Energetic charged particles are encountered in spaceflight as part of the galactic cosmic rays, where they pose a potential health risk to astronauts. On the other hand their destructive potential is also used for radiotherapy of deep seated tumours. The deposition of energy of these high energy and high charged (HZE) particles occurs mostly along the trajectory of the particle itself, but depending on its energy, there is some probability for energy deposition relatively far from the nominal trajectory, due to long-ranged delta rays produced. These delta rays are considered to induce non correlated DNA damage similar to low-linear energy transfer (LET) radiation (like X- or γ-rays), whereas the DNA damage induced by the dense ionizing track of HZE particles is assumed to be skewed towards more complex or clustered DNA damage, which is slowly repaired or is even irreparable. To study the spatiotemporal protein dynamics during and after charged particle irradiation, a remote controlled microscope device was used at the accelerator facility of GSI [1]. The system enables the acquisition of high-resolution fluorescence images of stained living cells during ion irradiation. The microscope setup allows us to study early radiation effects without the time lag of minutes presently conditional on limitations of access to the irradiation devices. Utilizing GFP-tagged repair proteins like 53BP1, NBS1 and XRCC1 allows us the spatio-temporal characterization of DNA damage in respect to the particle trajectory by direct visualization in human cells. To compare high LET (ions) and sparsely ionizing radiation (x-rays) induced DNA damage and to use the microscope between beamtimes, the system was now upgraded with a 35 kV x-ray tube operated at high dose rate (40 Gy/min).

Time-lapse series of GFP-coupled repair proteins like XRCC1 proved accumulations within seconds at sites of ion tracks indicating a very fast recognition of DNA damage in combination with a quite stable location of damage processing (Fig.1). In the study presented here, we used a spectrum of different particles over a broad range of LETs in addition to x-rays to address the dynamics of the early DNA damage response in regards to the damage density in living cells. The detailed analysis of NBS1-GFP revealed differences in the recruitment kinetics and retention at damage sites in connection to the LET and radial track structure of the particles. These differences might be explained by the increasing local density of DSBs along the ion track which results in a shift in the balance of molecules binding directly to the DNA damage and those binding to the surrounding chromatin domain.