Tumour BRCA testing success rates in routine diagnostic tissue samples

Dr. Tanush Vig[1] & Dr. Ray Lonsdale[2]
1. International Training Fellow (MTI-Path), Department of Cellular Pathology, Norfolk and Norwich University Hospitals NHS Foundation Trust
2. Consultant Histopathologist, Department of Cellular Pathology, Norfolk and Norwich University Hospitals NHS Foundation Trust

Norfolk and Norwich University Hospitals NHS Foundation Trust

INTRODUCTION: BRCA mutations are present in the tumours of ~22% of patients with epithelial ovarian cancer[(1–2).] Testing for germline and somatic *BRCA*1/2 gene mutations is a fundamental element in ovarian cancer care, due to its prognostic and predictive value for patients. Knowing a patient's BRCA mutation status before any treatments are initiated is valuable for determining therapeutic decisions. Patients with BRCA mutations are eligible and benefit from PARP inhibitor therapy under current NHS England reimbursement guidelines.

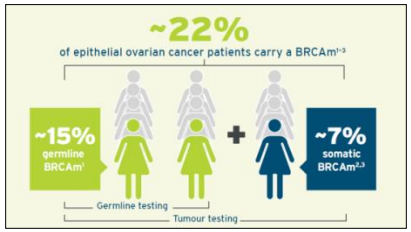


*Figure reproduced courtesy of AstraZeneca

AIM: To investigate the feasibility of tumour BRCA testing in clinical samples of high-grade serous carcinomas.

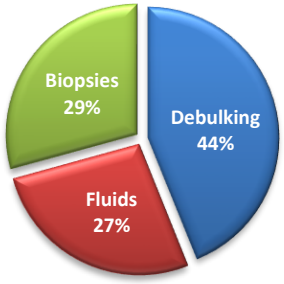
MATERIALS & METHODS: Samples from patients with high-grade serous carcinoma received in our laboratory from May 2020 to March 2021, including debulking specimens, effusions and diagnostic biopsies were tested for BRCA mutations at the Genomics Laboratory in Manchester.

RESULTS:

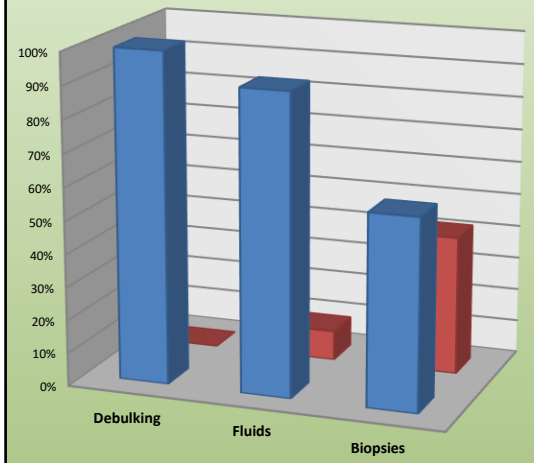
A total of 41 cases were included in the audit. All 18 debulking cases were successful for molecular testing. Of cytology samples (n=11) and diagnostic biopsies (n=12), successful testing was greater for cytology samples (n=10, 91%) than biopsies (n=7, 58%).

Four cases showed BRCA frameshift mutations (n=4, 9.75%), 3 involved the BRCA1 gene and 1 the BRCA2 gene .

TOTAL SPECIMENS



TEST RESULTS



	Debulking	Fluids	Biopsies
Successful Tests	100%	91%	58%
Failed Tests	0%	9%	42%

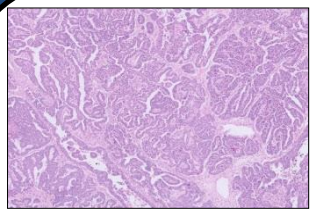


Figure 1: Photomicrograph of a debulking specimen showing well-preserved serous carcinoma arranged in papillary configurations and slit-like glandular spaces (H&E, 50X)

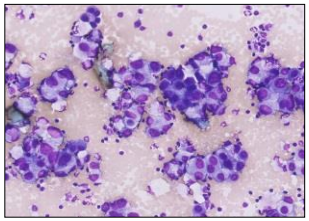


Figure 2: Photomicrograph of an effusion specimen showing a richly cellular sample with markedly pleomorphic malignant cells and a minority of background inflammatory cells (Giemsa, 100X)

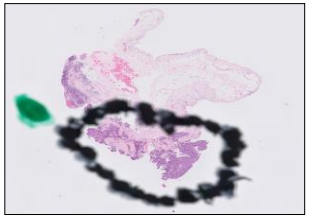


Figure 3: Core biopsy sample of serous carcinoma involving the omentum. The optimum area is marked by the pathologist for subsequent microdissection (H&E, 50X)

CONCLUSIONS:

- Our audit showed an overall technical BRCA test success rate of 85.3%.
- Successful somatic BRCA testing depends on adequate tumour cellularity, an accurate mark-up of sections for microdissection and optimal DNA preservation.
- Large debulking specimens allow selection of well preserved cellular tumour with a 100% success rate.
- Success with core biopsies was variable and depended on the number of tumour cells rather than core length or number.
- Effusion samples (ascites and pleural) were better than small biopsies for this test, as they are often highly cellular samples.

References:
1. Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. *Cancer*. 2005;104(12):2807-2816. doi:10.1002/cncr.21536
2. Moschetta M, George A, Kaye SB, Banerjee S. BRCA somatic mutations and epigenetic BRCA modifications in serous ovarian cancer. *Ann Oncol Off J Eur Soc Med Oncol*. 2016;27(8):1449-1455. doi:10.1093/annonc/mdw142