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Journal Name:	International STD Research & Reviews
Manuscript Number:	2013_ISRR_7983
Title of the Manuscript:	ONCOGENIC HUMAN PAPILLOMAVIRUS DETECTION IN PENILE LICHEN SCLEROSUS: AN UPDATE
Type of the Article	Short Research Article

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This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	The study includes 92 adult patients with penile LS and an equal number of males as control group: the data of 46 cases and 46 controls have been already published (ref. 10 of the manuscript). HPV prevalence was higher among cases than controls in both reports, but the figures differed: 8/46 (17.4%) and 4/46 (8.7%), respectively, in the first paper, and 15/46 (32.6%) and 10/46 (21.74%), respectively, in the subgroup added in the new paper. How do the authors explain this difference? How is the prevalence distribution over time? Methodology: the DNA extraction method is not indicated, and no information on evaluation of sample adequacy by amplification of a housekeeping gene is given; this is an important point because both FFPE specimens and cells from penile mucosa have been found	Variation in reported prevalence may be due to differences in sampling techniques, population studied, genital sites sampled, and HPV DNA detection methods used. Since none of these features has been changed during the course of this research study spanning through a 19-year period, it is reasonable to assume that the difference recorded among the two 46 patients subgroups (the one from the first paper and the newly recruited one) may suggest a tendency towards an increase of HPV prevalence with time. This interesting remark suggested by the reviewer has deserved a citation in the new version of the article. Whereas this finding is to be related to a general increasing trend of HPV infections, possibly due to changes in sexual habits, among the global population of sexually active non vaccinated individuals (recent population-based cohort studies have shown that vaccination strategies may significantly reverse this tendency by changing the dynamics of HPV transmission) cannot be established based on the data available from our study. DNA extraction was performed using a Qiagen kit (QIAamp DNA micro kit) and following the manufacturer's instructions. Sample adequacy has been established by spectrophotometric analysis and monitored through amplification of part of the b-globin gene. Since many of the examined LS cases have been retrieved from our past pathology files, obviously the control



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	inadequate in sizable fractions. Cases were collected during a 19-yrs period; when were the samples from the controls taken? The mean age between HPV-positive cases and HPV-positive controls (Table 1) is 68.1 and 56.9 years, respectively. Please comment.	samples have not been collected at the same time, but more recently during the last 10 years, when the retrospective evaluation of previously collected histopathological materials started. Previous studies have shown that there does not appear to be an association between age and HPV prevalence in men, in which the majority of HPV infections is reported to clear in less than 12 months (median time to clearance 6 to 7.5 months).¹ Our finding of a higher mean age in HPV-positive LS cases (68.1 yrs) compared to HPV-positive controls (56.9 yrs) may reflect a longer duration of HPV infection in LS patients as a result of a defective clearing capability. 1. Anic GM, Giuliano AR. Genital HPV infection and related lesions in men. Prev Med 2011;53(S1):36-41.
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments	The paper is quite similar to the previous report by the same authors (design, table, some statements)	This research was aimed to confirm the findings of the previous study by extending the investigation to a broader case series.