The challenges of genetic testing in patients diagnosed with Breast Cancer ; the Kent Oncology Centre experience

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Background:

- **NICE guidelines advise to offer genetic testing for *BRCA* mutations if the risk of being a *BRCA* carrier is over 10%**
- **In patients with a suggestive personal and/or family history, a specific predisposing gene is identified in <30% of cases.**
- **A *BRCA1* pathogenic mutation found in 45/308 participants in the TNT trial**
- **Women with triple negative BrCa <50years had a 20% BRCA1 mutation prevalence**

Aims:

- **To document the number of new pathogenic mutation carriers identified**
- **To estimate the expected number of carriers based on Family History and presentation**
- **To highlight the gap in case identification and offer solutions to optimise pathways**

Methods:

- **We acquired retrospective data for all new breast cancer cases from Jan 2014 to June 2014 from referral centres in Kent. We identified the prevalence of bilateral breast cancer, triple negative breast cancer, male breast cancer and also added family history details and calculated the Manchester risk score for all new BrCa referrals. (Figure 1)**
- **We then looked at the number of patients referred for Genetic Testing with documented test results.**
- **We compared this to the number of cases with genetic risk over 10% based on both family history and phenotypical characteristics.**

Results:

207 new BrCa cases (2 male) were referred to Oncology in this period with 10% being triple negative, 10% with bilateral breast cancer and with 30% having at least one affected relative. 11/207 (5.3%) were eligible for genetic testing based on the NCCN guidelines. 6/11 patients underwent genetic testing with 1 found to carry a pathogenic *BRCA2* mutation and 1 a *TP53* mutation (Li-Fraumeni) and 4 found not to carry a pathogenic mutation. (Figure 2)

5/11 patients eligible on the NCCN guidelines (3 patients with a Manchester score of over 15 and 2 patients with family history of ovarian cancer) did not undergo genetic testing. (Figure 3) A further 7/207 (3.4%) were eligible for genetic testing based on the current TNT trial data, which were not available during early 2014, making a total of 18/207 (8.7%) eligible. We estimate that 3 potential *BRCA* carriers were not identified. (Figure 4)

Conclusion:

Genetic referral pathways could be optimised to take into account both the family history as well as phenotypical characterisitics (triple negative BrCa, bilateral BrCa) often associated with a germline DNA repair pathway mutation.

Early identification of patients requiring genetic testing and a fast-track referral process would allow for different surgical approaches (mastectomy over breast preservation surgery) and chemotherapy treatment approaches (introduction of Carboplatin in neo-adjuvant and palliative chemotherapy regimens)

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Manchester scoring system

	BRCA1	*BRCA2*
FBC<30	6	5
FBC 30-39	4	4
FBC 40-49	3	3
FBC 50-59	2	2
FBC>59	1	1
MBC <60	5	8
MBC>59	5	5
Ovarian cancer <60	8	5
Ovarian cancer >59	5	5
Pancreatic cancer	0	1
Prostate cancer <60	0	2
Prostate cancer > 59	0	1

Pathology	BRCA1 adj	BRCA2 adj
Her2+	-4	0
Lobular	-2	0
DCIS only	-1	0
LCIS only	-4	0
Grade 1 IDC	-2	0
Grade 2 IDC	0	0
Grade 3 IDC	+2	0
ER pos	-1	0
ER neg	+1	0
Grade 3 triple neg	+4	0

Figure 1: Manchester Score calculation guide

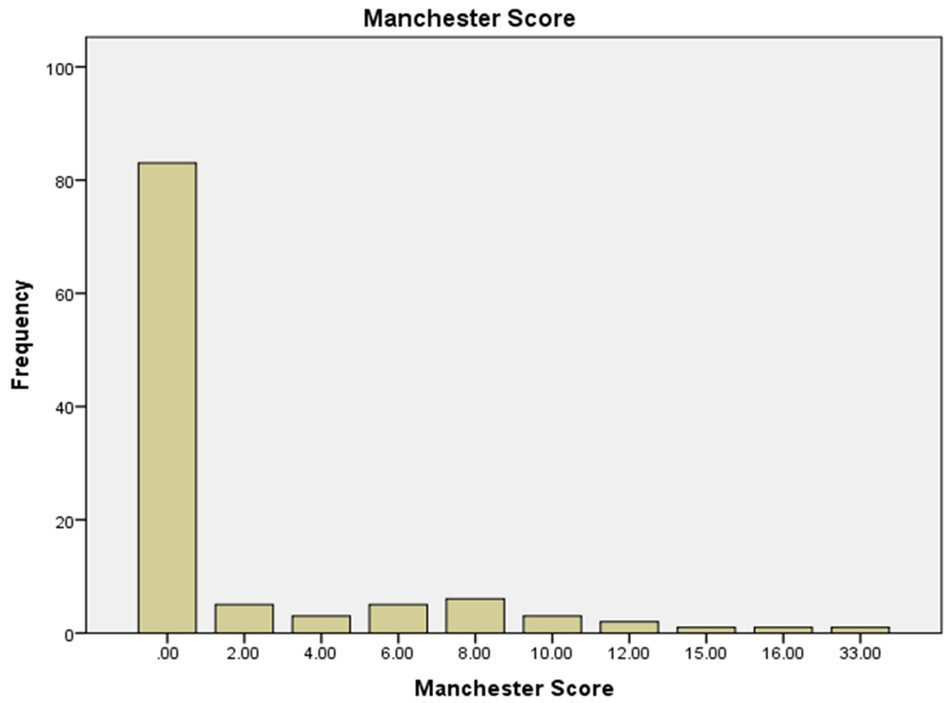

Figure 2: Frequency (percentage) of Manchester Score within our cohort based on Family History

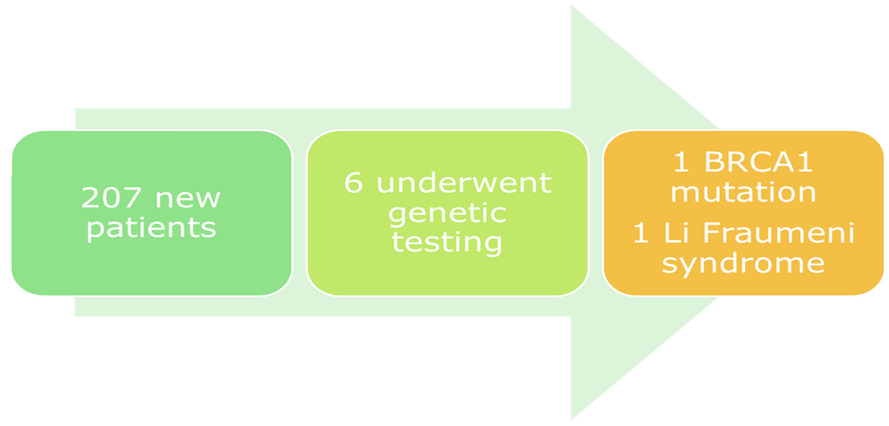

Figure 3: Number of patients referred for genetic testing with pathogenic mutations identified

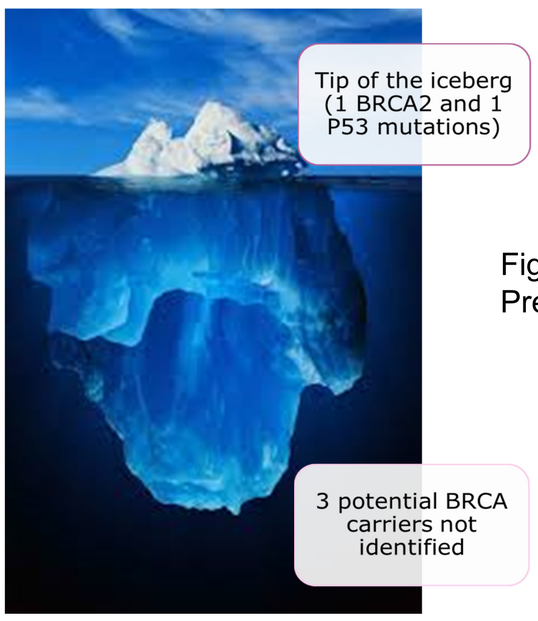

Figure 4: Breast Cancer Genetic Predisposition Iceberg paradigm

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