Evaluation of HER2 testing at a regional referral centre.

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Introduction:
HER2 is a key biomarker in the diagnosis and treatment of breast cancer, the level of tumour expression of HER2 predicts the response to targeted therapy [1] that can greatly increase response to treatment and progression free survival. University Hospitals of Birmingham performs HER2 testing for multiple sites in the West Midlands, an audit of the service from 2017 to 2018 was performed to determine positivity rates by IHC and FISH in addition to looking at quality aspects from a technical perspective.

Methods
HER2 IHC testing is performed using Ventana anti HER2/neu 4B5 antibody which is visually interpreted by trained consultant staff. HER2 FISH testing is performed on IHC cases scored as equivocal (2+) or uninterpretable/straight to FISH [2]. Testing is carried out using Abbott PathVysion HER2 probe kit and analysed by trained scientific staff. Data for the IHC and FISH results for specimens tested in 2017/2018 were extracted from their respective in-house databases and aggregated for statistical analysis using Microsoft Excel. Only cases of invasive breast cancer are included, gastric cancers are excluded.

Results

Data for reportable cases 2017-2018: HER2 IHC result Negative (0/1+)= 61.1%, Equivocal (2+) = 29.5%, Positive (3+) = 9.4%.
HER2 FISH result Not amplified = 78.7%, Amplified= 21.3%.
Overall HER2 positivity rate Amplified = 15.7%, Not Amplified = 84.3%.

The percentage HER2 IHC score for each antibody lot remained consistent, no trends were observed and standard deviation for result Negative (0/1+)= 3.15%, Equivocal (2+) = 2.97%, Positive (3+) = 1.66%.
Comparing consultant IHC scoring for each month showed correlation of 94.5% for Negative (0/1+), 91.9% for Equivocal (2+) and 81.5% for Positive (3+), comparing each consultant against themselves for the previous year showed average 99.7% correlation.

Also of note: the main cause for HER2 FISH failure was use of decalcification (34.5% of failed FISH cases).

Discussion/Conclusion

- The HER2 positivity rate was within expectations of the published literature which give a range of 15-30% [1] of cases being positive for HER2.
- The data did not represent heterogeneous or borderline cases effectively, 8.5% of cases were recorded as having heterogeneity and 7.2% of cases having a borderline FISH score but these are low estimates.
- Comparing the % HER2 IHC result for all antibody lots used in 2017-2018 showed consistency, no trends were identified suggesting comparable staining and interpretation across all lots used. This suggests that current batch acceptance testing methods are fit for purpose in determining equivalent staining.
- Consultant to consultant variation in % IHC scoring was observed: the largest variation was observed in the less experienced and confident consultants. This variation may require a concordance audit or review of equivocal cases for each consultant to determine if there is any clinical effect.

The data can be split by trust and fed back to service users, including data such as turnaround times and failure rates. If the audit is performed annually it would be beneficial for continuous monitoring for both the referring trusts and the testing centre.

Highlights areas of further investigation such as the inter-consultant variation, the true rate of heterogeneous and borderline cases and correlation between biopsy and excision specimens for the same patient, which can be audited to further improve the service.

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References
(1) NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE Single Technology Appraisal Pertuzumab for the adjuvant treatment of HER2-positive breast cancer Final scope. Issue Date: December 2017