

Patient underwent a probe curettage. The pathology report showed a grade 1 endometrioid type of endometrial carcinoma. A total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Final pathology report revealed that stage 1A endometrioid type of endometrium carcinoma.

Results Third day after surgery patient had fever (38 °C), tachycardia (102 beat/min) swelling was spread to the upper abdominal wall skin, vaginal discharge. She underwent a Hartmann procedure, abscess debridement and end sigmoid colostomy procedure. Patient then underwent extensive surgical debridement after 48 hours and a vacuum sealing drainage dressing was placed to cover the open abdominal wall and a negative sucker was placed upon the anus for 5 days. The dressing was changed every 3 days. Cultures of the exudates from the wound grew *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*. Antibiotic treatment was adjusted according to the sensitivity results. After 21 days of a negative pressure wound treatment, the abdominal wall defect was 15*15 cm diameter and the wound covered with a granulation tissue. Patient underwent a split thickness skin graft operation. In this video which we want to demonstrate how to reconstruct an open abdominal wall defect with a full thickness skin graft. After removing the granulation tissue, a good vascular supported tissue had seen and the necrotic wound had removed by a curette. The split thickness skin graft had taken from left leg's superolateral healthy skin with a measure of 10*25 cm diameter and 3 mm thickness. The skin is meshed to cover the large wound area. The graft covered the whole open abdominal wall and stitched up with 4,0 polipropilen sutures.

Conclusion Necrotizing fasciitis is an uncommon condition and has serious morbidity-mortality rate. Surgical debridement is the cornerstone of the treatment. NGWT combined with a STSG can help to heal wounds with NF.

Disclosures Picture 1:72 hours after STSG surgery

Picture 3: 3 months after STSG surgery

Translational research

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ACCUMULATION OF 53BP1 IN CIRCULATING TUMOR CELLS DURING TREATMENT WITH ERIBULIN IDENTIFIES CHEMOTHERAPY-RESPONSIVE METASTATIC BREAST CANCER PATIENTS

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Introduction/Background Evidence suggests that the DNA end-binding protein p53-binding protein 1 (53BP1) expression in breast cancer is associated with poor prognosis, especially in triple-negative breast cancer (TNBC). Circulating tumor cells (CTCs) provide accessible 'biopsy material' to track cell traits and functions and their alterations during treatment.

Methodology We prospectively monitored the 53BP1 status, as a parameter for intact DNA damage response, in CTCs from 63 metastatic breast cancer (MBC) patients with HER2- CTCs before, during, and at the end of chemotherapeutic treatment with Eribulin in the DETECT-IV trial. Nuclear 53BP1 staining and genomic integrity were evaluated by immunocytochemical and whole-genome-amplification-based polymerase chain reaction (PCR) analysis. We used mean 53BP1 scores in CTC samples as dividing criteria, i.e. compared patients with 53BP1 scores <50% and ≥50%. We analyzed PFS of the patients from these two groups using scores obtained with samples at different time points during the study.

Results We found a decline of mean CTC numbers from baseline to 12 weeks of treatment but a dramatic rise at the final visit due to disease progression in 10/13 of the cases (mean CTC-values at baseline: 18, 2nd visit: 2, final visit: 118). Comparative analysis of CTCs from patients with 15 triple-negative and 48 hormone receptor positive tumors revealed elevated 53BP1 levels in CTCs from patients with HR+ metastases, particularly following chemotherapeutic treatment. Kaplan–Meier analysis between nuclear 53BP1-positivity in CTCs and progression-free survival (PFS) revealed an increasing association during chemotherapy until last examination (p=0.065).

Conclusion Our data suggest that 53BP1 detection in CTCs could be a useful marker to capture dynamic changes of chemotherapeutic responsiveness in triple-negative and HR+ MBC.

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GENOMIC AND FUNCTIONAL CHARACTERISATION OF INTRA-TUMOURAL HETEROGENEITY IN HIGH GRADE SEROUS OVARIAN CANCER

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Introduction/Background High-grade serous ovarian cancer (HGSOC) is characterised by high degrees of genomic instability and heterogeneity, with most patients eventually acquiring resistance to platinum-based chemotherapy. Matching the best treatment options to patients remains problematic due to diverse platinum resistance mechanisms and limited effective predictive biomarkers. This study aims to understand the extent of intra-tumoural heterogeneity (ITH) in advanced stage HGSOC, at presentation and relapse, and to define the link between ITH at the genomic and phenotypic levels.

Methodology Patients (n=49) undergoing radical upfront-debulking for advanced HGSOC at Hammersmith Hospital, UK, underwent a tumour mapping of their tumour

dissemination patterns. Tumour biopsies were collected (range 4–15, median 9), placed in short-term cultures, treated with cisplatin (25 μ M overnight) and apoptosis/viability assayed. When relapsed, patients also had paired biopsies collected for genomic and phenotypic analysis. DNA was extracted from tumours (5 per patient, n=49 patients plus relapse samples) and Illumina Human OmniExpress genotyping performed. Allele-specific copy number (CN) was quantified using ASCAT. Genomic heterogeneity was quantified as the estimated number of CN aberration events distinct between each pair of tumour deposits. Clonal diversity within a patient's deposits was calculated using the difference between within-patient and between-patient heterogeneity.

Results Broad heterogeneity was detected in response to platinum treatment across cases at the phenotypic level in vitro (n=49), with higher variances in apoptosis induction observed in patients with platinum resistant disease. Genomic analysis revealed widespread variations in patterns of evolution for different patients' tumours, including the relationship between primary tumours and relapsed disease. Extensive variations in CCNE1, MYC and PTEN CN were observed across multiple tumours in the same patients, and overall higher CCNE1 CN associated with poorer patient outcome (p=0.038).

Conclusion Vast intra-tumoural heterogeneity is observed at the phenotypic and genomic level in HGSOE patients. Extensive copy number variations in genes such as CCNE1, MYC and PTEN across multiple disseminated samples within patients, indicates that sampling of a single tumour site does not accurately represent overall disseminated HGSOE biology and has implications for overinterpretation of studies relating to outcome and platinum-resistance.

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NOVEL 3D MODEL SYSTEMS TO ASSESS HETEROGENEITY IN RESPONSE TO PLATINUM THERAPY IN HIGH GRADE SEROUS OVARIAN CANCER

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Introduction/Background High-grade serous ovarian cancer (HGSOE) is the most common subtype of ovarian cancer, characterised by vast genomic instability and heterogeneity and acquired resistance to platinum-based chemotherapy. However, matching the most beneficial treatment options to patients is difficult to predict due to different platinum resistance mechanisms and limited effective predictive biomarkers. A study characterising intra-tumoural heterogeneity in HGSOE has identified variations in phenotypic responses to platinum treatment between different metastatic sites. In this study, we aim to develop novel clinically-relevant 3D ex-vivo models of HGSOE to investigate the effect of the local microenvironment on metastatic tumour cells' response to treatment, and potential use as a screening tool to predict drug responses.

Methodology Three different ex-vivo models were developed: organotypic, organoid and tumour slice. For organotypic and organoid models, tumour cells were extracted

from metastatic deposits obtained from defined anatomical regions during upfront radical debulking surgery of advanced stage HGSOE patients. Organotypic models were assembled using normal omental stromal cells embedded in Collagen-1 and tumour cells were added. Organoid models were propagated from tumour cells and embedded in basement membrane extract. For slice culture models, tumours were sliced into 350 μ m sections using a vibratome and cultured on cell culture inserts. All models were treated with cisplatin and assessed for apoptosis and viability read-outs.

Results Organotypic models showed that tumour cells cultured in 3D showed heterogeneity in response to cisplatin treatment, data showed a trend towards reduced response to treatment within 3D models compared to 2D (n=8). Changes in patterns of response to treatment between samples from 2D to 3D within the same patient was also demonstrated (n=5). Organoid models were successfully propagated from different metastatic sites and maintained long term growth (>15 passages). Histological read-outs for slice culture models demonstrated slices from different metastatic sites maintained viability in culture for up to 5 days.

Conclusion We have established growth, drug treatment conditions and assay read-outs for 3 different ex-vivo models of metastatic HGSOE. We have established that organoid culture must be generated within 24hours of tumour cell extraction. Furthermore, both fresh and viably frozen tumours can be used to generate organotypic and organoid models. The broader implication of establishing clinically-relevant complex tumour models as routine methodologies for screening novel therapeutics and capturing the complex heterogeneity of individual patients, may lead to better development of therapeutic strategies including tumour/microenvironment combination strategies and also better personalisation of therapy for patients with HGSOE.

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Trophoblastic diseases

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A CLINICAL AUDIT OF MOLAR PREGNANCIES AND GESTATIONAL TROPHOBLASTIC NEOPLASIA CASES OVER 1YR IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA WITH RESPECT TO THE INCIDENCE OF DISEASE, FACTORS RELATED TO ETIOPATHOGENESIS, DIAGNOSIS AND MANAGEMENT

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Introduction/Background A Clinical Audit of molar pregnancies and gestational trophoblastic neoplasia cases over 1yr was conducted at Kolkata Medical College & Hospital, a tertiary care hospital of Eastern India with respect to the incidence of disease, factors related to etiopathogenesis, diagnosis and management and effects on maternal morbidity and mortality.

Methodology A total of 10000 patients attended this institution during 2017 June to 2018 June for pregnancy or its complication in department of gynaecology & obstetrics. 85 molar