Histopathology of prostate cancer

Dr M. Sibony
Department of Pathology
Cochin Hospital
Rene Descartes University
Zonal anatomy of prostate
Mc Neal (1984)

• 3 parenchymal zones:
  – TZ, transition zone
  – CZ, central zone
  – PZ, peripheral zone

• 1 anterior fibromuscular stroma (AFMS)
Normal Histology

- Glands and ducts: epithelial bilayer
  - Interior cells
    - PSA + PAP + AR+
  - Outer cells: basal cells
    - CK 5/6 +, p63 +, CK 903 +,
    - PSA-, AR-
    - Never seen in cancer
Before therapeutic prostatectomy / focal therapies

• Local staging of PCa is more necessary than ever, as non confined tumors cannot be treated by focal therapies

• Standard biopsies
  – 12 cores, 6 sextants
  – 10 cores ?
  – > 12 cores ? Including anterior prostate

• MRI / Targeted biopsies
Considering the biopsies sampling

• Apex (apical one third)
  – PZ tissue
  – +/- AFMS

• Mid-gland (middle one third)
  – PZ
  – TZ

• Base (basal one third)
  – CZ
  – PZ
  – TZ
Anatomical prostate cancer

• Posterior and postero lateral
  – Arising in the PZ mostly
  – The most frequent cancers,
  – The most aggressive cancers

• Anterior (more and more frequent)
  – Apex : PZ
  – Mid and base : TZ
Zonal prostate cancer

- **Pca of external prostate (PZ and CZ)**
  - Moderately to poorly differentiated (GS 6-10)
  - Often multifocal
  - High PSA
  - Detected on MRI
  - If evoluated palpable on DRE

- **Pca of TZ**
  - Well differentiated (GS 4-6)
  - Low PSA
  - Can be seen on MRI
  - Sometimes sampled on PB
Multifocal prostatic cancer

3 PZ tumours, 1 TZ cancer
Prostatectomy specimens

- Macroscopic evaluation
- Handling and processing
- Reporting, staging
Prostatectomy specimens

• **Macroscopic evaluation**
  – Weight without seminal vesicles
  – 3 diameters (evaluation of volume)
  – External surface is painted (at least two colors: R and L)
  – Well fixed before sectionning (24 to 48hrs)

*(Consensus conference, Modern pathol 2010)*

• **My method**
  – Complete sampling
  – ~5 mm thick slices
  – Whole mount technique
Inked prostate

anterior face

posterior face
PROSTATECTOMY SCHEME

weight: g (without SV)
Measures: cm ht x cm large x cm antero-post

base / neck

base (if necessary)

apex

Dr M Sibony  Department of Pathology, Cochin Hospital  2012
If complete sampling is not done?

- We can miss
  - Small cancer < 3 – 5 mm or < 0.5 cm³

- Some prognostic informations
  - Extra prostatic extension (EPE)
  - Surgical margins (SM)

- No precise definition of
  - Tumor multifocality (very frequent: 60 to 90% of cases)
  - Tumor localization (PZ vs TZ)
  - Tumor volume evaluation which is correlated to tumor size
Reporting

• Histological type
• Grading according to the Gleason Score system
• Tumor multifocality (dominant or index tumor)
• Tumor volume (dominant or index tumor)
• TNM including SM status
Reporting

- Histological type
- **Grading according to the Gleason Score system**
- Tumor multifocality (dominant or index tumor)
- Tumor volume (dominant or index tumor)
- TNM including SM status
Gleason Score

- Since 1964
- appreciation of aggressiveness
- Prognostic factor, included in all predictive models before therapeutic
  - Findings at RP
  - Biochemical failure
  - Local recurrences
  - Lymph nodes or distant metastases

- Architectural criteria
- Sum of two grades
- Ex: 3+4 = 7
Modified GS
(ISUP 2005, J urol 2010)

• GS 2-4 not on biopsies
• Redefinition of grades 3 and 4
  – Cribriform = 4
• Scoring each BP or each sextant
• If tertiary pattern : mention it
  – On prostatectomy : ex 3+4+5
  – On BP : 3+4+5 $\Rightarrow$ 3+5
  – Or 4+3 (95% grade 4) $\Rightarrow$ 4+4
GS 5 (2+3)

TZ

GS 7 (3+4)
EPE +
R0

PZ
Reporting

- Histological type
- Grading according to the Gleason Score system
- Tumor multifocality (dominant or index tumor)
- Tumor volume (dominant or index tumor)
- TNM including SM status
Tumor multifocality
Question of: dominant/index tumor

The definition of the index tumor depends on the context

- Index or dominant tumor: the highest grade or stage regardless of the size
- If same GS: the largest tumor.

Van der Kwast, Consensus conference, Modern pathol 2010
Reporting

- Histological type
- Grading according to the Gleason Score system
- Tumor multifocality (dominant or index tumor)
- **Tumor volume (dominant or index tumor)**
- TNM including SM status
Tumor volume

- **Chen formula**
  - \( L \times l \times H \times 0.4 \)

- **Good estimation by measuring the largest diameter of the tumour**

  (Modern pathol 2010, Histopathology 2012)
Reporting

• Histological type
• Grading according to the Gleason Score system
• Tumor multifocality (dominant or index tumor)
• Tumor volume (dominant or index tumor)
• TNM including SM status
Figure 2. Schematic drawings of the 2010 TNM staging classification. EPE, extraprostatic extension; BNI, bladder neck invasion; SVI, seminal vesical invasion.
Substaging of pT2

• Its prognostic value is controversial and it lacks clinical relevance

• Becomes optional (modern pathology 2010)

Figure 1 Multifocality as a confounder of pT2 substaging. A single large prostate cancer, involving less than half of a single side would represent stage pT2a (TNM 2002 and 2010), whereas two very small cancers distributed in the left and right half are considered stage pT2c prostate cancer.

Van Der Kvast modern pathology 2010
• One new suggestion (histopathology 2012) for tomorrow?
  – pT2a the largest tumour dimension ≤ 5mm
  – pT2b the largest tumour dimension > 5mm but ≤ 16mm
  – pT2c largest tumour dimension > 16 mm

• Comment: majority of tumors with diameter ≤ 5mm have a tumor volume ≤ 0.5cm³
Extra prostatic extension EPE (pT3a)

- Cancer invading into periprostatic adipose tissue
- Cancer invading into perineural spaces of large neurovascular bundle in the posterolateral prostate (5 and 7 o’clock)
- Cancer in anterior prostate beyond normal confines of the prostate
- Cancer invading periseminal vesical soft tissue
Focal EPE vs non focal

• Focal vs established
  – Focal a few glands outside of the prostate
  – Established more extensive involvement

• Focal vs non focal
  – 1 hpf and $\leq 2$ separate sections
  – Non focal: more extensive involvement

• or radial distance cutoff
  – $< 0.75$ mm
  – $\geq 0.75$ mm
GS 7 (3+4)
EPE +
R0
PZ
Reporting

- Histological type
- Grading according to the Gleason Score system
- Tumor multifocality (dominant or index tumor)
- Tumor volume (dominant or index tumor)
- TNM including surgical margins (SM) status
Surgical margins

• Definition: when carcinomatous cells reach peripheral ink, it is called + surgical margin.

• R1, R0, Rx

• Extra prostatic +SM
• Intraprostatic +SM
• Artifactually +SM
Recommendations on SM

- Extent of +SM (mm) and or number or blocks *(consensus conference, Modern pathol 2010)*
  - Focal vs extensive

- Localisation of +SM (in particular apex)
Focal apical + SM

Apical positive Surgical Margins = pT2
MRI / histo Correlations
Corrélation
IRM / histo
Conclusion

• The prostatic zonal anatomy permits to better understand prostatic cancer.
• Correlations between MRI and whole mounted slices of prostate have improved comprehension of signals.
• On prostatectomy specimens, pathological report includes more precisely:
  – Anatomical location
  – Multiple foci (i.e dominant/index)
  – TNM (including EPE)
  – Surgical margins
Thank you for your attention,