Quantitative analysis of KSHV DNA in oral and cutaneous Kaposi sarcoma tumors in Zimbabwe

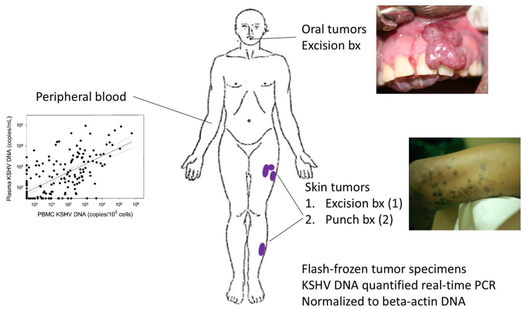
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BACKGROUND

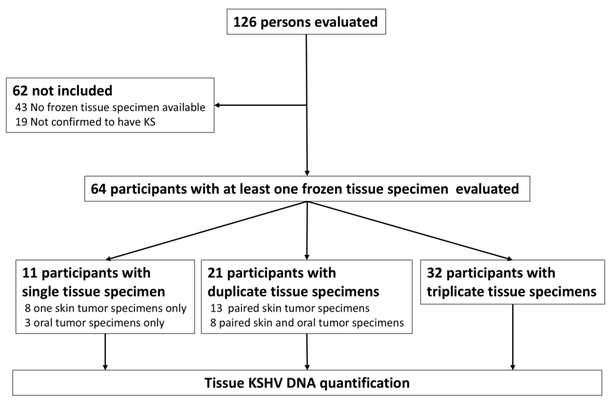
Detection of KSHV DNA in cutaneous tumors has been proposed to facilitate Kaposi sarcoma (KS) diagnosis in low resource settings. In addition to cutaneous tumors, KS often presents with oral lesions. Whether KSHV DNA content differs between cutaneous and oral tumors, and the relationship between them is unknown.

Quantification of KSHV DNA in different body compartments



METHODS

Biopsies of oral (N=43) and cutaneous KS tumors (N=106) were obtained from 64 persons with HIV-associated KS in Zimbabwe; median age 37 yrs, 44% female, 81% stage T1, median CD4+ lymphocytes 156/uL. All participants were antiretroviral and chemotherapy naïve. Presence of KS was confirmed by histopathology. Biopsy tissue was flash frozen in liquid nitrogen. KSHV DNA in tumor specimens and PBMC was quantified by PCR and normalized to total cellular DNA measured by quantitative PCR of β-actin DNA.

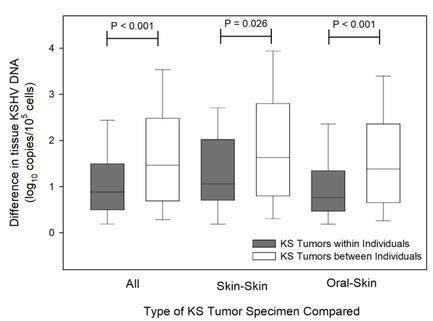


The amount of KSHV DNA in KS tumors is more similar within individuals than between individuals with HIV-associated KS

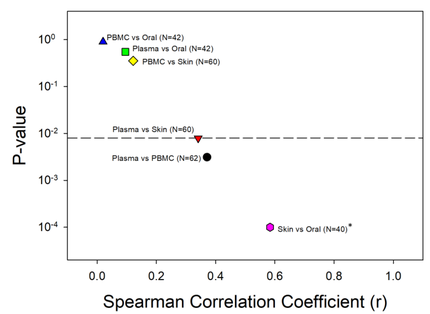
RESULTS

- Tumor KSHV DNA concentration was similar in oral (median 3.53, range <1 to 5.81 log10 copies/105 cells) and cutaneous tumor biopsies (median 3.75, range <1 to 6.53 log10 copies/105 cells, P=0.41) and was not associated with sex, age, CD4+ count, ACTG stage.
- Inter-person difference in KSHV DNA was greater than intra-person difference for both oral (median 1.38 vs. 0.77 log10 copies/106 cells, P<0.001) and cutaneous (median 1.63 vs. 1.06 log10 copies/105 cells, P=0.026) tumor biopsies.
- Weak correlation between KSHV DNA in plasma and skin tumor punch biopsies (r=0.33, P=0.03) from the same individual but there were no significant correlations between KSHV DNA in plasma or PBMC and skin or oral tumor biopsies (r<0.2, P≥0.2) in all other pairwise comparisons.
- KSHV DNA in replicate cutaneous tumor biopsies (skin excision vs skin punch) from the same individual was correlated (r=0.53, P=0.002) and KSHV DNA in biopsies of oral tumors and cutaneous tumors from the same individual was correlated (skin excision vs oral, r=0.74, P<0.001; skin punch vs oral, r=0.46, P=0.009).
- Bland-Altman plots showed similar agreement between skin-skin and skin-oral comparisons.
- In multivariate model, oral tumor KSHV DNA was the only significant predictor of skin tumor KSHV DNA

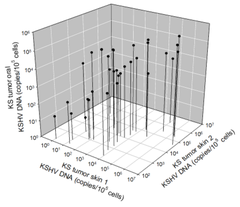
Inter-individual variability of tumor KSHV DNA is greater than intra-individual variability

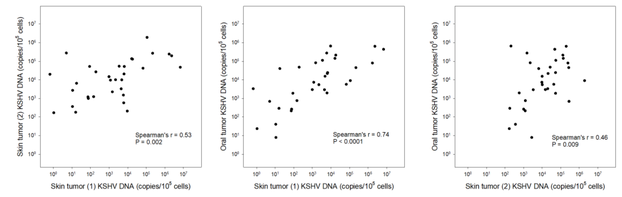


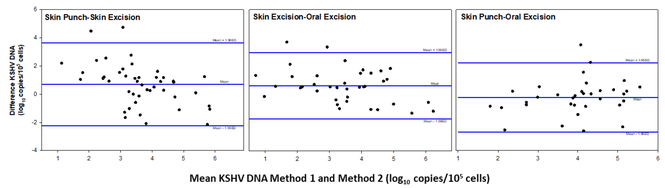
Univariate correlations between KSHV DNA in different body compartments



Relationship of tumor KSHV DNA in participants with triplicate specimens







CONCLUSIONS

- KSHV DNA concentrations in cutaneous and oral KS tumors span >5 log10 range but have similar variability and are quantitatively more similar within individuals than between individuals.
- The reasons for, and clinical significance of, inter-person differences in tumor KSHV DNA should be investigated further.

CONTACT INFORMATION

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PLAIN LANGUAGE SUMMARY

Kaposi sarcoma (KS) is caused by the Kaposi Sarcoma Herpes Virus (KSHV). We measured KSHV DNA in multiple skin and oral KS tumors in people with HIV-associated KS and found the levels were more similar within the same person then between people.