



Bethesda Sistemi, LAST ve PAP'ın Performansı

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Hacettepe Üniversitesi Tıp Fakültesi
Patoloji AD



Servikal Patolojiler ve Kolposkopi Derneği
TURKISH SOCIETY FOR COLPOSCOPY AND CERVICAL PATHOLOGY



Ulusal Kolposkopi ve
Servikal Patolojiler
Kongresi

7-10 Aralık 2017
Wyndham Grand, İzmir

Skuamoz Hücreli Karsinom Öncülleri

- 1886 Sir John Williams
- 1928 - Aureli Babes
- 1941 - Papanicolaou



PAP SMEAR TERMINOLOJİSİ

Pap Classes	Description	Bethesda 2001
• I	Normal	Normal and variants
• II	Reactive Changes	Reactive Change
•	Atypia	ASC, ASG
•	Koilocytosis	Low Grade SIL
• III CIN I	Mild dysplasia	Low Grade SIL
• III CIN II	Moderate dysplasia	High Grade SIL
• III CIN III	Severe dysplasia	High Grade SIL
• IV	Ca in situ, suspicious	High Grade SIL
• V	Invasive	Microinvasion (<3mm)
•		Frankly invasive (>3mm)

Clinique gynécologique de Bucarest
(Professeur C. DANIEL).

**DIAGNOSTIC
DU CANCER DU COL UTÉRIN
PAR LES FROTTIS**

Par A. BABES
Maître de Conférences à la Faculté de Médecine
de Bucarest.

Le diagnostic précoce du cancer du col utérin, comme d'ailleurs du cancer en général, est basé sur l'examen histopathologique de la biopsie faite au niveau des lésions.

Dans l'état actuel de nos connaissances, il existe deux caractères histopathologiques permettant le diagnostic précoce du cancer : l'hétérotypie, c'est-à-dire l'envahissement des éléments épithéliaux en profondeur, et l'atypie, la modification des cellules épithéliales.

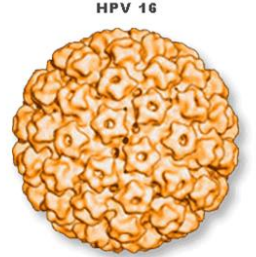
D'après les recherches les plus récentes, l'atypie, surtout en ce qui concerne le cancer du col utérin, précède l'apparition de l'hétérotypie. Nous en trouvons la preuve dans l'existence de cancers du col utérin, dans lesquels l'hétérotypie est totalement absente et dont les lésions sont limitées à l'atypie de l'épithélium qui a gardé sa situation et son étendue normales.

D'autre part sur les centaines de cancer du col examinés par nous, parmi lesquels beaucoup étaient incipients, nous n'avons point rencontré de cas dans lesquels l'atypie n'était pas considérable, étendue et variée.

Si des atypies cellulaires existent parfois aussi

Presse Médicale, 11th of April, 1928.

"The Bethesda System"



- **1988 Kurman öncülüğü**
 - Squamous İntraepithelial Lesion
 - (SIL)
 - İki farklı hastalık
- ***Düşük dereceli SIL (LSIL)***
 - Viral enfeksiyon
- ***Yüksek dereceli SIL (HSIL)***
 - Virus ilişkili prekanser
- Yeterlilik kriteri
- Tedavi ile uyumlu

- **1991**
 - Tanı kriterleri tanımlı
- **1994**
 - Bethesda Atlası
- **2001**
 - İnternet üzerinden veri toplama
- **2014**

BETHESDA SİSTEMİ

- Servikal sitoloji için geliştirildi, anüs, vajen de kullanılabilir
- ÖRNEK TİPİ
- ÖRNEK YETERLİLİĞİ
- YORUM ve SONUÇLAR
 - İntraepitelyal lezyon veya malignite açısından negatif
 - Epitelyal hücre anomalisi
 - Diğer Malign Tümörler
- EK TETKİKLER
- OTOMATİZE DEĞERLENDİRME
- EĞİTİCİ NOTLAR ve ÖNERİLER

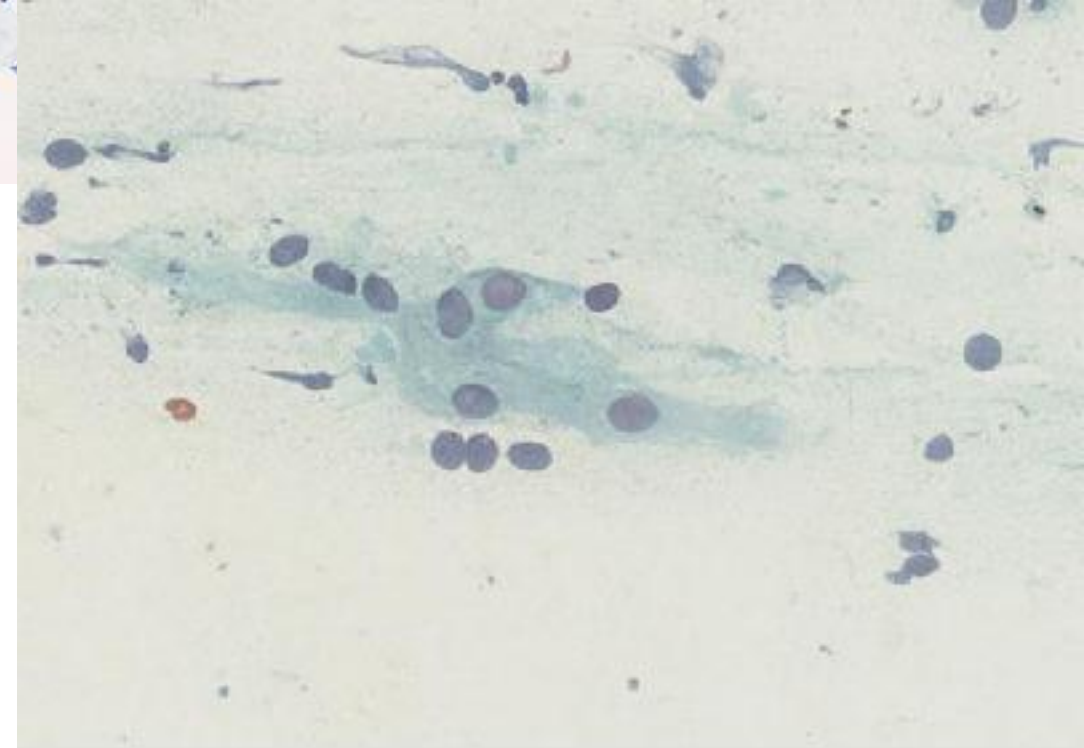
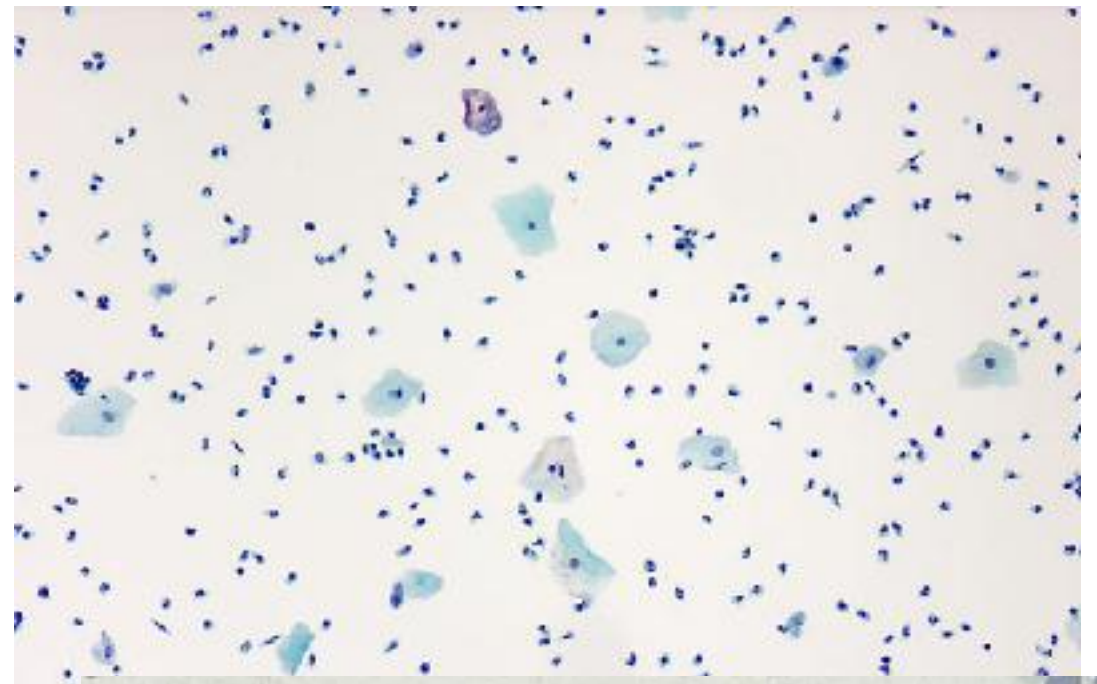
ÖRNEK TİPİ

- Konvansiyonel smear (Pap)
- Sıvı bazlı örnekler



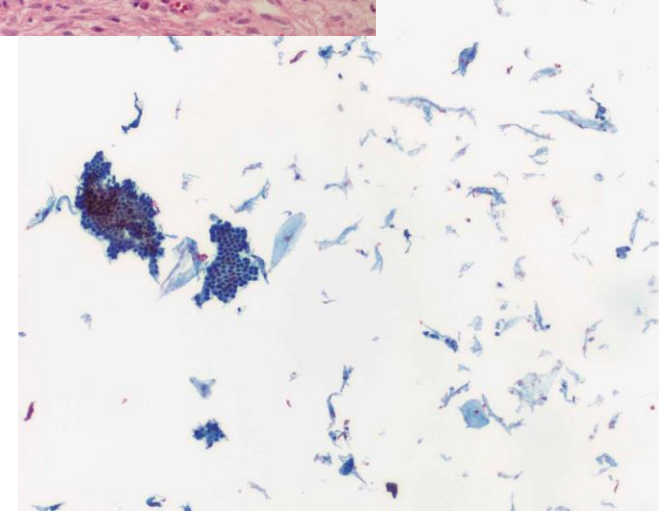
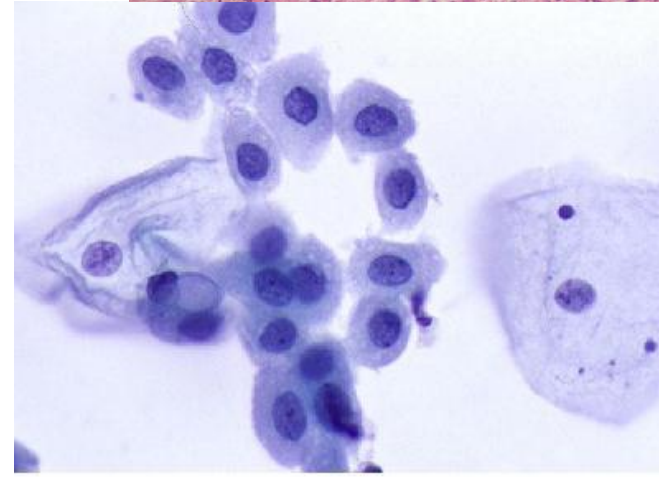
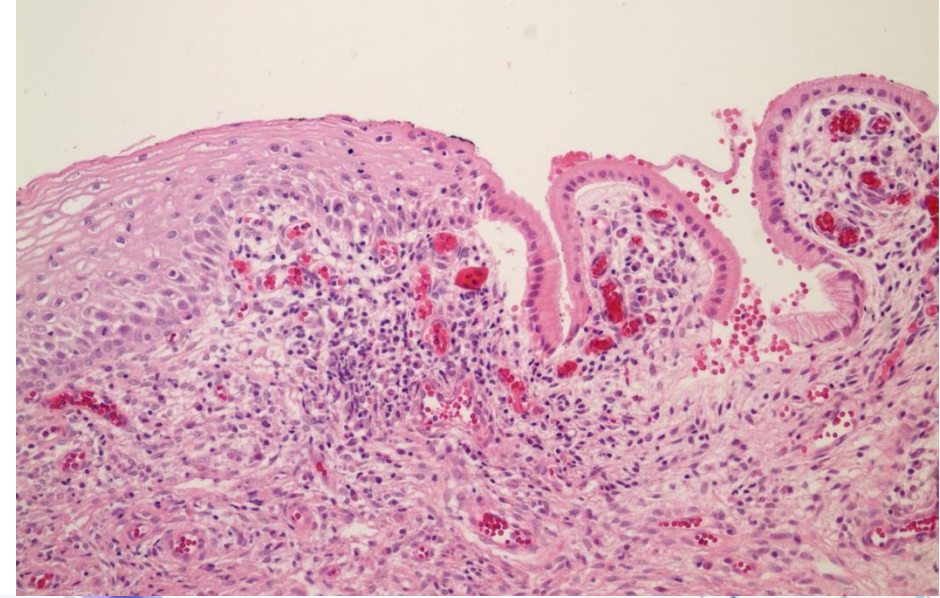
ÖRNEK YETERLİLİĞİ

- Değerlendirme için Yeterli
 - 8.000-12.000 skuamoz hücre
- *Değerlendirme için Yetersiz*
 - %1'den az olmalı
 - Ret edildi / Boyanmadı
 - Boyandı ve değerlendirildi
 - Az sayıda hücre
 - Kuruma artefaktı
 - Alanı örten eritrosit veya lökosit



Endoservikal/ Transformasyon (EC/TZ)

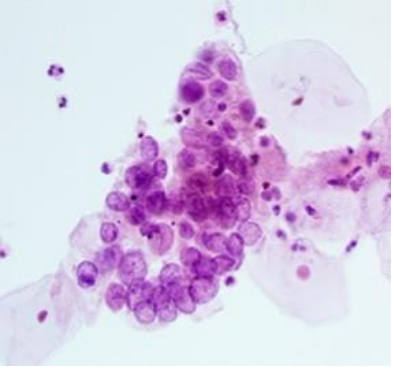
- Sitoloji negatif / EC/TZ yetersiz veya yok
- 10 endoser hüç / skuamöz met
 - %10 - %20
 - Atlanan hastalık???



"The Bethesda System"

Yorum / Sonuç

- Servikal sitoloji bir tarama testidir
 - Son tanı için klinik, laboratuvar ve biyopsi sonuçları
 - *Intraepitelyal lezyon veya malignite açısından negatif*
 - *Epitel Hücre Anomalileri*
 - Skuamöz hücreler
 - Glandüler hücreler
 - *Diğer Malign Neoplaziler*



EPİTELYAL HÜCRE ANOMALİLERİ

Skvamöz hücreler

- Atipik skvamöz hücreler
 - ASC-US / ASC-H
- Düşük dereceli SIL (LSIL)
- Yüksek dereceli SIL (HSIL)
- Skvamöz hücreli karsinom

Glandüler hücreler

- Atipik (AGS)
 - Endoservikal / Endometrial
- Endoservikal adeno CA insitu
- Adenokarsinom
 - Endoservikal / Endometrial / Ekstrauterin



Atipik Skuamöz Hücreler (ASC)

- En sık rapor edilen sitolojik anomali
- Morfolojik yorum sınırlılığı
- Tüm örnek için verilen bir yorum

- **ASC-US**
 - CIN 3+ için düşük risk
- **ASC-H**
 - CIN 3+ için ASC- US ve LSIL'den daha yüksek risk

Review

Natural History of Cervical Intraepithelial Neoplasia:
A Critical Review

Andrew G. Östör, M.D., FRCPA

TABLE 7. *Natural history of CIN: summary*

	Regress	Persist	Progress to CIS	Progress to invasion
CIN I	57%	32%	11%	1%
CIN II	43%	35%	22%	5%
CIN III	32%	56%	—	12%

- Öster CIN1 → CIN3 %2-34
- CIN1 izleminde CIN3 veya kanser gelişme riski %1.9 (Pretorius *et al*)

Histological ‘progression’ from low (LSIL) to high (HSIL) squamous intraepithelial lesion is an uncommon event and an indication for quality assurance review

Eleanor Y Chen, Ann Tran, Caroline J Raho, Chandler M Birch, Christopher P Crum & Michelle S Hirsch

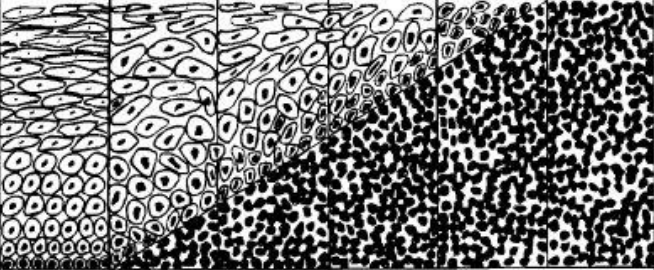
Modern Pathology (2010) 23, 1045–1051 (2010)
doi:10.1038/modpathol.2010.85
[Download Citation](#)

Received: 29 October 2009
Revised: 10 December 2009
Accepted: 12 December 2009

- LSIL, HSIL progresyonu
- İlk biyopside HSIL’in atlanması
- Yeni bir HPV bulaşması
- İzlemde yanlış HSIL tanısı

CIN (Cervical Intraepithelial Neoplasia)

- CIN 1/CIN 2/CIN 3
 - 1970 ve 1980 de yaygın kullanılıyor
- **TÜM LEZYONLAR TEK BİR HASTALIK**

	Grade 1		Grade 2	Grade 3	
Normal	Very Mild Dysplasia	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia	Ca-in-Situ
	Low Grade SIL		High Grade SIL		

SIL (Squamous intraepithelial Lesion)

International Journal of Gynecological Pathology
32:76–115, Lippincott Williams & Wilkins, Baltimore
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Original Article

The Lower Anogenital Squamous Terminology
Standardization Project for HPV-associated Lesions:
Background and Consensus Recommendations From
the College of American Pathologists and the American
Society for Colposcopy and Cervical Pathology

Teresa M. Darragh, M.D., Terence J. Colgan, M.D., J. Thomas Cox, M.D., Debra S. Heller, M.D.,
Michael R. Henry, M.D., Ronald D. Luff, M.D., Timothy McCalmont, M.D., Ritu Nayar, M.D.,
Joel M. Palefsky, M.D., Mark H. Stoler, M.D., Edward J. Wilkinson, M.D., Richard J. Zaino, M.D.,
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LAST ***(Lower Anogenital*** ***Squamous Terminology)***

- **HPV ilişkili skuamoz lezyonlar**
 - Viral enfeksiyonlar (LSIL)
 - Kanser öncülü lezyonlar (HSIL)
- **Ortak terminoloji**
 - Serviks, vajen, vulva, penis, anüs, perianüs, skrotum

- **TANI**
- HSIL / LSIL
- İlgili bölgeye ait (-IN)
 - CIN / VaIN / VIN / AIN
/ PAIN / PeIN
- LSIL (Kondilom)



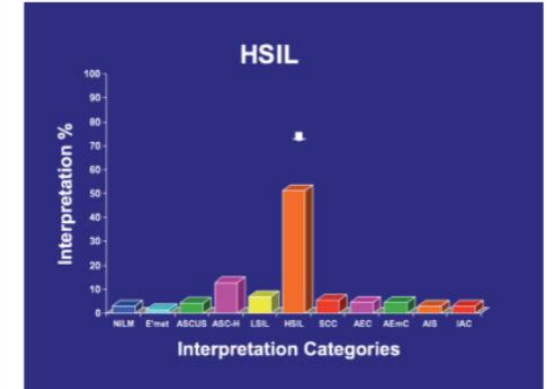
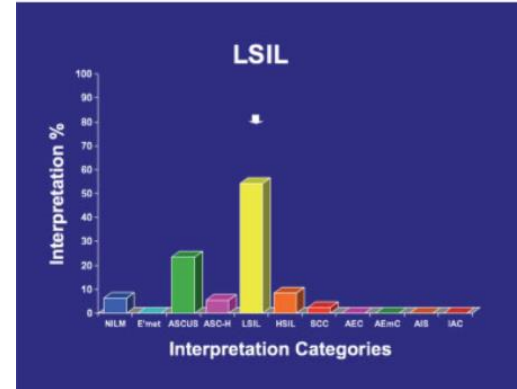
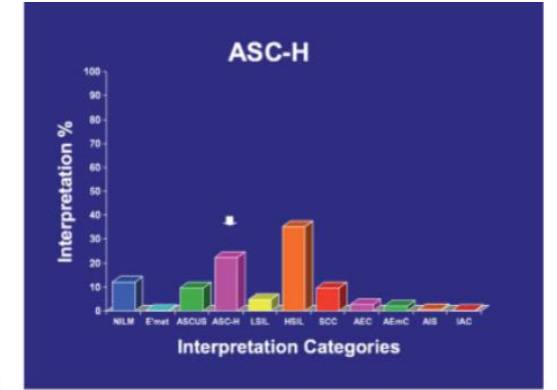
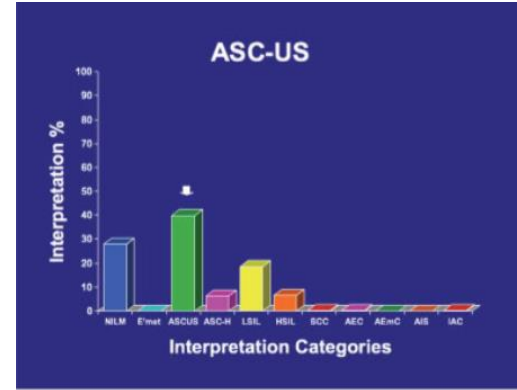
The Bethesda Interobserver Reproducibility Study (BIRST)

A Web-based Assessment of the Bethesda 2001 System for Classifying Cervical Cytology

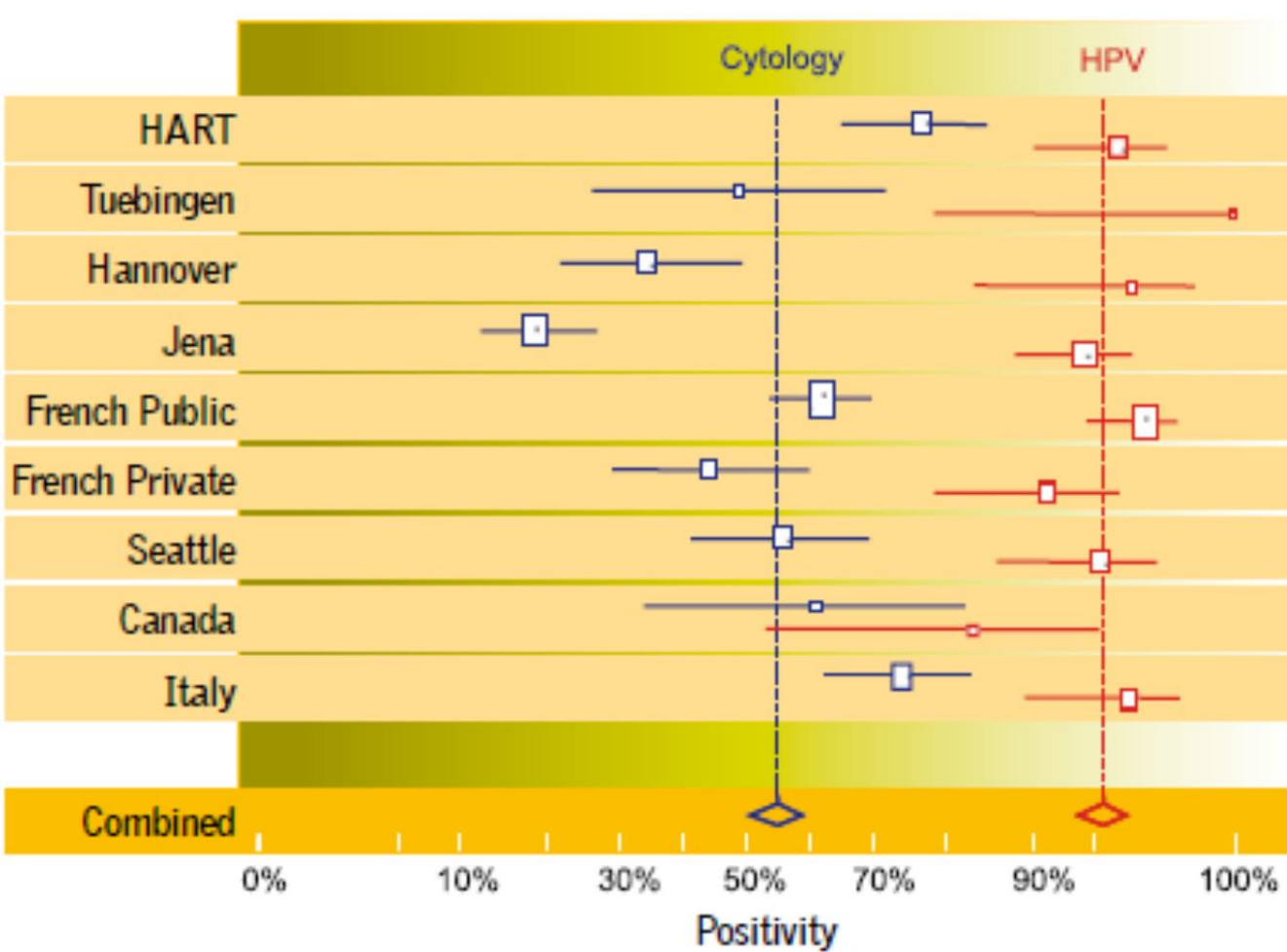
Mark E. Sherman, MD¹
Abhijit Dasgupta, PhD²
Mark Schiffman, MD, MPH¹
Ritu Nayar, MD³
Diane Solomon, MD⁴

CANCER (CANCER CYTOPATHOLOGY) February 25, 2007 / Volume 111 / Number 1

- Panelde uyum
 - Tam uyum %55.1%
 - %82.3 (Negatif X Pos)
 - En yüksek LSIL ve en düşük ASC-US / ASC-H
- Morfolojik görünüm en önemli belirleyici



Servikal Sitoloji



References: •Cuzick J et al. Int. J. Cancer 2006;119:1095-1101. •Ronco G et al. J Natl Cancer Inst 2006;98:765-74.

Primary Screening Sensitivity: CIN 2/3+				
Study	No.	Age	Pap	HPV
Cuzick J	11,085	30-60	76.6%	97.1%
Clavel C	4076	30-76	57.7% CP 84.4% LBP	100%

Screening Test	CIN2+		CIN3+	
	Corrected* Sensitivity (95% CI)	Corrected* Specificity (95% CI)	Corrected* Sensitivity (95% CI)	Corrected* Specificity (95% CI)
HC2	96.7% (92.6-100)	86.4% (85.4-87.4)	95.3% (83.9-100)	84.9% (83.8-86.0)
AHPV	92.0% (86.4-97.6)	91.8% (91.0-92.6)	95.7% (85.0-100)	90.3% (89.4-91.2)
Cytology	69.1% (60.0-78.1)	91.9% (91.1-92.7)	73.3% (55.6-91.0)	90.8% (90.0-91.7)

CIN = cervical intraepithelial neoplasia; HC2 = hybrid capture 2, the digene HPV Test®; AHPV = Aptima® HPV assay; CI = confidence interval *Adjusted for verification bias

- Yüksek yanlış negatiflik
- Yüksek spesifisite

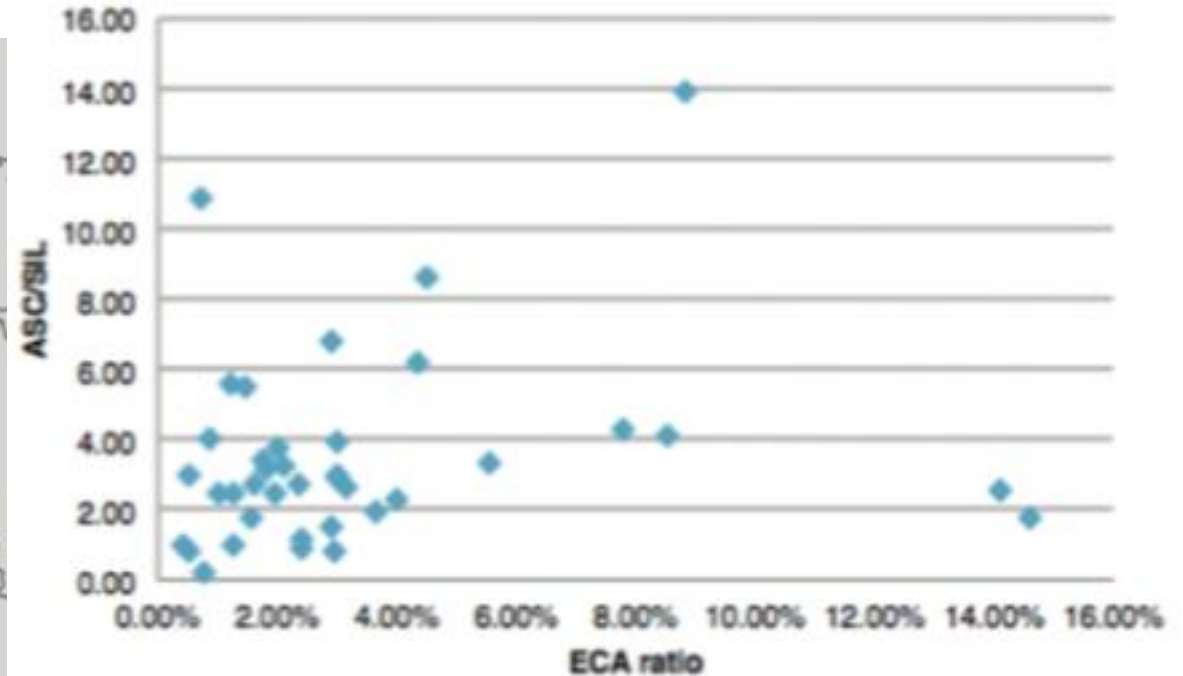
What does the Data of 354,725 Patients from Turkey Tell Us About Cervical Smear Epithelial Cell Abnormalities?

- The Epithelial Cell Abnormality Rate is Increasing
- Quality Control Studies and Corrective Activity are Musts

İlknur Çetinaslan TÜRKMEN¹, Alp USUBÜTÜN², Aslı ÇAKIR¹, Özlem AYDIN³, Filiz Aka BOLAT⁴,
Metin AKBULUT⁵, Serdar ALTINAY⁶, Sema ARICI⁷, Figen ASLAN⁸, Müzeyyen ASTARCI⁹, Emine Kılıç BAĞIR¹⁰,
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AYDIN¹⁵, Hale DEMİR¹⁶, Hayriye Tatlı DOĞAN¹⁷, Kamile Gülçin EKEN¹⁸, Selma Şengiz ERHAN¹⁹, Gülgün
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İclal GÜRSES²⁵, Nihan HABERAL²⁶, Dudu Solakoğlu KAHRAMAN²⁷, Gülçin Harman KAMALI¹⁹,
Yasemin Yuyucu KARABULUT²⁸, Mehmet KEFELİ²⁹, Meral KOYUNCUOĞLU³⁰, R. Doğan KÖSEOĞLU³¹,
Bahar MÜEZZİNOĞLU³², Binnur ONAL³³, Sevgen ÖNDER², Zuhul ÖZCAN³⁴, Elife KIMILOĞLU³⁴,
Hatice ÖZER³⁵, F. Cavide SÖNMEZ⁷, Sevinç ŞAHİN³⁶, Nurhan ŞAHİN³⁷, Tülin YALTA³⁸

24 şehir 45 hastane
EHA oranı: %5.08
ASC/SIL: 0,21-13,94
Ortalama: 2,61

Turkish Journal of Pathology



Factors related to inter-observer reproducibility of conventional Pap smear cytology: a multilevel analysis of smear and laboratory characteristics

A. Baena*, E. Guevara*, M. Almonte[†], J. Arias-Stella[‡], P. Sasieni[§] and G. I. Sanchez*

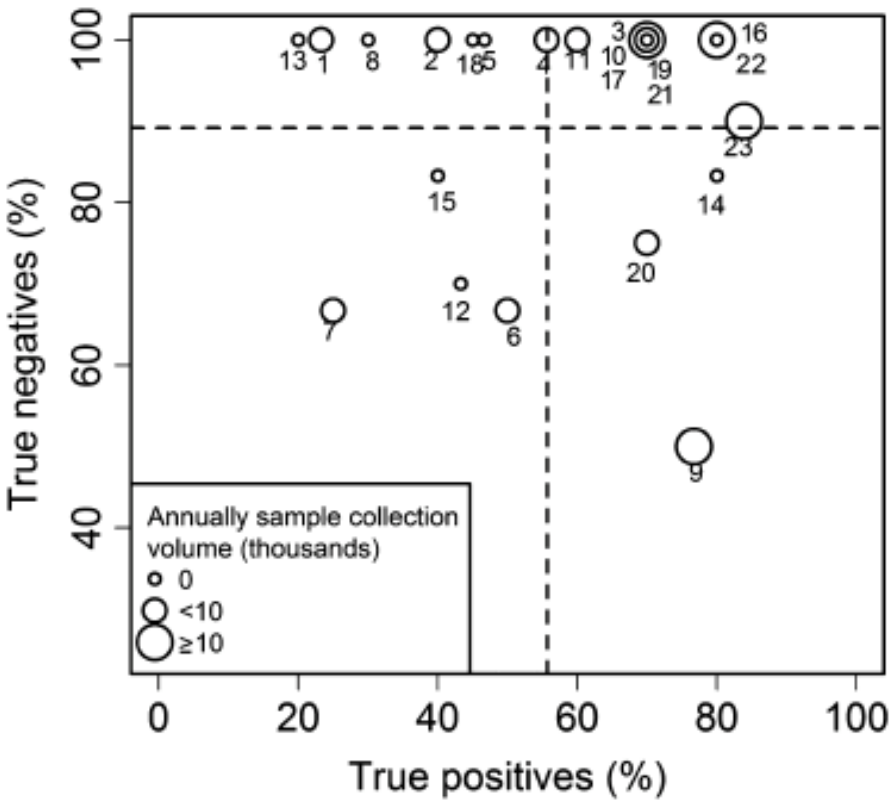
*Infection and Cancer Group, School of Medicine, Universidad de Antioquia, Medellin, Colombia, [†]Prevention and Implementation Group, International Agency for Research on Cancer, Lyon, France, [‡]Institute of Pathology and Molecular Biology, Arias Stella, Lima, Peru, [§]Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Accepted for publication 24 October 2016

A. Baena, E. Guevara, M. Almonte, J. Arias-Stella, P. Sasieni and G. I. Sanchez

- Kolombiya deneyimi
- Gerçek pozitif ve gerçek negatiflik oranları laboratuvarlar arası değişken

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Cytopathology 2017, **28**, 192–202



Cervical Histopathology Variability Among Laboratories

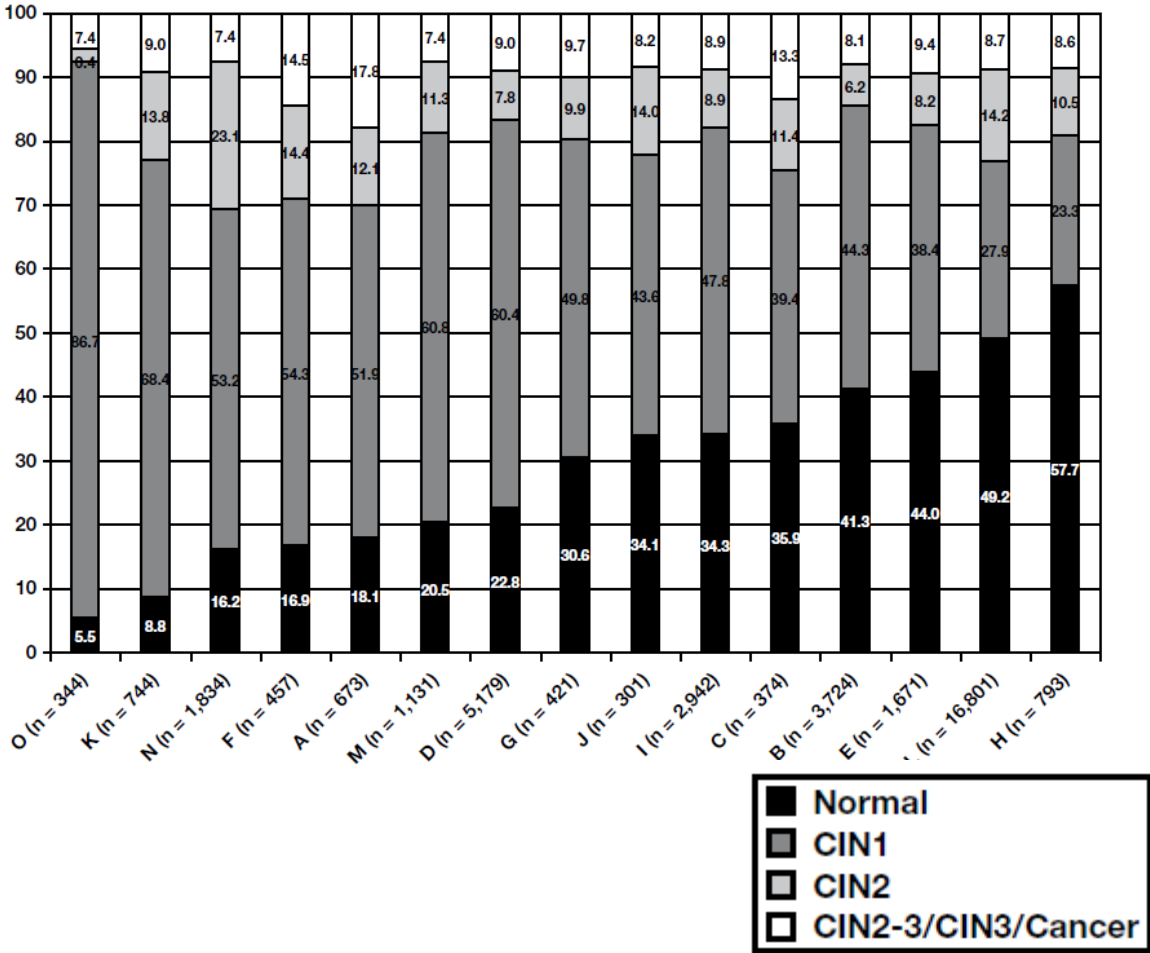
A Population-Based Statewide Investigation

Julia C. Gage, PhD, MPH,¹ Mark Schiffman, MD, MPH,¹ William C. Hunt, MA,² Nancy Joste, MD,² Arpita Ghosh, PhD,¹ Nicolas Wentzensen, MD, PhD,¹ and Cosette M. Wheeler, PhD,² for The New Mexico HPV Pap Registry Steering Committee

Key Words: Cervical intraepithelial neoplasia; Histopathology; Reproducibility

DOI: 10.1309/AJCPSD3ZXJP7NNB

Am J Clin Pathol 2013;139:330-335
DOI: 10.1309/AJCPSD3ZXJP7NNB



Short communication

Inter-laboratory variability in the presence of human papillomavirus in normal and abnormal cervical cytology samples

Christine Weyn^{a,b}, Christian Garbar^c, Jean-Christophe Noël^d, Birgit Weynand^e, Alain Verhest^f, Dominique d'Olne^g, Marc Arbyn^h, Yvon Englert^a, Véronique Fontaine^{a,b,*}

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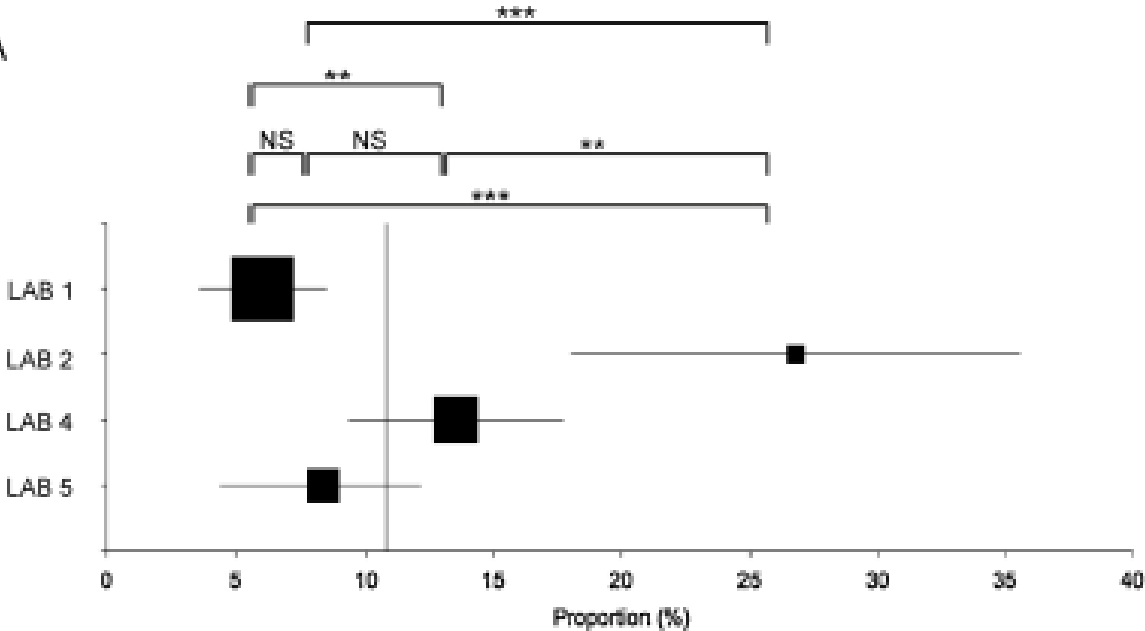
^eDepartment of Pathology, CHU Mont Godinne, Université Catholique de Louvain (UCL), Yvoir, Belgium

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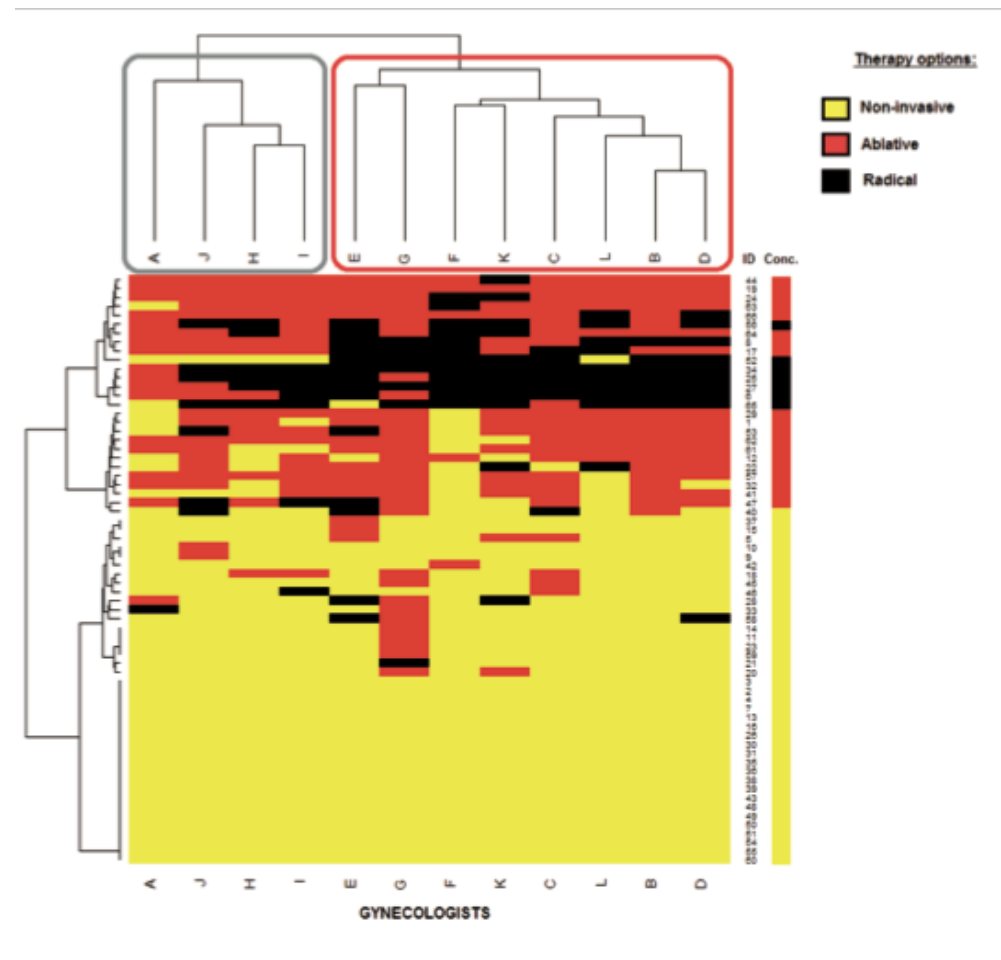
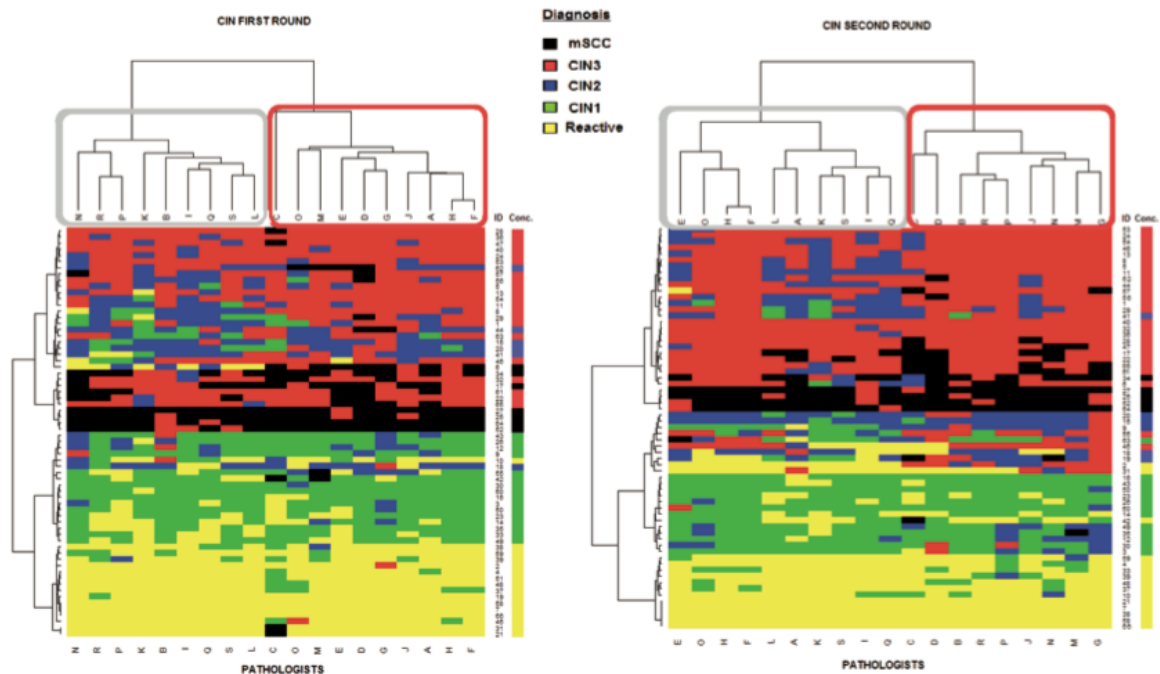
A



Diagnostic and Treatment Reproducibility of Cervical Intraepithelial Neoplasia / Squamous Intraepithelial Lesion and Factors Affecting the Diagnosis

Arzu SAĞLAM¹, Alp USUBÜTÜN¹, Anıl DOLGUN², George L. MUTTER³, M. Coşkun SALMAN⁴,
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Zerrin CALAY⁸, Funda EREN⁹, Derya GÜMÜRDÜLÜ¹⁰, Nihan HABERAL⁵, Şennur İLVAN⁸,
Şeyda KARAVELİ¹¹, Meral KOYUNCUOĞLU¹², Bahar MÜEZZİNOĞLU¹³, Kamil Hakan MÜFTÜOĞLU¹⁴,
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İLGİNİZ İÇİN TEŞEKKÜR EDERİM

