

# Breast Cancer Grading

## Nottingham Criteria

Accurate grading of invasive breast cancer requires good fixation, processing, section cutting, staining and careful application of grading criteria. In the UK, about 20% of symptomatic breast cancers are grade 1, 30% grade 2, and 50% grade 3. These proportions may be different in asymptomatic cancers detected by mammographic screening. Special type cancers (lobular, etc) should also be graded. Three separate scores are given:

### Gland (acinus) formation

Score 1: more than 75% of the whole carcinoma forms acini  
 Score 2: 10–75% of the whole carcinoma forms acini  
 Score 3: less than 10% of the whole carcinoma forms acini

Only score clearly formed glandular lumens surrounded by polarised cancer cells

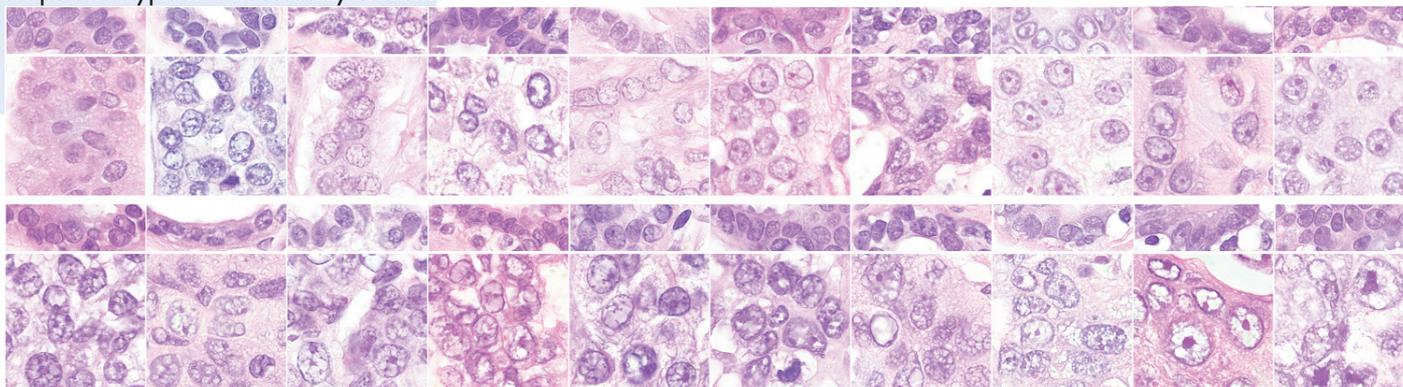
### Nuclear atypia/pleomorphism

Only about 5% of symptomatic cancers score 1 for nuclear atypia; about 50% score 3.

Score 1: nuclei only slightly larger than benign breast epithelium (< 1.5 × normal area); minor variation in size, shape and chromatin pattern

Score 2: nuclei distinctly enlarged (1.5–2 × normal area), often vesicular, nucleoli visible; may be distinctly variable in size and shape but not always

Score 3: markedly enlarged vesicular nuclei (> 2 × normal area), nucleoli often prominent; generally marked variation in size and shape but atypia not necessarily extreme



Nuclei of 20 consecutive breast cancers by increasing mean nuclear area (left to right, top to bottom). Paired non-neoplastic breast epithelium is shown above each case for comparison. Only one cancer (top left) has nuclei which score 1. The others in the top row score 2. All 10 in the bottom row score 3.

### Mitosis counts

Measure diameter of high power field (hpf) on your microscope to the nearest 0.01 mm. Always use same objective and eyepieces; if either is changed, measure again. Read score thresholds from table below. Scan sections to find area with most mitotic activity (often at tumour edge). In this area count definite mitoses in 10 consecutive fields. Skip fields with few carcinoma cells or obvious necrosis. Convert to score (1–3).

Table of mitosis score thresholds

Field diameter (mm)	Mitotic frequency score			Field diameter (mm)	Mitotic frequency score			Field diameter (mm)	Mitotic frequency score		
	1	2	3		1	2	3		1	2	3
0.40	≤4	5–9	≥10	0.50	≤7	8–14	≥15	0.60	≤10	11–20	≥21
0.41	≤4	5–9	≥10	0.51	≤7	8–14	≥15	0.61	≤10	11–21	≥22
0.42	≤5	6–10	≥11	0.52	≤7	8–15	≥16	0.62	≤11	12–22	≥23
0.43	≤5	6–10	≥11	0.53	≤8	9–16	≥17	0.63	≤11	12–22	≥23
0.44	≤5	6–11	≥12	0.54	≤8	9–16	≥17	0.64	≤11	12–23	≥24
0.45	≤5	6–11	≥12	0.55	≤8	9–17	≥18	0.65	≤12	13–24	≥25
0.46	≤6	7–12	≥13	0.56	≤8	9–17	≥18	0.66	≤12	13–24	≥25
0.47	≤6	7–12	≥13	0.57	≤9	10–18	≥19	0.67	≤12	13–25	≥26
0.48	≤6	7–13	≥14	0.58	≤9	10–19	≥20	0.68	≤13	14–26	≥27
0.49	≤6	7–13	≥14	0.59	≤9	10–19	≥20	0.69	≤13	14–27	≥28

### Final grading

Add scores for acinus formation, nuclear atypia and mitosis count. Total score must be in the range 3–9.

Total score 3, 4 or 5 = **grade 1** Total score 6 or 7 = **grade 2** Total score 8 or 9 = **grade 3**

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