

Objective: Chronic mechanical irritation (CMI) has been proposed as risk factor for oral cancer. Epigenetic alterations, particularly methylation, have been mentioned as early events in carcinogenesis, and it has been proposed that CMI could induce them. Thus, the aim of this study is to describe p16 and MGMT methylation in a specific CMI lesion: Chronic Traumatic Ulcer (CTU).

Study Design: A split-mouth design was used, and two samples per individual were taken using cytobrush: CTU lesion (according to Piemonte et al. modified criteria) and clinically normal mucosa of a contralateral site. After extracting DNA, p16 and MGMT methylation status was assessed using qPCR.

Results: 27 patients were studied, mean age 59.1. The most frequent CMI factor was Functional (70%), and CMI evolution time showed an average of 18.4 months. On CTU, methylation of both p16 and MGMT presented a statistically significant difference ( $p < 0,0001$  and  $p < 0,0005$ , respectively) when compared to control site.

Conclusion: CMI affected sites showed consistently more methylation of p16 and MGMT than mucosa devoid of CMI. Since in each case both control and study samples were from the same individual, effects of confounders were reduced. This suggests that CMI could foster carcinogenesis through epigenetic alterations.