

Monolayer Technology versus Conventional Pap Smear

By Thomas J. Bassler, Jr., MD, Michael W. deTar, M.D., and Felix Martinez, Jr., M.D.

In 1942, George Papanicolaou introduced what we now call the Pap smear to medical practice in the United States. Since that time, there had been little change in the technique until the development of monolayer (“liquid-based”) Pap testing in the late 1980s. While the new method was met with the usual level of healthy skepticism, the evolving medical literature on this issue clearly supports the superiority of the monolayer technique compared to the conventional test.^{1,2}

Of note, however, the April 5, 2003 *British Medical Journal* published a French study that concluded that monolayer cytology is less reliable and more likely to give false-positive and false-negative results than conventional cervical smear testing in screening for cervical cancer.^{3,4} There were serious methodologic problems with this study design, skewing the results in favor of the conventional method. Particularly, the authors first prepared a conventional Pap smear and then, with the remainder of the cellular harvest, rinsed the collection instrument into a monolayer vial. Previous studies have shown that this method significantly reduces the sensitivity of detection by starting out with a relatively cell-poor preparation.⁵

Another interesting result in the French study was that there were more inconclusive results in monolayer preparations than in conventional smears. This was certainly not the experience of several large studies in the United States conducted by the FDA to establish that validity of monolayer Pap testing. These studies consistently

demonstrated that monolayer technology was superior to the conventional smear preparation in the arena of inconclusive/unsatisfactory preparations, with far fewer cases showing technical problems such as air drying, excess blood, paucity of cells and the like.

We found over twice as many low-grade squamous intraepithelial lesions with the new monolayer technology, and we reduced our unsatisfactory rate by over 50%.

InCyte Pathology has been reviewing monolayer preparations for over two years. We have accumulated a significant body of valuable data on the relative value of monolayer cytology. From January to December, 2003, we reviewed 42,558 monolayer Pap preparations and 40,708 conventional Pap smears. We found over twice as many low-grade squamous intraepithelial lesions with the new monolayer technology, and we reduced our unsatisfactory rate by over 50%. While the ASCUS rate nearly doubled (but remained well below recommended guideline ranges), the rate of detecting HSIL increased by 67%. It may be asserted that the increased detection rate for

HSIL is counterbalanced by the increased rate of ASCUS, traditionally a problematic diagnostic category. Mitigating this apparent problem, however, is the recognition that HPV testing on the ASCUS category is helpful in resolving the diagnostic dilemma. These are impressive differences. The data certainly support the contention that monolayer Pap cytology enhances clinically significant disease detection.

For any questions pertaining to monolayer technology and HPV testing please feel free to contact client services, Molly Preston, Carol Brucick, or any of the Cytopathologists at 509-892-2700. ▲

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Diagnosis	Liquid-based Pap Smears Number (%)	Conventional Pap Smear Number (%)
Normal/Reactive	38,470 (90.4%)	38,794 (95.3%)
Low-grade squamous intraepithelial lesion (LSIL)	2041 (4.8%)	770 (1.9%)
High-grade squamous intraepithelial lesion (HSIL)	334 (0.8%)	200 (0.5%)
Atypical squamous cells of undetermined significance (ASCUS)	1,484 (3.5%)	701 (1.7%)
Carcinoma	4 (0.01%)	4 (0.01%)
Unsatisfactory	63 (0.15%)	116 (0.28%)
Atypical Glandular Cells of Undetermined Significance (AGC)	162 (.38%)	123 (.30%)

Quantitative Prostate Biopsy Pathology: Why individually identified prostate sextant biopsies are important

By David C. Hoak, M.D.

In 1988, Ragde, et. al. introduced the use of the Biopsy-gun with transrectal ultrasound (TRUS) to take prostate biopsies.¹ They demonstrated that the Biopsy-gun was superior to fine needle aspiration of the prostate for detecting prostate carcinoma.

In 1989, Dr. Thomas Stamey demonstrated that six *systematic* TRUS Biopsy-type biopsies were superior for detection of prostate cancer when compared to one or two *directed* TRUS guided Biopsy-type biopsies.² Thus, the “prostate sextant biopsy” was introduced. Urologists often routinely biopsy the apex, the midgland, and the base on both the right and left sides of the prostate for total of at least six biopsies. Today, about 70% of urologists submit one core from each area in individually identified specimen containers. Others submit three cores from each side in two containers. The latter approach saves money, but placing biopsies from the apex, midgland, and base in one container can result in loss of important staging information.

Individually labeled sextant biopsies allow for mapping tumor in the prostate gland. A large national commercial lab has been instrumental in promoting prostate cancer maps. Mapping the location of prostate carcinoma can help in planning for nerve sparing surgery. If the urologist knows that the carcinoma is predominantly in the apex of the gland, he or she can pay special attention to the apex at surgery. Mapping with sextant biopsies is also extremely helpful in planning for radioactive seed implants (brachytherapy). Also, if a small focus of atypical glands that are suspicious for, but not diagnostic of, cancer is found on a particular biopsy, or if a focus of High Grade Prostate Intraepithelial Neoplasia (HGPIN) is identified, the pathology report can help the urologist identify the precise area to re-biopsy.

More recently it has been demonstrated that, by using quantitative prostate biopsy data in combination with the serum PSA, a urologist can accurately predict –prior to therapy – if a patient’s prostate carcinoma is organ confined (OC), breaches the capsule (Cap+), involves the seminal vesicles (SV+), or is metastatic to lymph nodes (N+). The predictive models utilizing this data have been validated from hundreds of radical prostatectomies.^{3, 4, 5} The quantitative models rely on the percentage of positive cores.

Unfortunately, pathologists cannot always report a reliable percentage of positive cores if all the specimens from one side of the prostate are placed in one container. The fragile biopsies can become fragmented or tangled, in which case it can be impossible to tell if two or three biopsies are involved with cancer, or if one positive biopsy has fragmented into three pieces. This can obviously affect the predictive model. Technically, it is easier for the histotechnician to embed and cut sections of six prostate biopsies in six cassettes rather than six prostate biopsies in two cassettes, often because it is difficult to get the tangled

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biopsies to lay flat, thereby making it harder to obtain sections from the block. Valuable tissue can be lost in the process of “facing the block” if the specimens are not flat.

Recently, there have been several papers suggesting that sextant biopsies may not adequately sample the prostate, and that biopsies should also be taken from the posterolateral prostate as well. Taylor, et. al. found that the addition of more laterally directed biopsies increases the rate of cancer detection and that the majority of these detected cancers were clinically significant. Fink, et. al. found that the traditional sextant biopsy is only 53% sensitive and that additional cores from the lateral areas of prostate help increase sensitivity of prostate biopsy for cancer. Jonathan Epstein, noted prostate pathologist, states that urologists

at The Johns Hopkins Hospital “currently perform routine sampling of both the sextant and posterolateral aspects of the gland with 12 cores sampled per patient.” Peter Humphrey, another eminent prostate pathologist from Washington University in St. Louis, states “procurement of 8-13 biopsies is currently favored because of the increased cancer detection rate.” He notes that recent computer models “indicate that 10-12 core biopsies detect substantially more cancers than a sextant approach.” ▲



Biopsy-gun

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CLIENT ALERT

2005 Changes to Most Frequently Used ICD-9

Effective October 1, 2004, new codes were added to the 795.0 Abnormal Papanicolaou smear of cervix and cervical HPV category. The codes in this section now appear as listed below:

- 795** Abnormal Papanicolaou smear of cervix and cervical HPV – **requires an additional digit in order to be coded correctly.**
- 795.00** Abnormal glandular Papanicolaou smear of cervix
- 795.01** Papanicolaou smear of cervix with atypical squamous cells of undetermined significance (ASC-US)
- 795.02** Papanicolaou smear of cervix with atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H)
- 795.03** Papanicolaou smear of cervix with low-grade squamous intraepithelial lesion (LGSIL)
- 795.04** Papanicolaou smear of cervix with high-grade squamous intraepithelial lesion (HGSIL)
- 795.05** Cervical high risk human papillomavirus (HPV) DNA test positive
- 795.08** Unsatisfactory smear
- 795.09** Other abnormal Papanicolaou smear of cervix and cervical HPV

Consult the 2005 edition of the ICD-9-CM manual for a comprehensive list of changes. ▲

New Additions to Medical Staff at InCyte Pathology



PROFILE Mancong Zhang, M.D., Ph.D.

Mancong Zhang, M.D., Ph.D., joined InCyte Pathology in July 2004. Dr. Zhang graduated from Shanghai Medical University in China and completed a residency program at Massachusetts General Hospital in Boston. Her training includes completion of a dermatopathology fellowship at Harvard Medical School. Dr. Zhang is board certified in clinical and anatomic pathology as well as in dermatopathology.

Dr. Zhang and her husband enjoy gardening, biking, hiking, and fishing. She and her husband have a ten-year-old son and a two-year-old daughter. ▲



PROFILE Melissa Cessna, M.D.

Melissa Cessna, M.D., also joined InCyte Pathology in July 2004. A 1999 graduate of the University of New Mexico School of Medicine, Dr. Cessna completed a clinical and anatomic pathology residency program at the University of Utah. She continued her training at the U of U with a fellowship in hematopathology. Dr. Cessna holds board certifications in clinical and anatomic pathology as well as in hematology.

Dr. Cessna and her husband, Andy, enjoy snowshoeing, backpacking, hiking, and bike riding with their two-year-old son, James. ▲

The Coder's Corner

In order to comply with CMS Pap smear guidelines, laboratories are now required to submit the appropriate ICD-9-CM code when billing Medicare. The ICD-9-CM code must indicate the medical necessity for the Pap smear at the most detailed level. Please submit an ICD-9-CM code or verbiage on the requisition that represents the patient's specific symptom, complaint, current condition or past history. A signed and dated Advanced Beneficiary Notice (ABN) must accompany all routine Medicare Pap smears. These forms are available to you at no charge by contacting the laboratory. If you have any questions, please call (509)892-2700 and ask to speak to a coding specialist. ▲

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PathWays has items of interest for office personnel and assistants as well as for physicians, nurse practitioners, nurses and physician assistants. We recommend that, upon completion of circulation, your copy of **PathWays** be filed in the InCyte Pathology *Anatomic Pathology Services Manual* for future reference.

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