

ONLINE SUPPLEMENTARY DATA

Supplementary Table 1. The Delphi Questionnaire: “Part 1 - Clinical Practice”.

	SCORE (1-5)	Comments
1. In clinical practice		
Biopsy sampling:		
-A minimum of 3 synovial biopsies needs to be retrieved in large joints.		
-A minimum of 2 biopsies should be retrieved in small joints.		
-Biopsies should be performed in at least 2 different areas of the joint if large.		
-Biopsies should be performed in at least 3 different areas of the joint if large.		
-Biopsies should be performed in at least 2 different areas of the joint if small.		
-Bacteriological, fungal and mycobacteriological assessment should occur in each patient.		
-Polymerase chain reaction analysis for RNA 16S should be performed for each patient.		
-Polymerase chain reaction analysis for Lyme and Whipple diseases should be performed for each patient.		
Biopsy processing:		
-At least 2 biopsies should be formalin-fixed and paraffin-embedded.		
-The biopsies should spend 48 hours in formalin.		
-The biopsies should spend 24 hours in formalin.		
-1 biopsy should be snap frozen.		
-More than one biopsy should be snap frozen.		
-Sections should be 3 micrometers thick minimum.		
Histological criteria:		
-Synovial biopsy surface should be more than 2.5mm ² .		
-A synovial lining layer should be seen.		
-Morphology of the synovial tissue should be 100% preserved.		
-Synovial biopsy should include a minimum of 5 vessels.		
-Synovial biopsy should include a minimum of 10 vessels.		
-Stroma should represent up to 30% of the biopsy area.		
-Stroma should represent up to 50% of the biopsy area.		
-Stroma should represent up to 60% of the biopsy area.		
Staining and IHC:		
-An H&E staining should always be performed.		
-CD3 staining should always be performed.		
-CD19 or CD20 staining should always be performed.		
-CD68 staining should always be performed.		
- Additional CD4 staining should always be performed.		
-Additional CD4 and CD8 staining should always be performed.		
-FVIII or CD31 staining should always be performed.		
-Other staining should always be performed.		
- IHC results should be given using a semi-quantitative score (0-3)		
- IHC staining should be assessed using digital analysis software		
Biopsies interpretation and Pathologist's report.		
-A Krenn score should always be performed to assess inflammation.		
-Other scores for intensity of inflammation should be performed.		
-Lining layer hyperplasia should be scored.		
-Absolute number of vessels should be assessed.		
-Synovial pathotype should be described.		
-Presence or absence of lymphoid follicles within the membrane should be described.		
-A quantitative cell count using a digital analysis should be performed because it is more accurate.		
-A semi quantitative evaluation of the number of cells is accurate enough.		
-If a semi-quantitative or quantitative analysis is performed for a single biopsy, the assessment of a single area is sufficient.		
- If a semi-quantitative or quantitative analysis is performed for a single biopsy, at least 3 area of the biopsy should be assessed.		
- If a semi-quantitative or quantitative analysis is performed for multiple biopsies, average score should be calculated and given for the analysis of inflammation		
-Conclusion of the pathologist should always mention the likeliest diagnosis.		

Supplementary Table 2. The Delphi Questionnaire: “Part 2 - Translational Research”.

	SCORE (1-5)	Comments	
2. In clinical research			
Biopsy sampling:			
-A minimum of 3 synovial biopsies needs to be retrieved in large joints.			
-A minimum of 2 biopsies should be retrieved in small joints.			
-Biopsies should be performed in at least 2 different areas of the joint if large.			
-Biopsies should be performed in at least 3 different areas of the joint if large.			
-Biopsies should be performed in at least 2 different areas of the joint if small.			
Biopsy processing:			
-At least 2 biopsies should be formalin-fixed and paraffin-embedded.			
-The biopsies should spend 48 hours in formalin.			
-The biopsies should spend 24 hours in formalin.			
-1 biopsy should be snap frozen.			
-More than one biopsy should be snap frozen.			
-5 biopsies should be snap frozen to perform RNA extraction.			
-Sections should be 3 micrometers thick minimum.			
Histological criteria:			
-Synovial biopsy surface should be more than 2.5mm ² .			
-A synovial lining layer should be seen.			
-Morphology of the tissue should be preserved.			
-Synovial biopsy should include a minimum of 5 vessels.			
-Synovial biopsy should include a minimum of 10 vessels.			
-Stroma should represent up to 30% of the biopsy area.			
-Stroma should represent up to 50% of the biopsy area.			
-Stroma should represent up to 60% of the biopsy area.			
Staining and IHC :			
-An H&E staining should always be performed.			
-CD3 staining should always be performed.			
-CD19 or CD20 staining should always be performed.			
-CD68 staining should always be performed.			
-CD 131 staining should always be performed.			
- Additional CD4 staining should always be performed.			
-Additional CD4 and CD8 staining should always be performed.			
-FVIII or CD31 staining should always be performed.			
-Other staining should always be performed.			
Biopsies interpretation and Pathologist's report.			
-A Krenn score should always be performed to assess inflammation.			
-Other scores for intensity of inflammation should be performed.			
-Lining layer hyperplasia should be scored.			
-Absolute number of vessels should be assessed.			
-A quantitative cell count using a digital analysis should be performed because it is more accurate.			
-A semi quantitative evaluation of the number of cells is accurate enough.			
-If a semi-quantitative or quantitative analysis is performed for a single biopsy: the assessment of a single area is sufficient.			
- If a semi-quantitative or quantitative analysis is performed for a single biopsy: at least 3 area of the biopsy should be assessed.			
-Average score should be calculated and given for the analysis of inflammation and vascularization			
-Presence or absence of lymphoid follicles within the membrane should be described.			
-Synovial pathotype should be described			
RNA analysis			
-RNA extraction should be performed in each biopsy.			
-Biopsies of one patient should be pooled for RNA extraction.			
-A minimum of 10mg of synovial tissue should be used for RNA extraction.			