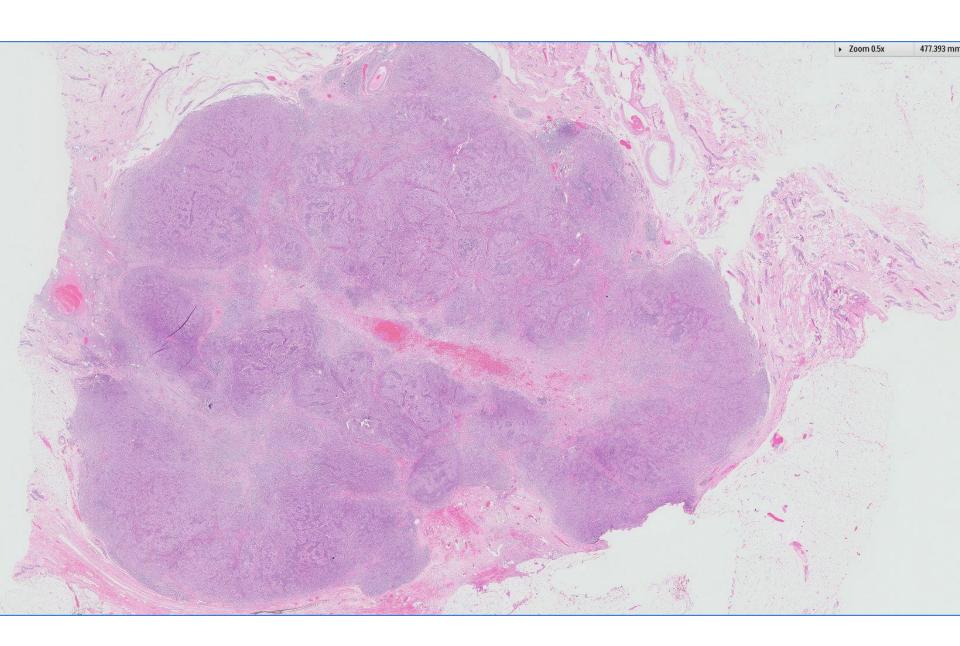
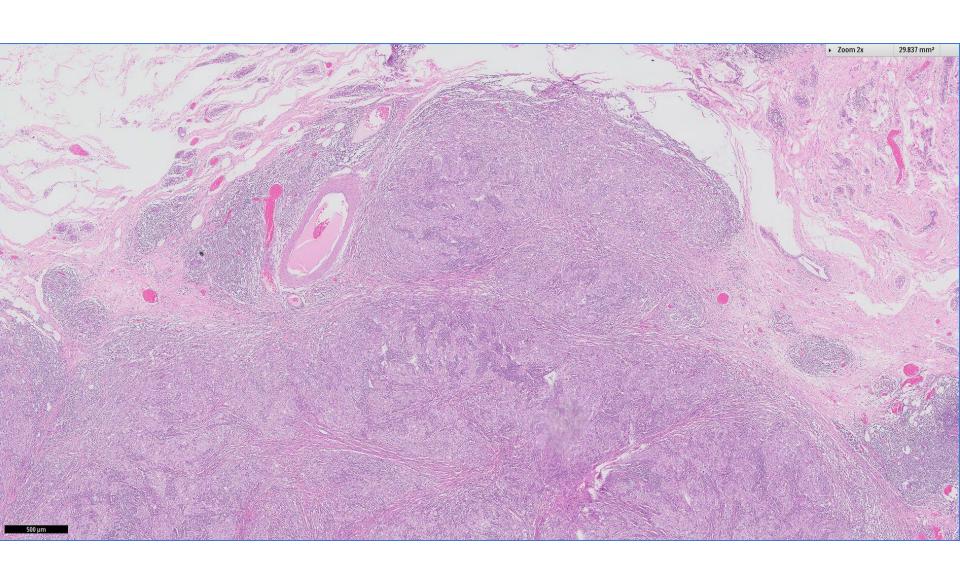
Case 29

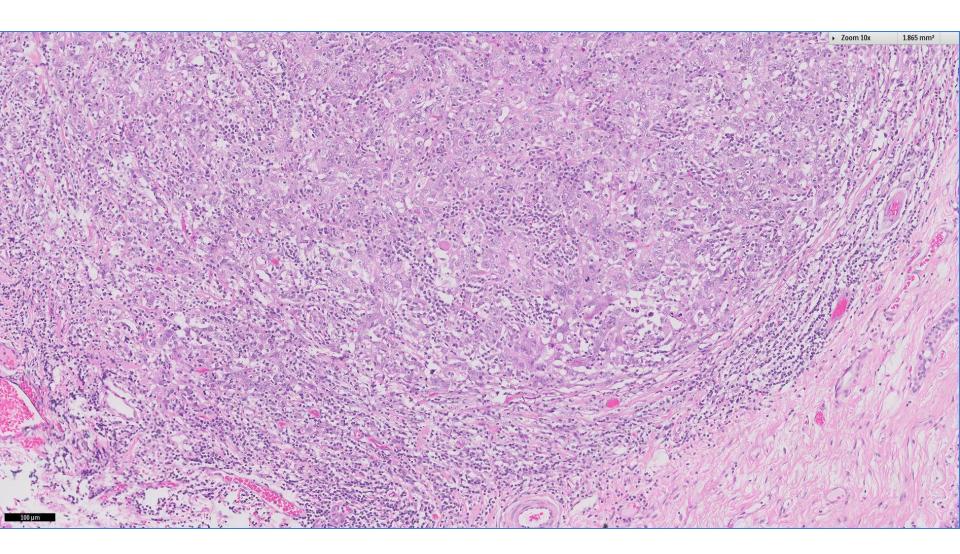
72 year old woman underwent right mastectomy for biopsy confirmed invasive carcinoma.

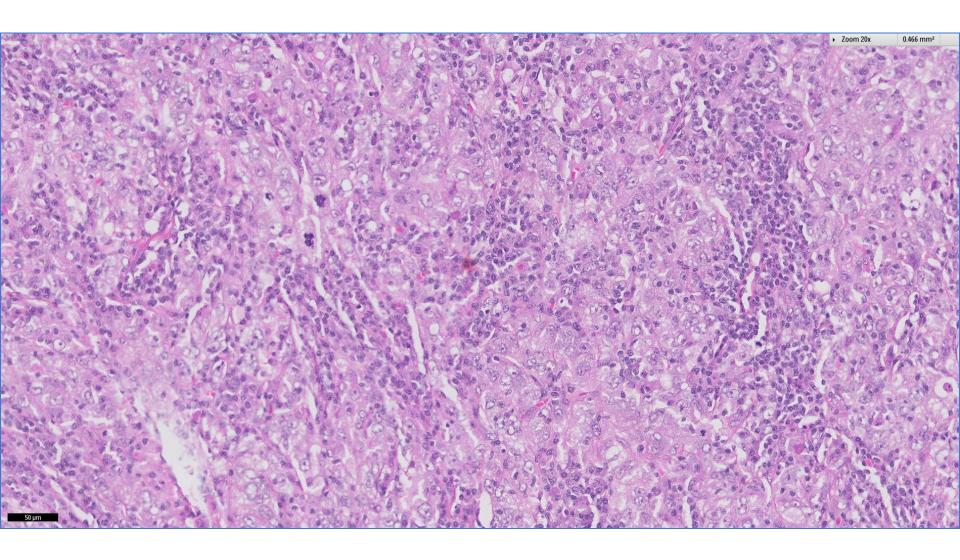


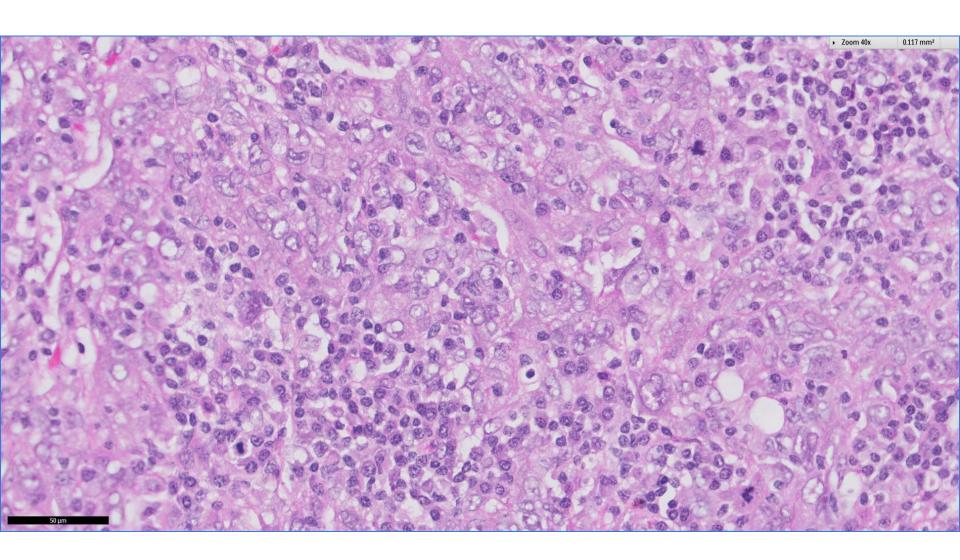




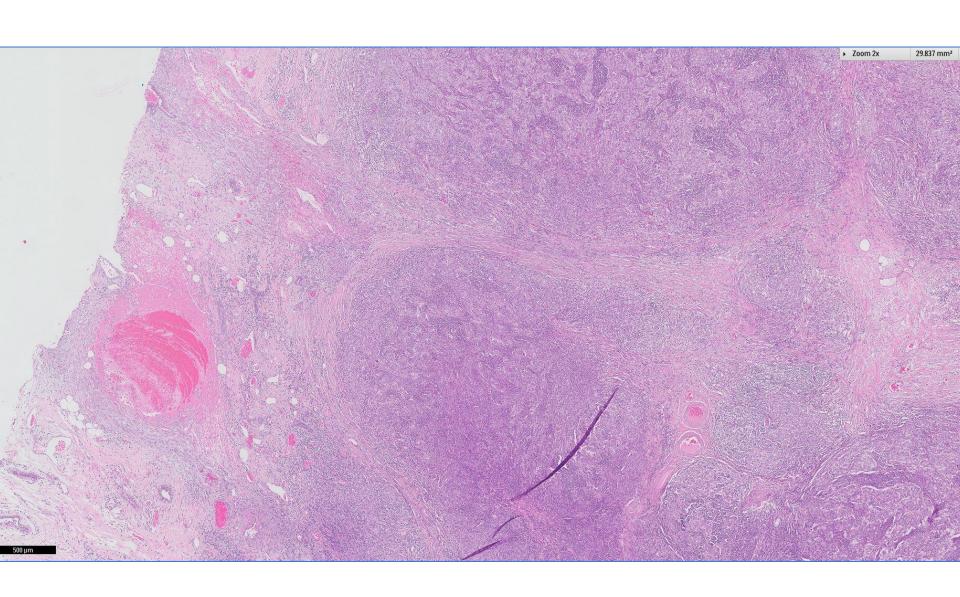


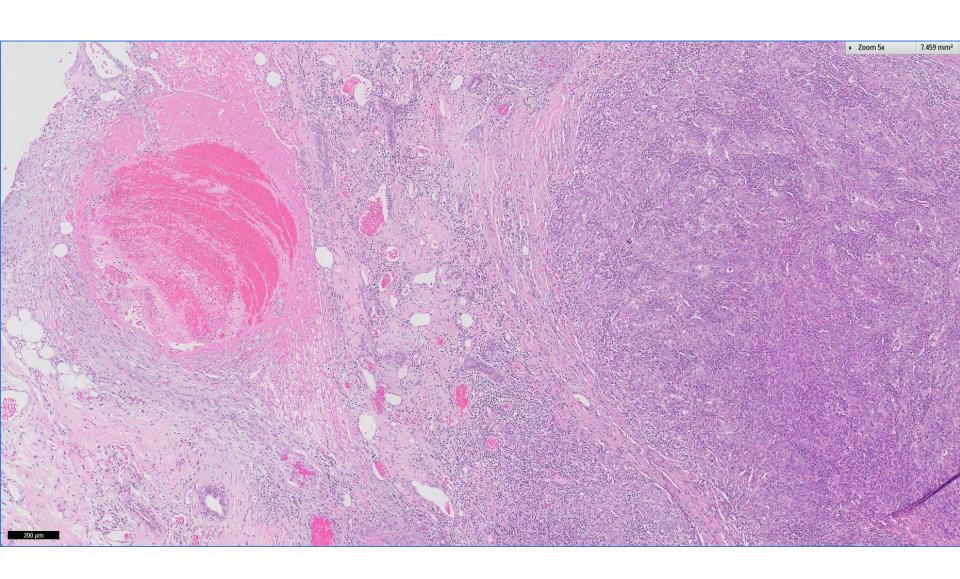


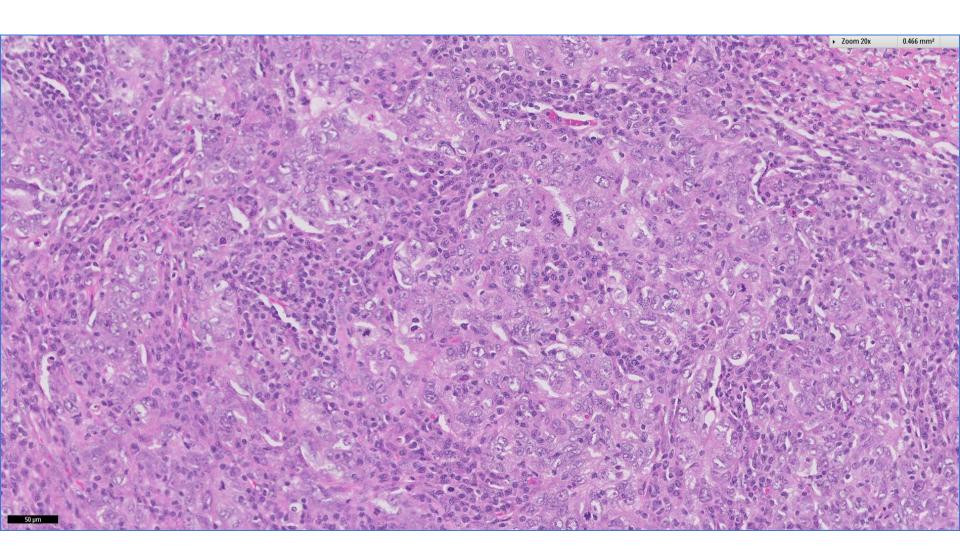


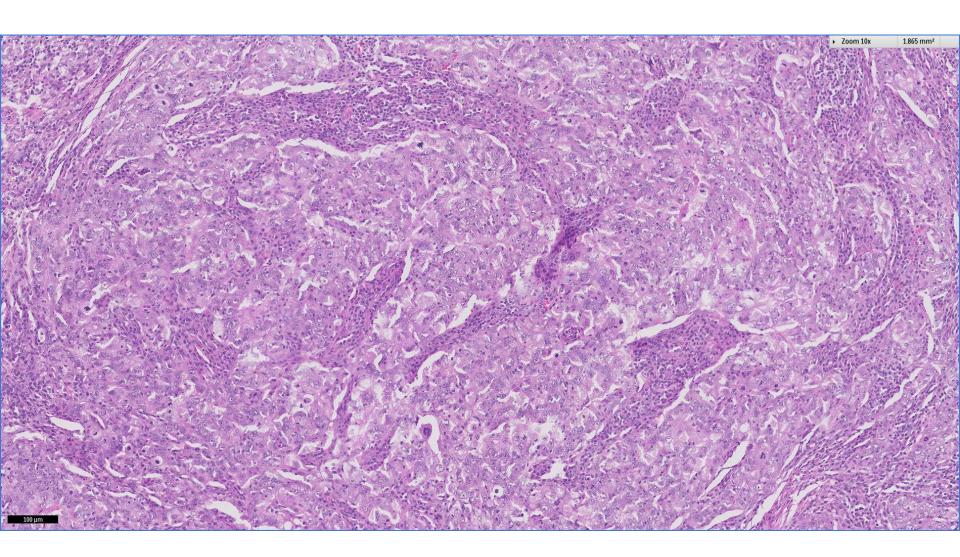


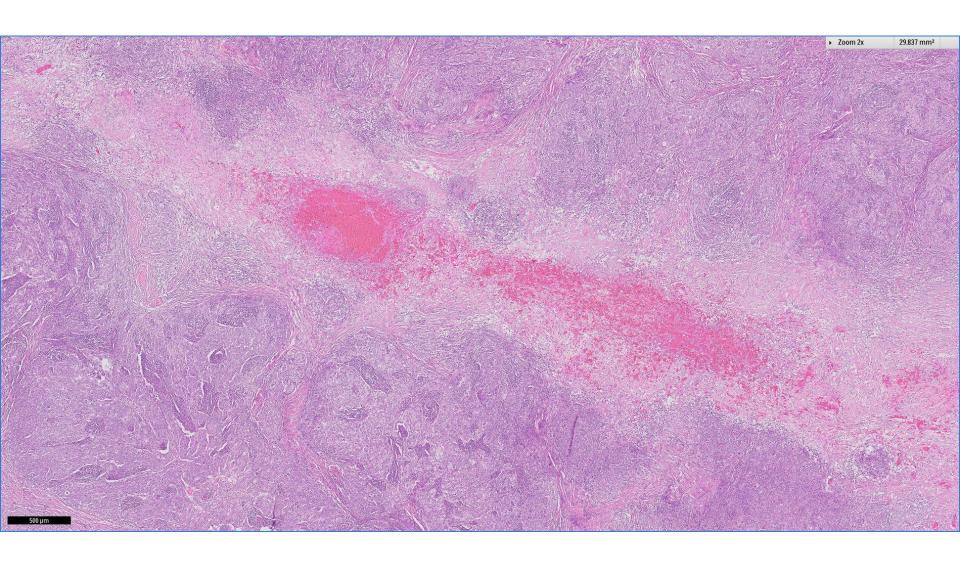


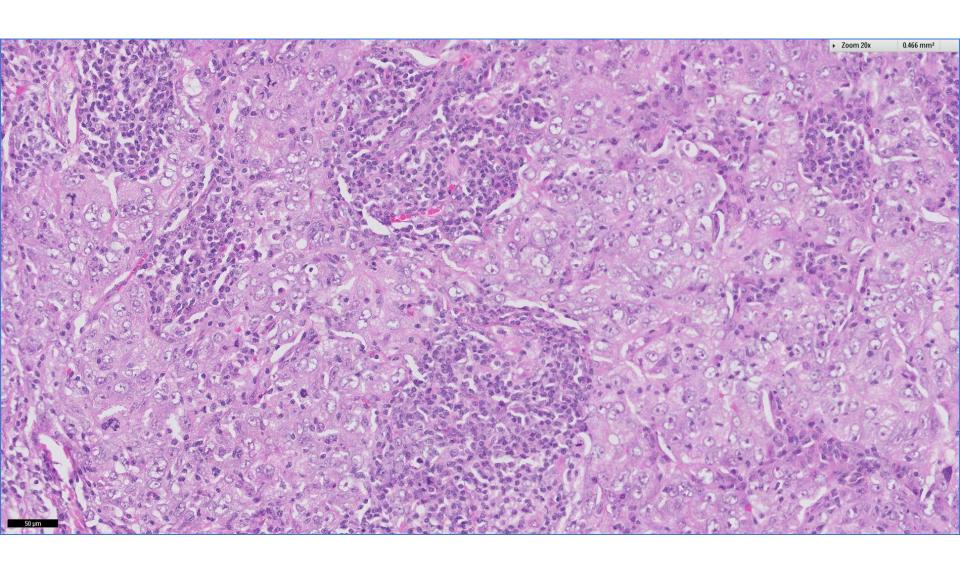


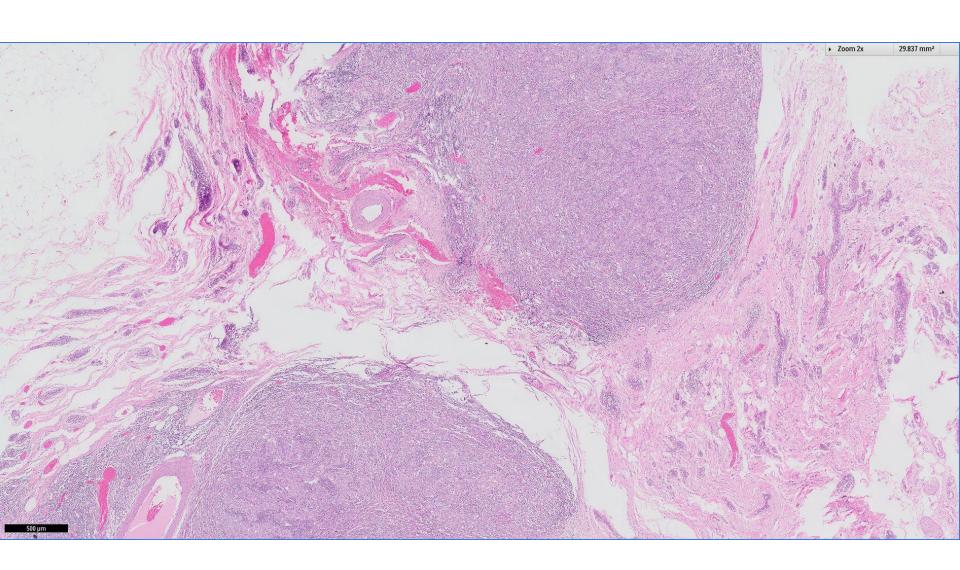












Right breast, mastectomy and axillary clearance:

Atypical medullary carcinoma, grade 3, 23mm.

2 out of 31 axillary lymph nodes show metastases.





Carcinomas with medullary differentiation

- Medullary carcinoma
- Atypical medullary carcinoma
- Invasive carcinoma of no special type with medullary-like features





Medullary carcinoma

Classical criteria:

- Syncytial architecture in > 75% of tumour mass.
- Histological circumscription with pushing margins.
- Lack of tubular differentiation.
- Prominent and diffuse lymphoplasmacytic infiltrate.
- High grade pleomorphic nuclei with brisk mitoses.





- Atypical medullary carcinoma
- Carcinoma with medullary-like features
 - Refer to tumours that do not fulfil all histological criteria.
- Difficulty in applying diagnostic criteria.
- Poor interobserver reproducibility.





Table 3.01 Comparative immunohistochemical profiles (% of cells expressing the given marker)

			ypical medullary reast cancer {634}	Invasive carcinoma with medullary features {1194}	Invasive carcinoma, grade 3 {1135}
Nielsen Basal profile (ER-negative/HER2-negative and keratin 5/6-positive and/or EGFR-positive)			Not evaluated for this signature	62.9%	18.9%
ER-negative		Triplo	89.5%	94.3%	38.5%
PR-negative	<u> </u>	Triple negative	48.7%	77.1%	34%
HER2-negative_		3	97.7%	100%	76.2%
Keratin 5/6-positiv	/e	Basal-	54.8%	60%	17.9%
P-cadherin-positiv	/e _	like	65.6%	40%	7.9%
p53-positive			69.3%	65.7%	31.6%
Ki67 > 50%			54.5%	91.2%	63.2%
Cyclin E			31.4%	65.2%	26.2%
P-cadherin-positive/Ki67 > 50% HER2-negative/p53-positive			54%	20%	0%
EGFR, epidermal growth factor receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.					

WHO Classification of Breast Tumours 2012

Carcinomas with medullary features

- Medullary carcinoma considered to have a favourable prognosis compared with grade-matched invasive cancer NST.
- 10 year distant relapse free survival rate of 94.9% vs 77.5% for invasive cancer NST (*Vu-Nishino et al. Int J Radiat Oncol Biol Phys 62: 1040-41, 2005*).
- Low reproducibility limits reliance on study results.
- Current practice of treating carcinomas with medullary features as basal-like triple negative disease with aggressive therapy.





Carcinomas with medullary features

- Prognostic importance of lymphoplasmacytic infiltrates.
- Expression levels of immune response genes are independent predictors of outcome in both ER positive and ER negative breast cancers with high proliferative activity.
- Improved clinical behaviour of medullary cancer may be related to the prominent lymphoplasmacytic infiltrates.





Carcinomas with medullary features: implications of 'new' WHO classification

- Acknowledges the low reproducibility of original criteria of medullary carcinoma.
- Allows widening the spectrum of these tumours with similar biological features:
 - Triple negativity.
 - Basal-like expression.
 - Hereditary breast cancer.





