**Supplement 2 – Histology findings descriptive**

**Page 2-31:** Table E1 - Overview of histological findings per group

* Qualitative descriptions per histological slide of the systematically assessed samples per group, as described while blinded to the allocated group or survival term. Remarkable findings are marked **bold.**

**Page 32-66:** Table E2 - Overview of histological findings in additional samples

* Qualitative descriptions of the additional histological slides taken per experiment, as described while not blinded. Remarkable findings are marked **bold.**

**Table E1:** Overview of histological findings per group

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| #  | **Survival term**  | **Group** | **Section** | **ID** | **Description (blinded)** |
| 1 | 5 days | NHS-POx | Central | E1 G1 | Patch material present with influx of immune cells (PNMs, macrophages, giant cells, lymphocytes). Minor infiltrate below the patch with some lymphocytes, PNMs and macrophages. Little neovascularization is seen. Single eosinophilic granuloma seen deeper in the parenchyma with no direct relation to the patch material. |
| Pleural overlap | E1 G2 | Section with patch material on top of pleura, cells can be seen scattered throughout the patch. Limited inflammatory response with macrophages and lymphocytes. |
| Fibrin/thrombin patch | Central | E1 T1 | Section with patch on top of pleura. Deep in the parenchyma and also reaching the pleural surface are extensive eosinophilic parasitic granulomas. The pleural interface shows young granulation tissue and collagen deposition with capillaries in the pleura/patch interface, with macrophages and PMNs also. Below this layer, there is inflammation with lymphocytes and plasma cells. |
| Pleural overlap | E1 T2 | Section with no recognizable patch. At the right side normal pleura can be seen. A single incisional wound is seen, with no healing and mainly blood clotting. In the lung parenchyma moderate inflammation is seen with extensive eosinophilic granulomas with parasites, surrounded by macrophages, lymphocytes and PMNs. The closest granuloma is located at 0,1 mm from the pleura. |
| Negative control | Central | E1 C3 | Mainly healthy looking lung parenchyma with some collapsed parenchyma just below the pleura. No significant immune rersponse, no patch material recognizable. Beginning of granulation tissue formation in areas of lung incision. |
| 2 | 5 days | NHS-POx | Central | E2 G1 | Patch identifiable on surface with mainly macrophages infiltrating from the pleural interface. Some inflammatory cells scattered throughout the patch and several giant cells around the patch. Some necrosis seen below the patch. Several eosinophilic granulomas seen within the lung parenchyma. |
| Pleural overlap | E2 G2 | Patch material on lung with scattered immune cells throughout patch. Minimal to moderate inflammation with polymorphonuclear cells, macrophages and lymphocytes. Eosinophilic granuloma seen deep in lung parenchyma.  |
| Fibrin/thrombin patch | Central | E2 T1 | Path on lung, with scattered lymphocytes, eosinophils and PNMs throughout. Below patch, some inflammation with lymphocytes, macrophages, giant cells and eosinophils. Also, many fibroblasts are seen in the granulation tissue below the patch. Eosinophilic granuloma without parasites seen in lung parenchyma. |
| Pleural overlap | E2 T2 | Section with patch on top of pleura, inflammatory response with mainly macrophages and plasma cells, some neutrophils and lymphocytes. Patch is diffusely infiltrated with immune cells, on top of patch also areas of granulation and inflammatory cells. |
| Negative control | Central | E2 C3 | No visible patch. Clearly identifiable incision lesions with neovascularization and granulation tissue. Some bleeding seen in subpleural alveoli. No major inflammatory reactions. No granulomas. |
| 3 | 5 days | NHS-POx | Central | E3 G1 | Section with patch material on top of pleura. Extensive hemorrhage is seen throughout the section, and blood is also seen in the patch. There is an extensive inflammatory infiltrate with PNMs (partly associated with hemorrhage), macrophages and giant cells and lymphocytes/plasma cells. Some fibrosis is seen around the patch, and healing mainly consists unorganized granulation tissue. |
| Pleural overlap | E3 G2 | Patch material remaining on lung, associated with surrounding fibrosis and neovascularization. Inflammatory response mainly subpleural with lymphocytes and plasma cells. Macrophages seen. No granulomas. |
| Fibrin/thrombin patch | Central | E3 T1 | Patch on lung surface. Below pleura, collapsed parenchyma with inflammatory cells (macrophages and lymphocytes and foreign body giant cells) and beginning of healing response. |
| Pleural overlap | E3 T2 | Patch material on top of pleura, extensive bleeding is seen between patch and pleura, also in alveoli. In blood cloths, some polymorphonuclear cells. Inflammatory response around patch with mainly macrophages and lymphocytes. Below patch, area of collapsed lung parenchyma. |
| Negative control | Central | E3 C3 | Recognizable patch material with areas of well-formed granulation tissue with groups of neovascularization. Inflammatory infiltrate below pleura consists mainly of lymphocytes, plasma cells and macrophages. Focally necrosis is seen. |
| 4 | 5 days | NHS-POx | Central | E4 G1 | Patch seen on pleura. Extensive bleeding/hematomas seen within the lung parenchyma / subpleural. Patch contains scattered immune cells. Immune reaction with mainly polymorphonuclear cells, **macrophages (also foamy macrophages adjacent to patch). Remarkable type II pneumocyte proliferation subpleural.** No granuloma. |
| Pleural overlap | E4 G2 | Section with patch material. Moderate infiltrate with macrophages and giant cells phagocytosing the patch. No necrosis. Some healing is seen in incisions. |
| Fibrin/thrombin patch | Central | E4 T1 | Patch material on the lung. Below, inflammatory infiltrate with mainly macrophages and lymphocytes. Blood and cells are seen throughout the patch material. Overlying the patch are cells and some macrophages and mesothelial cells. In the lung parenchyma below the patch, hemorrhage is seen. Deep in the lung parenchyma necrotizing/eosinophilic granulomas are seen. Focally, there may be some remnants of parasites. |
| Pleural overlap | E4 T2 | Patch material on lung with inflammatory reaction around patch with mainly macrophages and lymphocytes. Eosinophilic granulomas in the lung parenchyma. Minimal healing and fibrosis deposition is seen. |
| Negative control | Central | E4 C3 | No recognizable patch, difficult to interpret slide. Large bronchi and blood vessels present. Top section appears to be a thickened part of pleura corresponding to a part of lesion location, containing minimal inflammation with macrophages, PNMs and lymphocytes. Cluster of giant cells seen with foreign body material, but more deeply located close to a large bronchus. |
| 5 | 14 days | NHS-POx | Central | E5 G1 | Some patch material is identified with giant cell reaction, but the majority of the pleura shows mature fibrous tissue and neovascularization with minimal inflammatory infiltrate and with normal alveoli. Lymphoid tissue is seen deep in the lung parenchyma, and one granuloma is seen.  |
| Pleural overlap | E5 G2 | No recognizable patch. Thick fibrotic layer on top of pleura with broad band of capillaries. Just the below the surface fibrinoid material seen. Within this fibrosis, mainly macrophages (and fibroblasts). Directly subpleural also lymphocytes. No giant cells. |
| Fibrin/thrombin patch | Central | E5 T1 | Section with patch material. Below the patch, a moderate to packed infiltrate is seen, consisting of lymphocytes, macrophages and plasma cells. A foreign body giant cell reaction is seen on the remaining patch material. There are no clearly identifiable wounds/incision. |
| Pleural overlap | E5 T2 | Thickened fibrotic pleura with remaining fibrinoid material associated with **granulomatous rection with necrosis**, macrophages, giant cells, plasma cells, lymphocytes.  |
| Negative control | Central | E5 C3 | No patch. Narrow band of loose fibrosis on pleura with neovascularization. Minimal inflammatory response. |
| 6 | 14 days | NHS-POx | Central | E6 G1 | Patch material within fibrous layer on top of pleura. Some neovascularization. Patch material associated with macrophages, PMSs and giant cells. Some inflammation with lymphocytes and plasma cells directly sub pleural. |
| Pleural overlap | E6 G2 | Section with no recognizable patch material, showing extensive granulation tissue formation with neovascularization, collagen deposition, and macrophages. On top of the granulation tissue, **partial re-epithelization (of mesothelial cells) can be seen.** Below the granulation tissue, a band of predominantly lymphocytes and plasma cells is seen. Deep within the lung, normal air containing alveoli are observed, without evidence of granulomas or parasites. BALT tissues are seen associated with bronchi. |
| Fibrin/thrombin patch | Central | E6 T1 | Patch material on the lung with associated giant cell reaction. Below the patch a moderate to bread fibrotic band is seen with neovascularization and inflammatory cells, mainly consisting of plasma cells, macrophages and lymphocytes. |
| Pleural overlap | E6 T2 | Patch material present. Overlaying and underlying the patch, a band of fibrosis with grouped neovascularization and inflammatory cells. **Giant cells around the patch with formation of granulomas**, and lymphocytes, macrophages, plasma cells. |
| Negative control | Central | E6 C3 | No recognizable patch. Fibrous band on top of pleura with chronic inflammation (plasma cells, macrophages, lymphocytes). Single eosinophilic granuloma deep within the lung. Fat tissue deep within the lung parenchyma (but not associated with fibrosis so not scored as biomaterial response). |
| 7 | 14 days | NHS-POx | Central | E7 G1 | Patch on lung, diffusely infiltrated with macrophages and giant cells and associated lymphocytes. Fibrosis overlaying patch. Area of cloth/fibrin within patch with unknown substance. |
| Pleural overlap | E7 G2 | Section with patch material, diffusely infiltrated with macrophages and giant cells. Surrounding lymphocytes and plasma cells. Fibrosis layer on top of patch and below patch. |
| Fibrin/thrombin patch | Central | E7 T1 | Thickened fibrotic pleura with remaining area of fibrinoid material with **associated granulomatous reaction with necrosis**, mainly macrophages, giant cells, lymphocytes, plasma cells and scattered polymorphonuclear cells. |
| Pleural overlap | E7 T2 | Patch material on pleura, surrounded by lymphocytes, plasma cells and macrophages. Moderate fibrosis of pleura with broad band of capillaries. |
| Negative control | Central | E7 C3 | No recognizable patch. Clearly identifiable incision lesions with granulation tissue, fibrosis and neovascularization. Inflammation with minimal lymphocytes, macrophages and plasma cells. **Rare foamy macrophages**. |
| 8 | 14 days | NHS-POx | Central | E8 G1 | Patch material on the lung is completely infiltrated with macrophages, giant cells, lymphocytes and areas of hemorrhage. **Extensive degradation of the patch is seen by phagocytosis.** Below the patch, there is some inflammation in the parenchyma with collapsed alveoli, but normal air contents are seen. The entire surface of the patch is covered with fibrous tissue, inflammatory cells, mesothelium. On top of the patch necrotic tissue is seen.  |
| Pleural overlap | E8 G2 | Fibrotic layer on top of pleura, with neovascularization, and some patch material recognizable embedded in the fibrosis, associated with macrophages, lymphocytes and giant cells. **Focally, some foamy macrophages are seen.** |
| Fibrin/thrombin patch | Central | E8 T1 | Patch material on the lung. Moderate to broad fibrotic band seen with neovascularization. Inflammatory infiltrate below patch with mainly plasma cells, lymphocytes and macrophages. No incision identifiable. Scattered immune cells throughout the patch. Eosinophilic granuloma seen in the lung parenchyma. |
| Pleural overlap | E8 T2 | Patch material on lung with an extensive **inflammatory reaction, comprising macrophages at the material border**, surrounded by lymphocytes and plasma cells. There also is an area with no remaining patch material and a thick band of fibrosis on the pleura. |
| Negative control | Central | E8 C3 | No recognizable patch material. Fibrosis on top of pleura with neovascularization. Below inflammation with mainly lymphocytes, plasma cells and macrophages, no giant cells. |
| 9 | 6 weeks | NHS-POx | Central | E9 G1 | Thick band of fibrosis, on top of pleura, with areas of bleeding. Broad neovascularization. No patch material. Inflammation with mainly macrophages, including foamy macrophages. **Mix-up corrected with E9-T1.**  |
| Pleural overlap | E9 G2 | No patch seen. Partly loose, partly thickened fibrotic layer on top of pleura. Minimal associated immune cells (lymphocytes, macrophages). **Some residual foamy macrophages seen.** No granulomas.**Mix-up corrected with E9-T2.** |
| Fibrin/thrombin patch | Central | E9 T1 | **Severe intrapleural necrotizing granulomatous reaction to fibrinoid material with** macrophages, giant cells, lymphocytes, and plasma cells. **Extensive thickening of the pleura due to fibrosis and granulomatosis.** Normal lung parenchyma.**Mix-up corrected with E9-G1.** |
| Pleural overlap | E9 T2 | **Area of extensive and severe granulomas with some nuclear dust in the fibrous layer on top of pleura (reaction to patch?).** No parasites or eosinophils seen within the granulomas. This area of granulomas is associated with a chronic inflammation infiltrate with macrophages, plasma cells, lymphocytes. In the fibrous thickened pleura besides these granulomas, there is no patch material, and minor inflammatory cells.**Mix-up corrected with E9-G2.** |
| Negative control | Central | E9 C3 | No clear patch material on pleura. Layer of fibrosis with neovascularization on pleura, no relevant inflammation. |
| 10 | 6 weeks | NHS-POx | Central | E10 G1 | Fibrotic layer on top of pleura with neovascularization and fibrosis and remnants of inflammation. Granuloma with parasite seen (not eosinophilic) in lung parenchyma with one granuloma directly subpleural located. |
| Pleural overlap | E10 G2 | No recognizable patch. Thick fibrosis on area where the presumed patch used to be, normal pleura on edge of slide. Fibrosis layer seems well organized. Below this, a layer with loose connective tissue and **packed foamy macrophages with some associated inflammation (lymphocytes and plasma cells).** Single eosinophilic granuloma close to pleura without parasites. Fat tissue deep in lung tissue.  |
| Fibrin/thrombin patchFibrin/thrombin patch | Central | E10 T1 | No recognizable patch on top of pleura. Difficult to identify prior lesions. Minimal inflammatory response near the pleura seen with **some foamy macrophages**. Subpleural parenchyma is collapsed with interalveolar bleeding. No granulomas. |
| Pleural overlap | E10 T2 | No recognizable patch material. Moderate infiltrate of lymphocytes and macrophages, rare giant cells and fibrosis. Presence of foreign body (possible patch) material. On the pleural surface presence of PMNs. |
| Negative control | Central | E10 C3 | Thickened fibrotic pleura with rare inflammatory cells remaining. Granulomas deep in lung parenchyma. |
| 11 | 6 weeks | NHS-POx | Central | E11 G1 | Mostly unremarkable pleura with focal organized scar (incision) with some neovascularization and fibrosis, little to no inflammatory response. Several eosinophilic granulomas deeper within the lung parenchyma. |
| Pleural overlap | E11 G2 | No patch material. Moderate thickening of pleura over half of the total pleural surface with neovascularization and fibrosis. Minimal areas of inflammation with lymphocytes and macrophages. Parasitic granulomas deep in parenchyma. |
| Fibrin/thrombin patch | Central | E11 T1 | Section with remnant of fibrin patch material, **clear granulomatous reaction to the remaining patch material**; the patch itself is not infiltrated by immune cells. **Packed inflammation around the patch with macrophages, giant cells and lymphocytes with lymph follicle formation and granulomatous reaction to the patch.** Thick fibrotic band on top of parenchyma with area of chronic inflammatory cells. Normal parenchyma besides the area of the patch, and a single parasitic eosinophilic granuloma is observed. Area of fatty tissue (adipocytes) is seen deep in the parenchyma of the lung. |
| Pleural overlap | E11 T2 | Fibrosis on top of pleura with remaining patch material / **fibrinoid material with granulomatosis reaction** and minimal fat. Associated infiltrate of macrophages, lymphocytes and giant cells. Single granuloma in lung parenchyma. |
| Negative control | Central | E11 C3 | Section without patch. Entire pleural surface is covered with mature collagen, with some neovascularization, and minimal macrophages and lymphocytes. Some necrotizing/calcified granulomas deep in the lung parenchyma with focal presence of parasites. |
| 12 | 6 weeks | NHS-POx | Central | E12 G1 | Section with no recognizable patch material, well organizing fibrotic tissue. Complete mesothelial coverage on the pleural site. Between the pleural mesothelium and normal alveoli, there is a 1-3mm layer of organizing collagen fibers, neovascularization, signs of chronic inflammation with macrophages and lymphocytes, **and minimal presence of adipocytes with associated foamy macrophages.** |
| Pleural overlap | E12 G2 | Band of fibrosis in place of prior pleura with extensive neovascularization. No patch. Macrophages and lymphocytes present. Focally, some giant cells are seen. **Moreover, multiple foamy macrophages are seen in between fatty deposition.** Single eosinophilic granuloma with parasites right below pleura. |
| Fibrin/thrombin patch | Central | E12 T1 | No recognizable patch. Complete mesothelial coverage. Between mesothelium and lung parenchyma, there is a dense fibrotic area, which appears to have replaced a prior patch, with extensive neovascular ingrowth. Deep in the lung parenchyma, there are eosinophilic granulomas.  |
| Pleural overlap | E12 T2 | No recognizable patch material. Patch appears to be completely replaced by fibrous tissue. There is a broad fibrotic band between this fibrous tissue and the healthy parenchyma with neovascularization. Very minimal inflammation. The entire area is covered with mesothelium. There are several eosinophilic granulomas within the lung parenchyma with identifiable parasites. |
| Negative control | Central | E12 C3 | No patch. Pleura slightly thickened due to fibrosis with neovascularization. Some patchy areas of minimal inflammation with macrophages and lymphocytes. Parasitic granuloma deep in parenchyma. |

**Table E2:** Overview of histological findings in additional samples

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| **#** | **Survival term** | **Sample type** | **ID** | **Description**  |
| 1 | 5 days  | Control sample without lesion  | E1 C4 | Normal air containing alveoli. No inflammation. |
| Lymph node (4R) | E1 L1  | Lymph node **with eosinophilic granulomas.** No parasites seen. |
| Lymph node (10R) | E1 L2  | Lymph node with **eosinophilic granulomas with presence of parasites.** |
| 2 | 5 days  | Control sample without lesion | E2 C4 | Lung tissue with **prominent eosinophilic granulomatous inflammation.** No parasites seen. |
| Apical pleural biopsy  | E2 P1 | Muscle and fatty tissue. No mesothelial cells, no patch remnants, no inflammation |
| Lateral pleural biopsy  | E2 P2 | Parietal pleura and muscle tissue, no patch remnants, no inflammation |
| Pleural biopsy costodiaphragmatic recess  | E2 P3  | Muscle and fatty tissue, irritated mesothelium, no patch remnants |
| Lymph node (4R) | E2 L1  | Lymph node with **eosinophilic granulomas.** No parasites seen. |
| Macroscopic infiltrates (white spots on pleura)  | E2 E1 | Thickened pleura with fibrinous pleuritis. Underlying lung tissue with **eosinophilic granulomas**. No parasites seen. |
| 3 | 5 days  | Control sample without lesion | E3 C4  | Normal air containing alveoli. **One granuloma** without eosinophils or necrosis. **Pleura shows reactive changes with irritated mesothelial cells.** |
| Apical pleural biopsy  | E3 P1 | Muscle tissue mixed with fat tissue, parietal pleura, no patch remnants, no inflammation. |
| Lateral pleural biopsy  | E3 P2 | Muscle tissue mixed with fat tissue, parietal pleura, no patch remnants, no inflammation. |
| Pleural biopsy costodiaphragmatic recess  | E3 P3 | Muscle tissue and fatty, no mesothelial cells, no patch remnants, no inflammation.  |
| Lymph node (4R) | E3 N1 | Fatty and connective tissue. No lymph node. |
| Lymph node (10R)  | E3 N2  | Normal lymph node. Fat tissue around lymph node.  |
| Lymph node (2R) | E3 N3  | Normal lymph node surrounded with fat tissue.  |
| 4 | 5 days  | Control sample without lesion | E4 C4  | Lung parenchyma with **one large granuloma with central eosinophils**, **thickened pleura with (neo)vascularization and focal fibrinous exudate**. |
| Apical pleural biopsy  | E4 P1  | Muscle tissue mixed with fat tissue, **parietal pleura with reactive changes**, no patch remnants. No inflammation. |
| Lateral pleural biopsy  | E4 P2  | Parietal pleura with underlying muscle tissue mixed with fat tissue, no patch remnants, no inflammation.  |
| Pleural biopsy costodiaphragmatic recess  | E4 P3  | Parietal pleura with **fibrinous pleuritis**, underlying granulation tissue, no muscle tissue identifiable, no patch remnants |
| Lymph node (4R) | E4 N1  | Fat tissue, no lymph node.  |
| Lymph node (11R)  | E4 N2  | Collapsed but otherwise normal lung parenchyma, no lymph node.  |
| NHS-POx patch adhered to thorax  | E4 X1  | NHS-POx patch with underlying granulation tissue and some fibrinous exudate.  |
| Macroscopic infiltrate  | E4 X2 | Lung parenchyma with some prominent lymphoid aggregates (BALT).  |
| Macroscopic infiltrate | E4 X3 | Lung parenchyma with an **eosinophilic granuloma**, no parasites seen |
| 5  | 14 days  | Control sample without lesion | E5 C4 | Normal air containing alveoli without inflammation. **Thickened, fibrous pleura with minimal chronic inflammation.** |
| Apical pleural biopsy  | E5 P1 | Parietal pleura with muscle tissue mixed with fat tissue, no patch remnants, no inflammation.  |
| Lateral pleural biopsy  | E5 P2  | Parietal pleura with fibrosis and neovascularization, no muscle tissue identifiable, no patch remnants, no significant inflammation.  |
| Pleural biopsy costodiaphragmatic recess  | E5 P3  | Parietal pleura with fibrosis and neovascularization and **some reactive mesothelial cells,** no muscle tissue identifiable, no patch remnants, no significant inflammation |
| Pleural biopsy across control lesion  | E5 PC  | Parietal pleura with **fibrosis, neovascularization, reactive mesothelial cells, limited chronic inflammation. Focally, foreign body giant cell reaction to amorphous material.** |
| Pleural biopsy across NHS-POx | E5 PG  | Parietal pleura with **fibrosis, neovascularization,** **reactive mesothelial cells, limited chronic inflammation.** No patch remnants. |
| Pleural biopsy across fibrin patch | E5 PT  | Parietal pleura with **fibrosis, neovascularization, reactive mesothelial cells**, **limited chronic inflammation.** No patch remnants. |
| Lymph node (4R) | E5 N1 | Normal lymph node, presence of **eosinophilic granulomas**, some fat tissue around the lymph node. No parasites seen. |
| 6 | 14 days  | Control sample without lesion | E6 C4  | Normal air containing alveoli with **eosinophilic granulomas**, **thickened pleura with fibrin deposition, young fibrosis, mild chronic inflammation** with minor presence of PMNs |
| Apical pleural biopsy  | E6 P1 | Muscle tissue, parietal pleura with **mild reactive changes and mild chronic inflammation**, no patch remnants |
| Lateral pleural biopsy  | E6 P2 | Muscle tissue, parietal pleura with **mild reactive changes and mild chronic inflammation**, no patch remnants |
| Pleural biopsy costodiaphragmatic recess  | E6 P3 | Muscle and fatty tissue, no parietal pleura, no inflammation, no patch remnants |
| Pleural biopsy across control lesion  | E6 PC  | Parietal pleura with **reactive mesothelial cells,** **fibrosis, neovascularization.** No patch remnants. Presence of muscle tissue, and normal liver tissue.  |
| Pleural biopsy across NHS-POx | E6 PG | Parietal pleura with **reactive mesothelial cells,** fibrosis, neovascularization. Presence of muscle and fatty tissue, no patch. |
| Pleural biopsy across fibrin patch | E6 PT  | Parietal pleura with **mild reactive changes with loose fibrous connective tissue** and neovascularization. Presence of muscle and fatty tissue, no patch. |
| Lymph node (4R) | E6 N1  | Normal lymph node, no granulomas with central eosinophils, fat cells in lymph node, lymph node covered with fat tissue |
| Macroscopic infiltrate  | E6 X1 | **Thickened pleura, granulation tissue with macrophages** and PMNs, fibrin deposition, neovascularization, **granulomas with central necrosis.**  |
| 7 | 14 days | Control sample without lesion | E7 C4  | Normal air containing alveoli without inflammation. **Slightly thickened pleura with minor chronic inflammation.** |
| NHS-POx patch with white spot | E7 G3  | NHS-POx patch with **lymphohistiocytic inflammatory reaction**. Presence **of necrotic fatty and striated muscle tissue (likely originating from the parietal pleura).** |
| Apical pleural biopsy  | E7 P1 | Normal parietal pleura with muscle tissue with fat cells. No patch remnants. No inflammation. |
| Lateral pleural biopsy  | E7 P2  | Parietal pleura with **reactive changes with fibrosis and chronic inflammation with giant cells**. **Muscle tissue with degeneration**. No patch remnants. |
| Pleural biopsy costodiaphragmatic recess  | E7 P3  | Muscle tissue, with fat tissue. **Slightly reactive mesothelial cells.** No patch. |
| Pleural biopsy across control lesion  | E7 PC | Muscle tissue, with fat tissue. **Slightly reactive mesothelial cells.** No patch |
| Pleural biopsy across NHS-POx | E7 PG  | Muscle tissue, with fat tissue. **Slightly reactive mesothelial cells.** No patch |
| Pleural biopsy across fibrin patch | E7 PT | Muscle tissue, with fat tissue. **Slightly reactive mesothelial cells with minimal chronic inflammation**. No patch |
| Lymph node (4R) | E7 N1  | Normal lymph node with **eosinophilic granulomas**. No parasites. |
| Macroscopic infarct / infiltrate  | E7 X1 | **Thickened pleura with fibrosis and chronic inflammation with multinucleated giant cells**. At the border some alveoli seen. No infarction. |
| 8 | 14 days | Control sample without lesion | E8 C4  | Normal air containing alveoli, **focally peribronchial neutrophilic inflammation (active pneumonia).** No granulomas, no parasites, **slightly thickened pleura** |
| Apical pleural biopsy  | E8 P1 | Muscle tissue, fat cells, normal parietal pleura, no patch remnants, no inflammation |
| Lateral pleural biopsy  | E8 P2 | **Fibrinous pleuritis, fibrosis and neovascularization,** no patch remnants |
| Pleural biopsy costodiaphragmatic recess  | E8 P3 | Muscle tissue, fat cells, normal parietal pleura, no patch remnants, no inflammation |
| Pleural biopsy across control lesion  | E8 PC | Muscle tissue, fat cells, normal parietal pleura, no patch remnants, no inflammation |
| Pleural biopsy across NHS-POx | E8 PG  | No patch remnants, fat cells, muscle tissue mixed with pleura, **fibrinous pleuritis** |
| Pleural biopsy across fibrin patch | E8 PT | No patch remnants, no muscle tissue, **thickened pleura with neovascularization and mainly chronic inflammation** |
| Macroscopically thickened pleura | E8 X1 | Normal lung parenchyma and **excessively thickened pleura, granulation tissue,** neovascularization, fibrin deposition |
| White spot in thickened pleura | E8 X2 | **Thickened pleura, granulation tissue,** fibrin deposition, neovascularization, **suspicion of a granuloma with parasites** |
| Dark spot in thickened pleura  | E8 X3 | **Thickened pleura, inflamed spot** (with PMNs, plasma cells, leukocytes), granulation tissue, neovascularization, fibrin deposition |
| 9 | 6 weeks | Control sample without lesion | E9 C4 | Normal air containing alveoli, **thickened pleura**, no inflammation |
| Apical pleural biopsy  | E9 P1  | Normal muscle tissue, some fat tissue, normal parietal pleura, no patch remnants, no inflammation |
| Lateral pleural biopsy  | E9 P2 | Normal muscle tissue, some fat tissue, normal parietal pleura, no patch remnants, no inflammation |
| Pleural biopsy costodiaphragmatic recess  | E9 P3 | Normal fatty tissue, normal parietal pleura, no patch remnants, no inflammation |
| Pleural biopsy across control lesion  | E9 PC | Normal muscle tissue, some fat tissue, normal parietal pleura, no patch remnants, no inflammation |
| Pleural biopsy across NHS-POx | E9 PG | Normal muscle tissue, some fat tissue, normal parietal pleura, no patch remnants, no inflammation |
| Pleural biopsy across fibrin patch | E9 PT | Normal muscle tissue, some fat tissue, **slightly thickened parietal pleura,** no patch remnants, no inflammation |
| Lymph node (4R) | E9 N1 | Lung tissue with slightly thickened pleura, no lymph node |
| Lymph node (4R)  | E9 N2 | Normal lymph node, no granulomas or parasites |
| Lymph node (11R) | E9 N3 | Normal lymph node surrounded with fat tissue, no granulomas or parasites |
| Macroscopic infiltrate  | E9 X1 | **Granulomas with eosinophilic center with necrosis, thickened pleura** |
| Macroscopic infiltrate  | E9 X2 | **Granulomas with eosinophilic center with necrosis, thickened pleura** |
| Dark spot in thorax | E9 X3 | **Necrotic/ blood tissue packed with macrophages**, no granuloma |
| Biopsy of infiltrate during index surgery  | X9 X1 HE  | **Granuloma with necrosis**. Inflammation of lung tissue (PMNs, macrophages, lymphocytes, giant cells, plasma cells), infarct/bleeding in lung tissue.  |
| 10 | 6 weeks | Control sample without lesion | E10 C4 | Normal air containing alveoli, **thickened pleura, presence of granulomas with eosinophilic center and focal presence of parasites.**  |
| Apical pleural biopsy  | E10 P1 | Normal muscle tissue, some fat tissue, normal parietal pleura, no patch remnants, no inflammation |
| Lateral pleural biopsy  | E10 P2 | Normal parietal pleura, no inflammation, no patch |
| Pleural biopsy costodiaphragmatic recess  | E10 P3 | Normal muscle and fatty tissue, no mesothelial cells, no patch remnants, no inflammation. |
| Pleural biopsy across control lesion  | E10 PC | **Thickened pleura with foreign body giant cell reaction to Vicryl suture**. No patch material. |
| Pleural biopsy across NHS-POx | E10 PG | Normal parietal pleura with fatty tissue, no patch remnants, no inflammation |
| Lymph node (10R) | E10 N1 | Lymph node with prominent **eosinophilic granulomatous** reaction. No parasites seen. |
| Lymph node (11R) | E10 N2 | Lymph node with **prominent eosinophilic granulomatous reaction. Focal presence of parasites.** |
| Macroscopic infiltrate  | E10 X1 | Lung parenchyma with **granuloma with eosinophilic center and central necrosis**. No parasites seen.  |
| Macroscopic infiltrate  | E10 X2 | Lung parenchyma with **granuloma.** No necrosis or parasites seen. |
| 11 | 6 weeks | Control sample without lesion | E11 C4  | Normal air containing alveoli with **eosinophilic granulomas and central necrose, thickened pleura with fibrin deposition** and neovascularization. No parasites seen. |
| Apical pleural biopsy  | E11 P1 | Normal parietal pleura, muscle and fatty tissue, no patch remnants, no inflammation.  |
| Lateral pleural biopsy  | E11 P2  | Muscle tissue with fat cells and thickened pleura, no significant inflammation, no patch remnants |
| Pleural biopsy costodiaphragmatic recess  | E11 P3  | Normal parietal pleura, muscle and fatty tissue, no patch remnants, no inflammation |
| Pleural biopsy across control lesion  | E11 PC | **Muscle tissue with degeneration**, no patch remnants, **thickened pleura with granulation tissue** and neovascularization and **reactive mesothelial cells** |
| Pleural biopsy across NHS-POx | E11 PG | Parietal pleura with fibrosis and fatty tissue |
| Pleural biopsy across fibrin patch | E11 PT | Parietal pleura **with fibrosis, neovascularization, reactive mesothelial cells,** fatty tissue, no patch remnants, no significant inflammation |
| Lymph node (11R) | E11 N1 | Completely necrotic nodular tissue fragment.  |
| Lymph node (4R)  | E11 N2 | Lymph node with **eosinophilic granulomas and presence of parasites** |
| Biopsy of infiltrate during index surgery | E11 X1 | Lung parenchyma with focal suspicion of **eosinophilic granuloma.** |
| Macroscopic infiltrate  | E11 X2 | Lung parenchyma with **granuloma.** No evident necrosis. No parasites. |
| Thickened pleura  | E11 X3 | Lung parenchyma with **eosinophilic granulomas**. No parasites seen. |
| Macroscopic infiltrate (left lung) | E11 X4 | Lung parenchyma with **eosinophilic granulomas** **and presence of parasites.**  |
| 12 | 6 weeks | Control sample without lesion | E12 C4 | Normal air containing alveoli, no inflammation, **thickened pleura** |
| Apical pleural biopsy  | E12 P1 | Normal parietal pleura, muscle and fatty tissue, no patch remnants, no inflammation |
| Lateral pleural biopsy  | E12 P2 | Normal parietal pleura, muscle and fatty tissue, no patch remnants, no inflammation |
| Pleural biopsy costodiaphragmatic recess  | E12 P3 | Muscle and fatty tissue, no mesothelial cells, no patch remnants, no inflammation |
| Pleural biopsy across control lesion  | E12 PC | **Thickened, fibrotic pleura, no significant inflammation**, no patch remnants |
| Pleural biopsy across NHS-POx | E12 PG | Muscle tissue, fat tissue, **thickened, fibrotic pleura,** no significant inflammation, no patch remnants |
| Pleural biopsy across fibrin patch | E12 PT | Unremarkable parietal pleura. No patch remnants, no significant inflammation. |
| Lymph node (11R) | E12 N1 | Lymph node with **eosinophilic granulomas** and necrosis. No parasites seen. |
| Macroscopic infiltrate  | E12 X1 | **Thickened, fibrotic pleura**, underlying lung parenchyma with **eosinophilic granulomas with focal presence of parasites** |