (financial toxicity).

Several tools, centred on systemic medications, have been developed to assess the value of innovation in oncology treatments including: the ESMO (European Society for Medical Oncology) Magnitude of Clinical Benefit Scale (ESMO-MCBS), NCCN (National Comprehensive Cancer Network) Evidence Blocks and the ASCO (American Society of Clinical Oncology) Value Framework. There is currently far less attention paid to the value of non-pharmaceutical innovations.

Under the umbrella of the European CanCer Organisation (ECCO) and together with other European stakeholders in oncology and patient advocacy organisations, a project has been initiated to address this imbalance - the ECCO Value-Based Health Care Project (VBHC). The purpose is to evaluate ways in which policymakers may consider access and value more broadly across the entire cancer care spectrum. Existing value frameworks are primarily designed for the pharmaceutical market. The ECCO project will specifically consider locoregional treatments (radiotherapy, surgery, interventional radiology). Outcomes will be weighted and the potential to develop a value framework for non-pharmaceutical innovations will be considered.

The current status of the ECCO project will be presented and discussed, with the ultimate aim to come to a harmonized approach to value-based health care across the different oncologic disciplines.

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