The thermo-mechanical effects on the strain evolution within an EB-PVD thermal barrier coating (TBC) is presented in this work using in-situ characterization. Synchrotron x-ray diffraction at sector 1-ID at the Argonne National Laboratory provided both qualitative and quantitative in-situ data on the strain evolution under a thermal cycle with mechanical loading. The results show that at a critical combination of temperature and load, the stress in the thermally grown oxide (TGO) layer in the TBC reaches a tensile region. These significant findings enhance existing literature showing purely compressive strains within the TGO where mechanical loads have been neglected. The results have important implications on the effects on the overall life of the coating. Depth resolved quantitative strain is presented as contour plots over a thermal cycle highlighting the complementary strains in the adjacent layers including the bond coat and the TBC with time and temperature. Systematic identification of the appropriate peaks within the multi-layer TBC system provides guidelines for future strain studies using high energy x-rays. Piezospectroscopic studies with applied mechanical loading are further presented as verification of the room temperature XRD data for future development of the method as an operational technique to be used outside the laboratory environment.