The analysis of intact protein complexes by mass spectrometry is still challenging. Here we present an approach based on high-mass MALDI ToF mass spectrometry and chemical cross-linking. To circumvent the problem of dissociation when using MALDI ionization, a specific cross-linking protocol has been developed to stabilize covalently the samples. To solve the problem of detection, we are using a specially developed high-mass detection system, allowing sub-μM detection up to 1000 kDa. The use of this methodology presents a number of advantages: Sensitivity (sub-μM), tolerance for samples impurity, speed. We will present with details the high-mass technology used and show comparison spectra with MCP detection, the technology used in most of standard MALDI ToF instruments. We will also present examples of applications of this methodology in the field of protein complex analysis (intact protein complexes ranging from 40 to 1000 kDa), antibody characterization (Interaction analysis, Sandwich assays, Epitope mapping), Therapeutic protein aggregates analysis and drug discovery.