Changes in the fraction of total hypoxia and hypoxia subtypes in human squamous cell carcinomas upon fractionated irradiation: evaluation using pattern recognition in microcirculatory supply units.

Evaluate changes in total hypoxia and hypoxia subtypes in vital tumor tissue of human head and neck squamous cell carcinomas (hHNSCC) upon fractionated irradiation. Xenograft tumors were generated from 5 hHNSCC cell lines (UT-SCC-15, FaDu, SAS, UT-SCC-5 and UT-SCC-14). Hypoxia subtypes were quantified in cryosections based on (immuno-)fluorescent marker distribution patterns of Hoechst 33342 (perfusion), pimonidazole (hypoxia) and CD31 (endothelium) in microcirculatory supply units (MCSUs). Tumors were irradiated with 5 or 10 fractions of 2 Gy, 5×/week. Upon irradiation with 10 fractions, the overall fraction of hypoxic MCSUs decreased in UT-SCC-15, FaDu and SAS, remained the same in UT-SCC-5 and increased in UT-SCC-14. Decreases were observed in the proportion of chronically hypoxic MCSUs in UT-SCC-15, in the fraction of acutely hypoxic MCSUs in UT-SCC-15 and SAS, and in the percentage of hypoxemically hypoxic MCSUs in SAS tumors. After irradiation with 5 fractions, there were no significant changes in hypoxia subtypes. Changes in the overall fraction of hypoxic MCSUs were comparable to corresponding alterations in the proportions of acutely hypoxic MCSUs. There was no correlation between radiation resistance.
(TCD(50)) and any of the investigated hypoxic fractions upon fractionated irradiation. This study shows that there are large alterations in the fractions of hypoxia subtypes upon irradiation that can differ from changes in the overall fraction of hypoxic MCSUs.