

Audit of breast cancer excision specimens at the Histopathology Department, Rotherham NHS General Hospital, United Kingdom

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ABSTRACT

Introduction: Breast cancer is one of the common malignancies in Western countries. Breast cancer can be diagnosed by several ways; symptoms by the patient, periodic mammography screening in asymptomatic women aged 50-70 years and/or biopsy. According to the guidelines in the UK, breast cancer is predominantly treated with a multimodality therapy depending on cancer stage.

Methods: We have carried out an audit on breast excision specimens received in the histopathology department between April 2013 and March 2014. The findings from our audit were put to comparison with findings from our region; NEYH (North East, Yorkshire and Humberside) region and compared to national guidelines.

Results: There were 180 cases of breast malignancy identified in our study including both screen detected cases and symptomatic breast cancer. 171 (95%) of surgical procedures were roughly split equally between wide local excisions (WLE) and mastectomies. The incidence of Invasive ductal carcinoma, No special type (NST) was found in 124 (72.8%), and the commonest grade of the invasive carcinoma was Grade 2. The audit showed that 153 (85%) of cases were oestrogen receptor positive and only one (0.5%) case were progesterone Receptor positive. The department achieved an average turnaround time of 9 days for breast resection specimens.

Conclusion: This audit's findings have shown that our unit is broadly within overall regional and national guidelines and recommendations' limits. It also highlighted the distribution of breast cancer in the catchment zone of our community.

Key words: Pathology, histopathology, breast, oncology, oestrogen (ER), progesterone (PR), human epidermal growth factor receptor 2 (HER-2), screening, Ductal Carcinoma In-Situ (DCIS), Key performance indicators (KPI).

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Introduction

Surgical Breast cancer is one of the common malignancies in Europe and Western countries.¹ The age standardized incidence of breast cancer in 2006 was 110.3/100,000 (122.2/100,000 in the UK) making it the most common cancer diagnosed in Europe.¹ In 2010, it affected approximately 50000 women and 400 men in the UK.² In 2016, the mortality rate was estimated to 25.0/100,000.¹ A recent publication with global data has showed that the age-standardised 5-year net survival from breast cancer was 80% or higher in 34 countries around the world.³ Clinicians estimate prognosis using tools such as

the Nottingham Prognostic Index (NPI) or Adjuvant! Online. These tools use age of the patient, tumour size, nodal involvement, hormonal receptor status, histological grade, oestrogen receptor (ER) expression, human epidermal growth factor receptor type 2 (HER2). Over expression and comorbidities have been assessed and considered alongside patient preference when assessing risk and recommending therapies.^{2,4}

Breast cancer can be diagnosed by several methods, e.g. symptoms, periodic mammography screening in asymptomatic women aged 50-70 years and/or biopsy.⁵ Breast cancer is usu-

ally treated with a multimodality therapy depending on disease stage.⁵ The main treatment is surgical excision. Almost three quarters (74%) of breast cancer patients receive a major surgical resection as part of their cancer treatment.¹ Radiation therapy is considered if surgical excision margins are positive or to control locally recurrent disease. Anti-oestrogen medications are considered depending on tumour's hormonal status; Oestrogen score (ER score), and Progesterone score (PR score).^{1,2,5}

MATERIALS AND METHODS

The surgically excised specimens received in the Histopathology Department in Rotherham General Hospital during the year ending on 31st March 2014 were evaluated with respect to following parameters:

1. Gender distribution of cancers.
2. Type of Surgery undertaken.
3. Type of invasive malignancies identified.
4. Grading of tumours.
5. DCIS sub-classification.
6. Vascular Invasion.
7. ER, PR and Her-2 testing.

Breast excision specimens with benign and malignant neoplasia diagnosed this year were retrieved using Winpath (Pathology based Computer system), of which 249 cases were assessed.

RESULTS

A total of 180 cases of malignancy were identified out of the 249 cases. These included both screen detected and symptomatic breast cancers. The rest of the 69 cases were excluded as they were not malignant. Malignant cases comprised 179 females (99.4%) and 1 male (0.6%).

Table 1 shows the type of surgery undertaken. There is an almost equal distribution between Mastectomies and wide local excisions (WLEs). Our Mastectomy rate at Rotherham stands at 47.2% for 2013-2014 which is nearly similar to Departmental Audit of breast cancer in Rotherham during 2012 -2013 which was 46.7%. The choice of surgery is dependent on breast size, tumour

size, tumour stage, as well as the patients' choice. The 'other' surgeries include lumpectomies, tissue and cyst excisions.

Table 1: Type of treatment undertaken

Type of surgery	Number	%
Mastectomy	85	47.2
WLE	86	47.8
Others	9	5
Total	180	100

WLE: Wide lesion excision

The most common malignancy was invasive ductal carcinoma with 72.8% compared to 2012-2013 of 56.9%. Lobular cancer remains the same for 2013-14 as it did for 2012-2013. **See table 2**

Table 2: Type of Invasive malignancies

Type of Invasive tumour	Number	%
Ductal (D)	124	72.8
Lobular (L)	21	11.7
Mixed Ductal and Lobular	6	3.3
Tubular (T)	4	2.2
L & T	1	0.6
D & T	1	0.6
Mucinous	3	1.7
D & Mucinous	1	0.6
Not stated	12	6.7
Total	180	100

Of the 180 cases of Invasive cancers the grade distribution is in **table 3**. The likely explanation for not grading some of the invasive tumours is the prior history of neoadjuvant therapy and the poor tissue fixation in formaldehyde soon after surgery and giving it a sufficient length of fixation time prior to cut-up.

Table 3: Grading of tumours

Grade of Tumour	Number	%
1	24	13.3
2	102	56.7
3	50	27.7
Not graded	4	2.2
Total	180	100

Table 4 shows the classes of ductal carcinoma in situ (DCIS). In 47 patients (26.1%), they were high grade while 65 patients (36.1%) have no DCIS report.

Table 4: DCIS Sub-classification

DCIS Type	Number	%
High Grade	47	26.1
Intermediate Grade (Int.)	28	15.6
Low Grade	2	1.1
Low & High	1	0.6
Low & Int.	3	1.7
Int. & High	33	18.3
Low, Int. & High	1	0.6
No DCIS	65	36.1
Total	180	100

Most of the cases of invasive carcinomas had lymphovascular invasion (LVI) reported in the proforma based report. About two-thirds of cases have no lymphovascular invasion. See table 5

To ensure adequate staging of a tumour, nodal status must be attempted. The Department in Rotherham confirmed nodal status in all patients, with a positive nodal status in 37 cases (20%) of tumours. This is comparable with 20% Regionally (varied between 13% and 43%).⁵

Table 5: Lymphovascular Invasion

LVI	Number	%
Present	37	20.6
Absent	118	65.6
Probable / Possible	16	8.9
Not stated	9	5
Total	180	100

Oestrogen receptor is routinely performed for all invasive cancers and DCIS cases at Rotherham. Table 6 shows the Allred score distribution of the oestrogen receptor, in 153 (85%) the test was positive. In our hospital progesterone receptor testing was carried out in 29 patients (see table 7). For Herceptin- 2 testing see table 8.

Table 6: Oestrogen receptor tests

Allred Outcome	Number	%
Positive ≥ 3	153	85
Negative ≤ 2	27	15
Not done	0	0

Table 7: Progesterone receptor score

Allred Outcome	Number	%
Positive ≥ 3	1	0.5
Negative ≤ 2	28	15.6
Not done	151	83.9

Table 8: Herceptin-2 receptor Outcome

Her-2 Outcome	Number	%
Positive	16	8.9
Negative	138	76.7
Inadequate	1	0.6
Not done	25	13.9

Turnaround Times: The department achieved an average turnaround time of 9 days for breast resection specimens.

DISCUSSION

This is an audit on breast excision specimens received at the histopathology department between April 2013 and March 2014. The findings were compared to findings from our region; NEYH (North East, Yorkshire and Humberside) region and to national guidelines.

There were 180 cases of breast malignancy identified in our study. This included screen detected cancers and cases from the symptomatic group.

Surgical procedures were roughly split equally between wide local excisions (WLE) and mastectomies in 117 (95 %). This is in keeping with the findings from the first report of Breast Cancer Clinical Outcome Measures' (BCCOM) audit (2006) confirmed that mastectomy rates for symptomatic breast cancer varied by region from 36.4% to 53.2%.⁹

The incidence of male breast cancer was 0.6% of the cases of cancer reported and 0.4% of the total number of patients in our study. This is comparable to the National reported incidence rate of less than 1%.⁶

The incidence of invasive ductal carcinoma, no special type (NST), was found in 124 cases (72.8%) in our study. It is the most common type of invasive carcinoma of the breast. For the NEYH (North East, Yorkshire and Humberside) region 76% of tumours were found to be ductal carcinoma.^{6,7,8} The reason for this variation can be multifactorial. This may include interobserver variation amongst other potential factors. Further statistical analyses might be useful in identifying the significance of such regional variation. Regular annual audits on this subject would help to unravel some of these factors.

The commonest grade of an invasive carcinoma was Grade 2 (56.7% of total). This agrees with the statistics for screen detected breast cancers in NEYH region which found 53% of tumours were classified as grade 2.⁶

In 29.5% (including probable/possible) of cases vascular invasion was identified. This is in keeping with the findings of the English literature which lies in the same range as that reported in other studies: 28%, 46%, and 55% of patients with Lymph Node-positive Breast Cancer in different patient cohorts.¹⁰ The presence of vascular invasion is generally considered to be an adverse feature providing independent prognostic information about both local recurrence and survival.

Oestrogen receptor (ER) was positive in 85 % out of 180 cases that were tested for ER. This is lower than the Regional 92% positivity rate. Currently ER is performed on the needle core biopsy and if it is negative, the ER test will be repeated. If again this is negative, the ER is performed on the resection specimen. The department achieved an 85% positivity rate for invasive cancer cases. The presence of a positive oestrogen receptor (ER) status is a strong predictive marker of a positive response to anti-hormone therapy. It is acknowledged that factors such as tissue fixation (type of fixative and duration), choice of antibody, detection system/platform and threshold for interpretation of positive immuno-staining can affect test accuracy and reproducibility. These may account for the variation in rates of ER positivity at the service level.^{6,7,9,11}

Progesterone receptor (PR) was positive in 0.5% of cases. PR was performed routinely on ER negative cases at Rotherham, hence the low rate of positivity. The one case that showed PR positivity had an ER score of 3, therefore, ER and PR results are comparable.

Of the 180 cases of cancer, Her-2 was not performed in 25 cases as in these patients, a decision made at Multi-disciplinary team meetings based on comorbidity factors. Hence the test was performed in 86.1% of cases. There were 10.3% Her2 positive cases. Her-2 positivity is an important prognostic marker and predictor of response to chemotherapy and anti-HER-2 treatment. In the National Audit the average positivity rate of Her-2 status was 10% .^{6,9}

The most common malignancy was Invasive Ductal Carcinoma with 124 cases (72.8%) compared to 56.9% of the Departmental Audit of breast cancer in Rotherham during 2012 -2013. Lobular carcinoma in 2013-2014 remains the same as it did in 2012-13 according to the departmental audit in Rotherham. The most likely explanations for the apparent increase in Ductal carcinoma numbers in comparison to the previous years are firstly the implementation of strict criteria for diagnosing tubular carcinoma and therefore many of the cases that would have been classified as tubular cancer have been regarded as ductal carcinoma. Furthermore, immunohistochemistry stain (E-Cadherin) is being more frequently used to differentiate lobular carcinoma from other subtypes. Therefore, many of the apparent lobular and mixed carcinomas on Hematoxylin and eosin stain (H&E stain) were ultimately reclassified as ductal carcinoma on the final report after examination of E-Cadherin stain (author's opinion).

The department achieved an average turnaround time of 9 days for breast resection specimens. This was within the Key performance indicators (KPI) set by the department of turnaround time of ≤ 10 days for all cases.

CONCLUSIONS

This audit's findings have shown that the practice in our pathology department is broadly within the limits of the regional and national guidelines and recommendations about carcinoma of the breast. It also highlighted the distribution of breast cancer in the catchment zone of our community.

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Abbreviation list: Breast Cancer Clinical Outcome Measures (**BC-COM**), Ductal Carcinoma In Situ (**DCIS**), Haematoxylin and eosin stain (**H&E stain**), Human epidermal growth factor receptor type 2 (**HER2**), lymphoVascular Invasion (**LVI**), North East, Yorkshire and Humberside (**NEYH**), Oestrogen receptor (**ER**), Oestrogen score (**ER score**), Progesterone receptor (**PR**), Progesterone score (**PR score**), United Kingdom (**UK**), Wide Local Excisions (**WLEs**)

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