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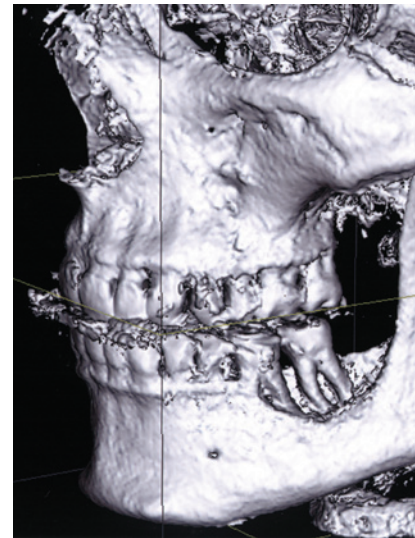
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ABOUT THE COVER

In 2007, the International Agency for Cancer Research presented compelling evidence that linked smokeless tobacco use to the development of human oral cancer. While these findings imply vigorous local carcinogen metabolism, little is known regarding levels and distribution of Phase I, II, and drug egress enzymes in human oral mucosa. The current study integrated clinical data, imaging studies, and histopathologic analyses of an oral squamous cell carcinoma that arose at the site of smokeless tobacco quid placement. The cover depicts a three-dimensional iCAT image of the buccal aspect of the patient's left mandibular body. The marked bone destruction associated with tobacco quid placement in the buccal vestibule adjacent to the patient's second and first mandibular molars is readily apparent. Immunoblot and immunohistochemical (IHC) analyses were employed to identify tumor and normal human oral mucosal smokeless tobacco-associated metabolic bioactivation and detoxification enzymes. Human oral epithelium contains every known Phase I enzyme capable of nitrosamine oxidative bioactivation with ~2 fold interdonor differences in protein levels. IHC studies confirmed that oral mucosal nitrosamine metabolizing enzymes reside in the basilar and suprabasilar regions, sites of ongoing keratinocyte DNA replication. Clearly, variations in product composition, capacity for nitrosamine oxidative metabolism and exposure duration will modulate clinical outcomes. The data presented here form a coherent picture consistent with the abundant experimental data that link tobacco-specific nitrosamines to human oral cancer. See article by Mallery and colleagues (beginning on page 23) for more information.



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