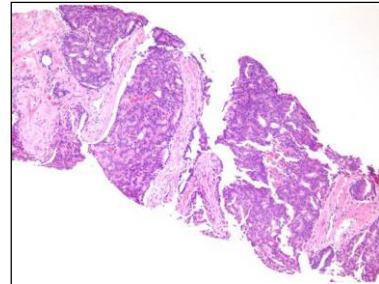


Intraductal Carcinoma of the Prostate

Murali Varma

Consultant Histopathologist
University Hospital of Wales
Cardiff, UK

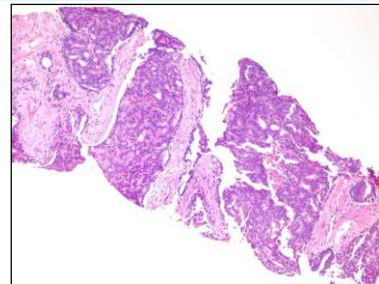
Maastricht 2018

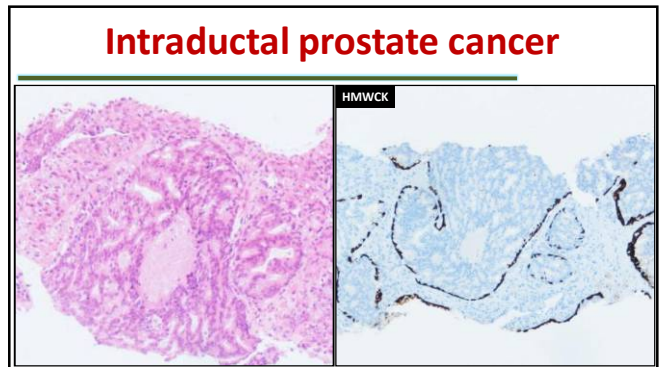
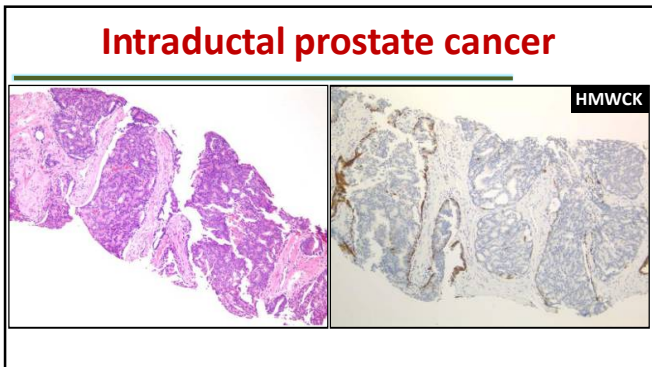
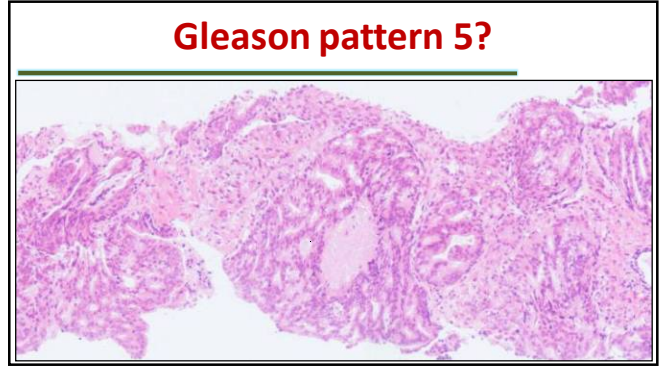
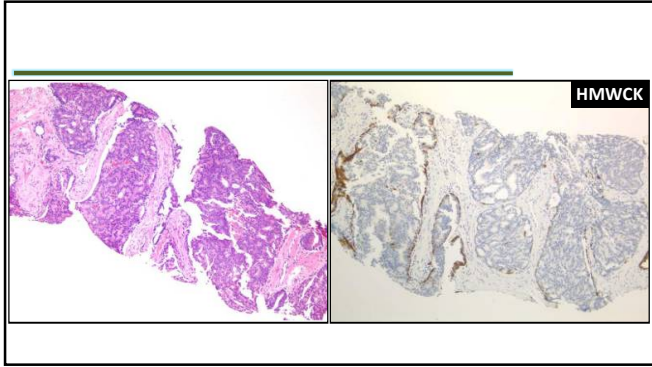


Intraductal carcinoma of prostate

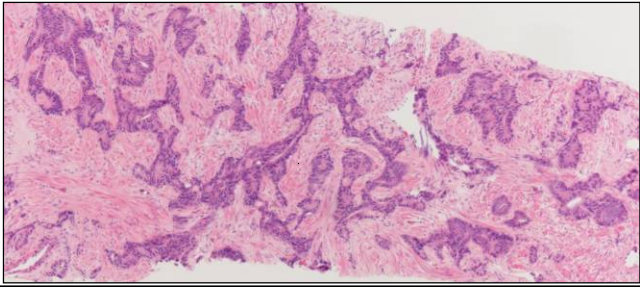
- Lumen spanning proliferation of neoplastic epithelium within enlarged pre-existing ducts

Gleason score 4 + 4 = 8?





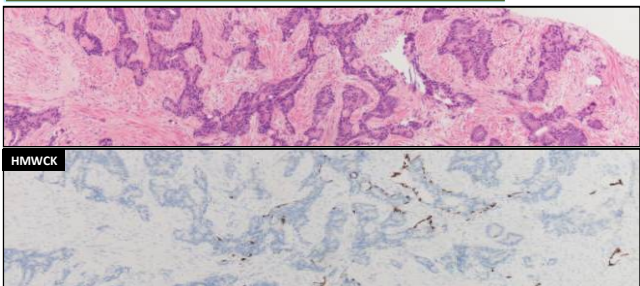
Invasive carcinoma?



Intraductal carcinoma of prostate

- Lumen spanning proliferation of neoplastic epithelium within enlarged pre-existing ducts
 - ~ Generally: colonisation of benign ducts by **invasive** carcinoma

Intraductal prostate cancer



Intraductal carcinoma of prostate

- Lumen spanning proliferation of neoplastic epithelium within enlarged pre-existing ducts
 - ~ Generally: colonisation of benign ducts by **invasive** carcinoma
 - ~ Rarely: a **pre-invasive** lesion with high risk of progression to invasive prostate cancer

Terminology:
Ductal vs. Intraductal cancer

Terminology:
Ductal vs. Intraductal cancer

- **Ductal**
 - ~ **Variant** of prostatic adenocarcinoma
 - ~ "ductal" refers to **phenotype**
- **Intraductal**
 - ~ **Growth pattern** of adenocarcinoma
 - ~ Not a variant of prostate cancer
 - ~ "---ductal" refers to **location** (within ducts)

Terminology:
Ductal vs. Intraductal cancer

- **Ductal**
 - ~ **Variant** of prostatic adenocarcinoma
 - ~ "ductal" refers to **phenotype**

Intraductal carcinoma of prostate

- **Lumen spanning proliferation of neoplastic epithelium within enlarged pre-existing ducts**
 - ~ Generally: colonisation of benign ducts by **invasive carcinoma**
 - ~ Rarely: a **pre-invasive** lesion with high risk of progression to invasive prostate cancer
- **New entity in WHO 2016**
 - ~ **Morphology code:** M8500/2

Intraductal prostate cancer
Consensus

Intraductal prostate cancer
Consensus

- Existence and nature
- **Poor prognosis (if with invasive)**
 - ~ Associated with high volume, high grade, high stage invasive cancer
 - ~ Significant risk of biochemical recurrence and metastasis

Intraductal prostate cancer
Consensus

Intraductal prostate cancer
Consensus

- Existence and nature

- Existence and nature
- Poor prognosis (if with invasive)
- **Active surveillance not appropriate for IDCP-invasive**

Intraductal prostate cancer Consensus

- Existence and nature
- Poor prognosis (if with invasive)
- Active surveillance not appropriate for IDCP-invasive
- Diagnostic criteria

Intraductal carcinoma of prostate Reproducibility issues

Intraductal carcinoma of the prostate: interobserver reproducibility survey of 39 urologic pathologists

Kenneth A. Iczkowski, MD^{1*}, Lars Egevad, MD², Jun Ma, MD³, Nicholas Harding-Jackson, MD⁴, Ferran Algaba, MD⁵, Athanasios Bilis, MD⁶, Philippe Camparo, MD⁷, Liang Cheng, MD⁸, David Clouston, MD⁹, Eva M. Comperat, MD¹⁰, Milton W. Datta, MD¹¹, Andrew G. Evans, MD¹², David F. Griffiths, MD¹³, Charles C. Guo, MD¹⁴, Seife Hallemariam, MD¹⁵, Wei Huang, MD¹⁶, Peter A. Humphrey, MD¹⁷, Zhong Jiang, MD¹⁸, Hillel Kahane, MD¹⁹, Glen Kristiansen, MD²⁰, Francisco G. Li Rosa, MD²¹, Antonio Lopez-Beltran, MD²², Gregory J. MacLennan, MD²³, Cristina Maggi-Galuzzi, MD²⁴, Jennifer Merriman, MD²⁵, Rodolfo Mostroini, MD²⁶, Adeboye O. Osunkoya, MD²⁷, Maria M. Picken, MD²⁸, Nagajun Rao, MD²⁹, Rajal B. Shah, MD³⁰, Jonathan H. Shanks, MD³¹, Steven S. Shen, MD³², Dakama W. Tawfik, MD³³, Lawrence D. True, MD³⁴, Theodoras Van der Kwast, MD³⁵, Murali Varma, MD³⁶, Thomas M. Wheeler, MD³⁷, Debra L. Zinger, MD³⁸, Nuzula Sahr, MD³⁹, David C. Bostwick, MD⁴⁰ *Annals of Diagnostic Pathology 18:333-342; 2014*

Microphotographs circulated
PIN – IDCP - Invasive

43% agreement for IDCP

Diagnostic criteria for intraductal cancer Guo and Epstein 2006

- Solid intraductal proliferation
OR
- Dense cribriform intraductal proliferation
OR
- Loose cribriform / micropapillary with either
 - ~ Marked atypia (≥ 6x nuclear enlargement)
 - or
 - ~ Non-focal comedonecrosis

Intraductal carcinoma of prostate Explanation for variation: 1

- Subjective application of diagnostic criteria

PIN

IDCP

Invasive

~ Morphological continuum

~ Difficult to standardise

Intraductal carcinoma of prostate

Explanation for variation: 2

- **Different rules used**
 - “ Diagnostic criteria
 - “ Reporting rules

Intraductal carcinoma of prostate reporting practice: A survey of **expert** European urologists

- **Survey of diagnostic criteria and reporting rules**
 - “ Questionnaire circulated
 - “ No microphotographs
- **Significant variation in diagnostic criteria and reporting rules**

Varma M, et al. J Clin Pathol 2016;69:852-857

Intraductal carcinoma of prostate

Explanation for variation: 2

- **Different rules used**
 - “ Diagnostic criteria
 - “ Reporting rules
- **Easier to standardise**
 - “ Establish consensus

Intraductal carcinoma of prostate reporting practice A survey of **practicing** pathologists

Murali Varma, Lars Egevad, Daniel Berney, Lukas Bubendorf, Eva Comperat, Ondrej Hes, Arno van Leenders and Glen Kristiansen

USCAP 2018

Intraductal Carcinoma of the Prostate

A critical re-appraisal

Understanding IDCP

- Some basic concepts

Intraductal carcinoma of prostate Issues

- **Management** of IDCP
- **Diagnostic criteria** for IDCP
- **Grade** IDCP?

Intraductal carcinoma in biopsies 2 distinct scenarios

- **Isolated (pure) IDCP**
 - “ No associated invasive component
- **IDCP associated with invasive cancer**

Intraductal carcinoma in biopsies
2 distinct scenarios

- **Isolated (pure) IDCP**
 - ~ Rare
 - ~ <0.3% of prostate biopsies
 - ~ Associated with **unsampled** aggressive invasive cancer
 - ~ **Management** controversial
 - ~ Urgent re-biopsy or radical Rx

Intraductal carcinoma of the prostate
2 different diseases

Intraductal carcinoma in biopsies
2 distinct scenarios

- **Isolated (pure) IDCP**
- **IDCP associated with invasive cancer**
 - ~ Common in bx and radicals with high grade prostate cancer
 - ~ **Reporting** (grade and tumour extent) controversial

Intraductal carcinoma of the prostate
2 different diseases

- **Pure IDCP and IDCP-invasive are biologically distinct diseases**

Intraductal carcinoma of the prostate **2 different diseases**

- Pure IDCP and IDCP-invasive are biologically distinct diseases
- **Pure IDCP:**
 - ~ Precursor lesion
 - ~ Analogous to HGPIN
- **IDCP-invasive:**
 - ~ Growth pattern of **invasive carcinoma**

Epstein criteria

- Designed for pure IDCP
- To identify patients who should receive radical Rx even in absence of co-existing invasive component

Diagnostic criteria for intraductal cancer **Guo and Epstein 2006**

- **Solid intraductal proliferation**
OR
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 - or
 - ~ Non-focal comedonecrosis

Epstein criteria

- Designed for pure IDCP
- To identify patients who should receive radical Rx even in absence of co-existing invasive component
- **Bar set very high**
 - ~ *Definitely* not HGPIN

Epstein criteria

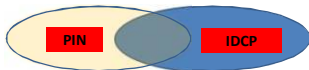
- Designed for pure IDCP
- To identify patients who should receive radical Rx even in absence of co-existing invasive component
- Bar set very high
- **Not minimum criteria for IDCP**
 - ~ Excludes IDCP with features overlapping with HGPIN

IDCP in prostate biopsy Issues

- **Management**
 - ~ Re-biopsy or radical Rx
- **Diagnosis**
 - ~ Diagnostic criteria
- **Reporting**
 - ~ Tumour grade

Epstein criteria

- Designed for pure IDCP
- To identify patients who should receive radical Rx even in absence of co-existing invasive component
- Bar set very high
- **Not minimum criteria for IDCP**
 - ~ Excludes IDCP with features overlapping with HGPIN



IDCP associated with invasive carcinoma Consensus

- Existence and nature
- Poor prognosis (if with invasive)
- **Active surveillance not appropriate for IDCP-invasive**

Pure intraductal carcinoma in biopsy
Management

- ~ Radical therapy?
- ~ Prompt re-biopsy?

**Intraductal carcinoma of the prostate without
invasive carcinoma on needle biopsy:**
Emphasis on radical prostatectomy findings

- **Pure intraductal carcinoma:**
 - ~ 83 cases in almost 10 years
- **Radical prostatectomy: 21 cases**
 - ~ At least pT3a: 52%
 - ~ Progression post-radical: 17%



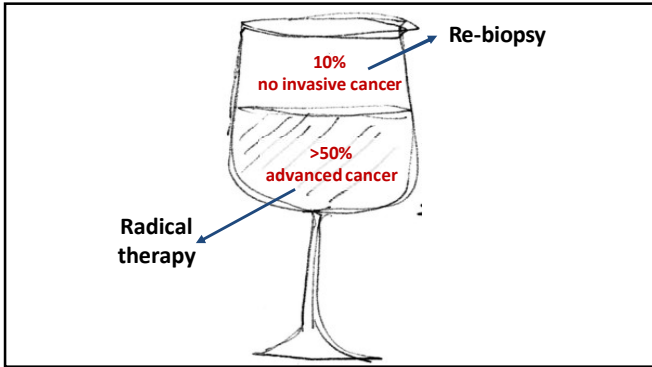
**Intraductal Carcinoma of the Prostate Without Invasive
Carcinoma on Needle Biopsy: Emphasis on Radical
Prostatectomy Findings**

Brian D. Robinson and Jonathan I. Epstein*

From the Departments of Pathology (BDR), Urology and Oncology, The Johns Hopkins Hospital (JIE), Baltimore, Maryland

**Intraductal carcinoma of the prostate without
invasive carcinoma on needle biopsy:**
Emphasis on radical prostatectomy findings

- **Pure intraductal carcinoma:**
 - ~ 83 cases in almost 10 years
- **Radical prostatectomy: 21 cases**
 - ~ At least pT3a: 52%
 - ~ Progression post-radical: 17%
- ~ **No invasive cancer: 2 (10%)**



Pure intraductal carcinoma in needle bx
Management controversy

- **Radical Rx**
 - “ Some patients over-treated for non-invasive disease?

Pure intraductal carcinoma in needle bx
Management controversy

Pure intraductal carcinoma in needle bx
Management controversy

- **Radical Rx**
 - “ Some patients over-treated for non-invasive disease?
 - “ However, current protocols overtreat some patients with clinically insignificant 3+3 invasive?
 - “ Most patients with pure IDCP in bx have advanced cancer in radical

Pure intraductal carcinoma in needle bx
Management controversy

- **Radical Rx**
 - “ Some patients over-treated for non-invasive disease?
- **Re-biopsy**
 - “ **Some patients may be undertreated**
 - “ Delay in treatment may be clinically significant

IDCP in prostate biopsy
Issues

- **Management**
 - “ Re-biopsy or radical Rx
- **Diagnosis**
 - “ Diagnostic criteria
- **Reporting**
 - “ Tumour grade

Pure intraductal carcinoma in needle bx
Management controversy

- **Radical Rx**
 - “ Some patients over-treated for non-invasive disease?
- **Re-biopsy**
 - “ **Some patients may be undertreated**
 - “ Delay in treatment may be clinically significant
 - “ **What if rebiopsy: benign or pure IDCP?**
 - “ Sampling error?

Diagnostic criteria for intraductal cancer
Guo and Epstein 2006

- **Solid intraductal proliferation**
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 - or
 - ~ Non-focal comedonecrosis

Nuclear size ($\geq 6x$ normal) criterion
Issue

- Nuclei larger than that acceptable in HGPIN
- Nuclear size “6x larger than normal” is an arbitrary cut-off described to improve reproducibility

Nuclear size ($\geq 6x$ normal) criterion
Issue

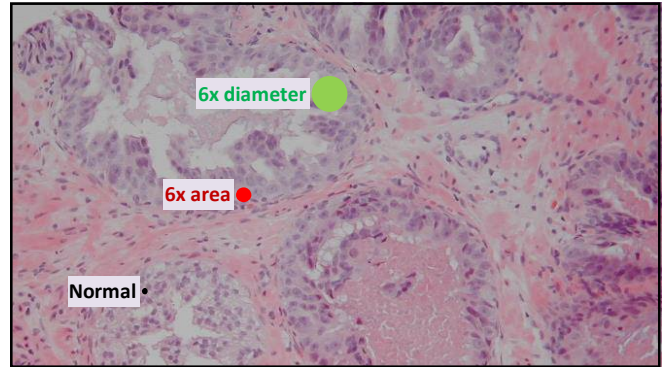
- Nuclei larger than that acceptable in HGPIN

Nuclear size ($\geq 6x$ normal) criterion
Issue

- Nuclei larger than that acceptable in HGPIN
- Nuclear size “6x larger than normal” is an arbitrary cut-off described to improve reproducibility
- **Ambiguous definition**
 - ~ Nuclear area or diameter?

If you use criterion "nuclear size $\geq 6x$ normal" then how would you define "nuclear size"?

- Nuclear *area* > 6x normal
- Nuclear *diameter* > 6x normal

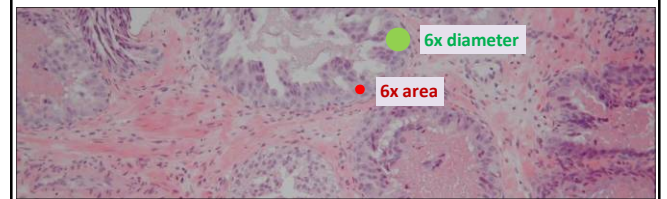


If you use criterion "nuclear size $\geq 6x$ normal" then how would you define "nuclear size"?

- Nuclear *area* > 6x normal: **54%**
- Nuclear *diameter* > 6x normal: **45%**

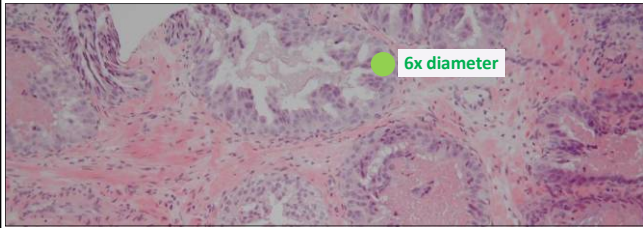
Nuclear size criterion Needs consensus clarification

- 6x normal area?
- 6x normal diameter?



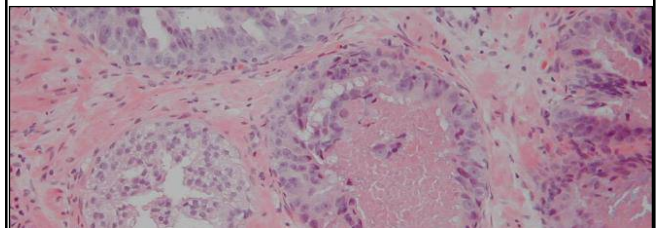
Nuclear size criterion
6x normal *diameter*

- Rarely if ever seen

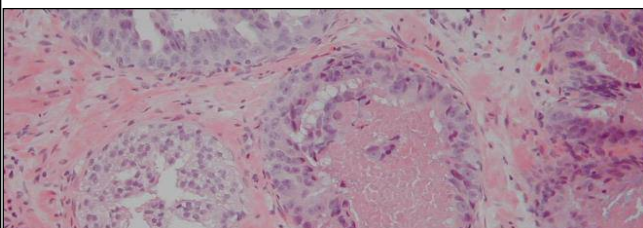


Nuclear size criterion
6x normal *area*

- Difficult to visually compare areas



Nuclear size criterion
6x normal *area*



Diagnostic criteria for intraductal cancer
Guo and Epstein 2006

- Solid intraductal proliferation
OR
- Dense cribriform intraductal proliferation
OR
- Loose cribriform / micropapillary with either
 - ~ Marked atypia ($\geq 6x$ nuclear enlargement)
 - or
 - ~ Non-focal comedonecrosis

“Dense cribriform” criterion
Cut-off

▪ **Guo and Epstein 2006**

~ “Solid areas predominate over luminal spaces”

~ **50%** cut-off?

“Dense cribriform” criterion
Which cut-off do you use?

- Solid component >50
- Solid component >70%

Differential Diagnosis of Intraductal lesions of the prostate

Wobker S, Epstein JI. Am J Surg Pathol 2016;40:e67–e82

Dense cribriform intraductal proliferation

~ Solid areas >**70%**

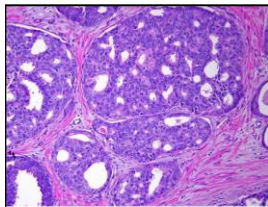


FIGURE 3. Dense cribriform IDC-P with >70% solid growth.

“Dense cribriform” criterion
Which cut-off do you use?

- Solid component >50%: **51%**
- Solid component >70%: **45%**

IDCP in prostate biopsy Issues

- **Management**
 - ~ Re-biopsy or radical Rx
- **Diagnosis**
 - ~ Diagnostic criteria
- **Reporting**
 - ~ Tumour grade

Intraductal carcinoma in biopsies 2 distinct scenarios

- **Isolated (pure) IDCP**
 - ~ No associated invasive component
- **IDCP associated with invasive cancer**

ISUP grading consensus meeting 2014

- IDC-P should not be graded
- Adopted by WHO 2016

IDCP: To grade or not to grade?

- **Pure IDCP**
 - ~ 92% respondents would **not** grade

Pure IDCP in needle biopsy
Rationale for not grading IDCP

- **If graded, may be misinterpreted as invasive cancer**
 - ~ Radical Rx may be inappropriate

IDCP associated with invasive
Rationale for not grading IDCP

- Gleason grading designed and validated for invasive cancer

IDCP: To grade or not to grade?

- **Pure IDCP**
 - ~ 92% respondents would **not** grade
- **IDCP associated with invasive**
 - ~ 87% respondents would **not** grade

Needle bx: IDCP with invasive cancer
Should IDCP component be graded?

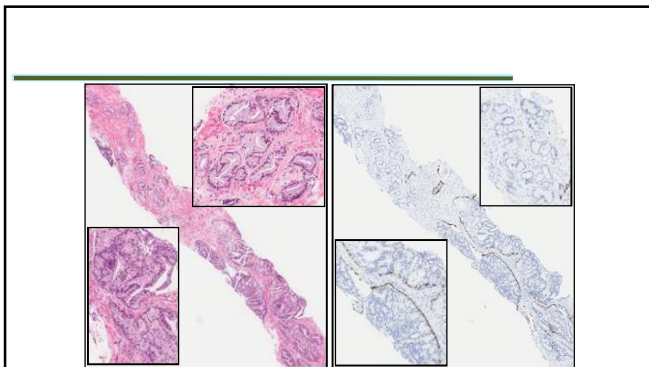
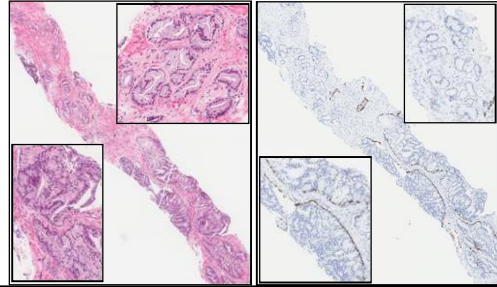
- **Most cases associated with high-grade invasive**
 - ~ Grading IDCP would not significantly change GS

Needle bx: IDCP with invasive cancer
Should IDCP component be graded?

▪ **Clinically relevant scenarios**

- ~ 3 + 4 invasive with comedonecrosis IDCP (3+4=7 or 3+5=8)
- ~ 3 + 3 invasive with comedonecrosis IDCP (3+3=6 or 3+5=8)

Gleason 3 + 3 + IDCP or 4 + 3?



Prostate Biopsy Specimens With Gleason 3+3=6 and Intraductal Carcinoma
Radical Prostatectomy Findings and Clinical Outcomes

Khani F, Epstein JI. Am J Surg Pathol. 2015;39:1383-1389.

TABLE 1. RP Findings of 16 Patients

Pathologic Stage	Gleason Grade (± IP%)	Extensive IDCP?	Lymphovascular Invasion	Lymph Node Metastases	Margin Status	Invasive Tumor Type	Prostate Weight (g)	How Submitted (Per Report)	Time to DCR (mo)
1	pT3a	3+4=7	Yes	No	Negative	Acinar	69	Representative	
2	pT3b	3+4=7	Yes	No	Positive	Acinar/sarcomatoid carcinoma component	85	NS	
3	pT3a	3+3=6	Yes	No	Positive	Acinar	64	Representative	
4	pT3a	4+3=7	Yes	No	Negative	Acinar	58	Entirely	
5	pT3b	4+4=8	Yes	No	Positive	Acinar	140	Representative	7
6	pT2c	3+4=7	Yes	No	Negative	Acinar	42	Representative	
7	pT3b	4+4=8	No	No	Negative	Acinar	37	Entirely	
8	pT2c	3+3=6	Yes	No	Negative	Mixed acinar/ductal	56	Representative	
9	pT2c	4+3=7	No	No	Negative	Acinar	33	Entirely	
10	pT2c	3+3=6	Yes	No	Negative	Acinar	106	30% submitted	52
11	pT3a	3+4=7	Yes	No	Negative	Mixed acinar/ductal	48	Representative	
12	pT2c	4+3=7	Yes	No	Negative	Acinar	42	90% submitted	
13	pT3b	3+4=7	Yes	No	Negative	Acinar	35	Entirely	69
14	pT3a	4+3=7	Yes	No	Negative	Acinar	58	Entirely	71
15*	pT2c	4+4=8	No	No	Negative	Acinar	88	Representative	
16†	pT2c	4+3=7	Yes	No	Positive	Acinar	84	Representative	

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1	pT3a	3+4=7	Yes	No	No	Negative	69	Acinar	Representative
2	pT3b	3+4=7	Yes	No	No	Positive	85	Acinar + sarcomatoid carcinoma	NS
3	pT3a	3+3=6	Yes	No	No	Positive	64	Acinar	Representative
4	pT3a	4+3=7	Yes	No	No	Negative	56	Acinar	Entirely
5	pT3b	4+4=8	Yes	No	No	Positive	140	Acinar	Representative
6	pT3c	3+4=7	Yes	No	No	Negative	42	Acinar	Representative
7	pT3b	4+4=8	Yes	No	No	Negative	42	Acinar	Entirely
8	pT3c	4+4=8	Yes	No	No	Negative	56	Mixed acinar/ductal	Representative
9	pT3c	4+4=8	No	No	No	Negative	23	Acinar	Entirely
10	pT3c	4+3=7	Yes	No	No	Negative	106	Acinar	30% submitted
11	pT3a	3+4=7	Yes	No	No	Negative	46	Mixed acinar/ductal	Representative
12	pT3c	4+3=7	Yes	No	No	Negative	42	Acinar	90% submitted
13	pT3b	3+4=7	Yes	No	No	Negative	35	Acinar	submitted
14	pT3a	4+3=7	Yes	No	No	Negative	58	Acinar	Entirely
15*	pT3c	4+4=8	No	No	No	Negative	88	Acinar	Representative
16†	pT3c	4+3=7	Yes	No	No	Positive	34	Acinar	Representative

3 (21%) only 3 + 3 in RP

ISUP grading consensus meeting 2014
Intraductal carcinoma of the prostate

- ?Pure IDCP
- ?IDCP associated with invasive cancer
- ?Both

ISUP grading consensus meeting 2014

- IDC-P should not be graded
- Adopted by WHO 2016

ISUP grading consensus meeting 2014
Intraductal carcinoma of the prostate

- ?Pure IDCP
- ?IDCP associated with invasive cancer
- ?Both

These scenarios were not separately discussed and voted on in 2014 consensus meeting

Intraductal carcinoma of the prostate

- Pure IDCP and IDCP-invasive are biologically distinct diseases
 - ~ Pure IDCP: Precursor lesion
 - ~ IDCP associated with invasive cancer: Growth pattern of invasive carcinoma

Intraductal carcinoma of the prostate

- Pure IDCP and IDCP-invasive are biologically distinct diseases
 - ~ Pure IDCP: Precursor lesion
 - ~ IDCP associated with invasive cancer: Growth pattern of invasive carcinoma
- WHO 2016 recommends in-situ morphology code (M8500/2) rather invasive (M8140/3)
- WHO 2016 IDCP: only pure IDCP?

Intraductal carcinoma of the prostate

- Pure IDCP and IDCP-invasive are biologically distinct diseases
 - ~ Pure IDCP: Precursor lesion
 - ~ IDCP associated with invasive cancer: Growth pattern of invasive carcinoma
- WHO 2016 recommends in-situ morphology code (M8500/2) rather invasive (M8140/3)

IDCP associated with invasive Arguments for grading IDCP

IDCP associated with invasive
Arguments for grading IDCP

- **All published data based on H&E**
~ "Comedonecrosis IDCP" graded as pattern 5 in all Gleason papers

Bx: 3+3 + IDCP
Presentation

- 7% had metastatic disease at presentation

Khani F, Epstein JI. AJSP 2015;39:1383-89

IDCP associated with invasive
Arguments for grading IDCP

- **All published data based on H&E**
~ "Comedonecrosis IDCP" graded as pattern 5 in all Gleason papers
- **Grading is for prognostication**
~ Associated with aggressive cancer

Bx: 3+3 + IDCP
Prostatectomy findings

- **High-grade:** 29% 4+3=7, 14% 4+4=8
- **High-stage:** 36% pT3a, 28% pT3b

Khani F, Epstein JI. AJSP 2015;39:1383-89

Biopsy: 3 + 3 + IDC-P
Prostatectomy: 29% 4+3; 14% 4+4

Khani F, Epstein JI. AJSP 2015

Hopkins data USCAP 2015

		Biopsy							
		3+3=6	3+4=7	4+3=7	3+5=8	5+3=8	4+4=8	GS 9,10	
Prostatectomy	3+3=6	72%	21%	9%	4%	5%	3%	1%	4609
	3+4=7	22%	56%	32%	36%	30%	11%	7%	2968
	4+3=7	4%	18%	40%	36%	20%	26%	10%	1246
	3+5=8	0%	1%	1%	13%	10%	1%	4%	86
	5+3=8	0%	0%	0%	0%	15%	0%	2%	18
	4+4=8	1%	1%	9%	2%	0%	38%	8%	364
	GS 9,10	1%	2%	9%	9%	20%	21%	67%	520
		5610	2216	1136	55	20	436	338	9811

Bx: 3+3 + IDCP

Arguments for grading IDCP

- All published data based on H&E
- Grading is for prognostication
- IDCP not part of clinical nomograms

Bx: 3+3 + IDCP

Outcome very different from bx 3+3*

- 7% had metastatic disease at presentation
- Radicals correlation:
 - ~ High-grade: 29% 4+3=7, 14% 4+4=8
 - ~ High-stage: 36% pT3a, 28% pT3b
- Poor outcome
 - ~ 20% disease progression in 3 years after RP/RT
 - ~ 13% ultimately developed metastatic disease
 - ~ 7% died of disease

*Khani F, Epstein JI. AJSP 2015;39:1383-89

Bx: 3+3 + IDCP

Arguments for grading IDCP

- All published data based on H&E
- Grading is for prognostication
- IDCP not part of clinical nomograms
 - ~ Risk of under-Rx
 - ~ 18% underwent active surveillance and 55% of these progressed*

*Khani F, Epstein JI. AJSP 2015;39:1383-89

Prostate Biopsy Specimens With Gleason 3+3=6 and Intraductal Carcinoma
Radical Prostatectomy Findings and Clinical Outcomes

Khani F, Epstein JI. Am J Surg Pathol. 2015;39:1383-1389.

TABLE 1. RP Findings of 16 Patients

Pathologic Stage	Gleason Grade	Extensive IDC/PT	Lymphovascular Invasion	Lymph Node Metastases	Margin Status	Invasive Tumor Type	Prostate Weight (g)	How Submitted (Per Report)	Time to BCR (mo)
1	pT3a	3+4=7	Yes	No	No	Negative	69	Representative	NS
2	pT3b	3+4=7	Yes	No	No	Positive	NS	NS	NS
3	pT3a	3+3=6	Yes	No	No	Positive	64	Representative	7
4	pT3a	4+3=7	Yes	No	No	Negative	56	Entirely	7
5	pT3b	4+4=8	Yes	No	No	Positive	140	Representative	7
6	pT2c	3+4=7	Yes	No	No	Negative	42	Representative	7
7	pT3b	4+4=8	Yes	No	No	Negative	37	Entirely	7
8	pT2c	3+3=6	Yes	No	No	Negative	56	Representative	7
9	pT2c	3+3=6	No	No	No	Negative	33	Entirely	33
10	pT2c	3+3=6	Yes	No	No	Negative	106	30% submitted	52
11	pT3a	3+4=7	Yes	No	No	Negative	46	Representative	46
12	pT2c	4+3=7	Yes	No	No	Negative	42	90% submitted	90%
13	pT3b	3+4=7	Yes	No	No	Negative	35	Entirely	69
14	pT3a	4+3=7	Yes	No	No	Negative	58	Entirely	71
15*	pT2c	4+4=8	No	No	No	Negative	NS	Representative	NS
16†	pT2c	4+3=7	Yes	No	No	Positive	34	Representative	NS

3 (21%) only 3+3 in RP

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One had EPE, another mixed acinar-ductal, third developed BCR

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TABLE 1. RP Findings of 16 Patients

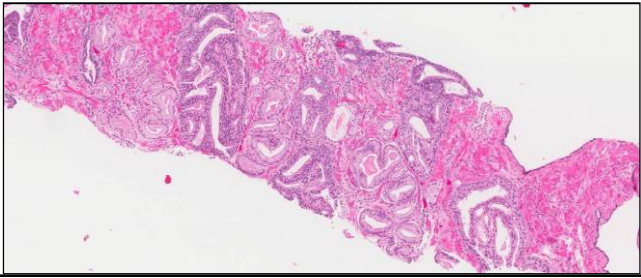
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All cases with 3+3 in radical were only partially embedded

Bx: 3+3 + IDC/PT
Arguments for grading IDC/PT

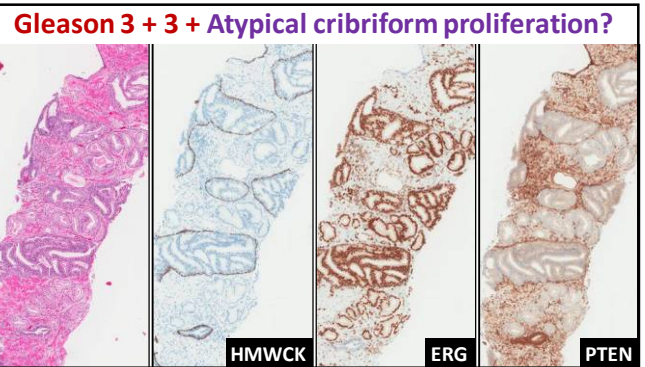
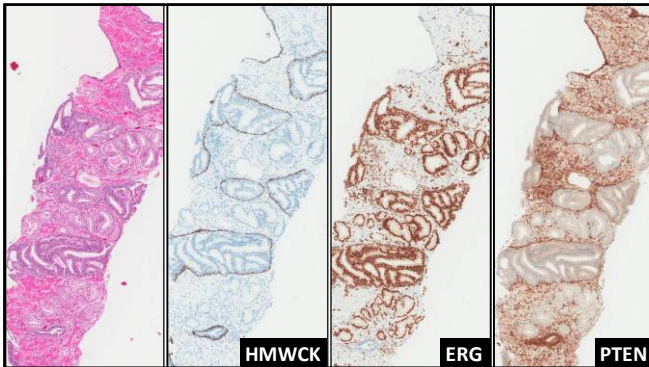
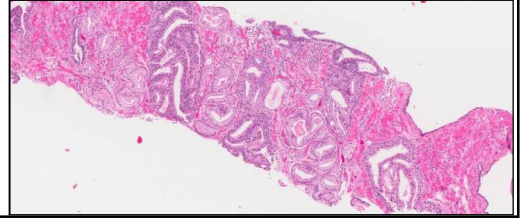
- All published data based on H&E
- Grading is for prognostication
- Distinction between IDC/PT and invasive can be impossible on morphology
 - ~ Would require frequent use of IHC in high-grade prostate cancer

IDCP not graded
A practical issue



IDCP not graded
A practical issue

- 3+3 + loose cribriform not amounting to IDCP



My approach to IDCP reporting

- A personal perspective

My approach Pure IDCP

- **Search hard for invasive component (even 3 + 3)**
 - “ Deeper levels
 - “ Recommend radical Rx for 3 + 3 + IDCP

My approach Diagnostic criteria for IDCP

- **Nuclear size** criterion: Do not use
- **Dense cribriform** cut-off: use 70%

My approach IDCP: To Grade or not to grade?

- **I do not grade pure IDCP**
 - “ May be mis-interpreted as invasive cancer

My approach

IDCP associated with invasive cancer

- **Grade by morphology rather than immunohistochemistry**
 - ~ Cribriform IDCP: pattern 4
 - ~ Comedonecrosis IDCP: pattern 5

My approach

IDCP associated with invasive cancer

- **Grade by morphology rather than immunohistochemistry**
- **Would add comment if grading based on IDCP component**

My approach

IDCP associated with invasive cancer

- **Grade by morphology rather than immunohistochemistry**
 - ~ Cribriform IDCP: pattern 4
 - ~ Comedonecrosis IDCP: pattern 5
 - ~ Micropapillary with marked atypia IDCP: do not grade

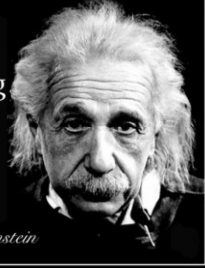
Intraductal carcinoma of prostate

Explanation for variation

- **Different rules used**
 - ~ Diagnostic criteria
 - ~ Reporting rules

Einstein's definition of insanity

Insanity:
doing the same thing
over and over again
and expecting
different results.



- Albert Einstein

3/6 cores, max 3mm/30%, Gleason 3 + 4 = 7 (Grade Group: 2)

5/6 cores, max 10mm/100%, Gleason 4 + 4 = 8 (Grade Group: 4)

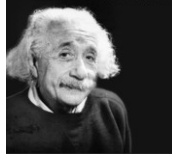
Histopathology reporting insanity?

Insanity's definition to insanity

Doing something very differently and
expecting the same result!

Insanity: doing the
same thing over
and over again
and expecting different
results.

ALBERT EINSTEIN



3/6 cores, max 3mm/30%, Gleason 3 + 4 = 7 (Grade Group: 2)
Suitable for active surveillance?

5/6 cores, max 10mm/100%, Gleason 4 + 4 = 8 (Grade Group: 4)
NOT suitable for active surveillance?

