

Skin microbiome as predictor and pathogenesis mechanism for severe radiodermatitis in breast cancer patients

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Radiodermatitis is commonly observed during radiotherapy in post-surgery breast cancer patients, reducing their quality of life. To date, neither the inter-individual differences nor the pathomechanism are sufficiently understood. To investigate the role of the skin microbiome in the development of severe radiodermatitis, we conducted a longitudinal pilot study with 20 female breast cancer patients undergoing radiotherapy. At 9 visits, the skin physiology was assessed and skin swabs for next-generation sequencing of the V1-V3 region of the 16S rRNA and quantitative PCR on both the affected and non-affected bodysides were taken on a weekly basis before, during and after radiotherapy (360 samples). All patients developed mild (n=7), moderate (n=9) or severe (n=4) radiodermatitis. Strikingly, low (<5%) relative abundance of skin commensals (*Staphylococcus epidermidis*, *Staphylococcus hominis*, *Cutibacterium acnes*) before radiotherapy was significantly predictive for the development of severe radiodermatitis with an accuracy of 100%. Instead, severe patients were characterized by higher *Corynebacteriaceae* relative abundance which was correlated with increased skin pH. Interestingly, severe patients only showed an increase in total bacterial load before the onset of severe radiodermatitis symptoms estimated by qPCR of the 16S rRNA copies in contrast to stable bacterial load in mild and moderate radiodermatitis patients. Summarizing, we observed a link between low commensals relative abundance before radiotherapy with an increase in total bacterial load in the early phase of radiation leading to severe radiodermatitis symptoms in the late phase of radiation. Our results hint towards a direct influence of microbes in the pathogenesis of severe radiodermatitis.