Clinical Performance of PapilloCheck®

Comparison of the clinical performance of PapilloCheck® human papillomavirus detection with that of the GP5+/6+-PCR-enzyme immunoassay in population-based cervical screening.

J Clin Microbiol. 2010 Mar;48(3):797-801. Epub 2009 Dec 30.
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We compared the clinical performance of the PapilloCheck® assay with the high-risk HPV GP5+/6+-PCR method, followed by enzyme immunoassay readout (GP5+/6+-PCR-EIA) on cervical samples originating from women of a population-based cervical screening cohort tested by combined cytology and GP5+/6+-PCR-EIA (POBASCAM trial). A random sample of 1,437 controls (defined as women with normal cytology (age 40-60 years) without evidence of ≥CIN2 within up to 8 years), and 192 cases (women aged 30-60 years with ≥CIN3 detected within up to 3 years of follow-up) were subjected to PapilloCheck® analysis. When all 17 (probably) hrHPV types were taken into account PapilloCheck® had a clinical sensitivity for ≥CIN3 of 96.4% (185/192; 95%CI: 93.7-99.7) and a clinical specificity for ≥CIN2 of 96.3% (95%CI: 95.3-97.3). After restricting PapilloCheck® analysis to the 14 hrHPV types targeted by GP5+/6+-PCR-EIA the clinical sensitivity and specificity figures were 95.8% (95%CI 92.8-98.8) and 96.7% (95%CI 95.7-97.7), respectively. By comparison, these figures were 96.4% (95%CI: 93.9-98.9) and 97.7% (95%CI: 96.9-98.5), respectively, for GP5+6+-PCR-EIA. When including all 17 (probably) hrHPV types non-inferiority score testing revealed that the clinical sensitivity for ≥CIN3 of PapilloCheck® was non-inferior (P<0.0001), but the specificity for ≥CIN2 inferior to that of GP5+/6+-PCR-EIA (P=0.08), using lower bounds of 90% and 98%, respectively. When restricting the analysis to the 14 hrHPV types targeted by GP5+/6+-PCR-EIA both clinical sensitivity and specificity of PapilloCheck® were non-inferior to that of GP5+/6+-PCR-EIA (non-inferiority score test; P<0.0001 and P=0.007, respectively). Thus, when considering the 14 hrHPV types detectable with hrHPV GP5+/6+-PCR-EIA the PapilloCheck® assay is clinically compatible to the GP5+/6+-PCR-EIA assay.

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Ordering-Number	Author	Title of Publication
F073 038	Hesselink et al. (2010)	Comparison of the clinical performance of PapilloCheck® human papillomavirus detection with that of the GP5+/6+-PCR-enzyme immunoassay in population-based cervical screening.
F073 034	Schopp et al. (2010)	Evaluation of the Performance of the Novel PapilloCheck® HPV Genotyping Test by Comparison With Two Other Genotyping Systems and the HC2 Test.
F073 023	Dalstein et al. (2009)	Analytical evaluation of the PapilloCheck® test, a new commercial DNA chip for detection and genotyping of human papillomavirus.
F074 051	Jones et al. (2009)	Comparison of the PapilloCheck® DNA micro-array Human Papillomavirus detection assay with Hybrid Capture II and PCR-enzyme immunoassay using the GP5/6+ primer set.

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Revision: 08/2010 – F074 040

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Scientific Publications of PapilloCheck®

Abstracts of Selected Publications

PapilloCheck® is part of the oCheck® product line from Greiner Bio-One GmbH

Performance Evaluation of PapilloCheck®

Evaluation of the Performance of the Novel PapilloCheck® HPV Genotyping Test by Comparison With Two Other Genotyping Systems and the HC2 Test.

J Med Virol. 2010 Apr;82(4):605-15
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The novel PapilloCheck® genotyping test was compared with SPF10 PCR LiPav1 and PGMY09/11 on hybrid capture 2 (HC2)-pretested samples. From results of 826 cervical samples detection rates and kappa values for the tests were calculated using a HPV type consensus definition. With PapilloCheck® HPV types 53, 56 and 33 were found with a sensitivity of 100%. The lowest detection rate was observed for HPV 35 (72.2%). The SPF10 PCR LiPav1 was found to be 100% positive for HPV 18, 31, 53, 56 and 35 and lowest for HPV 59 (81%). The PGMY09/11 system detected only HPV 59 at 100% detection rate and showed lowest sensitivity for HPV 56 (40.5%). Multiple infection rates ranged from 25.8% (PGMY09/11 PCR-LBA), over 39.5% (PapilloCheck®) to 55.9% (SPF10 PCR LiPav1). In samples with higher viral DNA load detection rates and concordance between the genotyping tests increases. The kappa values in comparison to the HPV consensus type ranged from k=0.21 to k=0.82 for comparing SPF10 PCR with the HPV consensus type, while values for PGMY09/11 PCR ranged from k=0 to k=0.96 and were best for the PapilloCheck® (k=0.49-0.98). Detection rates for the identification of high grade cervical intraepithelial neoplasia (CIN2+) ranged from 93.7% (PGMY09/11 PCR) to 98.4% (PapilloCheck®, SPF10 PCR, HC2). In conclusion, this study shows that the PapilloCheck® gives comparable results to established PCR methods. However, these results also show a necessity for the standardization of genotype-specific HPV detection assays.

Comparison of the PapilloCheck® DNA micro-array Human Papillomavirus detection assay with Hybrid Capture II and PCR-enzyme immunoassay using the GP5/6+ primer set.

J Clin Virol. 2009 Jun;45(2):100-4. Epub 2009 Apr 24
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BACKGROUND: Cervical screening detects precancerous cells and routine screening could be improved by testing for Human Papillomavirus (HPV), the virus that causes cervical cancer. HPV infection is common and the benefit of HPV testing would be identification of women who are HPV negative and at low risk of developing cancer. STUDY DESIGN: The aim of this study was to evaluate the Greiner Bio-One PapilloCheck® micro-array assay (PapilloCheck®) for detection of HPV in comparison with Hybrid Capture II (hc2) and PCR-enzyme immunoassay (PCR-EIA) using the GP5/6+ primers. RESULTS: Samples from a cytologically defined population (n=878) were analysed and 187 samples also had histology information. Overall, 674 out of 878 samples gave a consistent result (76.8%; 95% CI 73.83-79.52%) on all three platforms. The genotype results obtained by PapilloCheck® and PCR-EIA were compared and 94% were consistent (95% CI 92.1-96.4%). The main difference was the poor Kappa agreement for detection of high risk (HR) type 35 (Kappa=0.190) with all inconsistent results being HR positive by PCR-EIA assay but negative on the PapilloCheck® platform. There was no statistically significant difference between the performance of each assay when HR HPV positive samples were linked with clinical result (cytology and histology grade). PapilloCheck® detected the highest number of HR HPV infections in samples with histology confirmed as CIN1, CIN2 and CIN3 (76.6%, 85% and 91.7%, respectively). CONCLUSIONS: Overall, PapilloCheck® proved to be a sensitive, reproducible, robust molecular assay for HPV genotyping with the potential for high throughput of specimens in a clinical setting.

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Comparison of the clinical performance of carcinogenic HPV typing of the Linear Array and Papillocheck® HPV-screening assay.

J Clin Virol. 2010 Jan;47(1):38-42. Epub 2009 Nov 25
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BACKGROUND: HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66 are considered carcinogenic for human beings. DNA-chip technology, PapilloCheck® HPV-screening (Greiner) and reverse dot blot, Linear Array (LA) (Roche) are tools to assess the distribution of HPV genotypes. OBJECTIVES: The aim of the study was to compare the clinical performance of PapilloCheck® and LA assays using a clinical cut-off of CIN2+. The secondary aim was to comparatively assess the distribution of HPV types using these two assays. STUDY DESIGN: The study population comprised 239 women referred for colposcopy and histology. PapilloCheck®, LA, and Hybrid Capture II (HCII) tests were done on all samples. RESULTS: All tests showed good sensitivity and NPV (greater than 90%). None of the comparisons of sensitivities, specificities, PPVs, and NPVs showed statistically relevant differences between tests. High-risk HPV positivity rate was similar for all tests (PapilloCheck® 75%, LA 77%, and HCII 73%). Agreement between tests was good. The concordance levels between HCII and PapilloCheck® and between HCII and LA were 93% (k=0.82) and 92% (k=0.80), respectively. PapilloCheck® and LA tests showed a high overall concordance rate of 96% (k=0.90). HPV16 was the most detected type (45% with PapilloCheck®, and 47% with LA), and HPV31 was the second most detected type (13% with PapilloCheck®, and 14% with LA). CONCLUSIONS: The PapilloCheck® HPV-screening test and LA test have a good clinical sensitivity to detect HPV types in CIN2+ patients. These assays allow, in the same experiment, to detect and determine the virus type. Our study showed that HPV types 16 and 31/33 are the most prevalent.

Human Papillomavirus negative but dyskaryotic cervical cytology: re-analysis of molecular testing.

J Clin Virol. 2009 Apr;44(4):322-4. Epub 2009 Mar 4
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BACKGROUND: Evaluation of molecular Human Papillomavirus (HPV) testing into UK Cervical Screening Programmes is underway. In South Wales the current HPV prevalence in women attending routine screening is 13.5% with 76.3% HR HPV positive in cases with reported dyskaryotic cervical cytology [Hibbitts S, Jones J, Powell N, Dallimore N, McRea J, Beer H, et al. Human Papillomavirus prevalence in women attending routine cervical screening in South Wales, UK: a cross-sectional study. Br J Cancer 2008;99 (December (11)):1929-33]. OBJECTIVES: The aim of this study was to re-analyse the 23.7% cases with reported dyskaryotic cytology that were HR HPV negative (n=52 out of 219 in a population of 10,000). STUDY DESIGN: Three procedures were performed: (i) GP5+/GP6+ PCR-EIA repeat on original DNA extracts; (ii) DNA extraction and GP5+/GP6+ HPV PCR-EIA; (iii) DNA extraction and HPV typing using Greiner Bio-One PapilloCheck® DNA microarray. RESULTS: 51 out of 52 samples were re-analysed. Direct repeat HPV PCR-EIA identified 24% (n=12/51) of samples positive for HR HPV. Re-extracted DNA and PCR-EIA increased detection to 41.2% (n=21/51) and PapilloCheck® detected 78.4% (n=40/51). HR HPV detection by PapilloCheck® was significantly higher compared with the other methods of re-analysis. Eleven samples were persistently HR HPV negative but 4 tested positive for low risk HPV. CONCLUSIONS: This study identifies that up to 78% of samples with dyskaryotic cervical cytology that test negative for HPV can be found to be HPV positive on re-analysis. The reliance on a single negative HPV test result could lead to missed HPV related disease in a subset of patients, the number dependant on which HPV test is performed. The clinical significance of a false negative HPV result depends on the screening interval and how HPV testing is incorporated into screening.

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Analytical evaluation of the PapilloCheck® test, a new commercial DNA chip for detection and genotyping of human papillomavirus.

J Virol Methods. 2009 Mar;156(1-2):77-83. Epub 2008 Dec 17
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Recently, a commercially available HPV DNA chip, the PapilloCheck® test, developed by Greiner Bio-One, has become available for human Papillomavirus (HPV) genotyping. The PapilloCheck® test is a PCR-based test using a new consensus primer set targeting the E1 HPV gene. HPV oligoprobes immobilized on a DNA chip allow for the identification of 24 HPV types from the amplified product. In the present study, the analytical performance of the PapilloCheck® test is compared to the Linear Array HPV genotyping test (Roche Diagnostics). Cervical specimens collected in PreservCyt (Cytyc) solution and obtained from women who presented abnormal cytological findings were tested primarily by the Hybrid Capture 2 High-Risk assay (HC2-HR, QIAGEN). A total of 144 samples were selected according to the signal intensity obtained with the HC2-HR test, expressed as RLU/CO value, and divided into 4 groups as follows: [0-1] RLU/CO (negative HC2-HR result, 34 samples); [1-5] RLU/CO (positive HC2-HR result, 30 samples); [5-40] RLU/CO (positive HC2-HR result, 40 samples); >40 RLU/CO (positive HC2-HR result, 40 samples). The concordance levels between the HC2-HR test and each of the genotyping assays was similar (88.8%) and the crude agreement between these assays was considered as „good". The detailed analysis of the discrepant results confirmed a possibly high rate of false positive results of HC2-HR test in the 1-5 RLU/CO grey zone. Genotype-specific comparison analysis was limited to the 23 HPV types detected by both genotyping assays (HPV types 6, 11, 16, 18, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 55, 56, 58, 59, 66, 68, 70, 73 and 82). Of the 135 samples available for comparison, 91 (67.4%) showed absolute agreement between the assays (concordant genotype-specific results), 34 (25.1%) showed correspondence for some but not all genotypes detected by both assays (compatible genotype-specific results), and the remaining 10 (7.4%) samples did not show any similarity between the tests (discordant results). The majority of discordances were found in samples containing multiple HPV types and in samples harboring low amounts of HPV. For some HPV genotypes, there were slight differences in the detection rate between the two genotyping methods. The Linear Array test seemed to be more sensitive to detect HPV type 53 whereas PapilloCheck® test seemed to be more sensitive to detect HPV type 56. For the other genotypes, including HPV types 16 and 18, the results obtained by the two methods did not differ significantly. In conclusion, this study shows that the PapilloCheck® test and the Linear Array test give comparable results for detecting HPV in cervical specimens. However, these results also suggest that there is a need to standardize the type-specific sensitivity of genotyping methods and to evaluate their accuracy to detect multiple HPV infections. This would be a prerequisite for the use of genotyping assays in cervical cancer screening algorithms.

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