

**P026** Processing of complex DSB by BER and end joining proteins  
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Amongst the lesions induced by ionising radiation are complex DSB, defined as DSB with associated base lesions or abasic (AP) sites and/or 3' phosphoglycolate (PG) or phosphate (P) termini. These lesions are thought to be particularly detrimental. Synthetic oligonucleotides were synthesised with 8-oxoG or AP sites close to readily ligatable 3'-OH and 5'-P termini, to determine if complex DSB influence the efficiency of BER proteins to remove lesions or the efficiency of end joining DSB. The removal of 8-oxoG and AP sites by Fpg, hOGG1 and APE1 was severely retarded when the lesions were in close proximity to the oligonucleotide ends, however this retardation was partially overcome with NEIL1. 8-oxoG or AP sites result in retarded ligation by XRCC4/Ligase IV and T4 ligase if positioned two to three bases from the 3'-OH or six bases from the 5'-P termini. When two lesions are positioned across the break junction ligation is severely retarded. In addition, 8-oxoG does not influence the removal of PG from 3' overhanging termini if 8-oxoG is on the opposing DNA strand. Reduced efficiency of repair of complex DSB by BER and end joining proteins indicates that complex DSB, a signature of ionising radiation, are likely to persist longer than simple DSB, and as a consequence are predicted to be detrimental, thus they could be exploited as targets to increase the efficiency of radiation cancer therapy.