

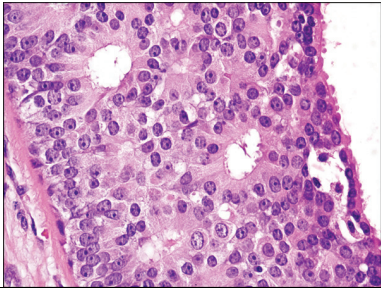
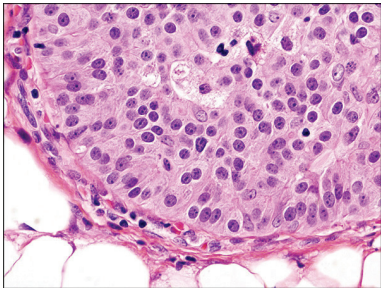
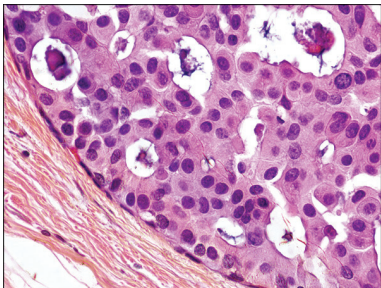
Ductal Carcinoma in Situ (DCIS)

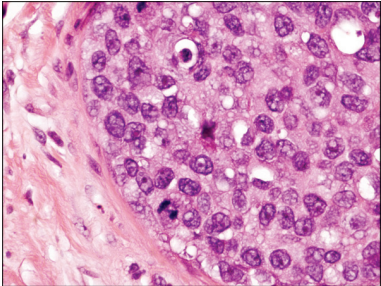
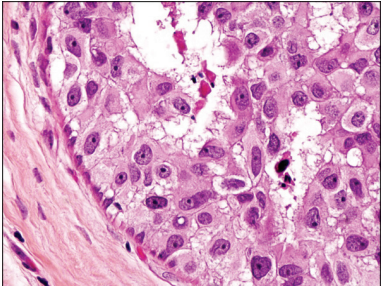
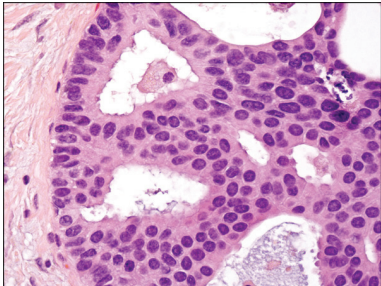
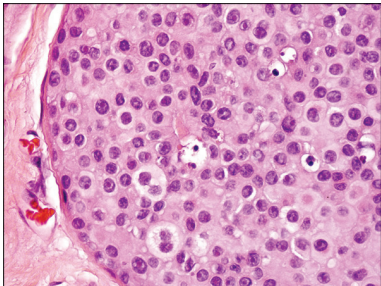
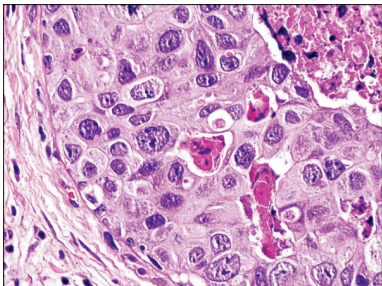
Heterogeneity of Histological Grade Within Cases

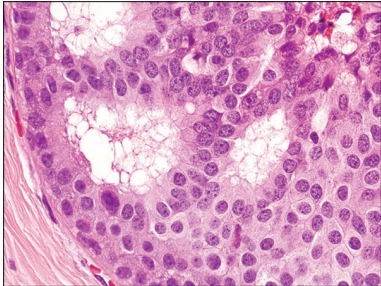
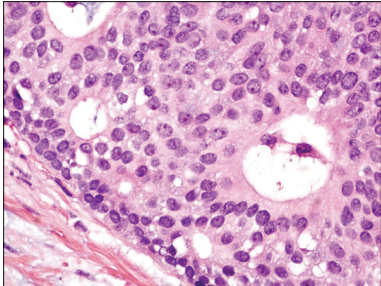
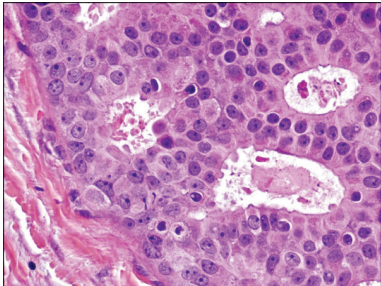
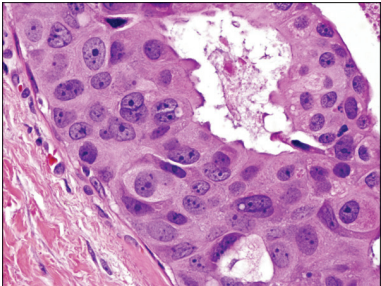
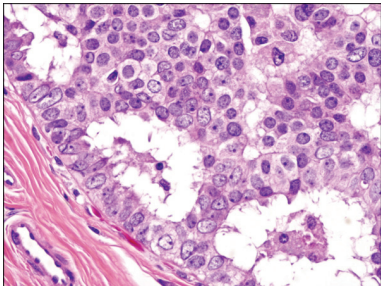
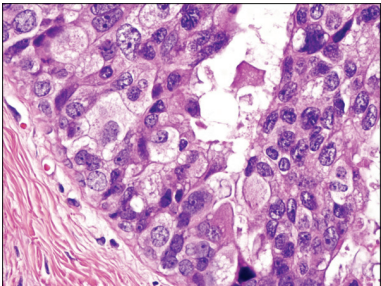
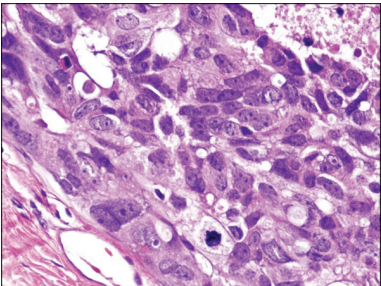
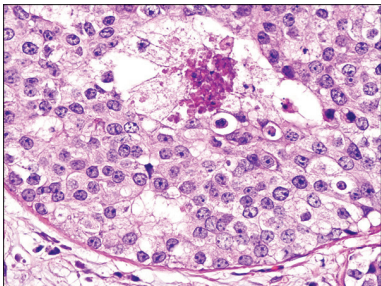
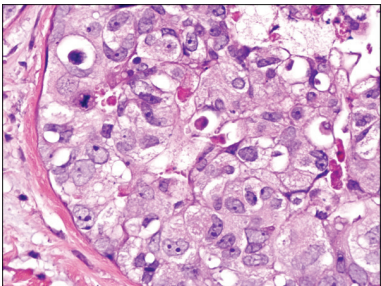
“Grade” refers to Black’s nuclear grading scheme as modified by Fisher (Cancer 36:1-85, 1975):

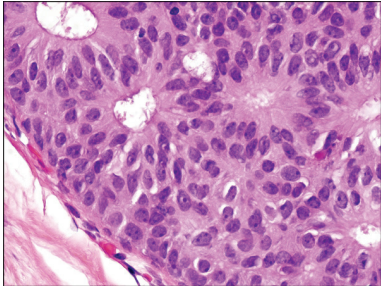
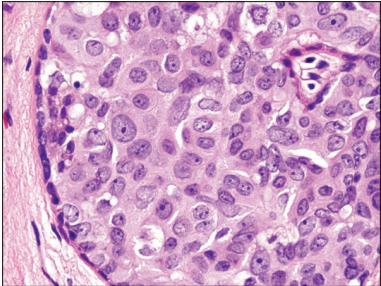
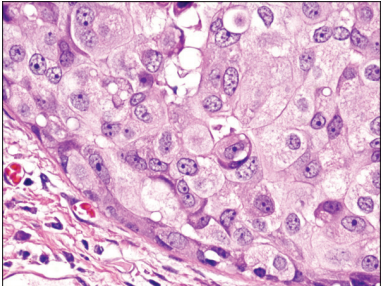
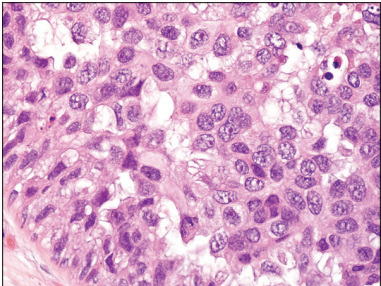
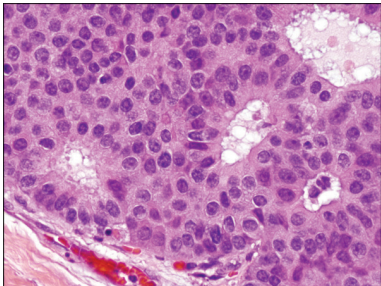
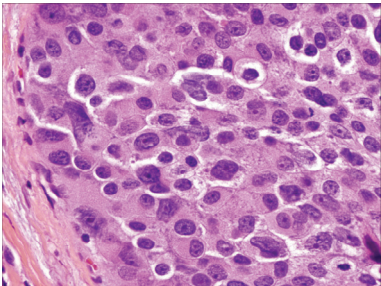
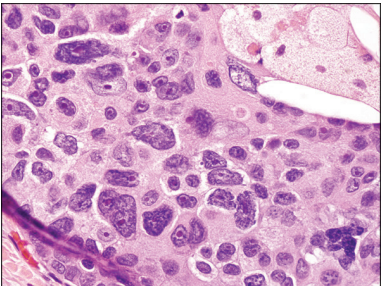
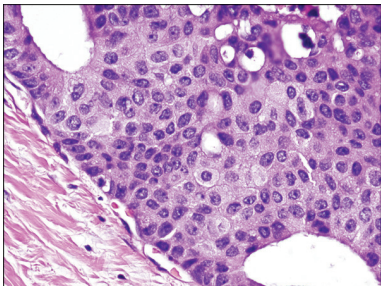
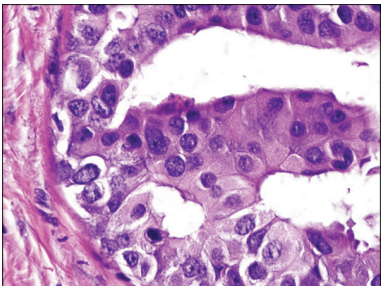
<u>Grade</u>	<u>Size</u>	<u>Pleomorphism</u>	<u>Nucleoli</u>	<u>Chromatin</u>	<u>Mitoses</u>
1	normal/small	normal/minimal	absent/rare	delicate	absent/rare
2	intermediate	intermediate	intermediate	intermediate	intermediate
3	large	marked/irregular	prominent	coarse	common

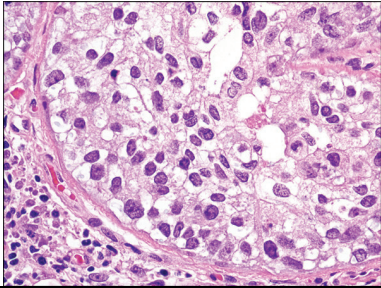
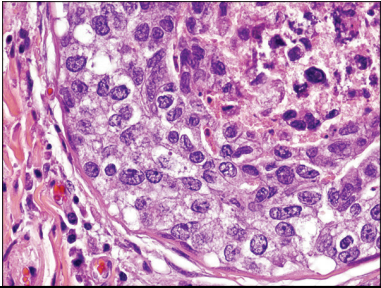
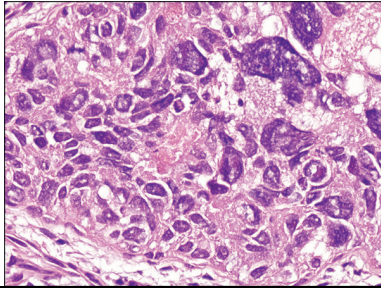
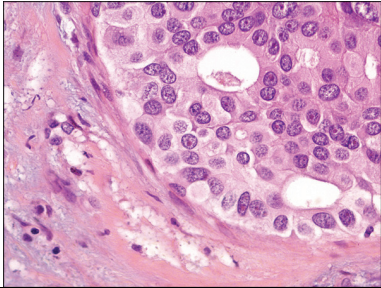
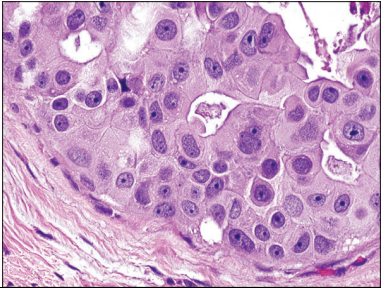
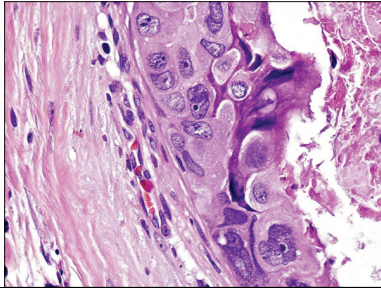
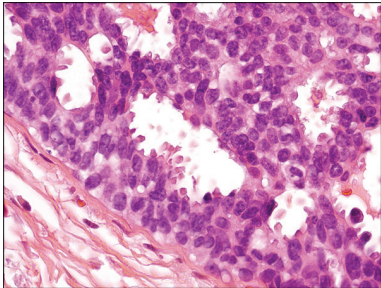
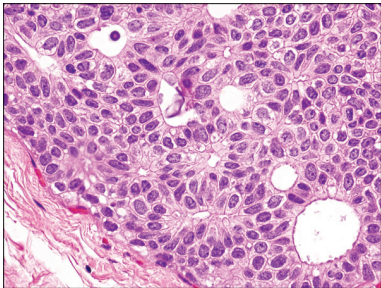
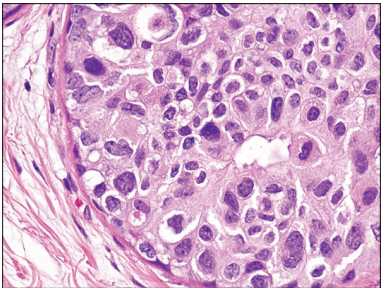
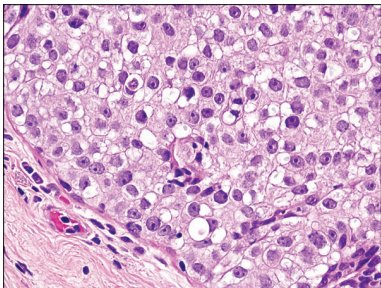
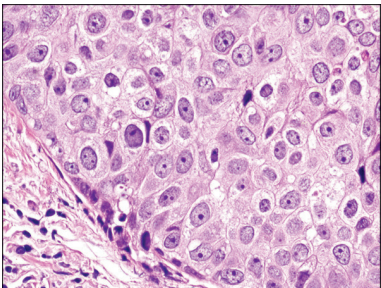
Note: These representative photomicrographs (all at 400X magnification) are from 120 recent consecutive cases in which at least 2 H&E-stained slides containing DCIS were available for review (average = 3.4 slides/case). The estimated percent contribution of each nuclear grade (minimum threshold = 5%) to the entire tumor is shown above each photomicrograph.

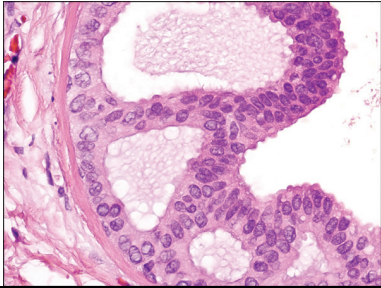
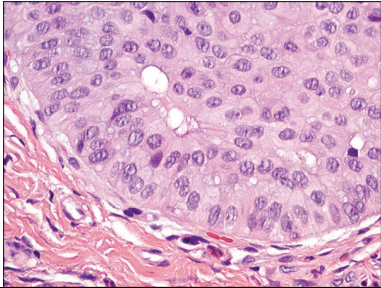
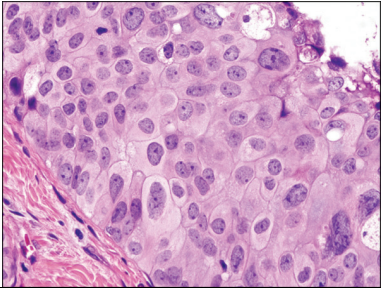
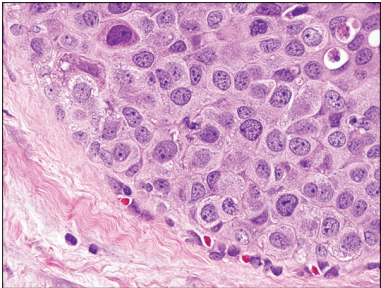
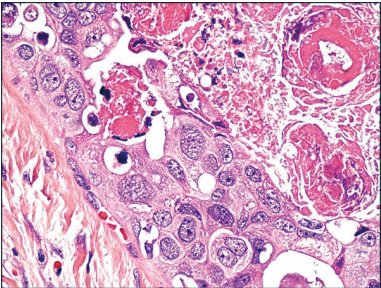
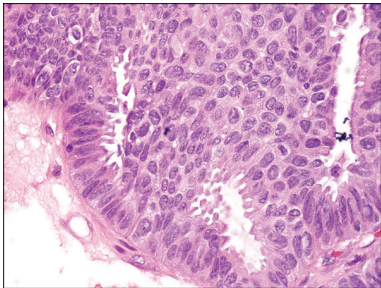
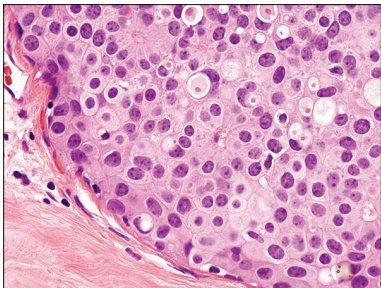
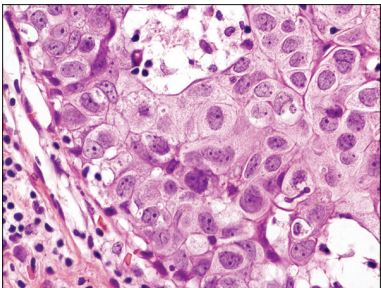
Case #	Grade 1	Grade 2	Grade 3
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002	~100% 	~0%	~0%
003	~100% 	~0%	~0%

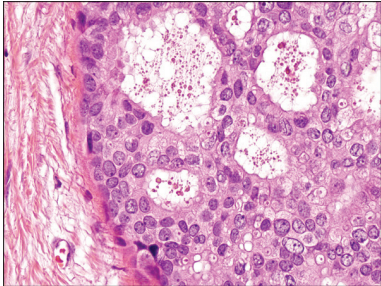
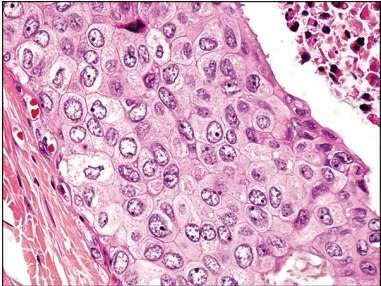
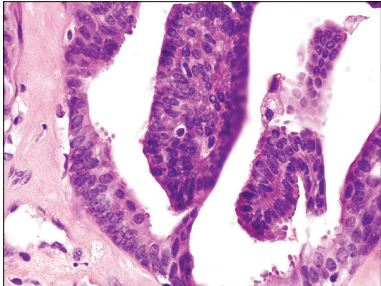
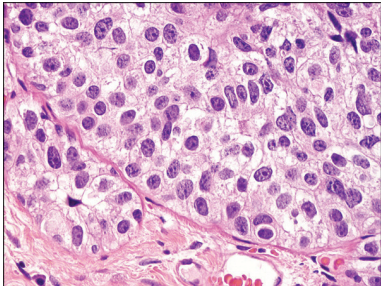
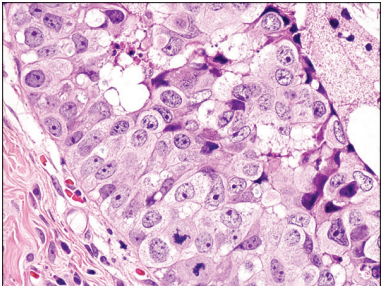
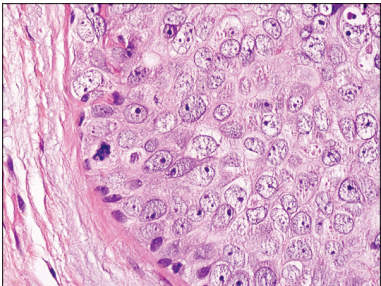
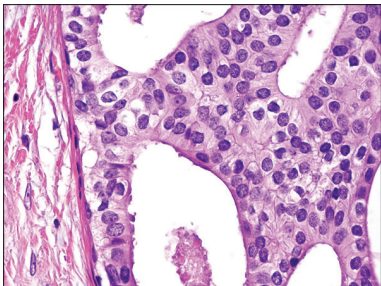
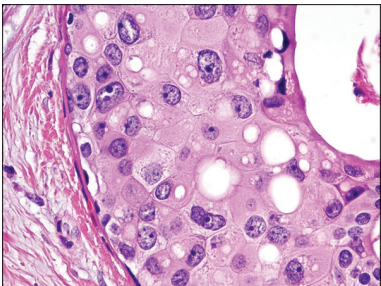
004	~0%	~100%	~0%
			
005	~0%	~100%	~0%
			
006	~100%	~0%	~0%
			
007	~100%	~0%	~0%
			
008	~0%	~0%	~100%
			

009	~100% 	~0% 	~0% 
010	~100% 	~0% 	~0% 
011	~60% 	~40% 	~0% 
012	~45% 	~50% 	~05% 
013	~60% 	~40% 	~0% 

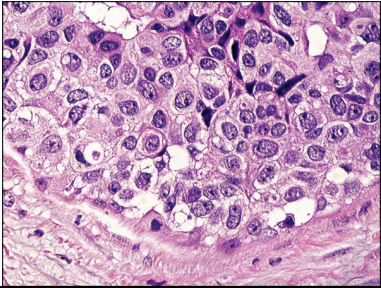
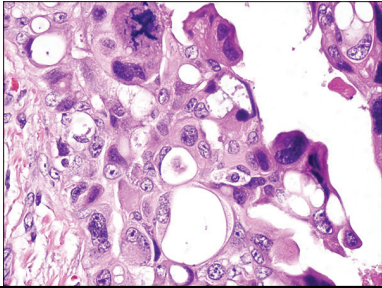
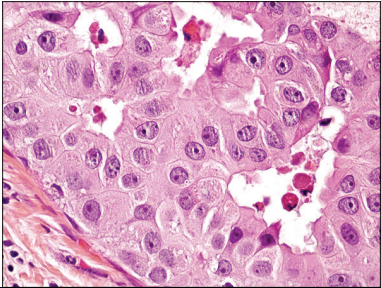
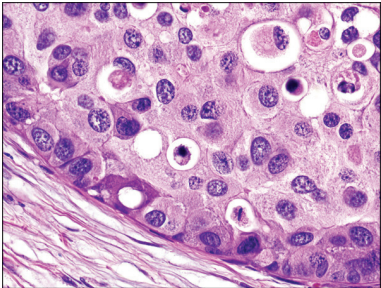
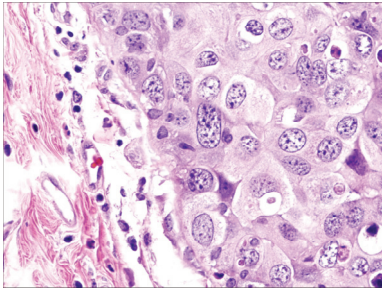
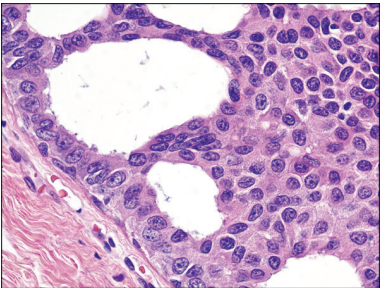
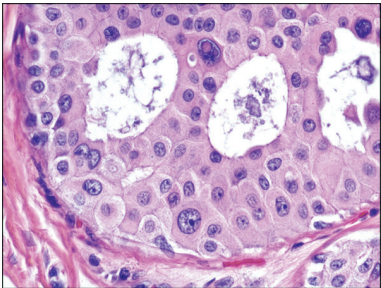
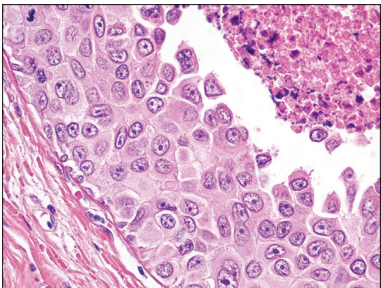
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015	~0% 	~100% 	~0% 
016	~0% 	~100% 	~0% 
017	~80% 	~15% 	~05% 
018	~80% 	~20% 	~0% 

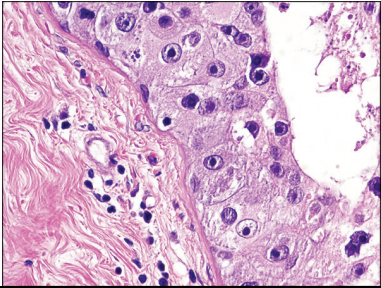
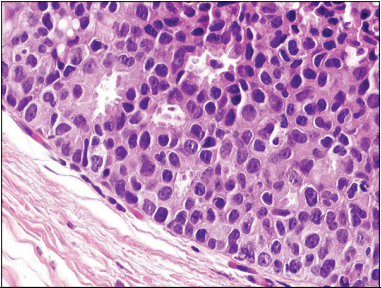
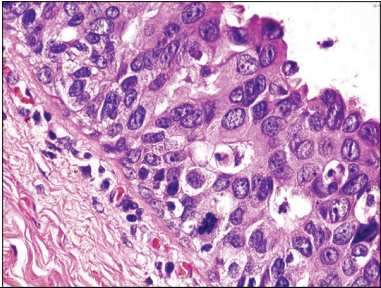
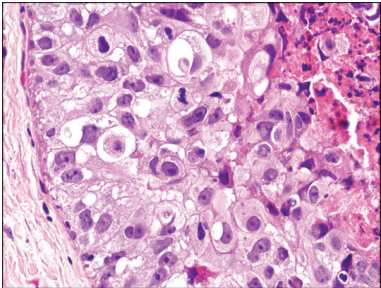
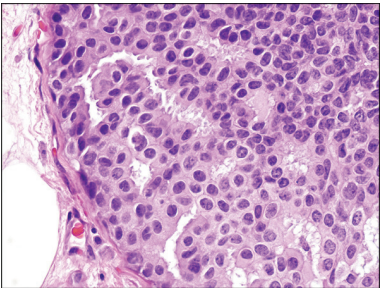
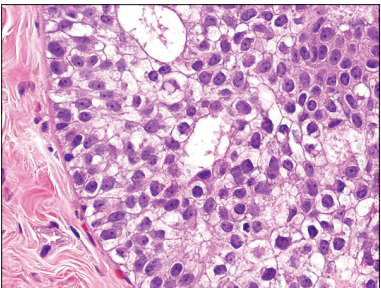
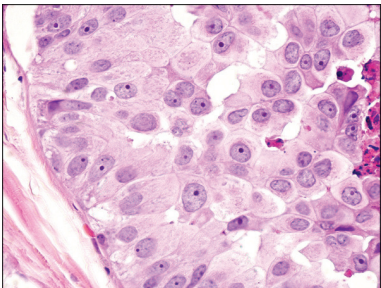
019	~10% 	~80% 	~10% 
020	~05% 	~70% 	~25% 
021	~100% 	~0% 	~0% 
022	~50% 	~50% 	~0% 
023	~80% 	~20% 	~0% 

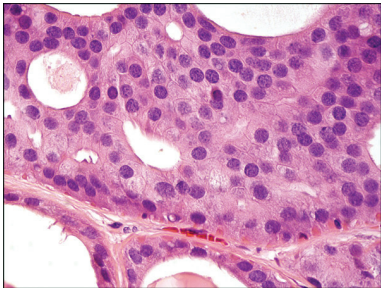
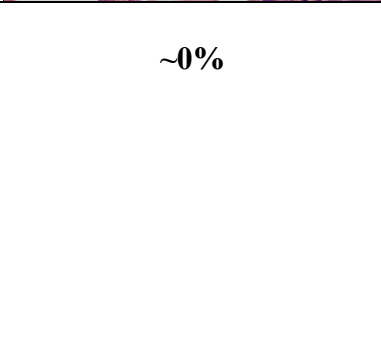
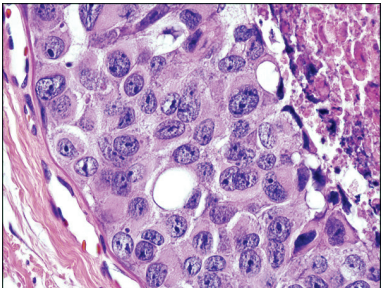
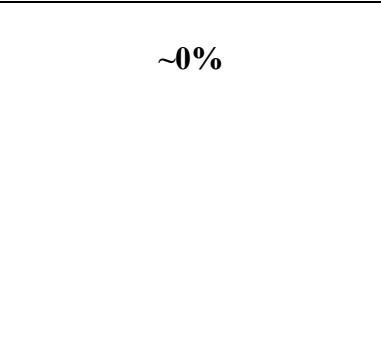
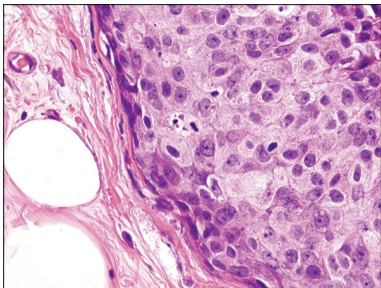
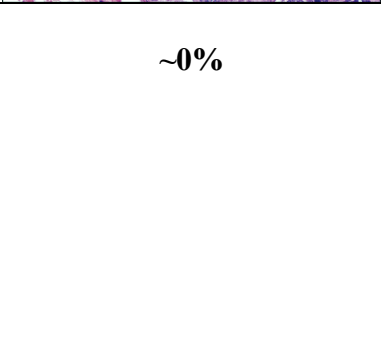
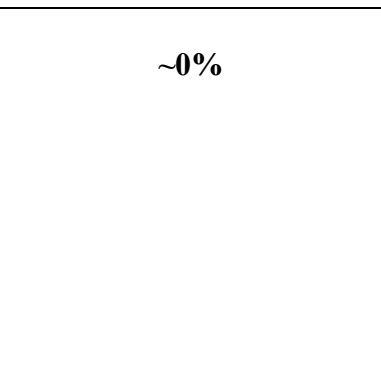
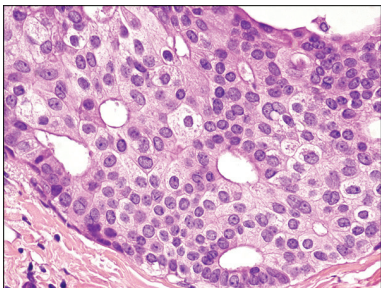
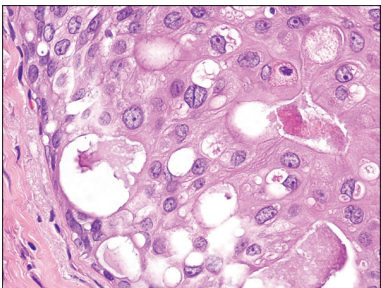
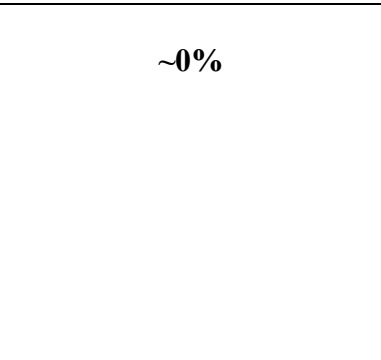
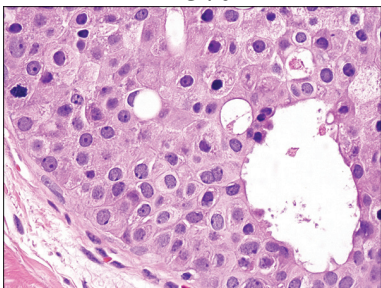
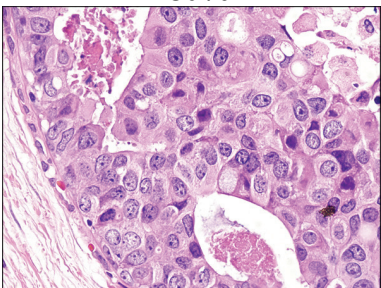
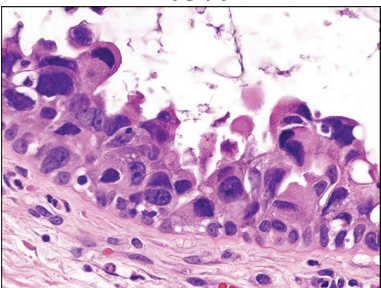
024	~100% 	~0% 	~0% 
025	~80% 	~20% 	~0% 
026	~0% 	~80% 	~20% 
027	~100% 	~0% 	~0% 
028	~80% 	~20% 	~0% 

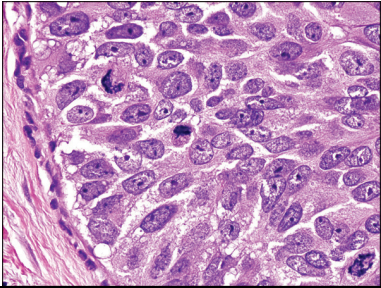
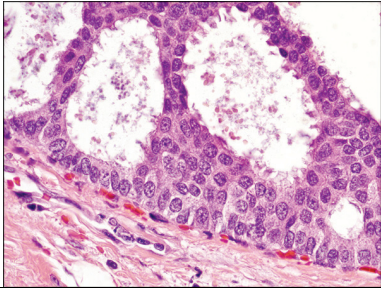
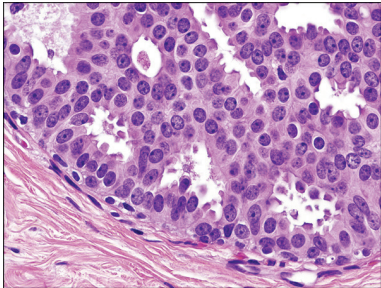
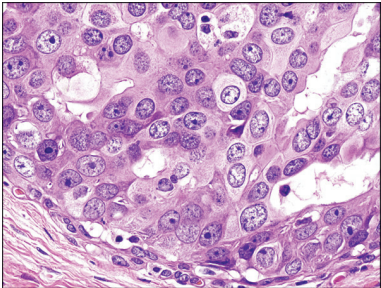
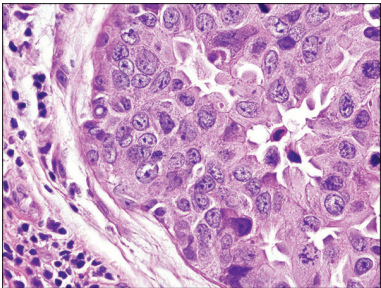
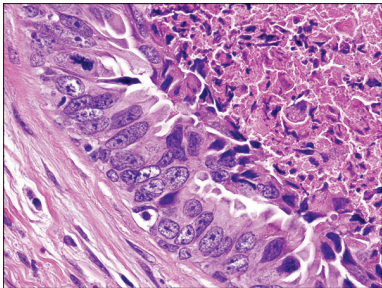
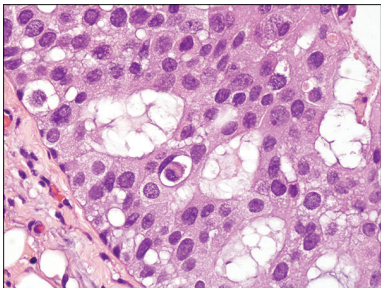
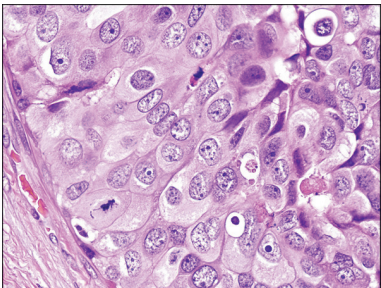
029	~95% 	~05% 	~0%
030	~100% 	~0%	~0%
031	~10% 	~90% 	~0%
032	~0%	~100% 	~0%
033	~05% 	~95% 	~0%

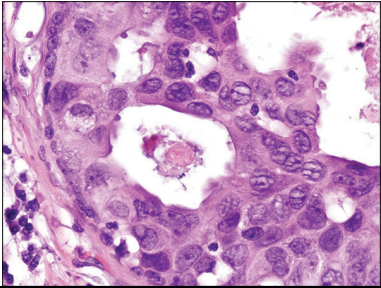
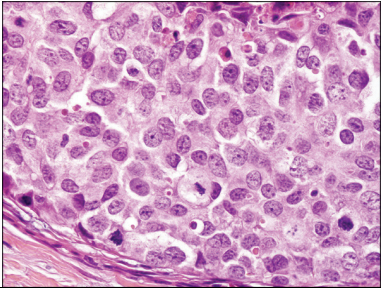
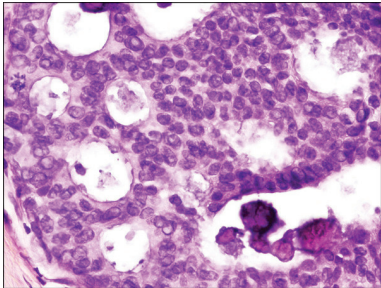
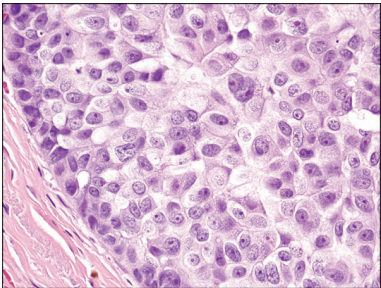
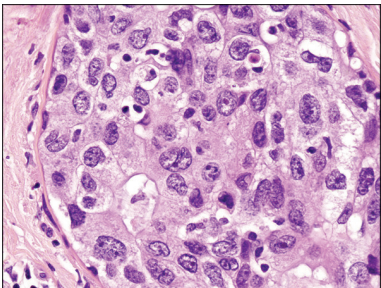
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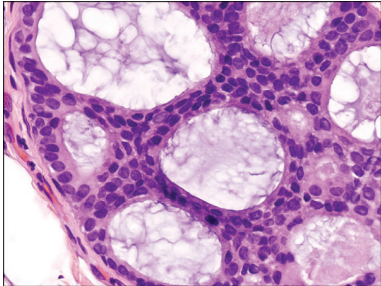
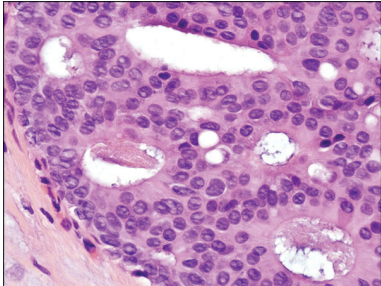
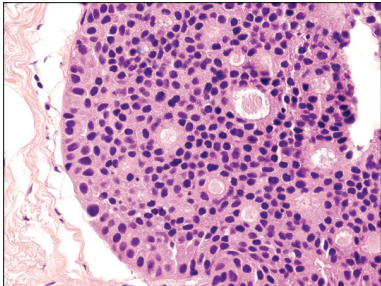
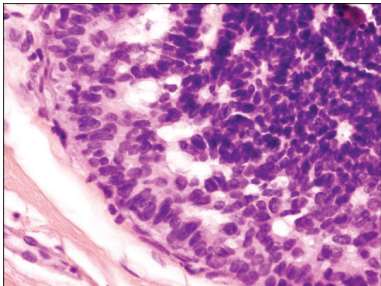
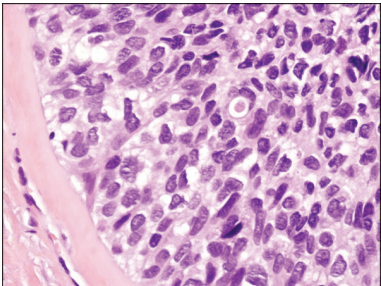
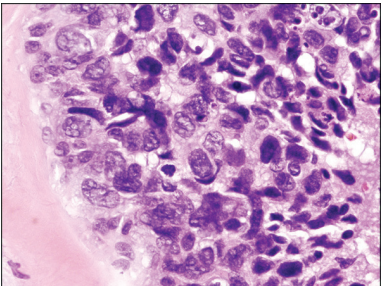
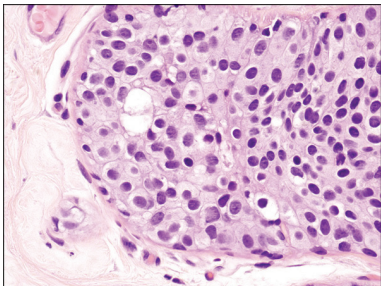
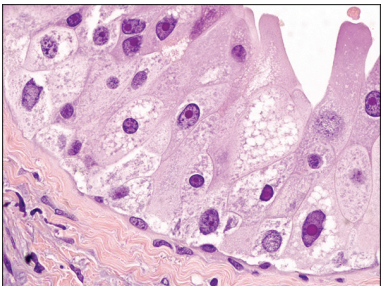
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043	~0%	~100%	~0%
			

044	~0%	~100%	~0%
			
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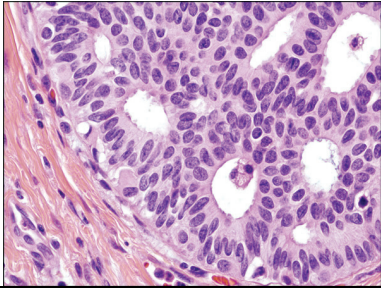
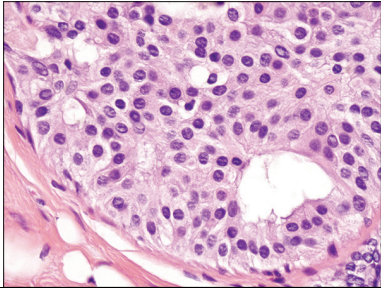
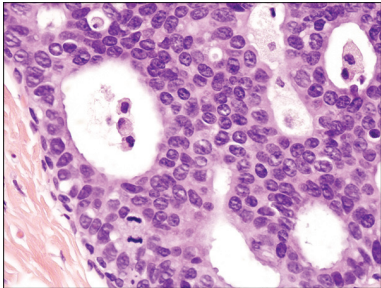
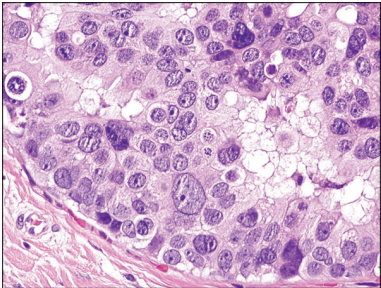
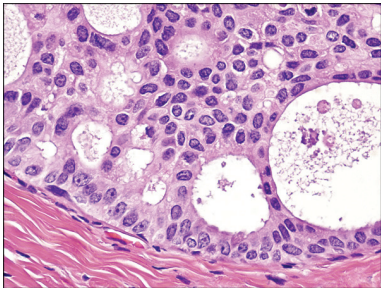
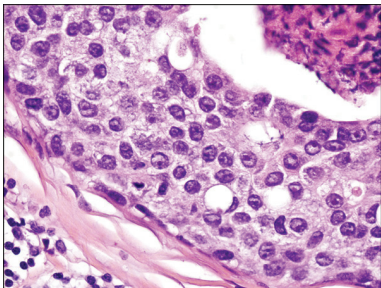
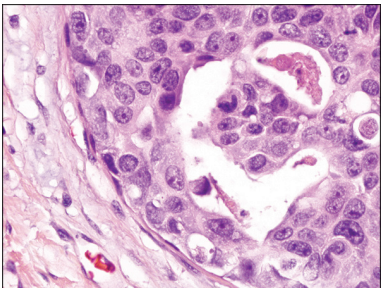
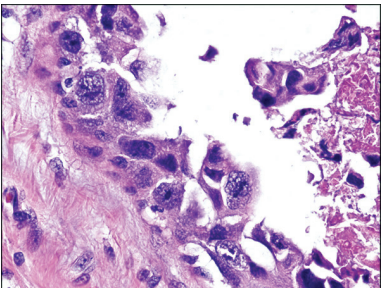
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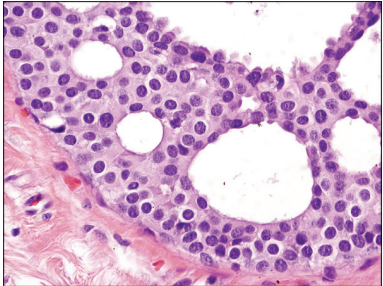
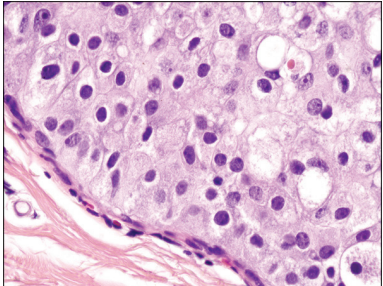
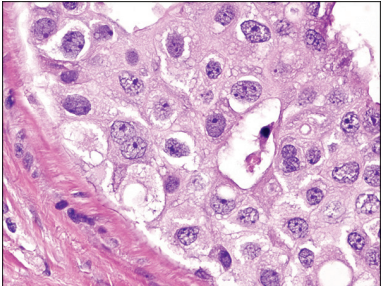
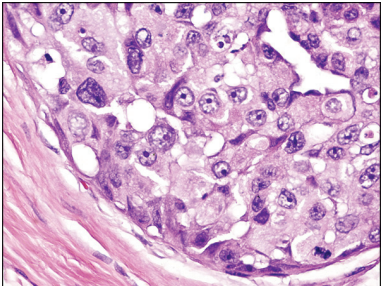
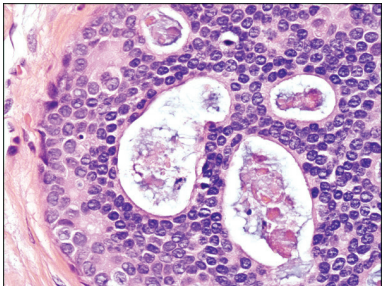
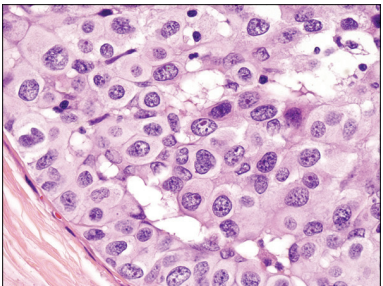
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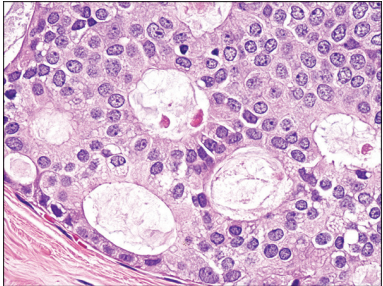
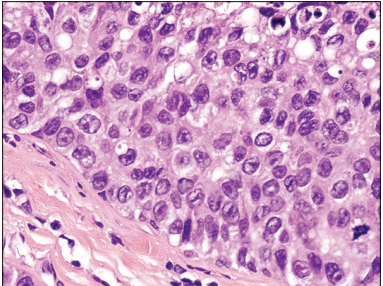
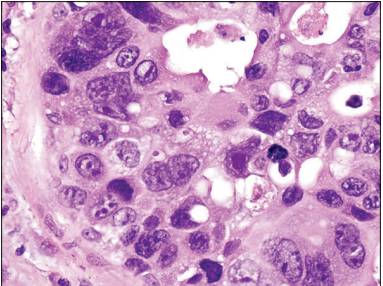
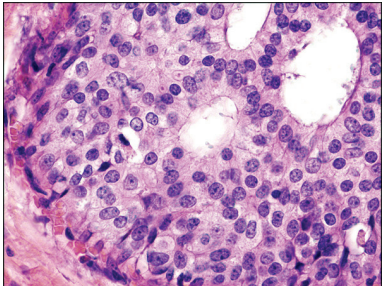
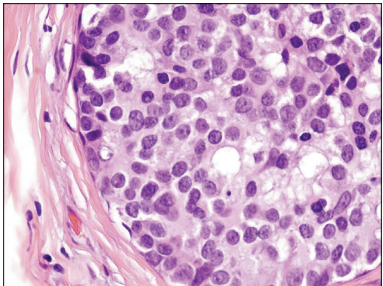
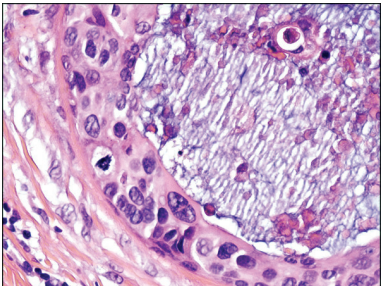
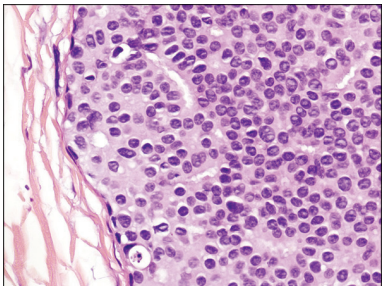
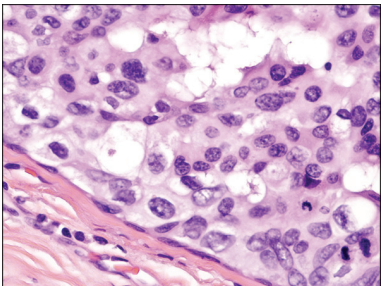
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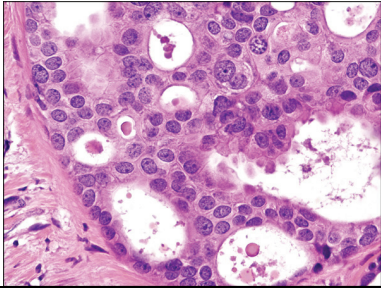
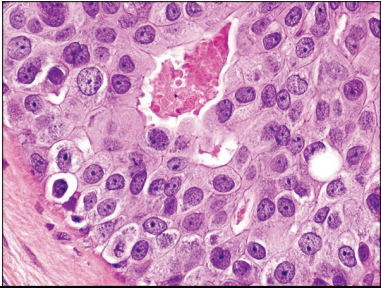
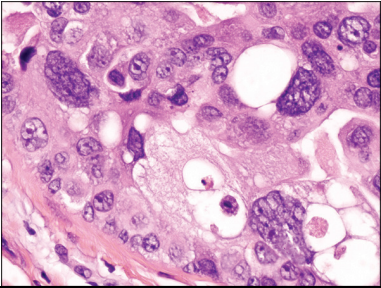
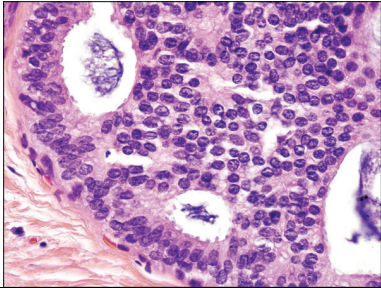
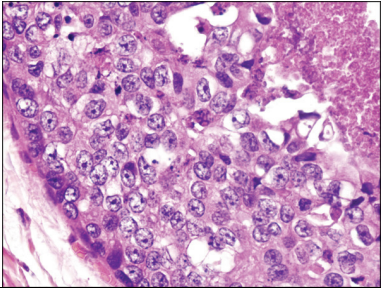
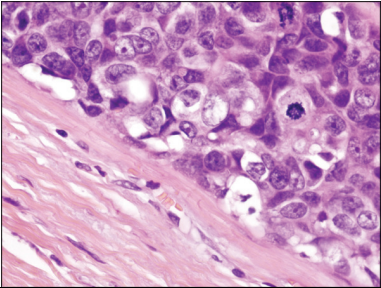
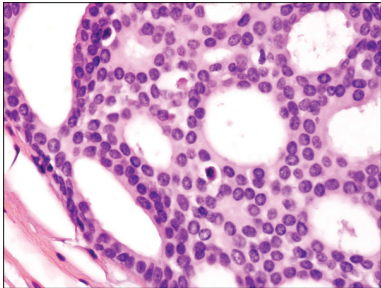
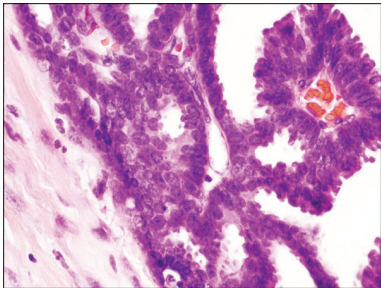
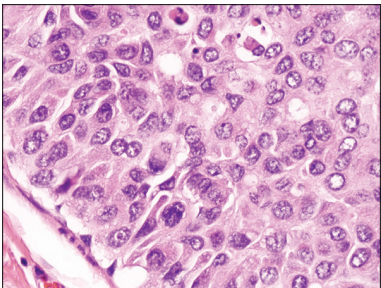
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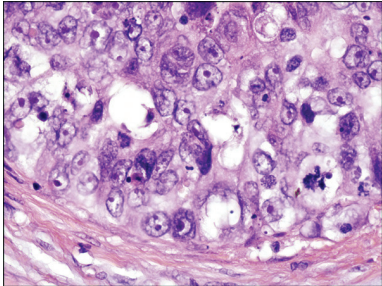
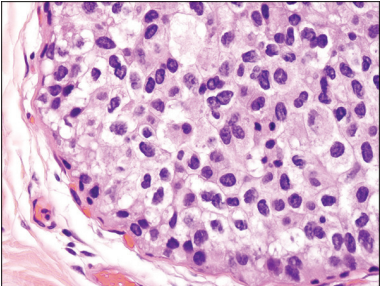
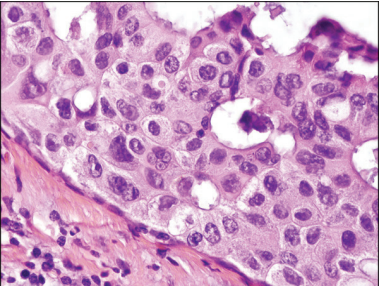
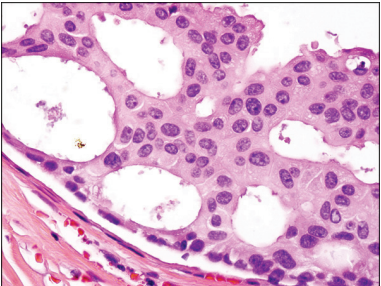
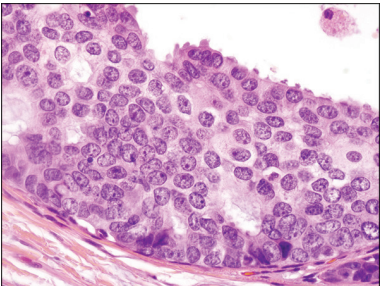
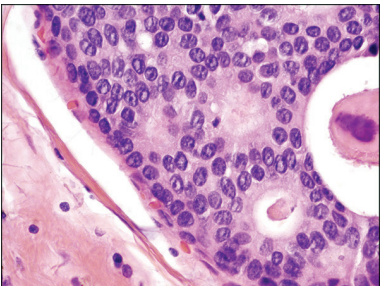
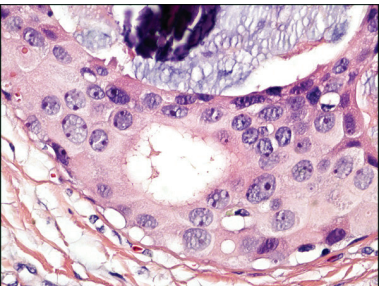
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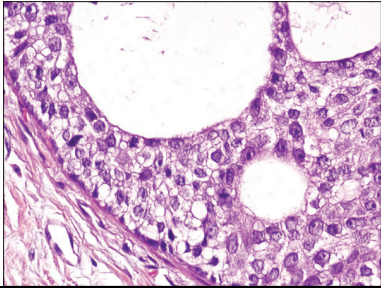
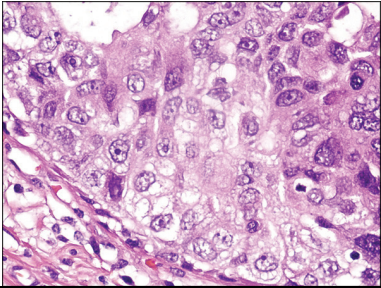
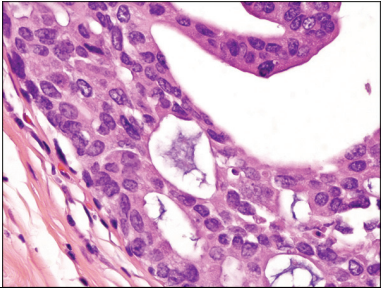
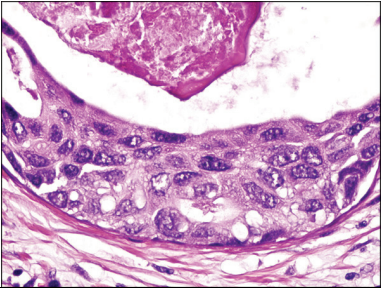
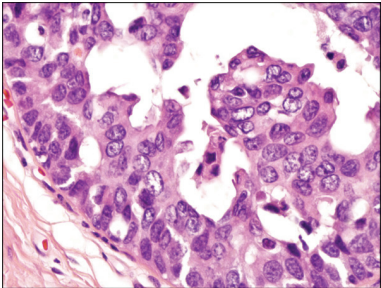
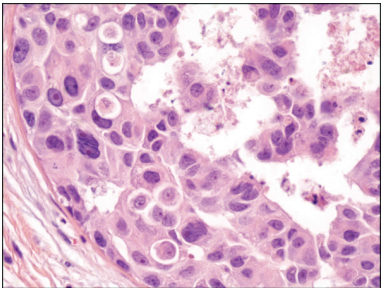
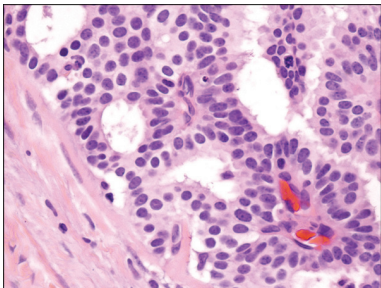
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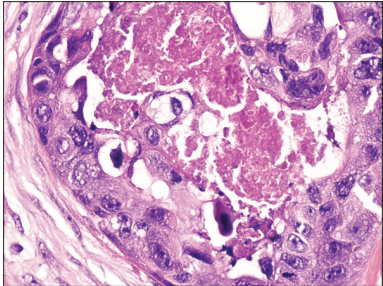
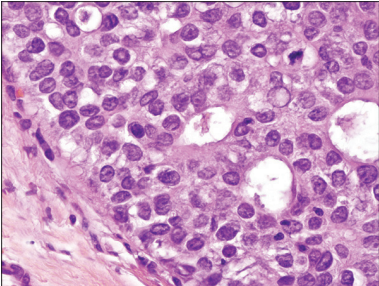
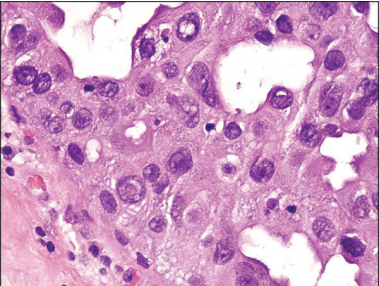
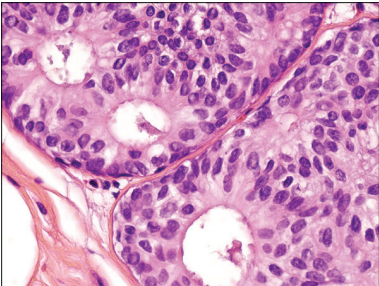
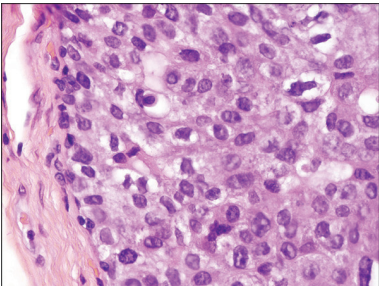
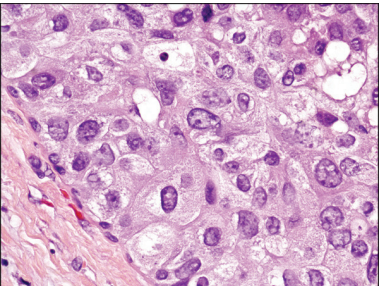
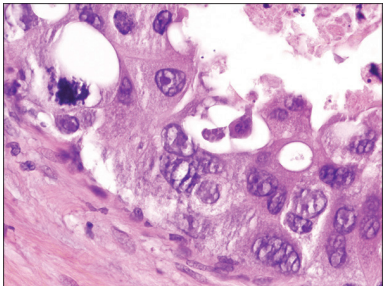
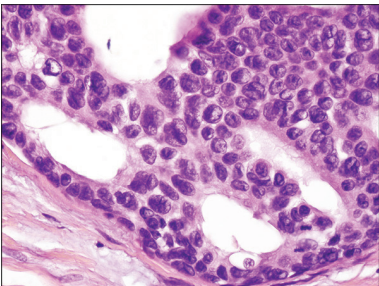
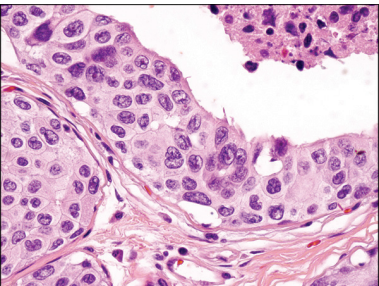
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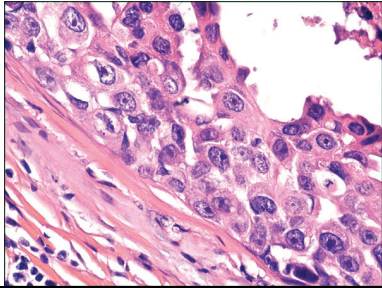
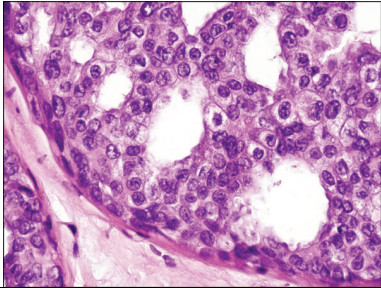
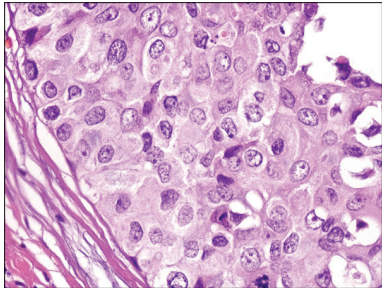
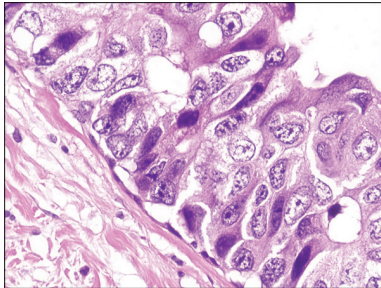
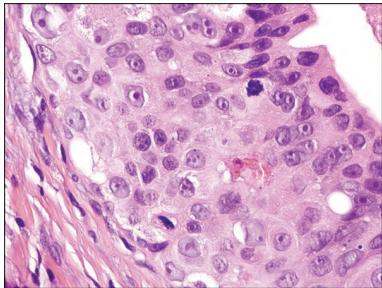
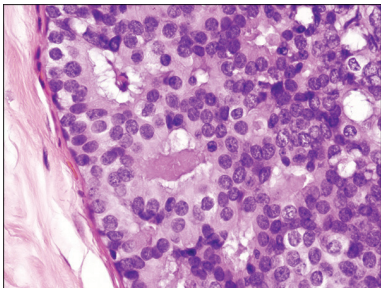
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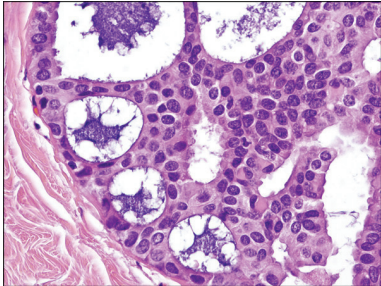
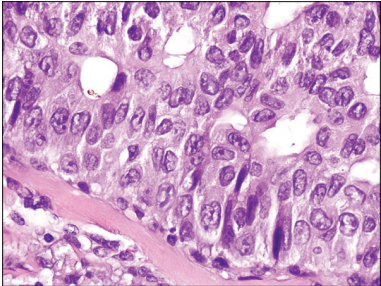
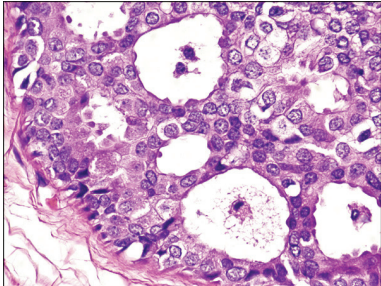
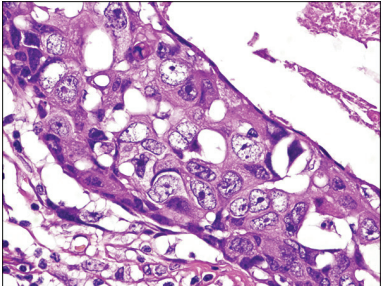
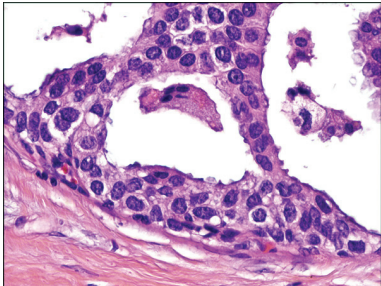
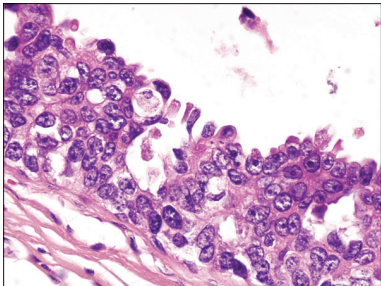
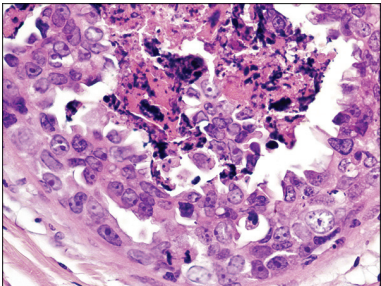
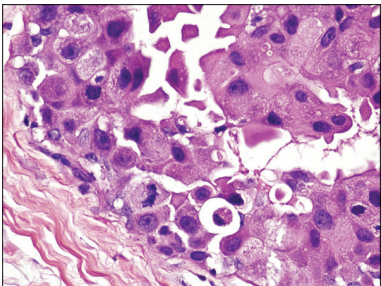
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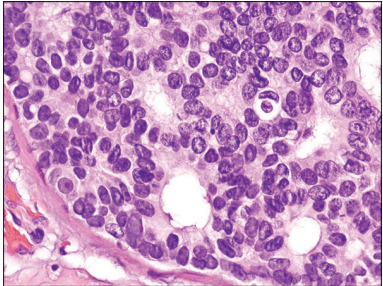
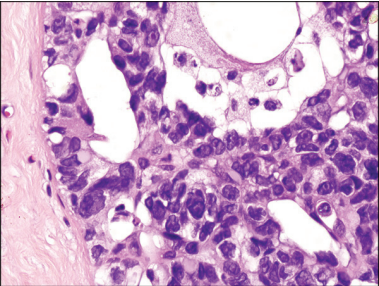
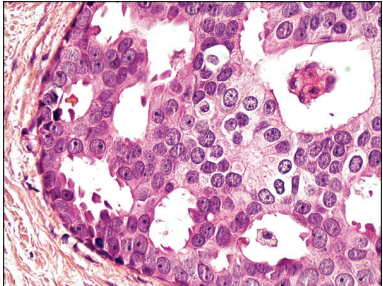
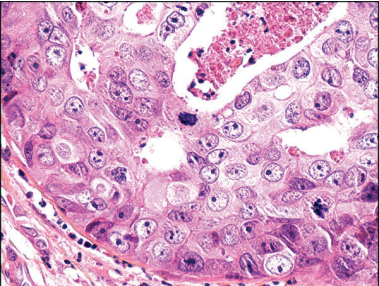
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104	~0%	~0%	~100% 
105	~70% 	~30% 	~0%
106	~100% 	~0%	~0%
107	~10% 	~85% 	~05% 
108	~70% 	~30% 	~0%

109	~0%	~100%	~0%
			
110	~100%	~0%	~0%
			
111	~0%	~60%	~40%
			
112	~0%	~100%	~0%
			
113	~100%	~0%	~0%
			

114	~90% 	~10% 	~0%
115	~60% 	~40% 	~0%
116	~100% 	~0%	~0%
117	~40% 	~60% 	~0%
118	~0%	~100% 	~0%

119	~80% 	~20% 	~0%
120	~50% 	~50% 	~0%

Supplemental Figure S2

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LOH at 15 Loci	Non High Grade	High Grade	P-Value
	DCIS (n=37-63)	DCIS (n=26-45)	
TPO/2pter	2%	11%	ns
D2S362/2q35	8%	15%	ns
D4S192/4q25	2%	8%	ns
D6S417/6qter (ER)	15%	14%	ns
D8S264/8p	21%	17%	ns
D9S157/9p	11%	9%	ns
D11S988/11p15	28%	24%	ns
D11S1328/11q23 (cyclin D)	20%	34%	.03
D13S137/13q13	15%	18%	ns
D14S62/14q24 (MTA1)	20%	17%	ns
D16S265/16q21 (E-cadherin)	34%	23%	.05
D17S960/17p13 (p53)	30%	36%	ns
NF1/17q11	24%	12%	.04
D17S597/17q21 (BRCA1)	19%	16%	ns
D178S787/17q25 (BRCA1)	18%	26%	ns
Average # LOH/Case	1.8/case	2.4/case	.13

LOH

at p53?

Yes (n=24)

No (n=95)

Average #LOH

2.96

1.65

p=0.0001

Supplemental Table S1. Proportion of Invasive Breast Cancers (IBCs) with a Component of Carcinoma in Situ (CIS).

<u>Type IBC</u>	<u>Number (% Total)</u>	<u>% With CIS</u>	<u>% CIS = DCIS</u>	<u>% CIS= LCIS</u>
NST	927 (81.2)	81.3	98.3	1.7
ILC	137 (12.0)	66.4	8.8	91.2
TUB	39 (3.4)	84.6	100	0
MUC	21 (1.8)	76.2	100	0
MED	18 (1.6)	22.2	100	0
Total	1142 (100)	78.6	na	na

Footnotes: Data derived from estimating % CIS in consecutive cases of IBC reviewed by one author (DCA) during the years 2002-2003 at Baylor College of Medicine affiliated hospitals. The material reviewed (average 1.8 H&E-stained slides/cases) represents <1% of total tumor volume and, thus, the estimated proportion of cases containing CIS is the lowest possible estimate. In our opinion, it is likely that a large majority (>90%) of IBCs contain a component of CIS, which most likely represents residual precursors. The IBCs evaluated in this study were restricted to the major subtypes (representing 98% of all IBCs evaluated). Abbreviations: NST = infiltrating ductal carcinoma of no special type; ILC = infiltrating lobular carcinoma; TUB = infiltrating tubular carcinoma; MUC = infiltrating mucinous carcinoma; MED = infiltrating medullary carcinoma.