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Transbronchial Lung Biopsy and Cryobiopsy in the Diagnosis of Fibrotic Interstitial Lung Diseases

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Problems of surgical lung biopsies in ILD

- Complications: 2-4% mortality at 90 days mainly for acute exacerbation, infections, 3-12% of prolonged air leak, >50% of pain at 12 months
- Can not be performed in many patients because of advanced age, comorbidities, severity of disease or patient deny
- For risk-benefit considerations, only about 10-20% of patients with fibrotic ILD undergoes a surgical lung biopsy
 - ... an alternative mode of biopsy that overcomes these problems without substantial loss of diagnostic accuracy would be invaluable..... Margaritopoulos, Wells. Rev Port Pneumol 2012;18:61-63



Transbronchial biopsy is useful in detecting UIP pattern Tomassetti et al. Respir Res 2012;13:96

Retrospective blinded review of TBB in 64 patients with various ILDs (40 UIP, 24 non UIP), all with a subsequent surgical lung biopsy

- TBB showing UIP (2 or 3 of the following: patchy fibrosis, fibroblastic foci, honeycombing): <u>specificity 100%</u>
- TBB showing just 1 lesion of UIP: specificity 85%
- Acceptable interpersonal agreement (k 0.61 for the presence of at least 1 lesion, k 0.46 for the exact number of lesions)
- TBB showing UIP: <u>sensitivity 20%</u> (32% in Berbescu et al, Chest 2006; 0% in Shim et al, Pathol Intern 2010)
- TBB in mimickers of UIP (f-NSIP, chronic HP, smokingrelated ILD): sensitivity 12.5%-16%, specificity 20%-25%









	N° of patients	Mean size	Diagnostic yield (after MDD)	N° of histologic diagnoses of UIP	Complications
Babiak, Respiration 2009	41	15.1 mm²	95.1%	15	Pnx 4.9%
Pajares, Arch Bronchopneumol 2010	10				None
Griff, Diagn Pathol 2011	15	17.1 mm²			None
Fruchter, Respirology 2013 (in lung transplant)	40	10 mm ²	100%		None
Fruchter, Lung 2013 (in immunosuppressed)	15	9 mm²	100%		None
Yarmus, Chest 2013 (in lung transplant)	17	≈50 mm²			None
Kropski, PLOS ONE 2013	25	64.2 mm²	80%	7	None
Casoni, PLOS ONE 2014	69	43.1 mm²		47	Pnx 28%, death due to acute exacerbation of IPF 1.4%
Fruchter, Respirology 2014	75	9 mm²	70% definite + 28% probable	7	None
Pajares, Respirology 2014	39	14.7 mm²	51.4%	7	Pnx 7,7%
Griff, BMC 2014	52	30.4 mm ²	79%	9	None
Hagmeyer, Clin Respir J in press	32		72%		Pnx 19%, bleeding 78% (none requiring surgery)
Hernandez-Gonzales, Arch	33		79%		Pnx 12%, mild bleeding

Diag	nostic yield	of trans intersti	sbronchia tial lung	ıl	Cor	nplications	Cryoprobe group n (%)	Conventional- forceps group n (%)	P-value
c	disease: a randomized trial Pajares et al. Respirology 2014;19:900-906				Blee G G G Pne	eding irade 0 irade 1 irade 2 irade 3 iumothorax	5 (12.8) 12 (30.8) 22 (56.4) 0 (0) 3 (7.7)	8 (21.1) 17 (44.7) 13 (34.2) 0 (0) 2 (5.2)	0.068
	Hist	opathologic	diagnosis				Multidisciplin	ary diagnosis	
	Histopathologic diagnosis	Cryoprobe group n (%)	Conventional- forceps group n (%)	<i>P</i> -val	ue	Diagnostic consensus	Cryoprol group n (%)	e Conventional- forceps group n (%)	P-value
	Nonspecific interstitial pneumonia	12 (30.8)	1 (2.6)			 Nonspecific interstitial pneumonia 	10 (25.7) 0	
	 Diffuse alveolar damage 	1 (2.6)	2 (5.3)			 Acute alveolar injury 	1 (2.6)	0	
	 Organizing pneumonia 	3 (7.7)	3 (8)			Infection	0	2 (5.3)	
	 Sarcoidosis 	1 (2.6)	2 (5.1)			 Organizing pneumonia 	3 (7.7)	3 (8)	
	 Bronchiolitis- associated DILD 	2 (5.1)	1 (2.6)			 Sarcoidosis 	1 (2.6)	2 (5.3)	
	 Hypersensitivity pneumonitis 	3 (7.7)	0			 Respiratory- bronchiolitis associated DIL 	2 (5.1) .D	1 (2.6)	
	 Eosinophilic pneumonia 	0	2 (5.3)			 Hypersensitivi pneumonitis 	ty 3 (7.7)	0	
	 Adenocarcinoma 	0	1 (2.6)			 Eosinophilic pneumonia 	0	2 (5.3)	
	 Usual interstitial pneumonia 	7 (17.9)	1 (2.6)		_	 Adenocarcinor 	ma 0	1 (2.6)	
	Total	29 (74.4)	13 (34.1)	< 0.00	01	Total	20 (51.4) 11 (29.1)	0.038

Procedure-related adverse events in patients

with ILD'S (Ravaglia et al, in progress)

	Cryobiopsy (235 patients)	Surgical lung biopsy (150 patients)	p value
Pnx	50 (21.3% - 16.6% needed drainage)	N/A	N/A
Drainage, days (mean/± SD)	0.7 (± 1.9)	3.8 (± 3.8)	<0.0001
Mild bleeding	13 (5.5%)	0 (0%)	0.003
Persistent feever	0 (0%)	7 (4.7%)	0.001
Prolonged air leak	1 (0.4%)	5 (3.3%)	0.035
Pneumonitis/ empyema	0 (0%)	3 (2%)	0.058
Death due to acute exacerbation	1 (0.4%)	4 (2.7%)	0.078
Hospitalization, days (median/range)	1 (17-0)	5 (48-3)	<0.0001

Cryobiopsies Forlì Hospital (Italy), March 2011-January 2015

- Retrospective review of 524 cryobiopsies in 310 patients with ILD and non diagnostic clinical-radiologic findings (including the 69 patients of Casoni et al, PLOS ONE 2014)
- No access to clinical data and special stains
- 1-6 biopsies for each patient
- Mean size of the biopsies (combined biopsies for each patient): 44.8 mm² Pleura in 92 patients (29.7%)



277 patients with adequate cryobiopsies • 64 (23.1%) UIP with high confidence: PF+FF with (14) or without (50) HC, and no ancillary findings against IPF













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 46 (16.6%) UIP with low confidence: 3 PF+HC, 7 FF+HC, 19 PF, 11 FF, 5 HC, and no ancillary findings against IPF





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- 46 (16.6%) UIP with low confidence: 3 PF+HC, 7 FF+HC, 19 PF, 11 FF, 5 HC, and no ancillary findings against IPF
- 167 (60.3%) ILDs different from UIP (sometimes with high, sometimes with low confidence - in case of low confidence, I had the possibility to add a second and a third choice diagnosis)

















Cryobiopsy in fibrotic ILD Some key questions				
• What is the capacity of cryobiopsy to recognize UIP/IPF, and to distinguish it from its main mimickers (fibrotic NSIP, smoking-related ILD, connective tissue diseases, chronic HP)?				
15 patients with cryob had a subsequent	15 patients with cryobiopsy (out of 310, 4.8%) had a subsequent surgical lung biopsy			
Cryobiopsy Surgical lung biopsy				
5 inadequate	2 UIP, 1 fibrotic NSIP, 1 LCH, 1 PAP			
5 UIP (low confidence) 2 UIP, 3 chronic HP (with UIP pattern)				
2 fibrotic NSIP (low confidence) 1 fibrotic NSIP, 1 UIP				
1 smoking-related ILD (low confidence) 1 smoking-related ILD				
1 LCH (low confidence)	1 fibrotic NSIP			
1 vasculitis (low confidence)	1 vasculitis (due to cocaine)			

My cryobiopsy diagnoses	MDD
64 UIP-H	58 IPF (90.7%), 2 drug-related ILD (3.1%), 1 HP (1.5%), 1 CTD (1.5%), 1 smoking-related ILD (1.5%), 1 unclassifiable (1.5%)

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46 UIP-L	27 IPF (58.7%), 7 CTD (15.2%), 4 HP (8.7%), 3 i-NSIP (6.5%), 3 smoking-related ILD (6.5%), 1 LCH (2.2%), 1 unclassifiable (2.2%)
36 NSIP-L	12 i-NSIP (33.3%), 10 CTD (27.8%), 2 COP (5.5%), 1 HP (2.8%), 1 drug- related ILD (2.8%), 3 IPF (8.3%), 1 sarcoidosis (2.8%), 1 lymphoma (2.8%), 5 unclassifiable (13.9%)

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My diagnoses	T. Colby diagnoses



My diagnoses	T. Colby diagnoses
64 UIP-H	35 UIP-H (54.7%), 21 UIP-L (32.8%), 3 NSIP (4.7%), 1 smoking-related ILD (1.5%), 1 OP (1.5%), 3 other/inadequate (4.7%)
46 UIP-L	22 UIP-L (47.8%), 13 UIP-H (28.2%), 5 NSIP (10.8%), 1 smo UIP H+L: 76% 1%), 1 LCH %)

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36 NSIP-L	24 NSIP (66.7%), 5 UIP-L (13.8%), 1 UIP-H (2.8%), UIP H+L: 16.6%

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36 NSIP-L	24 NSIP (66.7%), 5 UIP-L (13.8%), 1 UIP-H (2.8%), 1 HP (2.8%), 1 bronchiolitis (2.8%), 4 other/inadequate (11.1%)
14 SRILD (H+L)	10 SRILD (71.4%), 3 NSIP (21.4%), 1 other/inadequate (7.1%)

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11 HP-H	7 HP (63.6%), 2 NSIP (18.1), 1 bronchiolitis (9.1), 1 UIP (9.1%)
21 HP-L	9 UIP (42.8%), 5 HP (23.8%), 4 NSIP (19%), 3 other/inadequate (14.3%)

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21 HP-L	9 UIP (42.8%), 5 HP (23.8%), 4 NSIP (19%), 3 other/inadequate (14.3%)
Our agreement for UIP-non UIP: k 0.72 (0.64-0.80)	

Cryobiopsy in fibrotic ILD Some key questions

- What is the capacity of cryobiopsy to recognize UIP/IPF, and to distinguish it from its main mimickers (fibrotic NSIP, smoking-related ILD, connective tissue diseases, chronic HP)?
- What is the added diagnostic value of cryobiopsy in the real multidisciplinary approach to patients with fibrotic ILDs, and how much cryobiopsy is competitive with surgical lung biopsy in this setting?





Cryobiopsy in fibrotic ILD Conclusive remarks

- ... an alternative mode of biopsy that overcomes these problems without substantial loss of diagnostic accuracy would be invaluable..... Margaritopoulos, Wells. Rev Port Pneumol 2012;18:61-63
- Cryobiopsy is relatively safe, potentially increasing the number of patients with fibrotic ILD who can have a biopsy
- · Its diagnostic accuracy seems acceptable
- Further data will be necessary to more exactly clarify the role of cryobiopsy in this setting

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Thank you for your attention!