Journal Club

The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma

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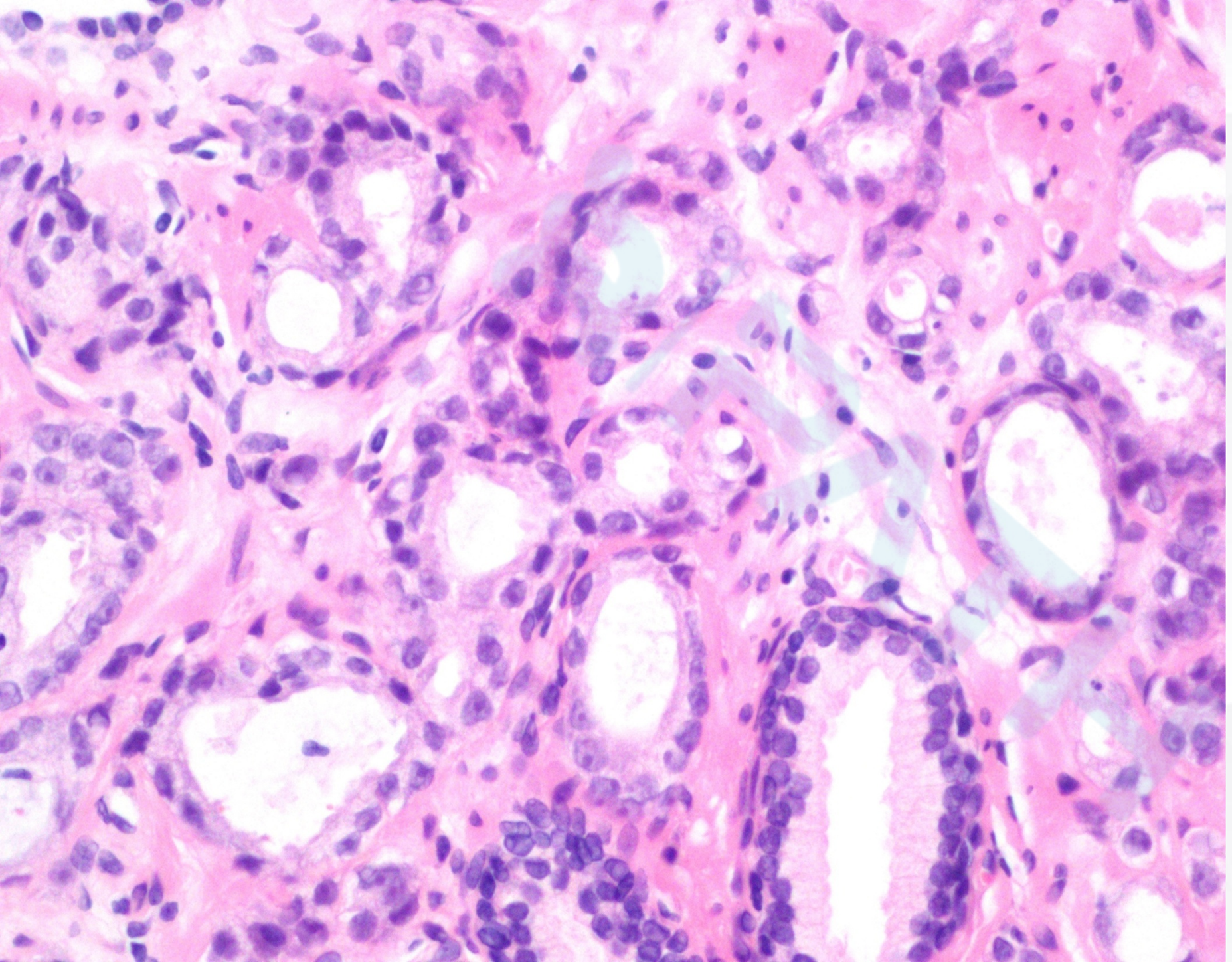
前列腺癌主要的组织学特征

结构
- ◆浸润性生长
- ◆小腺体或融合/不规则筛孔状腺体
- ◆排列拥挤的腺体
- ◆腔缘僵直

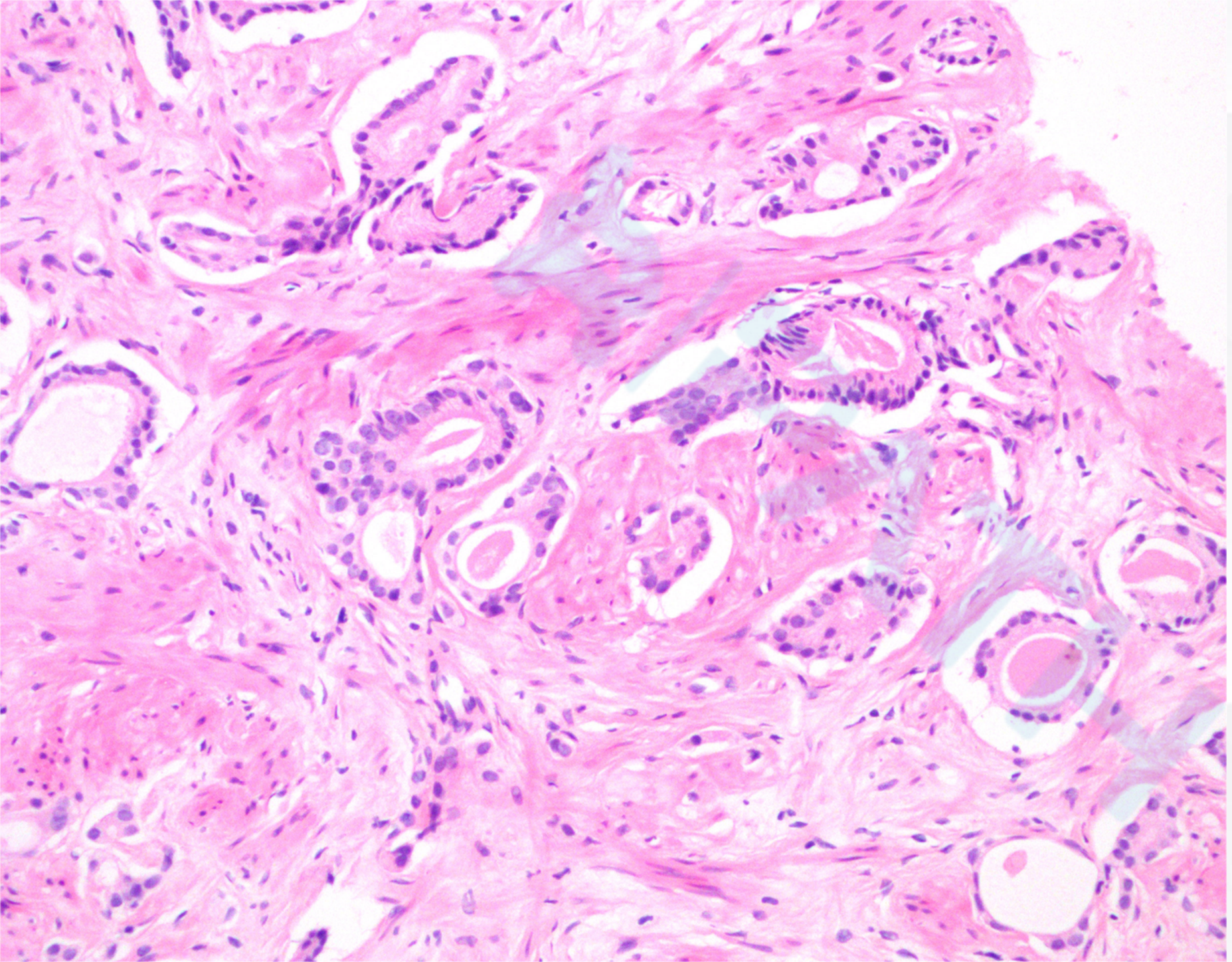
细胞核
- ◆核仁明显
- ◆核增大
- ◆核分裂

细胞浆
- ◆胞浆双嗜性
- ◆蓝染的粘液样分泌物
- ◆类晶体

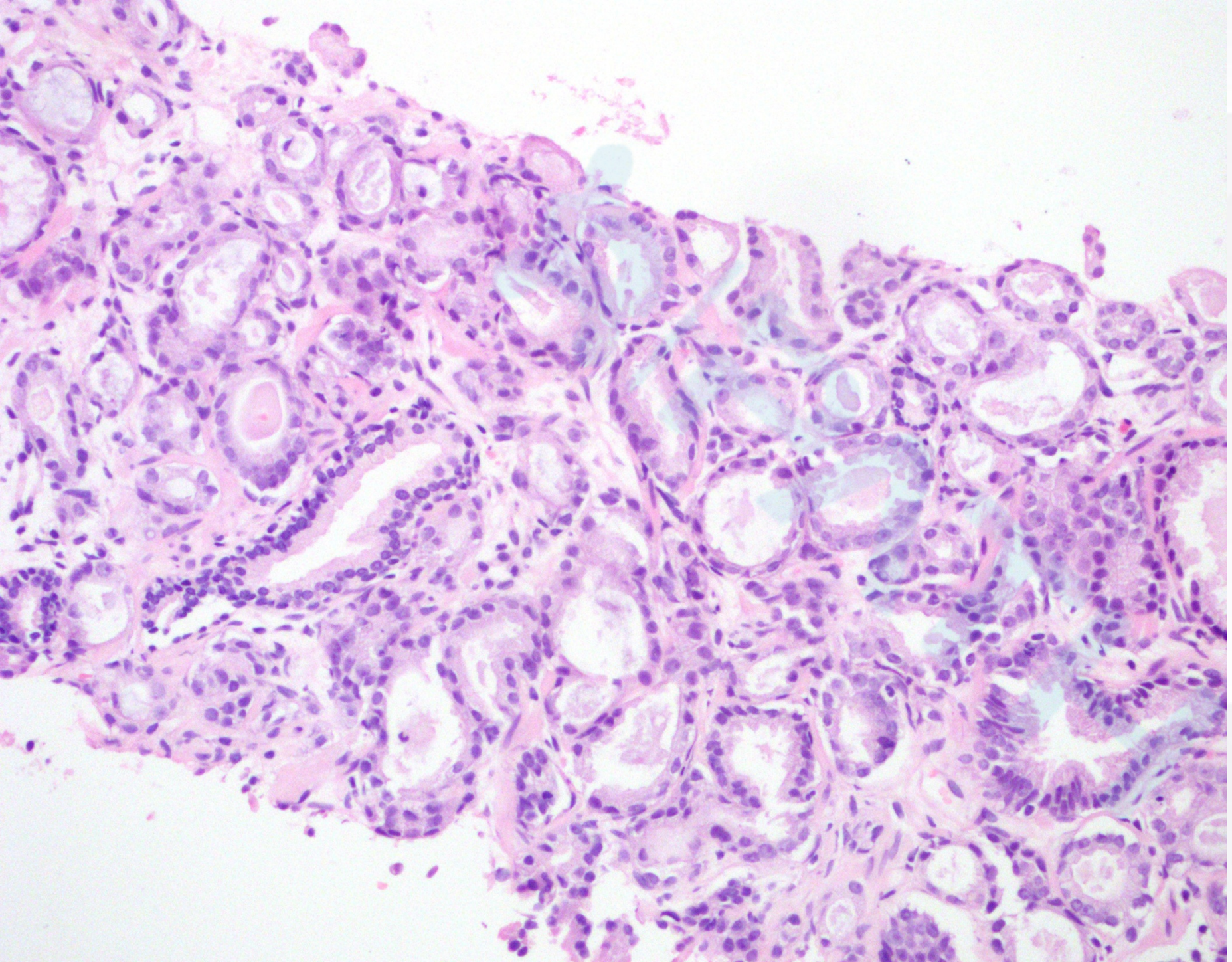


异常结构：浸润正常腺体

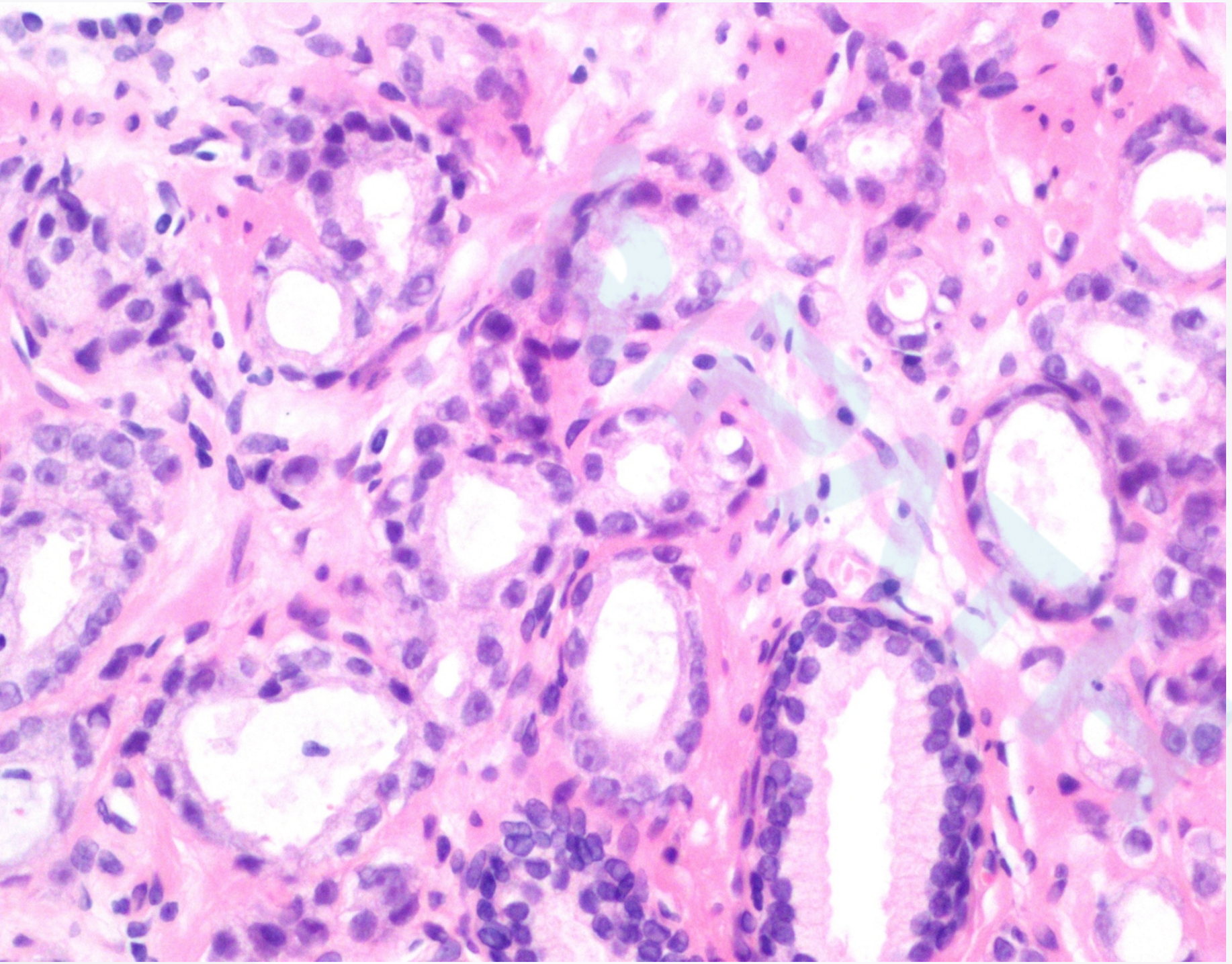
参考王哲主任课件



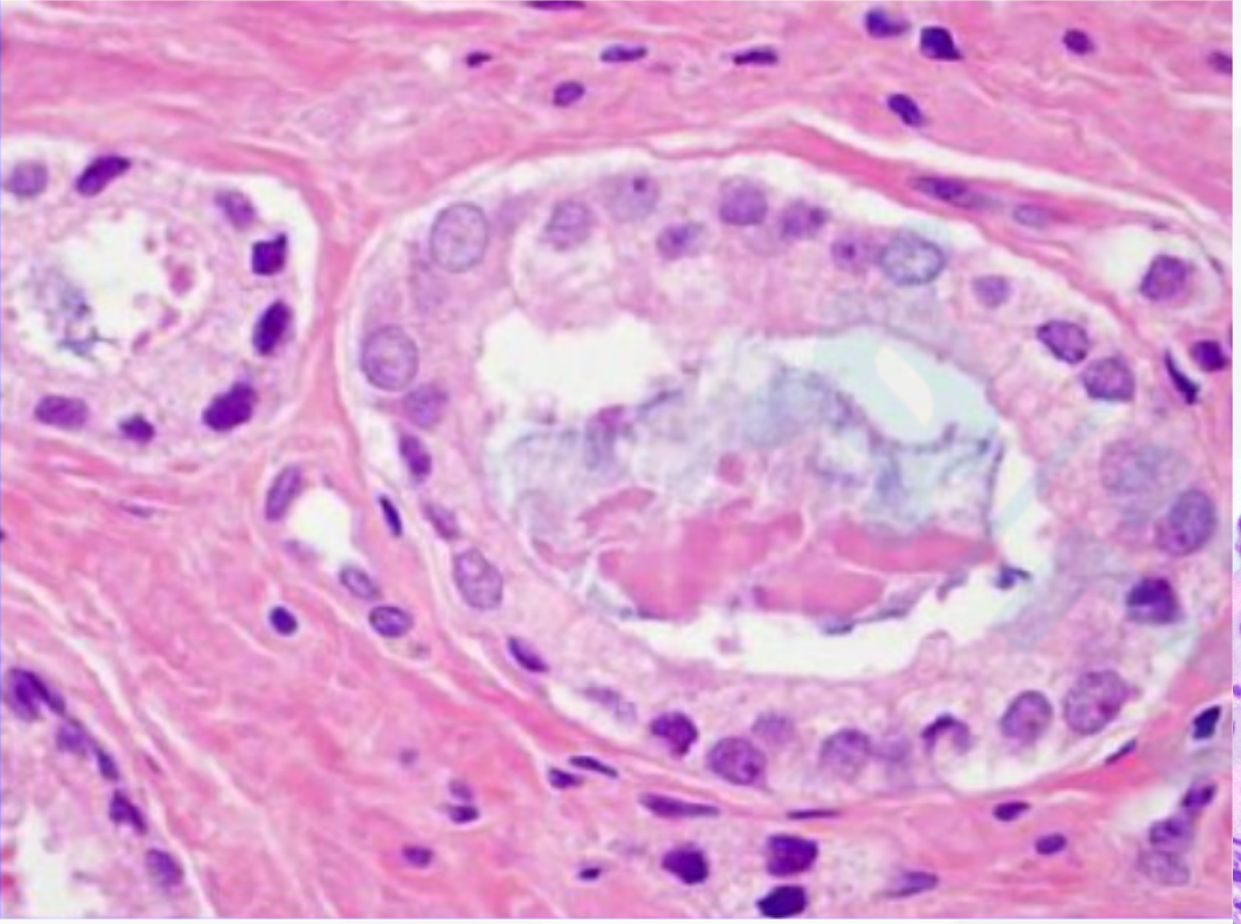
异常结构：小腺体，浸润性生长，排列不规则

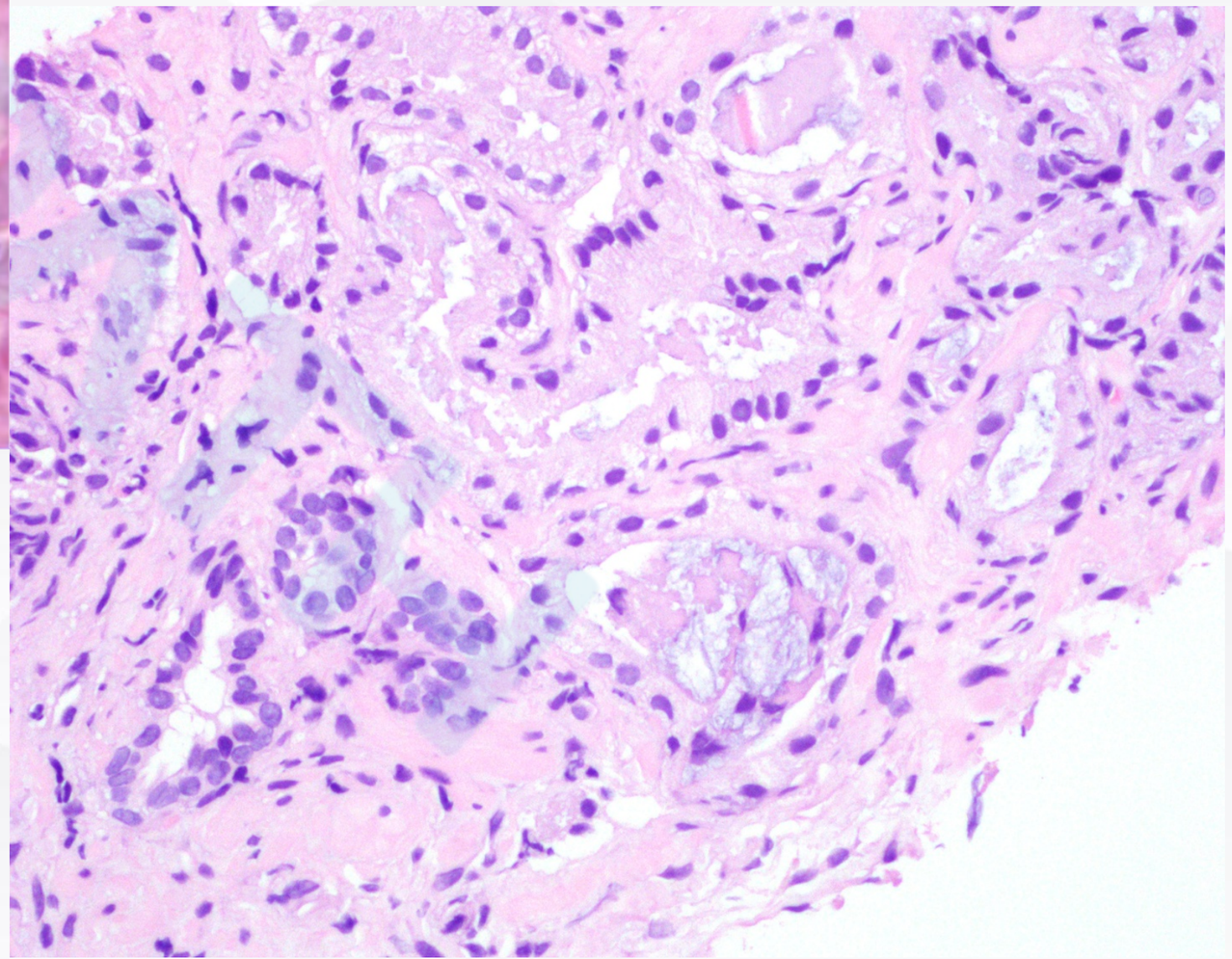


异常结构：腺体拥挤

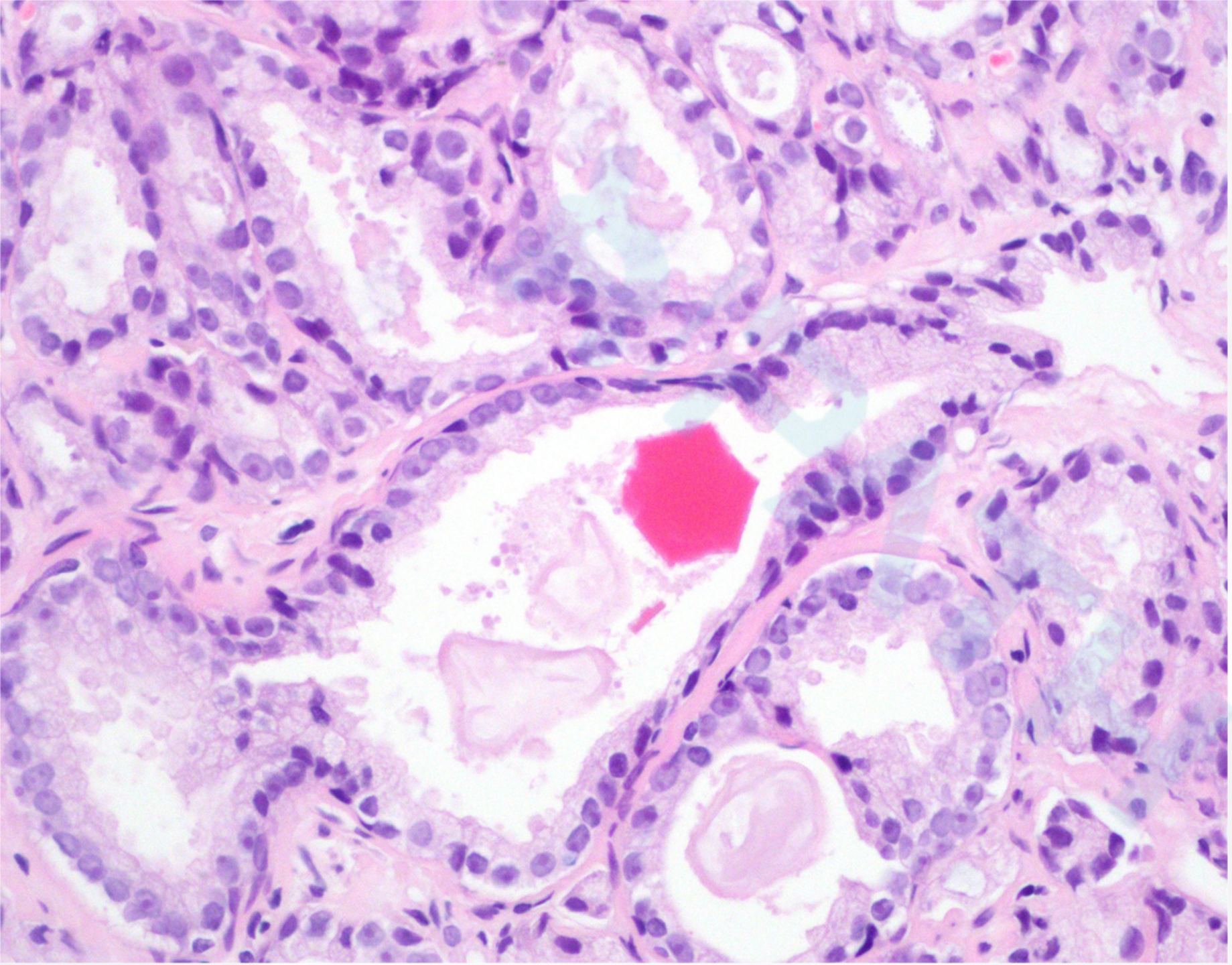


细胞核大核仁明显





腺腔蓝染的粘液样分泌物



红色类晶体

前列腺癌病理分级

- Gleason分级系统的历史与修订
- ISUP/WHO 2016预后分级分组系统
- 2019 ISUP 前列腺癌病理分级进展

最初的Gleason分级系统（1966-1972）

- 1974年由Dr. Donald Gleason提出
- 美国退伍军人管理部泌尿学研究协作组（VACURG）2911 patients
- 仅依据前列腺的结构特点，由于其良好的临床相关性，全世界大多数国家已广泛使用。
- Gleason评分是治疗前估计患者预后的重要参考数据，分级愈高，转移的机会愈大，局部治疗的效果愈差。

Gleason分级系统

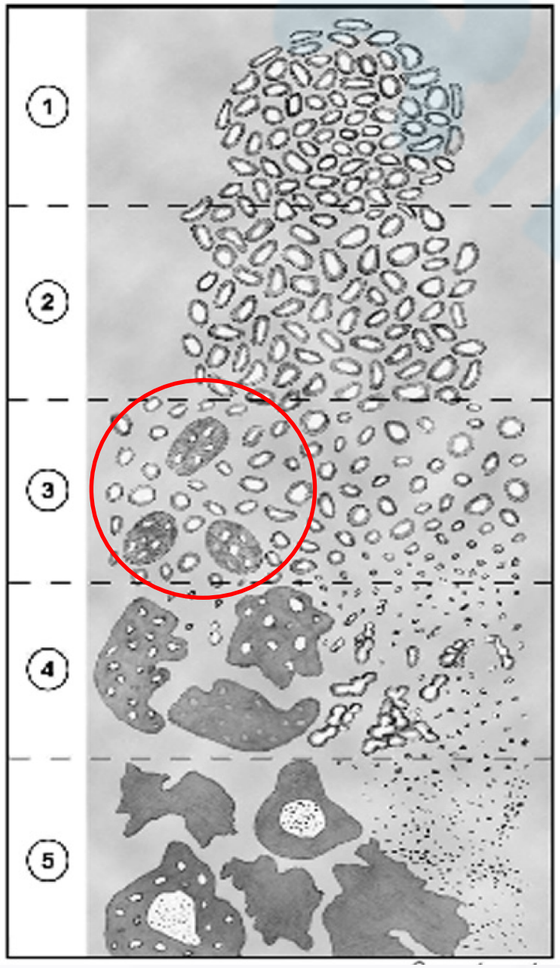
Gleason 最初分级系统（1966）

特点

- 仅依常规HE切片判断，一般不需要特殊染色和免疫组化
- 根据肿瘤组织结构，分为5种结构模式（pattern）/级别（grade）
- Gleason评分=主要结构模式（级别）+次要结构模式（级别），其范围为2-10。
- 从治疗和预后的角度，将Gleason评分划分为四组：2-4，5-6，7，8-10

Gleason分级系统

Gleason修改分级系统 (ISUP 2005)



特点

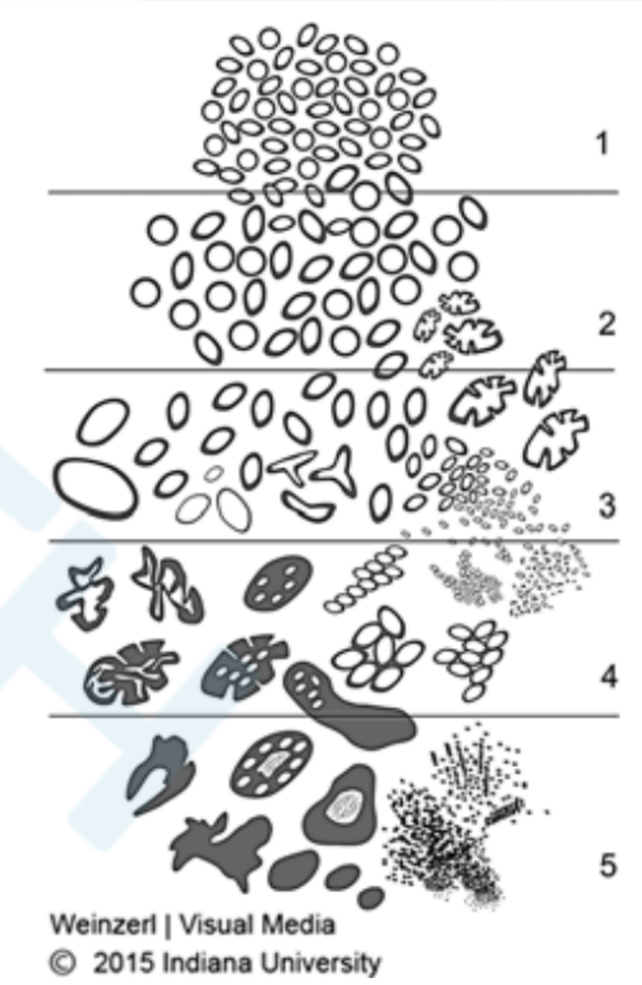
- Pattern 3中不能出现分化差的腺体
- 仅边界清楚光滑的筛状结构属Pattern 3
- 余筛状结构均为Pattern 4
- 最低级别5% cut off rule !原则

Gleason分级系统

存在的问题

- 修订Gleason分级系统几乎不再诊断2-5分。
- 老评分系统为Gleason2-10，实际工作中的最低分为6，可能使一些评分为6的患者误认为是中度危险选择过度治疗。
- 3+4=7 vs. 4+3=7 及 8 vs. 9-10 预后差异明显。

新分级系统 (WHO 2016)



新的ISUP/WHO预后分级分组系统

- Grade group 1(Gleason≤6) ：独立/边界清楚/分化好的腺体，极好的预后
- Grade group 2(Gleason 3+4=7)：分化好的腺体加少量分化差/筛状/融合腺体，极少转移
- Grade grou… …分化好的腺体，较差的预…
- Grade grou… …
- Grade group 5(Gleason 9-10)：无腺体形成区（坏死）及分化差/筛状/融合腺体，预后最差

- Grade group 1-5的根治标本5年无生化复发率分别为96%，88%，63%，48%，26%
- 5级分级系统提高根治标本与穿刺标本评分一致率

前列腺癌病理分级

- Gleason分级系统的历史与修订
- ISUP/WHO 2016预后分级分组系统
- 2019 ISUP 前列腺癌病理分级进展

TABLE 1. ISUP 2014 Modifications to Growth Patterns and Grade Grouping of Prostatic Carcinoma[1]

Assign cribriform glands as Gleason pattern 4, irrespective of size
Assign glome… …spective of size
Grade mucin… …its underlying growth patt… …tern 4
Do not assign… …te without invasive carcinoma. …sociation with aggressive prostate cancer
Use the 2014 modified 5-tier grading system[1] in conjunction with the Gleason system

- **将筛状腺体定为Gleason pattern 4**
- **不考虑大小将肾小球样腺体定为Gleason pattern 4**
- **没有浸润性癌时，勿将Gleason等级评分应用于前列腺IDC**

会议构成人员和内容

- 会议由ISUP理事会成员（K.A.I.，G.J.L.H.v.L，T.H.v.d.K.，D.J.G.）发起和准备。
- 共有来自四大洲的16位国际前列腺癌专家参加了工作组，其中包括13位泌尿生殖病理学家，1位泌尿外科医生、1位放射科医生和1位图像分析专家。出席会议有93人。
- 分配四个工作组，他们回顾了以下方面的相关文献：

（1）定量分级，包括将Gleason pattern 4和5百分比分配给活检和前列腺根治术标本，以及次要模式；

（2）浸润性筛状癌和导管内癌（IDC）的分级、意义和报告；

（3）等级异质性，包括根据整个病例，活检部位和单个核心的等级进行分级，并报告目标活检组织；

（4）分级的未来，包括合并人工智能（AI）和潜在的未来分级方案改进。

Part one

01

Working Group 1
Quantitative Grading

QUANTITATIVE GRADING, WORKING GROUP 1

High-grade Gleason评分的百分比

- 研究表明，对pattern 4的进一步量化具有临床意义。
- 活检标本中，GS 3 + 4 = 7且其中pattern 4 ＜肿瘤体积的5%时，在前列腺根治术，与GS 3 +3 =6的无复发生存率相似。

- 会前调查显示，有49%的受访者报告了根治性前列腺癌切除术中Gleason pattern 4和5的百分比；活检中微小病灶（<1 mm）的分级（例如GS 4+ 4 = 8）可能会导致过度治疗。

Ann Diagn Pathol.2016;20:48–51.

J Urol. 2019;20:77–82

QUANTITATIVE GRADING, WORKING GROUP 1

次要模式

- 两种Gleason模式，评分=主要模式（级别）+次要模式（级别）
- 三种Gleason模式，且最高级别成分数量最少
  - ＜5%时，评分=主要模式（级别）+次要模式（级别）
  - ＞5%时，评分=主要模式（级别）+最高模式（级别）

Epstein JI.Am J Surg Pathol. 2017;41:e1–e7.

QUANTITATIVE GRADING, WORKING GROUP 1

提案与投票

TABLE 3. Grade Quantification Voting Results

Statement	Voting Result
Percent Gleason pattern 4 should be reported in biopsy for score 3+4 = 7	100% agree
Percentage Gleason pattern 4 should be reported in biopsy for score 4+3 = 7	94% agree
Percent Gleason patterns 4 and 5 should be reported for all radical prostatectomies	42% disagree, no consensus
For radical prostatectomy, any amount of Gleason pattern 5 $\geq$ 5% should be included in the GS as the secondary pattern	77% agree
For radical prostatectomy, any amount of Gleason pattern 4 $\geq$ 5% should be included in the GS as the secondary pattern	79% agree
For radical prostatectomy, any amount of Gleason pattern 4 < 5% should be reported as "minor pattern," but not included in the score	72% agree
For radical prostatectomy, any amount of Gleason pattern 5 < 5% should be reported as "minor pattern," but not included in the score	85% agree
For radical prostatectomy, any amount of Gleason pattern 5 < 5% should be included in the score as the secondary pattern	67% disagree, consensus against
For radical prostatectomy, any amount of Gleason pattern 4 < 5% should be included in the score as the secondary pattern	66% disagree, no consensus

Part two

02

Working Group 2
IDC and Tumor Growth Patterns

IDC and Tumor Growth Patterns

Intraductal Carcinoma(IDC-P)

- **定义：前列腺腺泡内和/或导管内上皮的肿瘤性增生，具有部分HGPIN的特征，但其组织学和/或细胞学的异型性更高，并与高级别、高分期的前列腺腺癌的发生显著相关。预后较差。**

- **ICD-O　8500/2**

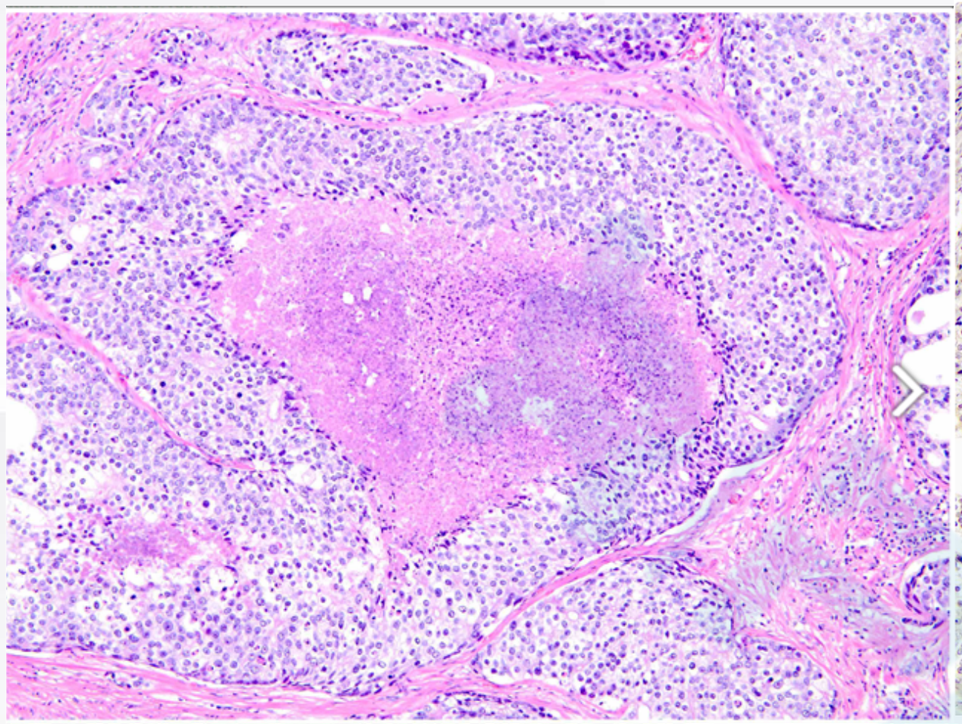
- **组织学：**

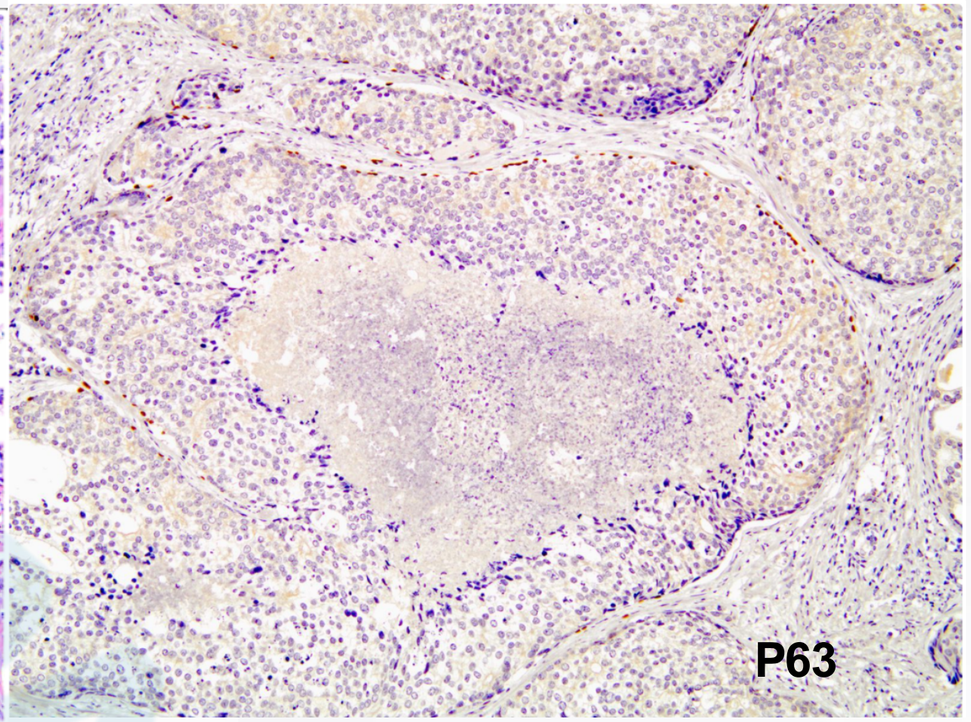
- **前列腺腺癌的细胞局限在腺泡内或者导管内，并且可以沿着导管和腺泡进行播散，基底细胞层可部分保存。**

IDC-P的诊断标准（WHO 2016）

具有基底细胞的导管内，出现

1. 实性结构；
2. 致密筛状结构；
3. 疏松筛状或微乳头状结构伴明显的核异型性（达到正常前列腺上皮细胞核的6倍）；
4. 中央粉刺样坏死，但并不总是存在。

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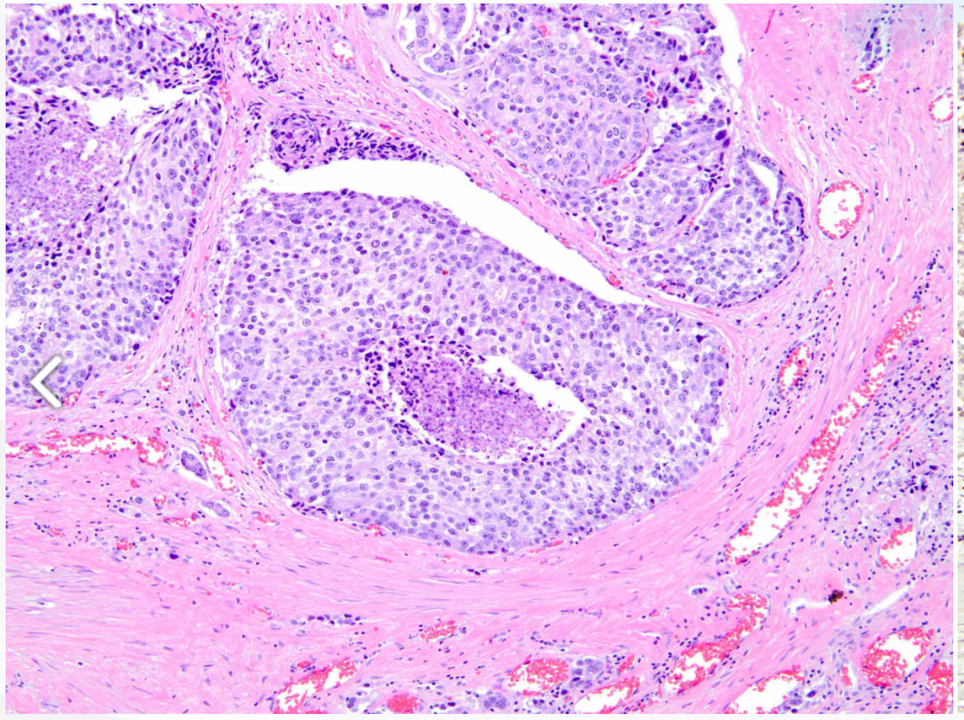

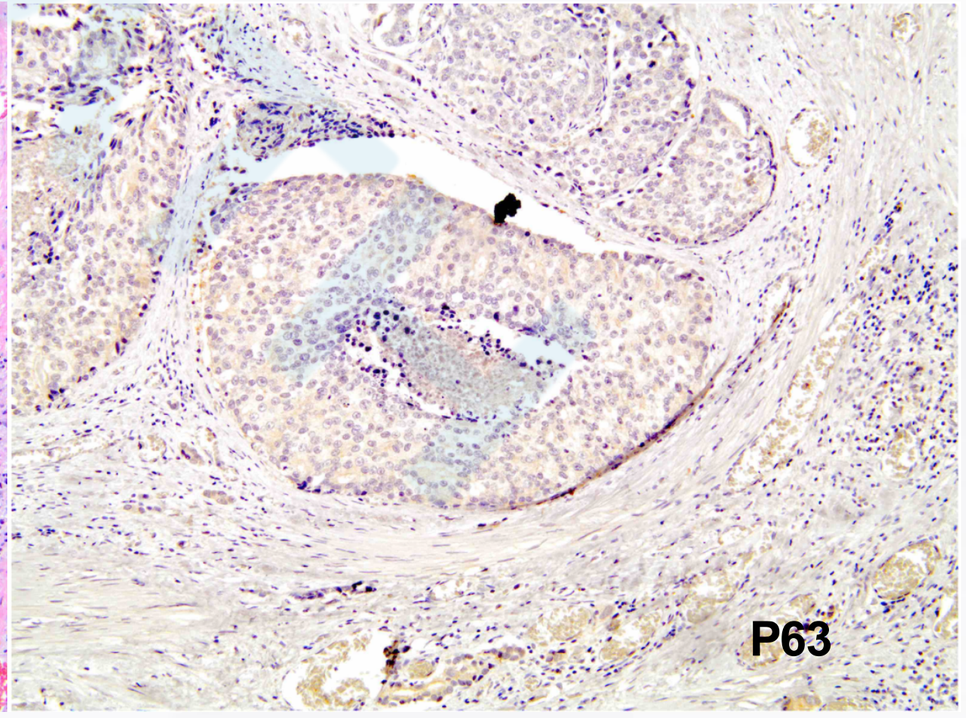
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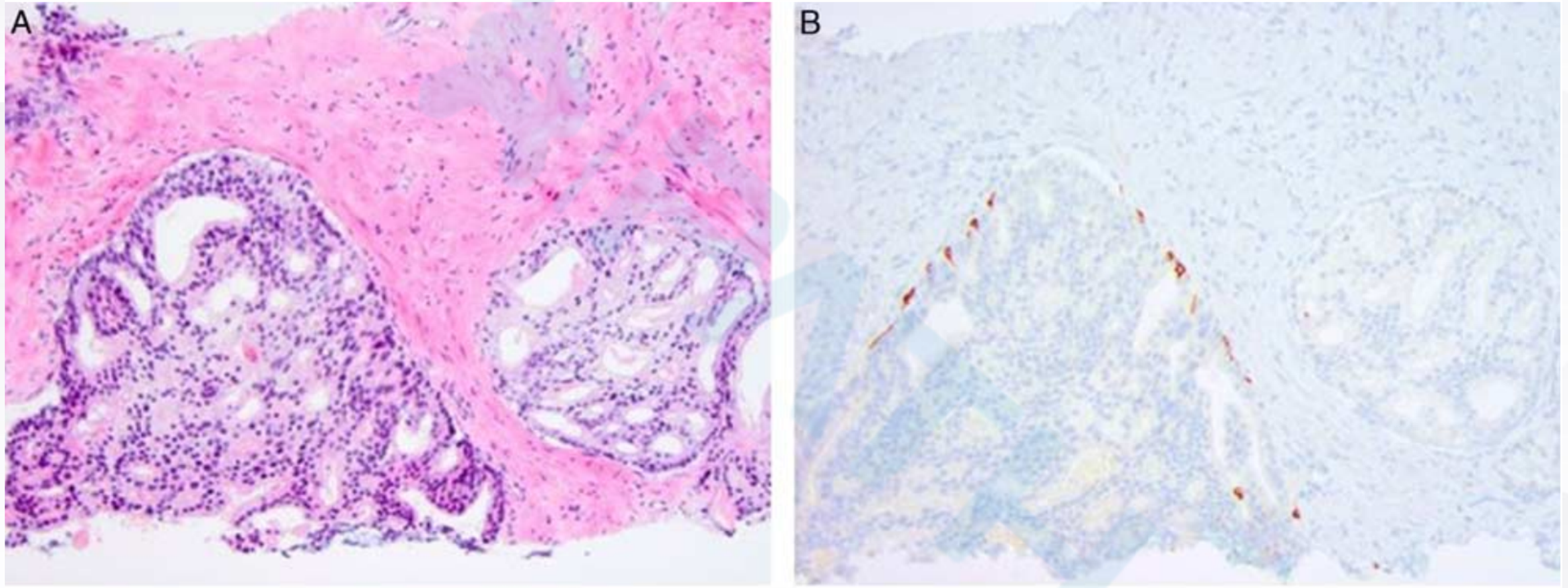

A
B

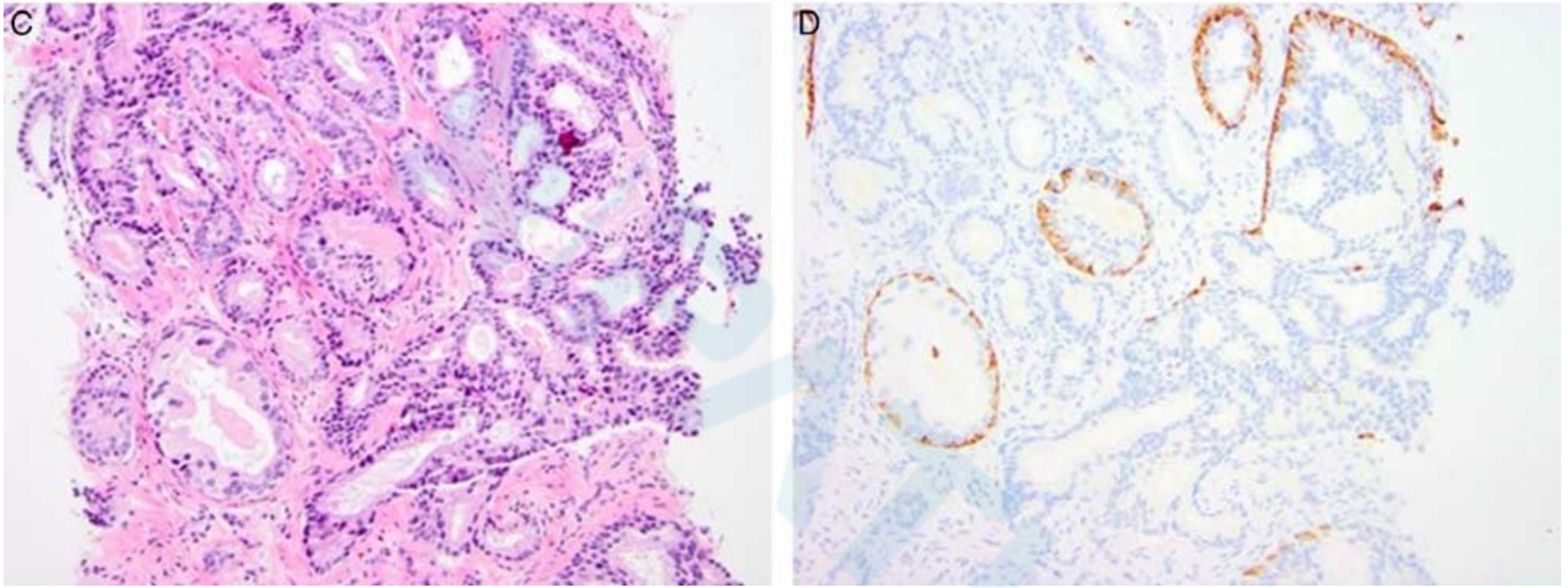


FIGURE 1. Cribriform epithelial proliferations showing overlap between IDC and invasive cribriform Gleason pattern 4. A and B, Two adjacent cribriform proliferations, one (left) having scattered basal cells, the other (right) without basal cell layer. The left structure fulfills the criteria of IDC. The right structure may represent either invasive cribriform carcinoma, or IDC without basal cells due to sampling artifact in this section. C and D, Cribriform proliferation with a basal cell layer compatible with IDC with irregular tubular outgrowths. Classification of outgrowth is unclear as either IDC, IDC transitioning to Gleason pattern 3, or IDC and invasive cribriform carcinoma. A and C, hematoxylin-eosin; B and D, high molecular weight cytokeratin.

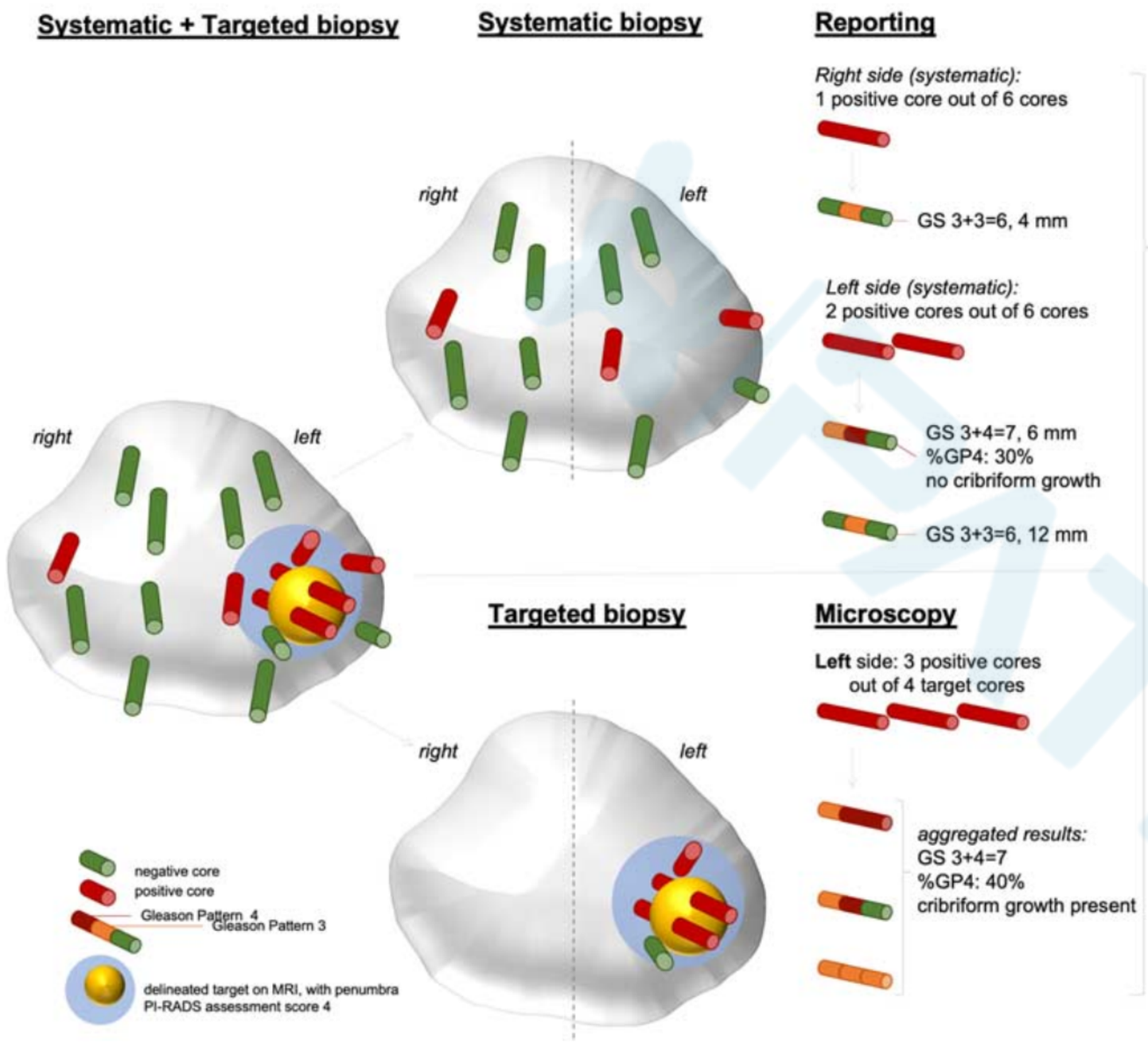
IDC and Tumor Growth Patterns

提案与投票

TABLE 4. IDC and Tumor Growth Pattern Voting Results

Statement	Voting Result
Pure IDC should not be graded	91% agree
Presence of invasive cribriform cancer should be commented on in GS 7 cases	97% agree
Presence of invasive cribriform cancer should be commented on in GS 8 cases	84% agree

- 91%的共识认为无浸润癌的IDC不应分级
- 76%建议将与浸润性癌相关的IDC纳入GS
- 由于IDC可能具有独立的预后意义，因此83%同意IDC的存在和意义
- 93%同意将浸润性癌的筛状IDC分级为GP 4
- 分别有97%和84%同意在活检和根治性前列腺切除术中报告GS 7和GS 8中的浸润性筛状癌



ISUP recommendations:

Report

- (individual) results for systematic biopsy per vial
- aggregated results for systematic biopsy, global or per side (optional)
- aggregated results for targeted biopsy per lesion
- possible histology explanation in case all targeted cores are negative

FIGURE 2. Schematic overview of reporting systematic and mpMRI-targeted biopsies. GP indicates Gleason pattern.

2019ISUP推荐：

- 在系统穿刺中，应对每处病灶分别进行GS评价
- 在系统穿刺中，应对两叶整体或分叶进行总体GS评价
- 在靶向穿刺中，应对每处病灶进行总体GS评价
- 对于靶向穿刺中所有穿刺针均阴性的患者，应进行可能的组织学解释

TABLE 2. Summary of ISUP 2019 Modifications to Prostate Cancer Grading

Report in biopsies the percentage Gleason pattern 4 for all GS 7 (ISUP GG 2 and 3)
For radical prostatectomies, include the presence of tertiary/minor Gleason patterns 4 and 5 in the GS, if constituting > 5% of the tumor volume
Report in radical prostatectomies presence of tertiary/minor Gleason patterns 4 and 5
Do not grade IDC without invasive cancer
Incorporate the grade of IDC into the GS when invasive cancer is present
Comment on the presence and significance of IDC in biopsies and radical prostatectomy specimens
Comment on the presence and significance of invasive cribriform cancer in biopsies and radical prostatectomy specimens
Report in systematic biopsies a separate GS (ISUP GG) for each individual biopsy site
Report in mpMRI-targeted biopsies a global (aggregate) GS (ISUP GG) for each suspicious MRI lesion
Report specific benign histologic findings in suspicious (PIRADS 4-5) MRI-targeted biopsies without cancer

2019 ISUP共识主要内容：

1.GS7需报告活检组织pattern 4百分比

2.根治标本中第三种/GS5的报告方式

3.IDC不伴浸润性癌不进行评分

4.将IDC整合到浸润癌GS中

5.在活检和根治标本中述评IDC/筛状癌的临床意义

6.系统活检每个部位进行单独评分

7.对mpMRI的每个可疑病灶进行总体评分

8.对mpMRI 假阳性病灶进行病理解释

2019 ISUP共识后的前列腺病理报告内容

- 前列腺腺癌，系统穿刺Gleason评分4+3=7分，每条组织分别评分；
- ISUP/WHO 2016 分级分组：第3组；
- 肿瘤总体占比50%；
- Gleason分级4的成分占70%，其中筛状4占60%，分化不良腺体占40%；
- 另含10%筛状型IDC-P成分；
- 磁共振靶向穿刺位点1为腺癌， Gleason评分4+4=8；
- 磁共振靶向穿刺位点2为肉芽肿性炎；
- 未见治疗反应。

感谢聆听

Thanks