HRD testing of high-grade ovarian cancers: experience from a cancer centre

Triantafyllakis P[1], Isakjee D[2], Butler S[2], Boyle W[1], Ganesan R[1]

[1]Cellular Pathology, Birmingham Women's Hospital, United Kingdom

[2]West Midlands Regional Genetics Laboratory, Birmingham, United Kingdom

Introduction

Germline and somatic mutations in BRCA1/2 (tBRCA – detected in tissue samples) are detected in 17–25% of patients with advanced, high grade, tubo-ovarian carcinomas. BRCA1/2-mutated patients have homologous recombination deficiency (HRD) in their cells; a further 20% of high-grade ovarian cancer patients also have HRD but are BRCA1/2 wildtype. HRD status is based on a combined result of tBRCA status and Genomic instability score (GIS), measured by the Myriad MyChoice CDx assay. Identifying women with HRD allows for addition of Poly (ADP-ribose) polymerase (PARP) inhibitors to the treatment protocol and provides a significant survival advantage compared to conventional chemotherapy alone.

Objectives

In this study, we audited the HRD/tBRCA testing pathway at Birmingham Women's Hospital against the BAGP/BGCS consensus recommendations (figure 1) for BRCA testing in ovarian cancer.

Methods

Data was collected retrospectively and analysed, from results on formalin fixed, paraffin embedded (FFPE) samples sent for testing between May and September 2021.

Figure 1: BAGP/BGCS consensus recommendations for tBRCA/HRD testing.

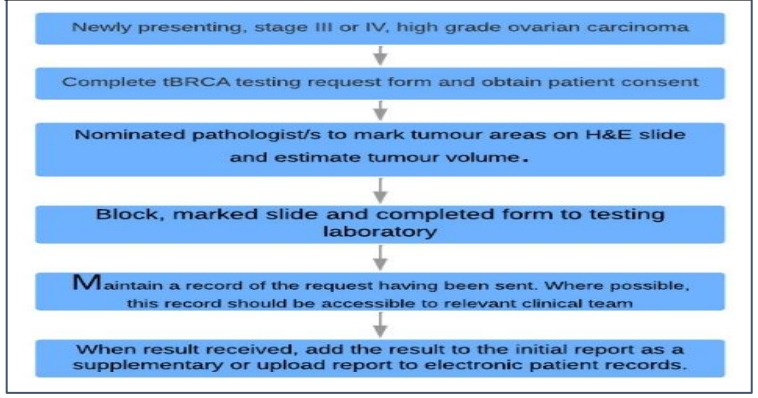


Table 1.

Age range (median)	35-81 (66)
Tumour content % range (median)	<20-95 (80)
GIS range (median)	5-75(28)
Sample type	13/30 biopsies 17/30 resections
Tissue sites	Omentum, Ovary, Adnexa, Peritoneum, Groin node, Colon, Uterus
Diagnosis	26/30 HGSC, 2/30 CCC, 1/30 carcinosarcoma, 1/30 High grade ca NOS
Turnaround time range (median)	8-34(13) days (receipt at testing laboratory (Myriad) to return of results)

Figure 2.

HRD outcomes in 4 samples with <20% TC

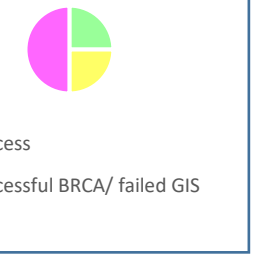


Figure 3.

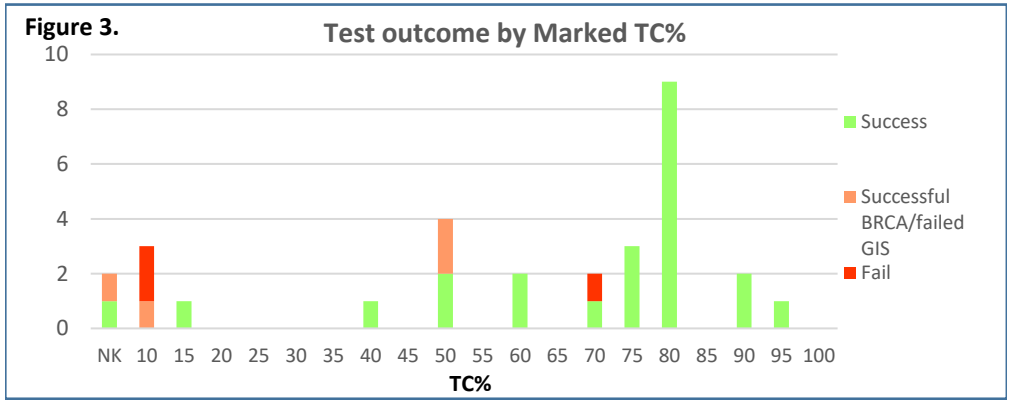
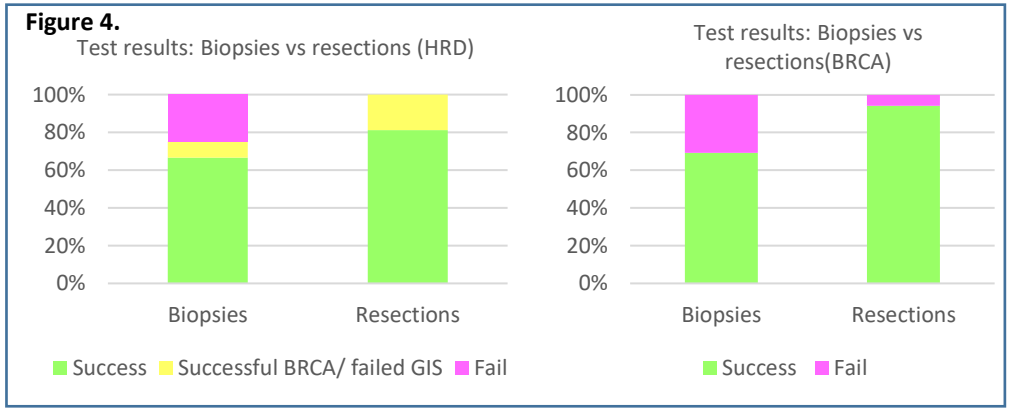


Figure 4.



Results/Discussion

- Our sample comprised 13 biopsies and 17 resections (Table 1).
- All cases were consented and had tBRCA/HRD test request forms completed.
- 2 recurrent tumours were tested only for somatic BRCA mutations.
- The majority of cases were high grade serous carcinomas (86.7%), followed by clear cell carcinoma(6.7%), 1 case of carcinosarcoma and 1 case of high grade carcinoma NOS (Table 1)
- Tumour content was documented in the significant majority of cases (28/30, 93.3%) (Figure 3).
- Successful testing for tBRCA with or without GIS testing was observed in 9/13 biopsies(69.2%) and 15/17 resections (88%)
- Median turnaround time was 13 days (range, 8-34 days)

Our analysis showed a higher success rate in resection samples compared to biopsies (Figure 4). Successful testing was also associated with a tumour content of 70% or more, in the majority of cases. Among the failed tests, there was one sample with high tumour content (70%), but low cellularity. Among cases with 20% tumour content or less, one was successful on testing(Figures 2, 3).

These findings suggest that tumour content does not always predict successful test outcome. Assessment of both cellularity and tumour content on H&E slides by pathologists might be a better predictor of sample adequacy and successful testing. A rigorous and systematic approach to such analysis is required to overcome the known problem of suboptimal inter-observer concordance.

Conclusions

The role of the pathologist is crucial in assessing the adequacy of the sample and accurately marking the tumour content. In this small study, successful testing was not always predicted by tumour content. The small number of cases is among the limitations of this study.