




Role of cryobiopsy in lung transplant surveillance

M. Angeles Montero
 Royal Brompton and Harefield NHS Trust
 Imperial College University, London
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Royal Brompton & Harefield 
Imperial College 

I have no conflicts of interest

TBB is the gold standard for the monitoring of lung TX patients

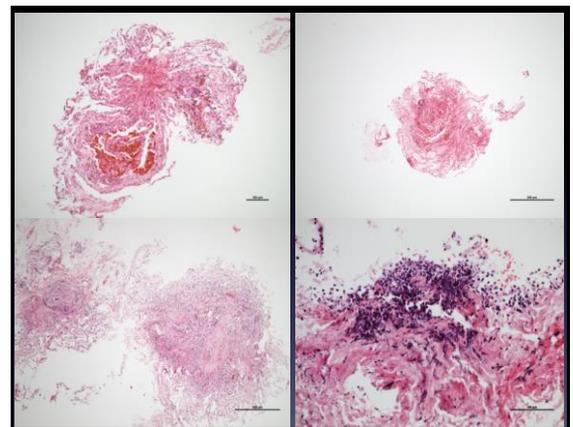
Adv Anat Pathol • Volume 12, Number 4, July 2005

TABLE 2. Reliability of Transbronchial Biopsy ^{22,45,46-48,50}
High Utility
Lung cancer and some metastases
Sarcoidosis
<u>Opportunistic infections in immunocompromised patients</u>
<u>Lung transplantation</u>

Minimum of 5 fragments of lung parenchyma, each with

- 100 alveoli
- One bronchiole

Yousem SA et al. *J Heart Transplant* 1996; 15:1-15



Pathologic Interpretation of Transbronchial Biopsy for Acute Rejection of Lung Allograft Is Highly Variable

American Journal of Transplantation 2011; 11: 320-328

Ansary et al.

TBB IN ILD

Author	Diagnosis		
Anderson 1978 N=939 (rev. por Churg)	31%	Non spec	44%
		Normal/Inad	25%
Poletti 1988 N=801	29%	com Clin Dx	37%
		Non spec	34%
Ensminger 2006 N=603	38%	Useful	76%
		Non useful	24%

Cryobiopsy in ILD

Articles	P	Size	Diagn %	No Dg	deaths [⊙]	Mild-Mod C [★]	Sev C	Pneumt %
Fruchter	75	9 mm	75	29	0	4%	0	2.6
Casoni	69	43.11 mm ²	76		1		0	28
Hdez-Glez	33	4	79	21	0	30%	0	12
Pajares	77	14.7 mm ²	74.4	25,6	0	56.4%	0	7,7
Kropski	25	8.7	76	20	2 (worsening)		0	0
Babiak	41	15.11 mm ²	95		0		0	4.8
Griff	52	6,9	79		0		0	

- ★ Mild to moderate bleeding which resolved with clinical manouvers
- ⊙ Deaths or clinical worsening

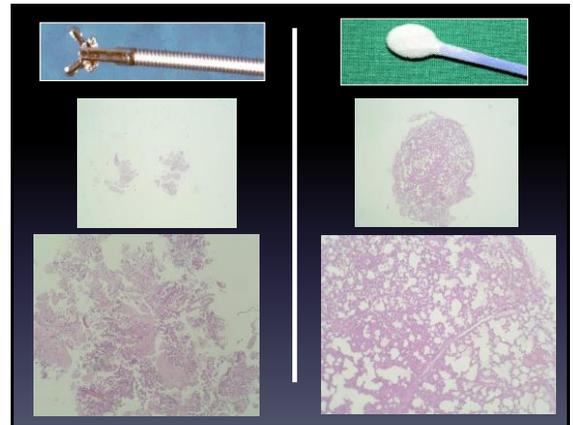
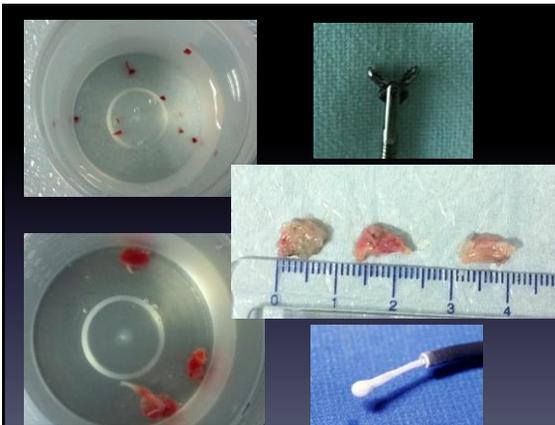
Hypothesis

- Cryobiopsies will improve the diagnostic yield in the monitoring of lung TX patients.

Aims

- To evaluate the diagnostic yield and the quality of the TBB obtained by cryoprobes.

IN TRANSPLANTED PATIENTS



Methods

- Restrospective, non randomized, comparative and observational study.
- 81 consecutives biopsies in 58 lung TX patients, single or bilateral lung transplantation.
- Period: January to December 2011.

All patients agreed to participate in this study and the study was approved by the ethics committee in HUVH

- Forceps biopsies: UCI
- Cryobiopsies: rest of patients

Results

Patients	Forceps	Cryoprobe	p
Biopsies	41	40	
Fragments	3,65	3,78	0,5
Size mm ²	25,0	82,4	< 0,0001
Num alveoles	97,3	399,1	<0,0001
No diagnosis	10 (25%)	1 (2,5%)	<0,009
Diag. probable	9 (22,5%)	12 (29,3%)	ns
Diag. Certain	21 (52,5%)	27 (66%)	ns
Complications	7	16*	0,056

	Total	Forceps	Cryobiopsy	P - value
Diagnostic	48	26	28	0.638
Probable	22	6	12	0.250
Non diagnostic	11	9	1	0.014
Acute cellular rejection	18	6	12	
Chronic rejection	6	-	6	0.0257
AMR	10	4	6	
No rejection	46	29	17	0.0048

	Total	Forceps	Cryobiopsy	P - value
Biopsies				
Procedure	81	41	41	
RLL/LLL/others	43/29/9	25/13/3	18/16/6	
Histology				
Area (mm ²)	225 - 4	56 - 4	225 - 20	< 0.0001
Alveoles	325 - 0	87 - 0	325 - 25	< 0.0001
Artefact	9	9	0	< 0.007
Vessels	43	13	30	< 0.0003
Num vessels	0.85±1	0.46±0.9	1.2±1.1	0.001

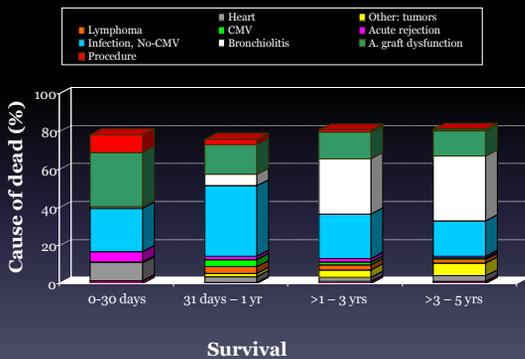
TBB in lung transplant

GRAFT DYSFUNCTION (more frequent):
INFECTION VS REJECTION
 Any time
 Specimen: 3 to 5 fragments

TREATMENT CONTROL (frequent):
 Doubts in the clinical evolution
 1-2 weeks post clinical TBB
 Specimen: 3 to 5 fragments

SURVEILLANCE (single):
 2^a-5^a week POST-TX

CAUSES OF DEATH (1982-2000)



Lung Allograft Rejection

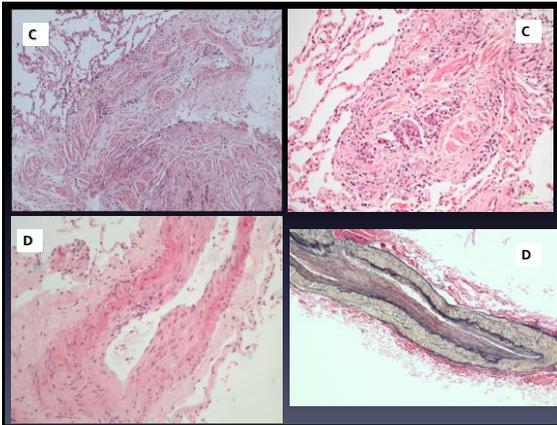
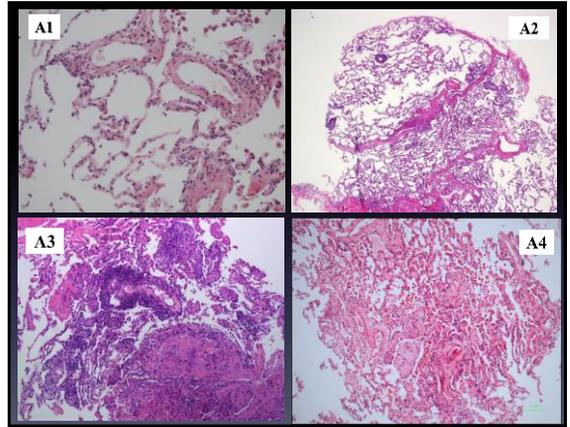
Revision of the 1996 "Working Formulation" for the standardization of nomenclature in the diagnosis of lung rejection
(JHLT, 2007;26(12):1229-1242)

A. Acute rejection
 Grade 0 - none
 Grade 1 - Minimal
 Grade 2 - mild
 Grade 3 - Moderate
 Grade 4 - Severe

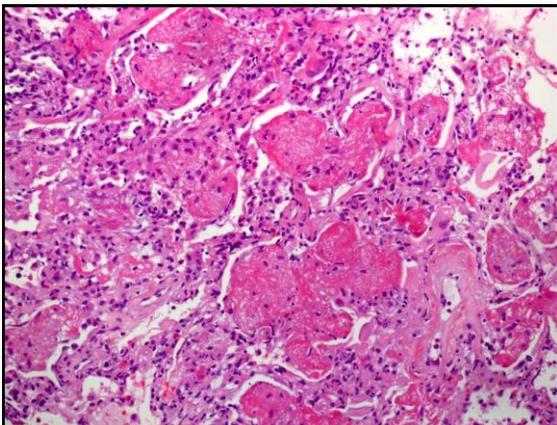
B. Airway inflammation:
 Lymphocytic bronchiolitis
 Grade 0 - no inflam
 Grade 1R - Low grade
 Grade 2R - High grade
 BX. Ungradable

C. Chronic airways rejection
Obliterans bronchiolitis (BOS)
 Grade 0 - absent
 Grade 1 - Present

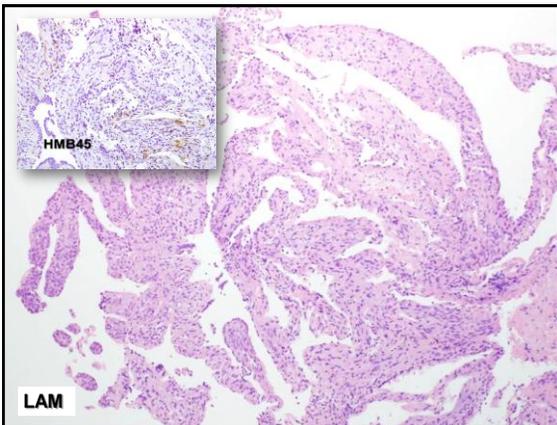
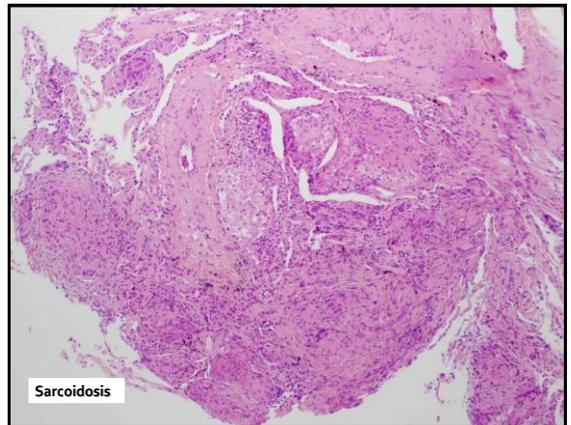
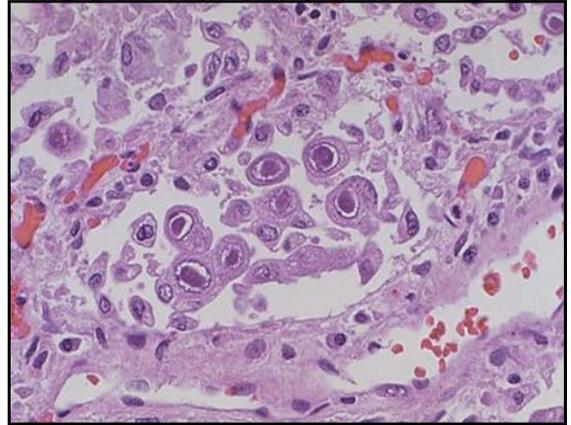
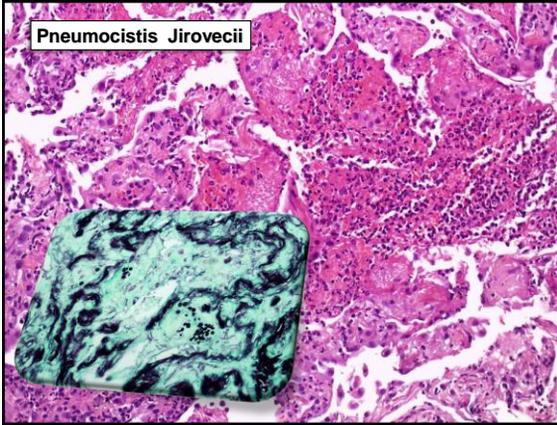
D. Chronic vascular rejection
(accelerated graft vascular sclerosis)

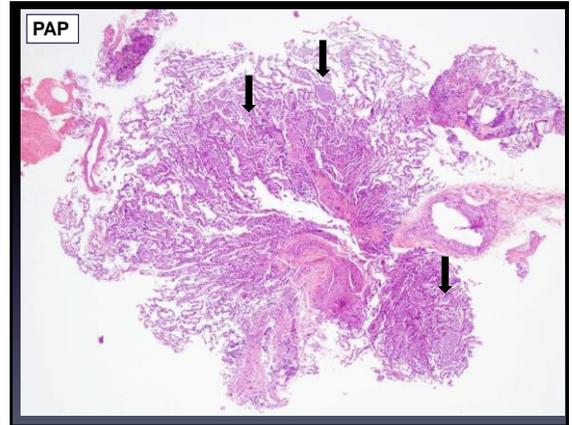
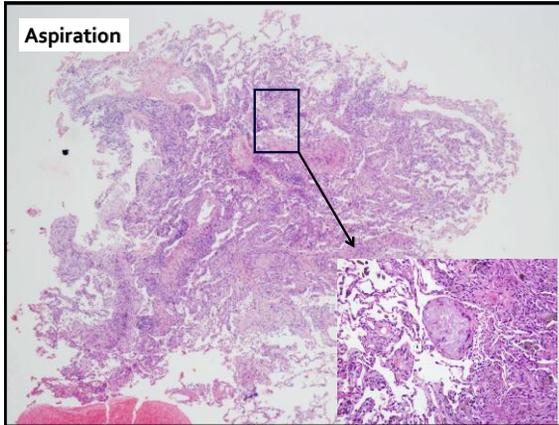


Primary Graft Dysfunction



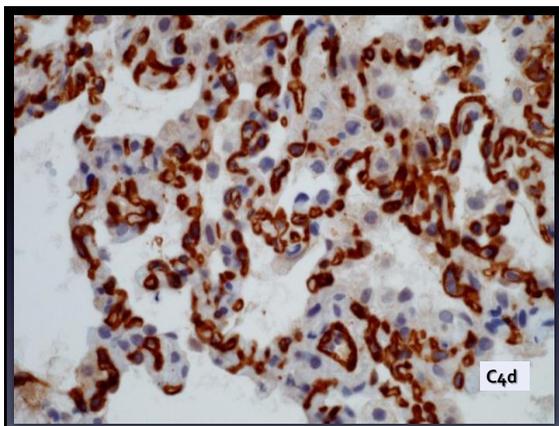
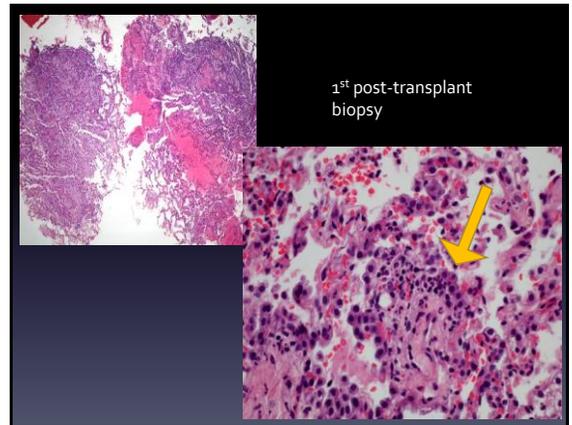
Infections





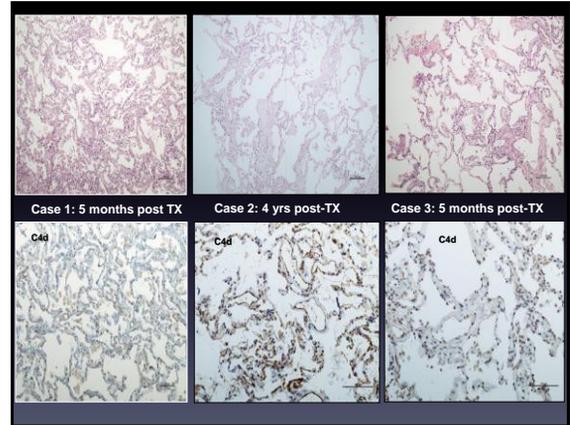
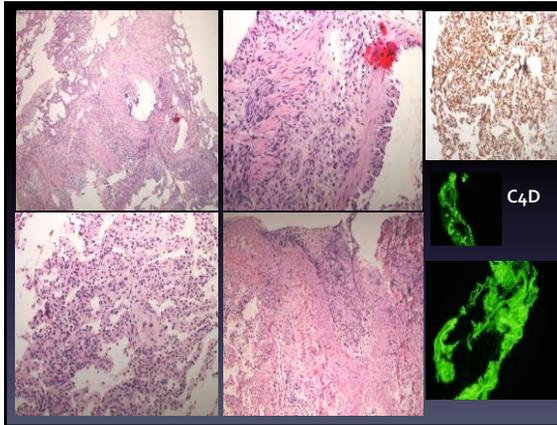
EARLY AMR

- BSSLTX: DAD secondary to pneumonia (H1N1)
- Pre-transplant sensitized with High DSA.



Late AMR

- Graft dysfunction after 3 years post –TX.
- DSA positive.
- Clinical and radiological improvement



Conclusions

- Cryobiopsy allows harvesting:
 - larger and well expanded biopsies
 - Decrease in non-diagnostic biopsies
 - Safe procedure



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