

P045 High-resolution 3D quantification of the development of insulinitis and destruction of b-cell mass in the NOD mouse
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The NOD mouse represents one of the best and most used animal models for T1D. It spontaneously develops insulinitis that eventually leads to the destruction of β -cells and overt diabetes. Using a tomographic imaging and computational processing technology, optical projection tomography (OPT) we have analyzed the process of β -cell destruction leading to overt diabetes. This approach allowed us to measure of islet β -cell volume distribution directly and to analyze the entire islet-volume distribution for each pancreas. As expected diabetic NOD mice sibling pairs displayed a lower total volume of insulin-producing b cells as compared to their nondiabetic littermates. A striking feature was the degree of variation from pancreas to pancreas not only in terms of islet number, but also in the distribution of islet sizes and in the splenic versus duodenal pancreas. The quantitative distribution analysis was combined with spatial assessments of β -cell destruction in interactive 3D reconstructions at different ages reflected different levels of insulinitis development . Such analyses of representative pancreata including those from overt diabetic and non-diabetic NOD littermates indicate that the peripheral islets are the first to disappear, whereas the larger and more centrally located islets initially remain unaffected or increased in size. These results suggest that parallel degenerative and generative processes may be ongoing during the autoimmune attack of the β cells in the NOD mouse.