GEISINGER IHC

Stains are a good thing ... **Quality** stains are our thing.

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In this issue:

Updates in Diagnostic Immunohistochemistry (IHC) in *Archives of Pathology & Laboratory Medicine*

Geisinger Pathology Group is pleased to announce their contribution to two upcoming Special Issues (December 2014 and January 2015) of *Archives of Pathology & Laboratory Medicine*. Organized by Dr. Fan Lin and contributed by Geisinger pathologists and many expert pathologists from other medical centers, these Special Issues feature 14 review articles covering updates in IHC automation, standardization of diagnostic IHC, and the role of IHC in diagnosing tumors in major organs and tumors of unknown primary.

This series begins with an article emphasizing standardization of diagnostic IHC in the preanalytic, analytic and post analytic phases. The second review article compares and contrasts the recent technological advances in new-generation automated IHC platforms from all major companies. The third comprehensively reviews some diagnostic strategies and algorithms for tumors of unknown origin and updates many recently described diagnostic markers. The remaining 11 review articles are devoted to organ-specific diagnostic IHC, with detailed discussion of diagnostic IHC panels and the utilities and pitfalls of commonly used IHC markers, including many recently described biomarkers, such as ankyrin repeat domain 30A (NY-BR-1), arginase-1, BRAF, cadherin-17, CD146, CD160, CD200, c-MYC, C-reactive protein, desmocollin-3, desmoglein-3, ERG, forkhead box L2 (FOXL2), GATA3, glucose transporter 1, glutamine synthetase, hepatocyte nuclear factor 1 alpha, hepatocyte nuclear factor 1 beta, hepatocyte nuclear factor 4 alpha, HGAL/GCET2, IDH1, IMP3, INI1, IRTA1, LEF1, LFAB, LMO2, maspin, Merkel cell polyomavirus (MCPyV), MUC4, MUM1, Nanog, NKX2.2, NKX3.1, OCT4, p40, p57, PAX2, PAX8, pVHL, S100P, SALL4, SATB2, SDHB, serum amyloid associated protein, SOX10, SOX11, SOX2, STAT6, stathmin, steroidogenic factor 1 (SF-1) and TROP2.

New Antibodies

Geisinger IHC recently validated two new mutation-specific antibodies for clinical use.

IDH1 R132H

Isocitrate dehydrogenase 1 (IDH1), an enzyme involved in Krebs cycle, is frequently mutated in human tumors. IDH1 R132H is the most common mutant form and is found in a majority of low-grade diffuse and anaplastic gliomas and secondary glioblastomas, spindle cell hemangiomas, a subset of acute myeloid leukemias and, more recently, in some breast, prostatic, and colonic adenocarcinomas arising in a background of inflammatory bowel disease. Using IHC to detect this specific mutation is a recent development, and comparative studies have shown good concordance with DNA sequencing results.

IDH1 R132H IHC is particularly useful in the diagnosis and risk stratification of gliomas. Figure 1 demonstrates a positive granular cytoplasmic staining pattern in a glioma. This allows pathologists to confidently differentiate diffusely infiltrating tumor cells in a low-grade diffuse glioma from surrounding reactive gliosis. It also helps to identify tumor cells in post-therapy specimens with extensive background reactive changes. In addition to its neuropathology applications, the stain has also been suggested to help differentiate chondrosarcoma (positive) from chrondroblastic osteosarcoma (negative).

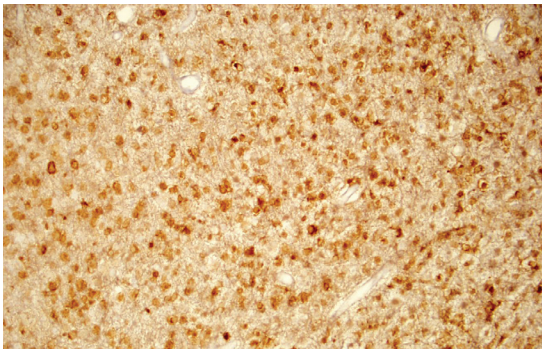

Figure 1. IDH1 positive in glioma

BRAF V600E

BRAF is an important cell-signaling protein involving the mitogen-activated protein kinase pathway (MAPK). It is frequently mutated in various human cancers, including melanoma, colorectal carcinoma (CRC) and papillary thyroid carcinoma (PTC). The most common mutation is BRAF V600E, accounting for essentially all BRAF mutations in CRC and greater than 90% in melanoma and PTC. A selective BRAF inhibitor therapy is currently available to treat advanced melanoma and PTC in patients whose tumors harbor BRAF mutation.

Using IHC to detect mutant BRAF V600E is a rather recent development. Although some early studies showed controversial results, the recently published data have clearly demonstrated its potential clinical use. The assay can achieve a sensitivity and specificity comparable to molecular detection methods, provided that it is carefully validated and results correctly interpreted. In our lab, we went through an extensive validation process by testing more than 100 CRC samples with or without confirmed BRAF mutation using both TMA and large tissues. Our validation data revealed an excellent concordance between IHC and PCR results. Figure 2 shows an example of BRAF V600E-positive CRC with diffuse and strong granular cytoplasmic staining in tumor cells but not in normal glands.

Our lab has adopted an algorithm for universal screening of Lynch syndrome in all patients with CRC resection using a mismatch repair protein (MMR) IHC method. As a result, tumors with MLH1 loss or MLH1/PMS2 concurrent loss are submitted for BRAF V600E molecular testing, which is costly and time consuming. Using BRAF V600E IHC as a triage step in the algorithm reserves the molecular testing only for those rare cases with indeterminate IHC results, thus decreasing test cost and improving turnaround time. BRAF V600E IHC also has proven clinical value in PTC diagnosis and prognosis. Its potential use as a predictive marker for selective BRAF inhibitor therapy in patients with advanced PTC and melanoma requires further testing.

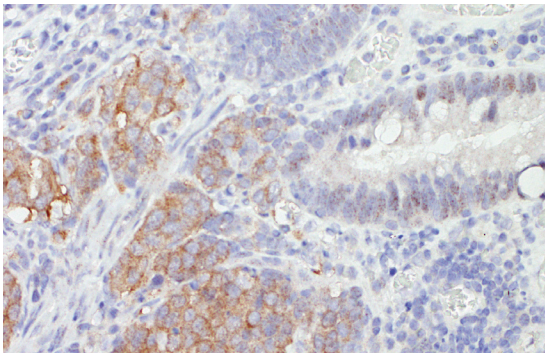

Figure 2. BRAF positive in CRC

CPT Coding for 2015

Contributed by Diane M. Shulski

Medicare's implementation of G codes for 2014 caused confusion for laboratories trying to interpret unit of service and multiplex stain billing. 2015 brings clarification to IHC coding along with a parallel method for reporting in situ hybridization (ISH). In 2015 the unit of service is specimen, not block, and additional codes help to clarify single vs. multiplex stains.

Immunohistochemistry (IHC) and ISH code groups have been created to include a primary code and add-on codes identified by a + in front of the code. The multiplex codes (for multiple separately identifiable antibodies or probes applied to the same specimen) are part of the group but are not considered add-on codes. The multiplex code is to be billed in place of the primary code. Changes are indicated in red in the following tables.

IHC or Immunocytochemistry (ICC); per specimen:

Code	Status	Use
88342	Revised	Initial single antibody stain procedure
+ 88341	New	Each additional single antibody stain procedure (use in conjunction with primary code 88342)
88344	New	Each multiplex antibody stain procedure
88343	Deleted	Replaced by multiplex code 88344

When multiple separately identifiable antibodies are applied to the same specimen (i.e., multiplex antibody stain procedure), use one unit of 88344. When multiple antibodies are applied to the same slide that are not separately identifiable (i.e., antibody cocktails), use 88342

Morphometric analysis, tumor, IHC (e.g., Her-/neu, estrogen receptor/progesterone receptor); quantitative or semiquantitative, per specimen

Code	Status	Use
88360	Revised	Each single antibody stain procedure; manual
88361	Revised	Each single antibody stain procedure; using computer-assisted technology

Morphometric analysis of a multiplex antibody stain should be reported with one unit of 88360 or 88361, per specimen

CPT codes for ISH have been revised and new codes have been added to model the IHC billing structure.

Qualitative ISH: per specimen; single vs. multiplex stain

Code	Status	Use
88365	Revised	Initial single probe stain procedure
+ 88364	New	Each additional single probe stain procedure (in addition to code 88365 for primary procedure)
88366	New	Each multiplex antibody stain procedure

Morphometric analysis, ISH (quantitative or semi-quantitative), using computer–assisted technology, per specimen:

Code	Status	Use
88342	Revised	Initial single antibody stain procedure
+ 88341	New	Each additional single antibody stain procedure (use in conjunction with primary code 88342)
88344	New	Each multiplex antibody stain procedure

Morphometric analysis ISH (quantitative or semi-quantitative), manual, per specimen:

Code	Status	Use
88368	Revised	Initial single probe stain procedure
+ 88369	New	Each additional single probe stain procedure (in addition to code 88638 for primary procedure)
88377	New	Each multiplex antibody stain procedure

Laboratory groups hope that Medicare will adopt the new code structure and discard G codes for IHC testing, thereby simplifying coding of qualitative and quantitative IHC and ISH. Technical reimbursement for the add on + codes remains a question based on the Medicare 2015 HOPPS Final Rule—Bundling of Laboratory Services into APCs.

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NEWS

Look Inside for:

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