FROZEN-SECTIONS ANALYSES

Uropathology vs clinical Urology Beyrut 15/10

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FSA indications

□ IoFS only justified if implicating a dramatic change in decision making during surgery

IoFS misdiagnosis index, very significant for patients Is generally low or tempered by the level of expectations

FSA limitations

Sampling conditions

- Small fragments need total exam
- Whole specimen imply (sujective) selection of representative parts
 - Poor sampling \rightarrow 9.5% of errors
 - Whole mount \rightarrow true histology (PLND)
- Tissue freezing >>> loss of subtle details, false positive (RCC)
- Reduced number of sections >>> lack of deep layers: 25% of underDiagn



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Review

Intraoperative Frozen Section Diagnosis in Urological **Oncology**

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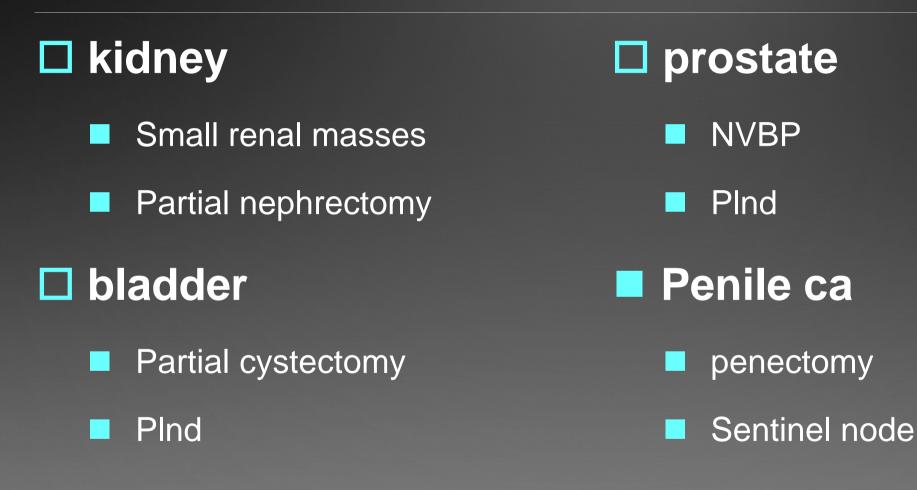
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Abstract

The intraoperative frozen sections are indicated if the pathological findings change the surgical procedure. In urological oncology is not recommended, as a general attitude, in the tumor diagnosis/staging during the surgery. The assessment of the surgical margins is recommended in partial surgical resections but the literature discourages its systematic use in the radical surgical resections. The assessment of the lymph nodes is specially indicated in the penile cancer with intermediate or high risk and non-palpable nodes, and is debated its utility in non-palpable lymph nodes of cystectomies and prostatectomies.

FSA indications





FSA kidney

Small renal masses

□ 16.9% of SRM NOT Ca

- Dubious surgeries 13%
- Benign tumours
- Mets / sarcomas >> Surg Resec
- Cost effectiveness

Partial nephrectomy

- False negative : 20 37%
- False positive : up to 34%

FSA kidney

Small renal masses



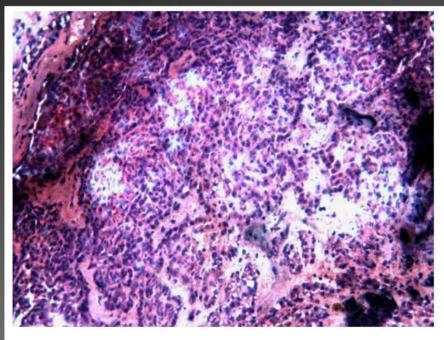


Fig. 1. Frozen section from a renal cell carcinoma. The crushed cells difficult the correct evaluation.

Poor specimen (site or necrosis)

Cystic masses (FNA ??)

freezing

- Cyto-architecture altered
 - RCC vs TCC indication of
 - complete Spec, LND, ureter

FSA kidney

- Small renal masses
 - Partial nephrectomy

SM in nephron sparing

Major REC : multifocality // cell subtypes



Fig. 2. Complete frozen section of a nephron-sparing specimen. The arrows indicate the surgical margin inked.

Specimen 2 types

- Small suspicious fragments
- Specimenb PNX: inked margin
- Relation of tumour cells to ink

FSA bladder

□ bladder

Partial cystectomy



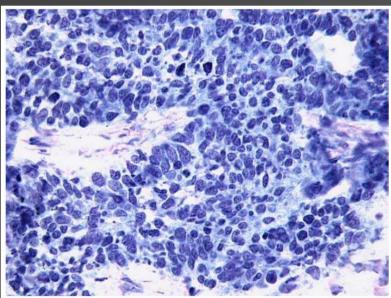


Fig. 3. High grade urothelial carcinoma.

Open partial CX

- Fragment / whole sp
- Inking of SM
- Perpendicular slices
- Differentiation UTT
 - Low = endourology
 - High = radical tt (75%)

• OBJECTIVE:

- To assess the utility of routine frozen section analysis of ureters at the time of radical cystectomy (RC) for urothelial cancer (UC), and the long-term outcomes of adverse ureteric pathology.
- <u>Satkunasivam R</u>1, <u>Hu B</u>1, <u>Metcalfe C</u>1, <u>Ghodoussipour</u> <u>SB1</u>, <u>Aron M</u>2, <u>Cai J</u>1, <u>Miranda G</u>1, <u>Gill I</u>1, <u>Daneshmand S</u>1.

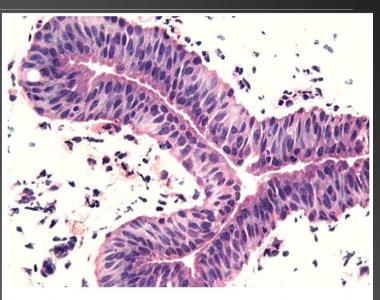


Fig. 4. Ureteral frozen section with normal urothelium. The slight swelling of the cells is a consequence of the frozen.

• PATIENTS AND METHODS:

- Pathological data on 2 047 patients undergoing RC for UC with routine frozen section analysis of ureters (January 1971 to December 2009) were analysed.
- Univariate and multivariable logistic and Cox proportional hazards models were used to determine the risk of
 - upper tract UC (UTUC) recurrence,
 - local recurrence and
 - overall surviva
- I in those identified as having adverse pathology (severe atypia/carcinoma in situ [CIS] or UC) at time of frozen section analysis.
- <u>Satkunasivam R</u>1, <u>Hu B</u>1, <u>Metcalfe C</u>1, <u>Ghodoussipour SB</u>1, <u>Aron M</u>2, <u>Cai J</u>1, <u>Miranda</u>
 <u>G</u>1, <u>Gill I</u>1, <u>Daneshmand S</u>1.

• **RESULTS**:

- Adverse pathology was identified by frozen section analysis in 178 patients (8.6%).
- Frozen section analysis was found to have poor sensitivity in identifying adverse pathology (59.1%), which was improved in patients with preoperative CIS (68.0%).
- After a median (interquartile range) follow-up of 12.4 (1.9-10.1) years, 28 patients (1.4%) developed UTUC recurrence.
 - There were no uretero-enteric anastomotic recurrences.
 - Adverse pathology on frozen section analysis was associated with UTUC recurrence on univariate analysis (hazard ratio [HR] 6.2, 95% confidence interval [CI] 2.9-13.5), but 15/28 patients (54%) with UTUC recurrence had benign ureteric frozen section analysis on initial sectioning.
 - Adverse pathology on frozen section analysis was not independently associated with the risk of local recurrence (HR 1.08, 95% Cl 0.61-1.89) or overall survival (HR 1.12, 95% Cl 0.94-1.35) in multivariate models.

• CONCLUSIONS:

- Ureteric frozen section analysis has poor sensitivity and may be marginally improved in pre-existing CIS.
- UTUC recurrence is rare and can occur despite negative frozen section analysis.
- Our data question the utility of routine frozen section analysis of the distal ureteric margin at the time of RC. <u>Satkunasivam R1</u>, <u>HU B1</u>, <u>Metcalfe C1</u>, <u>Ghodoussipour SB1</u>, <u>Aron M2</u>, <u>Cai J1</u>, <u>Miranda</u> <u>G1</u>, <u>Gill I1</u>, <u>Daneshmand S1</u>. BJU Int. 2016 Mar;117(3):463-8. doi: 10.1111/bju.13081. Epub 2015 Apr 21.

FSA bladder

Radical cystectomy urethra



Fig. 4. Ureteral frozen section with normal urothelium. The slight swelling of the cells is a consequence of the frozen.

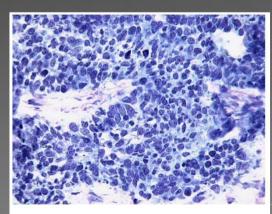


Fig. 3. High grade urothelial carcinoma.

Bx with preop settings

Indicates urethrectomy

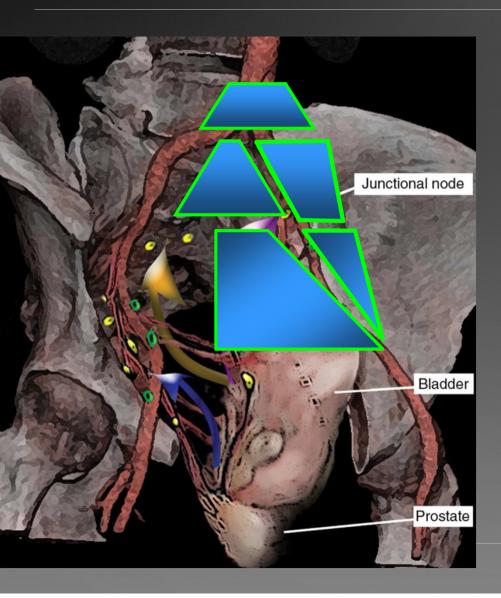
Avoid change in diversion model

Radial SM on specimen

Belongs to definitive PA report

IFS if changes in RCX

FSA Radical cystectomy



Pelvic LND

- Macro LN dis \rightarrow poor 3 yrs DFS
- Micro LN dis \rightarrow 55% at 5 yrs
- IFS not advisable if normal LN
- Extended LND = diagn + cure
- Belongs to definitive PA report
- IFS if changes in RCX

FSA Testis

- Classical diagnosis
 Good correl IFS /final
 - □ Clin, echo, CT, markers
- Testis sparing
 - □ Solitary
 - Bilateral disease
 - □ Non GCT

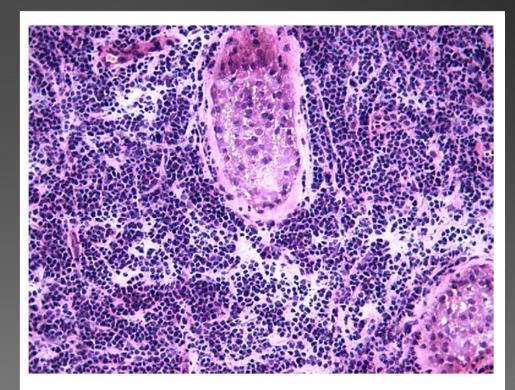


Fig. 5. Testicular involvement for a lymphoproliferative proliferation.

FSA Prostate

Biopsies

- □ NO FS on core biopsies !
- □ Gleason score ???

TURP specimen

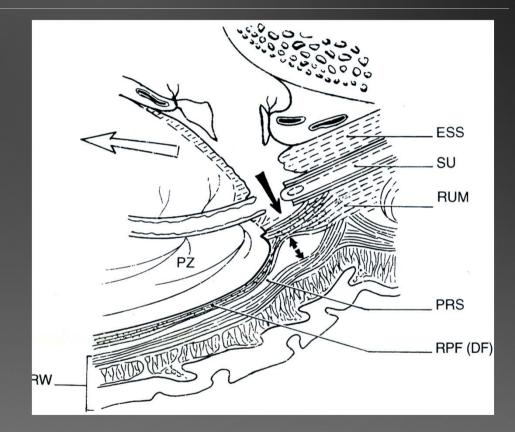
- FS not recommended
- Sample representative?
- Separate sampling better

LN assessment

- See nomograms for indications
- Full LND to be preferred
- Ilio-obturator / limited LND
 - □ Lack of 50% info
- □ Large nodes : oligomets if + ??
- Multimodal therapies

FSA Prostate

- Surgical margins
- - Apex if retrograde
 - Bladder neck if perineal
 - Postero lateral if MiS
 - **PPV 73%**
 - □ NPV 95% (2005)



FSA Prostate

Surgical margins function of fascial dissection

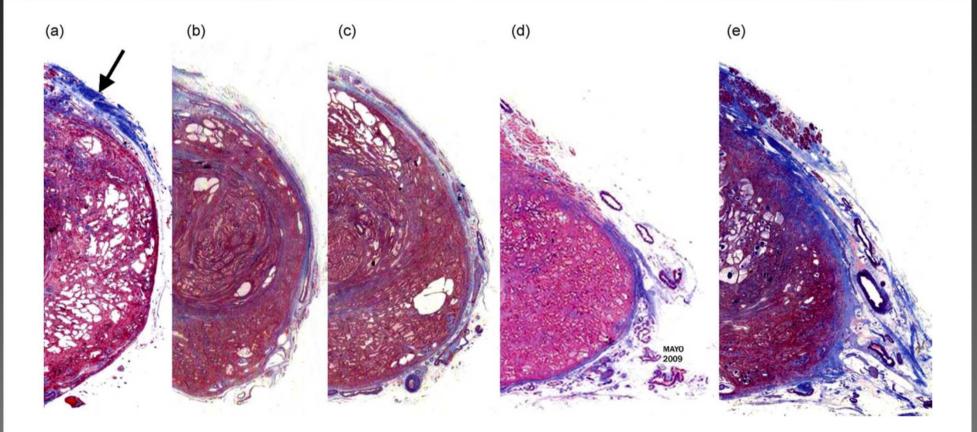


Fig. 6 – Variation of prostate capsule to prostatic fascia (PF) on the lateral surface of the prostate. Masson-trichrome staining: fascia stains bright blue; smooth muscle stains red. (a) Capsule present but no PF visible (arrow: fascial tendinous arch of pelvis); (b) PF fused to capsule; (c) capsule fused to PF; very fine levator ani fascia lateral to vessels; (d) fascia-capsular interface, variable and poorly defined; (e) relatively thick PF present but no capsule visible. Reproduced with permission from the Mayo Clinic.

FSA Penile Ca

- IFS not recommended for diagnosis
 - Squamous cell diff vs hyperplasia with ca

Surgical margins

- Easy specimen: distal/ subtotal penectomy
- □ All structures to be examined

□ LN assessment

Low risk = non palapable LN \rightarrow **no IFS**

 \Box Intermediate risk = palapable nodes \rightarrow IFS on sentinel

Conclusions

- The indications of frozen section diagnosis in **uropathology** are quite specific, and this explains the fact that they amount to a mere 7.3% of the frozen sections performed in general hospitals.
- Generally speaking, frozen sections are not warranted to identify the nature of a tumoral mass, with the following exceptions:
 - (1) renal masses of a doubtful parenchymal origin or located in the urinary tract,
 - (2) testicular neoplasias, when the possibility of a conservative treatment arises,
 - (3) determination of the presence of a prostate adenocarcinoma in an organ donor with high serum prostate-specific antigen (but even in these circumstances the need is widely controversial).
 - F. Algaba Analytical and Quantitative Cytopathology and Histopathology

Conclusions

- Intraoperative determination of surgical margins is particularly useful in
 - (1) partial nephrectomies (it may be limited to inspection after dyeing the margin with India ink; bed freezing is very seldom needed)
 - (2) partial penectomies (always studying the urethral margin and the cavernosal and spongiosal corpora margins).

• F. Algaba

 <u>Analytical and Quantitative Cytopathology and Histopathology</u> [2015, 37(1):23-28]

Conclusions

- The study of the nodes is a widely debated issue,
 - except for those cases in which unexpectedly increased node size is found,
 - systematic frozen sections are indicated neither of the bladder nor of the prostate.
 - The situation regarding penis carcinoma is different, as in the groups with intermediate and high risk of node metastasis; frozen section is recommended, particularly of radioisotope-marked sentinel nodes.
 - F. Algaba
- <u>Analytical and Quantitative Cytopathology and Histopathology</u> [2015, 37(1):23-28]