Practical Approach to Intraoperative Consultation (IOC)

“Intraoperative Consultation (IOC) for a brain biopsy is among the most stressful situations that a surgical pathologist will encounter.”

* G Fuller, January 25, 2013 Austin
IOC Principles

PRE-IOC Preparation

*AGE of the patient*
PRE-IOC Preparation

• AGE of the patient
• ANATOMIC LOCATION of the lesion

PRE-IOC Preparation

• AGE of the patient
• ANATOMIC LOCATION of the lesion
• IMAGING characteristics of the lesion

NEUROIMAGING 101
The Importance of Imaging Studies to the Pathologist Cannot be Stressed Enough!

Rubin’s Pathology
6th Edition
2011

Rubin’s Pathology
6th Edition
2011
Contemporary neuroimaging techniques provide the first look at the “gross pathology” of a CNS lesion and constitute a rich source of information that can be utilized by the pathologist to formulate a refined differential diagnosis prior to surgical biopsy and tissue examination.
Go to the Operating Room
Peter C. Burger
Am J Surg Path 1988

“…the radiographs on display in the operating theater are as relevant to the work of the pathologist as they are to the neurosurgeon.”
Practical Illustration

Importance of Knowing what the Pre-operative MRI Scans Show
Importance of Pre-op MRI

DX: Low-Grade Diffuse Glioma

Pre-operative MR Imaging
Importance of Pre-op MRI

YIKES!

The biopsy was NOT representative!
Our patients are best served by a collegial Team Approach – surgeon, oncologist, radiologist, pathologist

You must know what the imaging shows - Talk to the neuroradiologist!

To talk to the neuroradiologist, you must be able to speak their language
Practical Basic Neuroimaging

Information Gained from MRI

Anatomic location of the lesion(s)
Information Gained from MRI

Anatomic location of the lesion(s)

Nature of interface of lesion border with brain parenchyma (sharp margin vs. diffuse infiltration)

Presence or absence of contrast enhancement

If contrast-enhancing, pattern of enhancement
Patterns of Contrast Enhancement

Smooth ring
Ragged ring
C-shaped ring
Solid, uniform
Cyst w/ nodule
Dark ring*

*T2, T2-FLAIR, T2-GRE, T2-SWI

Patterns of Contrast Enhancement

Abscess
GBM, Metastasis
Demyelinating pseudotumor
Meningioma, PCNSL
JPA, PXA, Ganglioglioma
Cavernoma, Abscess

*T2, T2-FLAIR, T2-GRE, T2-SWI
Patterns of Contrast Enhancement

Magnetic Resonance Imaging

3 Planes of Section

- Axial
- Coronal
- Sagittal
Magnetic Resonance Imaging

4 “Work horse” Sequences

• T1 without contrast
• T1 with contrast (post-contrast)
• T2
• T2-FLAIR (fluid attenuation inversion recovery)

Magnetic Resonance Imaging

2 Simple Principles

• On T2-weighted images, water (H₂O) is hyperintense (bright, white)
Magnetic Resonance Imaging

2 Simple Principles

\[ T2 = H_2O \]

- On T2-weighted images, water (H\textsubscript{2}O) is hyperintense (bright, white)

- White matter is rich in myelin; myelin is a lipid; thus, normal white matter contains less water than gray matter; thus white matter is darker (hypointense) than gray matter on T2-weighted images

$T2$-weighted image (H\textsubscript{2}O)

- Cerebrospinal fluid (CSF) is very bright (white, hyperintense)

- Gray matter, because it has more water, is brighter (more hyperintense) than white matter
If the CSF is Bright (White, Hyperintense), it’s a T2 Sequence

If the CSF isBright (White, Hyperintense), it’s a T2 Sequence

$T1$-weighted image

• Cerebrospinal fluid (CSF) is dark (black, hypointense)

• Gray matter is darker (more hypointense) than white matter

Compare Cortex with White Matter (in an area of normal brain away from the lesion)

If Cortex is **Brighter** than White Matter: T2

If Cortex is **Darker** than White Matter: T1
Whether or not a lesion exhibits enhancement is assessed on T1-weighted sequences (the contrast agent is gadolinium)

![T1-pre](image1.jpg)  

Whether or not a lesion exhibits enhancement is assessed on T1-weighted sequences

![T1-pre](image2.jpg)  ![T1-post](image3.jpg)
Whether or not a lesion exhibits enhancement is assessed on T1-weighted sequences.

DO NOT CONFUSE T2 Brightness (Water: CSF, Edema) with Contrast Enhancement!

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DO NOT CONFUSE T2 Brightness (Water: CSF, Edema) with Contrast Enhancement!
T1 without (pre) or with (post) contrast? Look for bright blood vessels, choroid plexus
**T2-FLAIR sequence**

- Normal H$_2$O (CSF) signal is suppressed; thus the ventricles and subarachnoid spaces are dark (black, hypointense)

![T2-FLAIR Image](image)

- **But...** gray matter is still brighter (more hyperintense) than white matter (so it is a T2-based sequence, not a T1)

![T2-FLAIR Image](image)

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The Ventricles are Black:

Is the sequence a T1 or T2-FLAIR?
The Ventricles are Black:
Is the sequence a T1 or T2-FLAIR?

Compare Cortex with White Matter to Determine if the Scan is a T1 or T2 weighted sequence!
The Ventricles are Black: Is the sequence a T1 or T2-FLAIR?

![T2-FLAIR](image1) ![T1-pre](image2)

The Ventricles are Black: Is the sequence a T1 or T2-FLAIR?

![T2](image3) ![T2-FLAIR](image4) ![T1-pre](image5)

You see Abnormal Bright Signal!
You see Abnormal Bright Signal!
Is it contrast enhancement on a T1 post, or is it edema on a T2 or T2-FLAIR ???

The cortical gray matter is hyperintense to white matter, thus it’s a T2 sequence
You see Abnormal Bright Signal!
Is it contrast enhancement on a T1 post, or is it edema on a T2 or T2-FLAIR ???

The cortical gray matter is hyperintense to white matter, thus it’s a T2 sequence

The ventricles are dark, thus it’s a T2-FLAIR

It’s a T2-FLAIR, thus the bright signal is edema, not contrast enhancement!

You see Abnormal Bright Signal!
Is it contrast enhancement on a T1 post, or is it edema on a T2 or T2-FLAIR ???

The cortical gray matter is hyperintense to white matter, thus it’s a T2 sequence

The ventricles are dark, thus it’s a T2-FLAIR

Sensitivity of T2 & T2-FLAIR compared to T1-postcontrast
Sensitivity of T2 & T2-FLAIR compared to T1-postcontrast

Do you see an obvious lesion?

Sensitivity of T2 & T2-FLAIR compared to T1-postcontrast

ADVANTAGE OF T2-FLAIR over T2
ADVANTAGE OF T2-FLAIR over T2

Do you see an obvious lesion?

ADVANTAGE OF T2-FLAIR over T2

For a Quick Look: T2-FLAIR and T1-Post Contrast
For a Quick Look: T2-FLAIR and T1-Post Contrast

**DWI: Diffusion-Weighted Imaging**

"Restricted Diffusion"

Bright on DWI - Dark on ADC map - Bright on T2-trace

- Acute Infarct (within 6 hrs. of stroke – 7d)
- Abscess
- Epidermoid cyst
- Hypercellular tumors (PCNSL, PNET, etc)

**DWI: Diffusion-Weighted Imaging**

Restricted diffusion: Abscess
DWI: Diffusion-Weighted Imaging

Restricted diffusion: Abscess

T2-GRE (T2\(^\ast\)): Gradient Echo

Useful for detecting:

- Blood products
- Iron
- Calcium

all appear hypointense (dark, black)

Cavernous Angioma
SWI: Susceptibility-Weighted

Useful for detecting:

• Blood products

• Iron  
  all appear hypointense  
  (dark, black)

• Calcium

• Small Veins

Proton MR Spectroscopy

MR Spectroscopy

MRS
Measurable Proton Metabolites

- Choline 3.2 ppm
- Creatine 3.0 ppm
- NAA 2.0 ppm
- Lipids/Lactate 0.9-1.4

Proton MR Spectroscopy

"Up is good (normal), down is bad (tumor)"

“up” = “Hunter’s angle”, a 45-degree upslope
What About All of Those Other Advanced Imaging Techniques?

Advanced imaging techniques continue to evolve rapidly; many are used for pre-surgical planning and intra-operative neuronavigation; others for screening diagnosis in specific clinical situations.

21st Century Neuroimaging Modalities

- Time of Flight MR Arteriography & Venography (TOF MRA)
- MR Perfusion for Vascular Permeability
- Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)
- Functional MR
- Three Dimensional Computed Tomography Reconstruction
- Diffusion Tensor Imaging: Fiber Tractography Vector Mapping
TOF MR Angiography
(no contrast agent)

3D CT: Vascular Anatomy
RECOMMENDATIONS
Currently, no official standardized societal recommendations exist for IA screening in patients with ADPKD, but various recommendations can be found in the literature. They include (only) screening patients with both ADPKD and a family history of IA or SAH, prior aneurysm rupture, high-risk occupations, undergoing major elective surgery, or having a “warning headache” or severe anxiety regarding the issue.144,145 Weber et al144 provided recommendations for following unruptured IAs in any high-risk population (including ADPKD): annual MRA/CTA for 2–5 years, then every 2–3 years thereafter if the aneurysms are stable. Butler et al145 suggested screening every 2–3 years in patients with ADPKD with a family history of IA and every 5–20 years in those without. Torres et al144 advised rescanning every 5–10 years in patients with initial negative screening examination findings. In patients with ADPKD with known aneurysms considered suitable for surveillance, they suggested bimennial or annual imaging to confirm stability and then transitioning to less frequent intervals. Xiu et al146 strongly recommended screening patients with ADPKD with a family history of IA or SAH, though they did not provide detailed guidelines or specifically comment on patients without this history.

If one incorporates the most recent data regarding the incidence, screening, treatment risk, and cost-benefit analyses, screening patients with ADPKD via CTA or MRA will improve outcomes for patients with ADPKD by non-contrast 3T TOF MRA at the time of initial diagnosis with follow-up scans at intervals of at least 1 year, depending on patient-specific risk factors, including the presence of symptoms, hypertension, smoking, alcohol abuse, high-risk professions (such as pilots), or those undergoing major elective surgery. We would consider coil embolization of most posterior circulation aneurysms and anterior circulation aneurysms of >7 mm, though treatment of smaller IAs may be contemplated on the basis of additional patient and aneurysm risk factors (including irregular morphology). Patients with aneurysms unsuitable for coil embolization with adjunctive balloon or stent-assisted techniques may be offered surgical clipping or multidisciplinary convergence. Newly diagnosed IAs would undergo bimennial TOF MRA imaging for the first 2 years and every 2–3 years thereafter if stable. Appropriate medical management to reduce modifiable risk factors for aneurysm growth/rupture: smoking/allochotic cessation, antihypertensive therapy, and, when possible, avoidance of blood thinners is also recommended.

21st Century Neuroimaging Modalities
Time of Flight MR Arteriography & Venography (TOF MRA)
MR Perfusion for Vascular Permeability
Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)
Functional MR
Three Dimensional Computed Tomography Reconstruction
Diffusion Tensor Imaging: Fiber Tractography Vector Mapping
Diffusion Tensor Imaging
Colorized Fiber Tractography

Diffusion Tensor Imaging
Presurgical Planning
POP QUIZ!

Circumscribed Intraventricular Mass Lesion
Choroid plexus papilloma
• Atypical choroid plexus papilloma
• Choroid plexus carcinoma
• Choroid plexus meningioma
• Choroid plexus xanthogranuloma
• Ependymoma
• Subependymoma
• Subependymal giant cell astrocytoma
  • **Central neurocytoma**
  • Solitary metastasis to the choroid plexus (especially renal cell carcinoma)

Circumscribed Intraventricular Mass Lesion

Circumscribed Cyst with Enhancing Nodule in the Cerebellum
• Pilocytic astrocytoma
• Hemangioblastoma
• Cystic metastasis
Circumscribed Cyst with Enhancing Nodule in the Cerebellum in a 56yo Man

- Hemangioblastoma
- Cystic metastasis
Circumscribed Intraventricular Mass Lesion in the Atrium (glomus choroideum)

Central neurocytoma LESS LIKELY

MENINGIOMA MORE LIKELY

METASTASIS MORE LIKELY
Sellar / Suprasellar Mass

- Pituitary adenoma
Sellar / Suprasellar Mass

- Pituitary adenoma
- Pituitary adenoma
- Pituitary adenoma
- Pituitary adenoma
- Pituitary adenoma
- Pituitary adenoma
- Pituitary adenoma

Sellar / Suprasellar Mass

- Pituitary adenoma
- Granular cell tumor
- Pituicytoma
- Etc.
T2-FLAIR sequence

DIFFUSE T2-Hyperintense Lesion

DIFFUSE T2-Hyperintense Lesion
  • Diffuse glioma
**DIFFUSE T2-Hyperintense Lesion**

- Diffuse glioma
- Lymphoma
Smooth ring Enhancing (Rim Enhancing) Mass

• Abscess

• Check DWI sequence for restricted diffusion
Ring Enhancing (Rim Enhancing) Mass

Smooth ring

- Abscess
- Glioblastoma
- Metastasis

Pineal Region Mass
- Germinoma
- Pineal Region Mass

- Meningioma
- CPP
- Ependymoma
- PTPR
- Metastasis
Diffuse Enlargement of the Pons

• DIPG (diffuse intrinsic pontine glioma)
Multiple Lesions

Metastasis
Multiple Lesions

- Metastasis
- Multiple abscesses

- Tumor Predisposition Syndrome (multiple primary tumors; eg, NF2)

- Multiple vascular malformations
Multiple Lesions
- Multiple vascular malformations
- Multiple parasites (e.g., cysticercosis)

Ring Enhancing Mass

Ragged ring
Ring Enhancing Mass

**Ragged** ring
- Glioblastoma
- Metastasis

(less likely, but check DWI)
Uniformly Enhancing Periventricular Masses

PCNSL
(primary CNS large B-cell lymphoma)
Dura-Based Mass

- Meningioma
- • SFT/HPC Family Tumor
- • Plasmacytoma
- • Granulocytic Sarcoma (Chloroma)
- • Dural Marginal Zone (MALT-like) B-cell lymphoma
- • Solitary metastasis
- • Calcifying pseudotumor (fibro-osseous lesion)
- • Inflammatory pseudotumor
- • Idiopathic hypertrophic pachymeningitis
- • Sarcoidosis
- • Rosai-Dorfman Disease
- • Castleman Disease

PRE-IOC Preparation

- AGE of the patient
- ANATOMIC LOCATION of the lesion
- IMAGING characteristics of the lesion
- PAST MEDICAL HISTORY of the patient
PRE-IOC Preparation

• AGE of the patient
• ANATOMIC LOCATION of the lesion
• IMAGING characteristics of the lesion
• PAST MEDICAL HISTORY of the patient
• TYPE and DURATION of presenting signs & symptoms

• WHAT TYPE of SURGICAL PROCEDURE?

• WHAT WILL THE SURGEON NEED TO KNOW?
IOC PRINCIPLES

• Cytology and Architecture are Complementary – Use Both!

• Diff-Quik and H&E stains for cytology are Complementary – You Can Use Both!
IOC PRINCIPLES

• Know what the surgeon needs to know about the lesion intraoperatively!

• The surgeon needs to know information that is needed to successfully complete the operation and will determine the subsequent course of the operation

Indications for IOC
IOC PRINCIPLES
Some Indications for IOC

• Is adequate, representative tissue present?

• Is the disease an infectious process?

• If tumor, is it of a type amenable to gross total surgical resection
IOC PRINCIPLES

Some Valid Indications for IOC

• Is adequate, representative tissue present?
• Is the disease an infectious process?
• If tumor, is it of a type amenable to gross total surgical resection
• Is viable GBM present? (if so, Gliadel wafer, Gliacyte balloon, other intraoperative treatment can proceed)

IOC PRINCIPLES

• Cytology and Architecture are Complementary – Use Both!
• Don’t freeze all of the tissue if possible
• Know what the surgeon needs to know about the lesion intraoperatively!
• Plan for tomorrow!

IOC PRINCIPLES

• Plan for tomorrow!
IOC PRINCIPLES

- Plan for tomorrow!

For very small biopsies (e.g., stereotactic bx), ensure adequate specimen for IHC:
  - unstained touch preps
  - unstained sections cut from FS block
IOC PRINCIPLES

• Plan for tomorrow!

For very small biopsies (e.g., stereotactic bx), ensure adequate specimen for IHC:

  - unstained touch preps
  - unstained sections cut from FS block
  - order unstained from paraffin block ("biopsy processing")

IOC PRINCIPLES

• Know what the surgeon **DOES NOT** need to know about the lesion intraoperatively!

  Important example: the *specific type* of diffuse glioma (astro, oligo, mixed oligoastro)
IOC PRINCIPLES

• The specific type of diffuse glioma **WILL** need to be determined with the help of diagnostic molecular studies for the **final diagnosis**, but this level of specificity is generally not required to complete the surgical procedure.

IOC PRINCIPLES

• Common cause of intraoperative diagnosis / final diagnosis discrepancy: misdiagnosing oligodendroglioma as astrocytoma on frozen sections.

IOC PRINCIPLES

• Freezing distorts oligo nuclei and makes them appear more pleomorphic and thus astrocytoma-like

• The characteristic cytoplasmic clearing (perinuclear “halos”, “fried egg” appearance) is only seen in FFPE tissue, not in frozen sections
IOC PRINCIPLES

• One Caveat

The pathologist must ensure that representative tumor has been obtained with respect to grade (correlate with the preoperative imaging studies; enhancing diffuse gliomas are usually high-grade; “undersampling” and hence “undergrading” of diffuse gliomas is very common in stereotactic biopsies)

INTRA-IOC

Perform a Cytologic Prep!
Cytologic Preparations

- Touch (Imprint)
- Smear (Squash, Crush)
- Scrape
- Drag

<table>
<thead>
<tr>
<th>Technique</th>
<th>Tissue Consistency</th>
<th>Representative Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Touch</td>
<td>Soft and discohesive</td>
<td>Pituitary adenoma</td>
</tr>
<tr>
<td>Smear</td>
<td>Soft</td>
<td>Gliomas, Most Brain Tumors</td>
</tr>
<tr>
<td>Scrape</td>
<td>Dense fibrous tissue</td>
<td>Dural and Paraspinal Metastases</td>
</tr>
<tr>
<td>Drag</td>
<td>Necrotic</td>
<td>Necrotic metastasis, Stereotactic radiosurgery site resection</td>
</tr>
</tbody>
</table>

INTRA-IOC

Specific Problematic Issues
INTRA-IOC ISSUES

• Specimen is non-representative

How do you know?

Hypothesis 1:
The surgeon will tell me….
NOT!

INTRA-IOC ISSUES

• Specimen is non-representative

How do you know?

Imaging Studies!
INTRA-IOC ISSUES

• Specimen is very small
  (endoscopic bx or fragment of stereotactic bx)

• Specimen is very small
  (endoscopic bx or fragmented stereotactic bx)

Perform a cytologic preparation
(imprint or drag prep) before freezing

• Specimen is seriously small!
INTRA-IOC ISSUES

• Specimen is *seriously* small!

So minute and/or of a consistency such that there is concern that it will not surviving processing, potentially resulting in a Final Dx of “Tissue lost in processing”…YIKES!

INTRA-IOC ISSUES

• Specimen is *seriously* small!

*Options:*
  • Submit to Cytology Lab for cytospin

INTRA-IOC ISSUES

• Specimen is *seriously* small!

*Options:*
  • Submit to Cytology Lab for cytospin
  • Smear entire specimen
INTRA-IOC ISSUES

• Specimen is extensively cauterized

Bisect specimen and perform cytologic drag prep using freshly cut surface before freezing

INTRA-IOC ISSUES

• Specimen is extensively necrotic
INTRA-IOC ISSUES

• Specimen is extensively necrotic

Perform cytologic drag preps on multiple tissue fragments on the same slide to maximize sampling and detection of any viable cells

INTRA-IOC ISSUES

• Specimen is extensively bony

Perform a cytologic drag prep
INTRA-IOC ISSUES

• Specimen is densely fibrous

Perform a cytologic scrape prep before freezing

POST-IOC ISSUE
POST-IOC ISSUE

A Final

BUT VERY IMPORTANT

Topic

Practical Clinical

Molecular Subclassification

of the Diffuse Gliomas

Diffuse Glioma Classification
Diffuse Glioma Classification

• Classical Morphologic Feature-Based
  H&E stain (used for past 65 years)

• Molecular Profiling (Personalized Med)
  Genomic / Transcriptomic / Proteomic / Methylomic / Metabolomic / Etc. (Coming)

• Combined Morphologic-Molecular
  H&E + IDH1-R132H immuno + 1p/19q in situ hybridization (2013)
Molecular Classification of the Diffuse Gliomas

**Just 2 Markers**

• 1p / 19q Deletion Status

• Isocitrate Dehydrogenase (IDH) Mutation Status

Why is this VERY GOOD NEWS for the General Surgical Pathologist?

What is a “mixed oligoastrocytoma”? 
Mixed Oligoastrocytoma

- Astrocytoma
- Oligodendroglioma

- Astrocytoma
- Oligodendroglioma
Mixed Oligoastrocytoma

“This is the single most controversial and subjective area of contemporary brain tumor classification and a common, extremely vexing problem for the surgical pathologist”

* G Fuller Austin
January 25, 2013

The “answer” to this problem is being provided by 2 simple molecular marker studies:

• 1p/19q deletion status (FISH)
• IDH1 mutation status (IHC)

Both tests are run on routine FFPE surgical tissue sections using commercially available reagents
Molecular Classification of the Diffuse Gliomas

**Just 2 Markers**

1p/19q Codeletion *and* IDH Mutation are both **FAVORABLE GENETIC SIGNATURES** in Diffuse Gliomas.

Molecular Classification of the Diffuse Gliomas

**Just 2 Markers**

1p/19q Codeletion is highly correlated with classical oligodendroglial morphology (85%) and is considered to be the “molecular definition of oligodendroglioma”.

Molecular Classification of the Diffuse Gliomas

**Just 2 Markers**

IDH Mutation Status can be used to substratify Non-1p/19q Codeleted Diffuse Gliomas (Astrocytomas) into Favorable (mutation Present) and Unfavorable (mutation Absent) prognostic groups.
1. If the H&E shows classic oligodendroglioma features, there is an 85% probability of combined 1p/19q deletion (and 100% of 1p/19q co-deleted gliomas exhibit IDH mutation) and the diagnosis is Oligodendroglioma.

2. If the morphologic features are NOT classical oligo, the trend is to classify the tumor as an Astrocytoma.

3. FISH testing for combined deletion of 1p and 19q has become standard of care, and co-deletion constitutes the “molecular definition” of oligodendroglioma.
1. If the H&E shows classic oligodendroglioma features, there is an 85% probability of combined 1p/19q deletion (and 100% of 1p/19q co-deleted gliomas also exhibit IDH mutation) and the diagnosis is Oligodendroglioma.

2. If the morphologic features are NOT classical oligo, the trend is to classify the tumor as an Astrocytoma.

3. FISH testing for combined deletion of 1p and 19q has become standard of care, and co-deletion constitutes the "molecular definition" of oligodendroglioma.

4. IHC for IDH1 mutation (and sometimes sequencing for less common IDH1 and IDH2 mutations) permits substratification of non-codeleted diffuse gliomas into favorable and unfavorable groups.

Molecular Classification of Diffuse Gliomas

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Principles of Molecular Diagnostics and Personalized Cancer Medicine

Dongfeng Tan and Henry Lynch, eds.

Philadelphia: Wolters Kluwer Health / Lippincott Williams & Wilkins, 2012 (December)

Chapter 40

Molecular Diagnosis of Diffuse Glioma

Adriana Olar, Greg Fuller
...has already reached textbook status...
Diffuse Glioma (H&E Diagnosis)

- Diffuse Glioma Grade II-III
- Classical Glioblastoma (poor prognosis)

IDH Mutation Present

- IDH Wild-Type (poor prognosis)

1p/19q Codeleted (best prognosis)

No 1p/19q Codeletion (intermediate prognosis)

Olar, Fuller. In: Principles of Molecular Diagnostics and Personalized Cancer Medicine, 2012
Diffuse Glioma Diagnosis Using *Combined Morphologic-Molecular Criteria*

MDACC Path Report Format
Diffuse Glioma Diagnosis Using *Combined Morphologic-Molecular Criteria*  
MDACC Path Report Format

**DIFFUSE GLIOMA**  
WHO Grade II  
Mitotic index (PHH3): 1/1000  
Ki-67 index: 2%  
IDH1-R132H Mutation: NEGATIVE  
1p/19q: INTACT

(low-grade diffuse astrocytoma)

**ANAPLASTIC DIFFUSE GLIOMA**  
WHO Grade III  
Mitotic index (PHH3): 13/1000  
Ki-67 index: 55%  
IDH1-R132H Mutation: POSITIVE  
1p/19q: CO-DELETED

(anaplastic oligodendroglioma)

**ANAPLASTIC DIFFUSE GLIOMA (ANAPLASTIC OLIGODENDROGLIOMA)**  
WHO Grade III  
Mitotic index (PHH3): 13/1000  
Ki-67 index: 55%  
IDH1-R132H Mutation: POSITIVE  
1p/19q: CO-DELETED
### Neuropathology References 2013

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### Histology for Pathologists

*4th Edition 2011*

Fuller & Burger
Chapter 11
Central Nervous System
Histology for Pathologists

World Health Organization
Classification of Tumours of the Central Nervous System


World Health Organization CNS Tumor Classification Consensus Committee

Spring 2014 Amsterdam

Short Course #46

"Neuropathology After Dark: Surviving Intraoperative Frozen Section Consultation"

Chris Fuller & Greg Fuller