CT Imaging of Ischemic Stroke

Michael Meuse, M.D.
Outline

- Introduction/anatomy/physiology
- Goals of Imaging in the Acute Setting
- Modalities Employed
- Emphasis on Cerebral Perfusion CT
- Cases
Stroke Epidemiology

- 3rd leading cause of death
- #1 cause of disability
- 750,000 new stroke/year
- 8% die within 30 days, 29% die within 1 year
- Survivors
  - 16% require institutional care
  - 31% require assistance caring for self
  - 20% require assistance walking
- $43 billion per year in direct and indirect costs
Vascular Anatomy

- Aortic Arch
  - Innominate
  - L carotid
  - L subclavian
- Subclavians
  - Vertebral
- CCA
  - ICA
  - ECA
Vascular Anatomy
(ant circulation)

- ICA
  - Cervical
  - Petrous
  - Cavernous
  - Intracranial
    - Ophthalmic a.
    - PCOMM
    - Ant choroidal
    - ACA
    - MCA
Vascular Anatomy
(post circulation)

- Vertebral
  - PICA
- Basilar
  - AICA
  - Sup Cerebellar
  - PCA
    - PCOMM
Vascular Anatomy

- Circle of Willis
  - Supraclinoid ICA
  - A1-ACA
  - ACOMM
  - PCOMM
    - thalamoperf
  - P1-PCA
    - thalamoperf
ACA

- Smaller of 2 term branches ICA
- Courses
  - medially and anteriorly
- A1
  - Before ACOMM
  - Med lenticulostriates
- A2
  - After ACOMM
MCA

- Larger of 2 term branches ICA

- Courses
  - Lat and horiz along Sylvian F.

- M1
  - Before trifurcation
  - Lat lenticulostriates

- M2
  - After trifurcation
PCA

- Arise from terminal basilar a.
- Courses
  - Initially within interpedunc cistern
- P1
  - Before PCOMM
- P2 / P3
  - After PCOMM
Vascular Territories & Deficits
ACANH

- Medial frontal and parietal lobes

<table>
<thead>
<tr>
<th>Branch</th>
<th>Side</th>
<th>Deficit</th>
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<tbody>
<tr>
<td>Hemispheric</td>
<td>Either</td>
<td>Leg weakness</td>
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<tr>
<td></td>
<td>Both</td>
<td>Incont, akin mutism</td>
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<tr>
<td>Med Lenticulosatriates</td>
<td>Either</td>
<td>Facial weakness</td>
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<tr>
<td></td>
<td>Left</td>
<td>Dysarthria (±/- motor aphagia)</td>
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**MCA**

- Lateral areas of frontal, temporal, and parietal

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<th>Side</th>
<th>Deficit</th>
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</thead>
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<tr>
<td>Hemispheric</td>
<td>Either Left Right</td>
<td>Weakness face/arm &gt; leg Motor (a) / Receptive (p) / Global (a&amp;p) Aphasia Visual spatial deficits</td>
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<td>Lat Lenticulostriates</td>
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<td>Variable lacunar syndrome</td>
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## PCA

- **Medial occipital lobes**

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<td>Thalamoperferators</td>
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<td>Somnolence</td>
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<td>Sensory disturbance</td>
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Cerebellum

<table>
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<th>Branch</th>
<th>Side</th>
<th>Deficit</th>
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<tbody>
<tr>
<td>PICA, AICA, SCA</td>
<td>Either</td>
<td>Ataxia, vertigo, vomiting</td>
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</tbody>
</table>
Watershed

- Between major vascular territories

<table>
<thead>
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<th>Branch</th>
<th>Side</th>
<th>Deficit</th>
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</thead>
<tbody>
<tr>
<td>ACA / MCA / PCA</td>
<td>Either</td>
<td>“Man-in-a-barrel syndrome”</td>
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<tr>
<td></td>
<td>Bilateral</td>
<td>Sev Memory deficits</td>
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Deficits

- Based on the anatomic variability/extent of thrombus, and presence/absence of collateral flow the clinic exam can be extremely humbling
Venous Anatomy

- SSS
- ISS
- Straight
- Great v. Galen
- Occipital
- L/R Transverse
- Sigmoid
- Inferior petrosal
Normal Physiology

- Cerebral blood flow (CBF)
  - Ave 50-55 ml/100 g/minute
  - gray matter 3-4X > white matter
- Cerebral perfusion pressure (CPP)
  - 60-180 mm Hg
Autoregulation

- Maintains narrow range blood flow
  - Increased MAP -> vasoconstriction
  - Decreased MAP -> vasodilation
  - Failure of autoreg in ischemia
Pathophysiology

- **Injury**
  - Degree ischemia
  - Duration ischemia

- **CBF Threshold (10-20 mL/100g/min)**
  - < 22: reversible injury starts
  - < 18: cortical neurons lose spontaneous action potentials
  - < 12 (>2hrs): infarct (primates)

- **Cell sensitivity**
  - Neurons > oligodendrocytes > astrocytes
Penumbra

- CBF not as low as in center of infarct
- Possible reversible ischemia region
- Reversible neurologic deficits after intervention
- MR: discordance between area of T2 hyperintensity and area of slow flow
Stroke Acute Phase

- Structural changes as soon as 20 mins
- Microscopic
  - < 6 Hrs: Swollen disorganized mitochondria
  - > 6 Hrs: neuronal shrinkage, cytoplasmic eosinophilia, ribosomal aggregation, synaptic “encrustation”
- Macroscopic
  - < 2 Hrs: No changes
  - 2-6 Hrs: Cytotoxic edema— failure of Na/K pump
  - 3-8 Hrs: Vasogenic edema
Cytotoxic Edema

- Time: <6 hours
- Fluid: Transudate
- CT: Isodense
- MR: Swelling (T1WI)

Vasogenic Edema

- Time: >3–8 hours
- Fluid: Exudate
- CT: Hypodense
- MR: Hyperintense (T2WI)
Management Pre- MID-1990’s

- Supportive care in the acute setting
- Diagnostic w/u
  - Define cause of symptoms for which Rx might be instituted
  - Goal: To prevent future events
Rule out other pathologic processes that can present with stroke-like symptoms

- Neoplasm
- Acute extra-axial fluid collections
  - Epidural & subdural hematomas
- Infections
- Cause of seizure
  - Masses, vascular malformations
Management Pre- MID-1990’s

- Rule out hemorrhage associated with an area of cerebral infarction
  - That would contraindicate anticoagulation Rx

- Cerebral angiography performed later…
  - Anything amenable to surgical (endarterectomy) or medical (antiplatelet or anticoagulation) Rx
National Institute of Neurological Disorders and Stroke

- 1995 study of IV t-PA
- Thrombolysis as treatment of ischemic lesions of the MCA territory
- Reduction in the # of patients with poor functional outcomes when treated within 3-6 hours
- But, higher risk of hemorrhage and death within 10 days post-treatment
Primary Purpose of Imaging

- To ensure selection of the appropriate patients for thrombolytic therapy and/or stroke intervention
  - To reduce severe complications
  - t-PA associated with 10-fold increased risk of intracranial hemorrhage
Risks of Thrombolysis

- Risk increased as the time interval from acute event to treatment increased.
- Summary: a better outcome is more likely if treated within 3 hours rather than 3-6 hours.
FDA Approval in 1996

- IV t-PA
- Administer within 3 hours of symptom onset
- End point: little or no disability 3 months after the event
More recent data allows for IV t-PA administration up to 4.5 hours in patients who meet certain criteria:

- <80 y/o
- No h/o diabetes
- Not on coumadin
t-PA Exclusion Criteria

Exclusion Criteria:

- Uncontrolled hypertension at the start of treatment with tPA (SBP > 185 mm Hg and/or DBP > 110 mm Hg.)
- Evidence of intracranial hemorrhage on pretreatment evaluation.
- Suspicion of subarachnoid hemorrhage.
- Recent intracranial surgery, serious head trauma within past 3 months.
- Lumbar puncture within 7 days.
- Major surgeries and/or trauma < 15 days.
- Active internal bleeding within 21 days.
- Intracranial neoplasm, AVM or aneurysm.
- Known bleeding diathesis, including INR > 1.7, heparin within the last 12 hours and a PTT > 1.5 times normal, platelet count < 100,000.
- Patient or family declines and understands risks and benefits of treatment.
- Glucose < 50 or > 400 mg/dL at time of bolus. (Hyperglycemia-Relative Contraindication)
- Arterial puncture in non-compressible site. (Relative Contraindication)
- Minor or rapidly improving stroke within previous 7 days. (Relative Contraindication)
- Acute pericarditis
- Recent MI within 3 months. (Relative Contraindication)
- Previous stroke within the past 3 months. (Relative Contraindication)
- History of intracranial hemorrhage. (Relative Contraindication)
- Seizure at onset of stroke. (Relative Contraindication)
- Life expectancy < 1 year or severe co-morbid illness. (Relative Contraindication)
- Pregnancy (Relative Contraindication)
- Diabetic hemorrhagic retinopathy or other ophthalmic bleeding (Relative Contraindication)
t-PA: 3 Hour Window
Benefit Vs Harm

- For every 8 patients treated, 1 benefits.
- For every 16 treated, 1 is harmed by ICH.
- For every 34 treated, 1 dies of ICH.

Thus for every 4 patients who benefits 1 dies.

So is t-PA “highly efficacious”? 
Uses in ACA Thrombi

- Shown to be efficacious up to 6 hours after symptom onset
- As of 12/2004, FDA has not approved its use for this purpose
Primary Purpose of Imaging

- Acute intracranial hemorrhage and nonvascular causes of stroke symptoms need to be ruled out within 3/4.5 hours of symptom onset
  - So that use of IV t-PA can be considered
Primary Purpose of Imaging

- Can potentially identify subgroups of patients who might benefit most from aggressive therapy beyond the accepted “therapeutic window” of 3/4.5 hours

...Stroke intervention
Stroke Intervention

- Currently considered appropriate up to 8 hours for anterior circulation
- Up to 24 hours in the posterior circulation
90d Mortality, Stratified by Age and Revascularization

% of 90d Mortality (mRS=6) vs. Age

- Age <60 (n=278)
- Age 60-69 (n=199)
- Age 70-79 (n=222)
- Age >79 (n=170)

Revascularization:
- TICI=3 (n=243)
- TICI=2b (n=245)
- TICI=2a (n=208)
- TICI=0-1 (n=173)
Goals of Imaging

- Exclude intracranial hemorrhage
Goals of Imaging

- Other lesions that can mimic ischemic stroke:
  - Tumor, infection, vascular malformations
Goals of Imaging

- Differentiate between irreversibly affected brain tissue ("dead brain") and reversibly impaired tissue ("tissue at risk")
  - Which might benefit from early treatment
Goals of Imaging

- Differentiate between irreversibly affected brain tissue (“dead brain”) and reversibly impaired tissue (“tissue at risk”)
  - Which might benefit from early treatment
“Tissue at risk”

- **Penumbra**
- Area of markedly reduced perfusion with loss of function of still viable neurons
- Timely reperfusion of this tissue may prevent cell death and help reestablish normal function
Goals of Imaging

- Identify stenosis or occlusion of major extra- and intracranial arteries
Identify Stenosis or Occlusion
Identify Stenosis or Occlusion
Modalities Employed

- Nonenhanced CT
- CT-Angiography
- Cerebral Perfusion CT
- MRI
Nonenhanced CT

- Predominant imaging modality for initial evaluation of suspected stroke
Nonenhanced CT

- Most CT scans are negative with respect to early signs of an acute ischemic process in the first 6 hours after symptom onset
  - Which is the current “therapeutic window” during which pharmacologic intervention can affect patient outcome
Subtle parenchymal findings

- Reflects underlying cytotoxic edema
  - An early pathophysiologic finding in ischemia
- Parenchymal hypoattenuation
- Sulcal effacement
Obscuration of the lentiform nucleus

- Increasing hypoattenuation due to cytotoxic edema
  - Loss of normal attenuation difference of the GP and/or putamen with respect to contiguous white matter structures
- Within 2 hours of onset
Obscuration of the lentiform nucleus
Obscuration of the lentiform nucleus
Obscuration of the lentiform nucleus

- Prone to early irreversible damage
- Lenticulostriate branches of the MCA are end-vessels
Insular Ribbon Sign

- Hypoattenuation of the insular cortex
  - “blurring” of the gray matter-white matter jx due to decreased attenuation of the gray matter

- Loss of usual slightly increased attenuation of the insular cortex just superficial to the external/extreme capsules
Insula
Insular Ribbon Sign
Insular Ribbon Sign

- Watershed position far from collateral supply of both ACA and PCA
- Therefore, early irreversible damage
Insular Ribbon Sign
Hyperattenuating media sign

- “Hyperdense MCA”
- MCA occluded by fresh thrombus
- Hyperattenuating relative to normal contralateral MCA
Hyperattenuating media sign

- Secondary to local slow intravascular blood flow due to intra-arterial thrombus
- May represent direct visualization of the thrombus itself
Hyperattenuating media sign

- Indicates occlusion, not infarction
- Within 90 minutes
- Usually seen in M1 segment of MCA
- Specificity nearly 100%
- Sensitivity about 30%
European Cooperative Acute Stroke Study

- Studied patients with stroke symptoms <6 hours
- CT findings: demonstrable ischemic changes involving < 1/3 of MCA territory
European Cooperative Acute Stroke Study

- Abnormal CT:
  Have relatively worse outcome than those with symptoms but negative CT

- BUT may still benefit if parenchymal changes involve < 1/3 of a vascular territory
Limitations of Nonenhanced CT

- Extent of irreversibly damaged brain tissue
  - Avoid hemorrhage during thrombolysis of ischemic lesions
- Identify tissue at risk
- Goal: Avoid unnecessary thrombolytic Rx
Limitations of Nonenhanced CT

- Distinguishing between the following:
  - Potentially salvageable tissue that is at risk for infarction
    - The ischemic penumbra
  - Extensive infarct
Nonenhanced CT Report

- Presence or absence of hemorrhage
- Presence and extent of any ischemic parenchymal changes
- Presence or absence of nonvascular etiologies of stroke-like symptoms
CT-Angiography

- Time-optimized bolus of contrast material for the opacification of vessels
- Performed in as little as 20 seconds
- Requires relatively little patient cooperation
CT-Angiography

- Intracranial vessel occlusion/stenosis
- Carotid Artery pathology
- Vasospasm or aneurysm?
CT-Angiography

- Therefore, can potentially identify the source of an ischemic process to aid in the planning of (sometimes emergent) definitive therapy
CTA – Right MCA Aneurysm
MRI
Cerebral Perfusion CT
Cerebral Perfusion CT

- Basic Theory
- Technique
- Clinical Indications
Basic Theory

- Serial CT scans are acquired rapidly to dynamically track a bolus of IV contrast material as it travels through the brain at a single location or several contiguous locations.
Basic Theory

- Hemodynamic maps of brain perfusion are generated as this contrast bolus passes through the brain.
Technique

- Central volume principle
- Relates the following:
  - Cerebral Blood Flow (CBF)
  - Cerebral Blood Volume (CBV)
  - Mean Transit Time (MTT)
Definitions: Time-to-peak (TTP)

- Time that elapses between the start of an IV contrast injection and the maximal attenuation of contrast-enhanced blood as it passes through a defined region of brain.
Definitions: Mean Transit Time

- Time it takes blood to flow from a major cerebral artery feeding a given region of brain to the major cerebral vein draining that region
Definitions: Cerebral Blood Volume

- Volume of blood in a defined portion of the brain at any given time
Definitions: Cerebral Blood Flow

- CBV/minute
- Can be measured or calculated
Technique

- Central Volume Principle
- CBF = CBV/MTT
Technique

- Linear relationship between contrast agent concentration and attenuation
- Contrast agent causes a transient increase in attenuation proportional to the amount of contrast agent in a given region
Technique

- Contrast agent time-concentration curves are generated:
  - in an arterial region of interest (ROI)
  - in a venous ROI
  - and in each pixel
Technique

- Deconvolution of arterial and tissue enhancement curves...
  - Gives the Mean Transit Time
Technique

- Cerebral Blood Volume = area under the curve (in a parenchymal pixel) divided by the area under the curve in an arterial pixel
Technique

- Then, solve the equation for CBF
- Knowing MTT and CBV,
  - \( CBF = \frac{CBV}{MTT} \)
Protocol

- Unenhanced Head CT
- 4 adjacent 5-mm-thick sections are selected
  - Start at the level of the basal ganglia
    - All 3 supratentorial vascular territories are visualized
    - Avoid clips/metal/etc.
Protocol

- 50mL nonionic contrast agent
- Inject at a rate of 4mL/sec
- At 5 seconds after initiation, a cine (continuous) scan is initiated
- For 50 seconds
Protocol

- 1-second images are reformatted at 0.5-second intervals
- 5-mm sections are reformatted into two 10-mm-thick sections
  - Lessen beam-hardening artifacts
  - Better signal-to-noise ratio
  - Improved temporal resolution
Radiation

- Overall effective dose required is only slightly higher than that required for routine head CT
- 2.0-3.4 mSv vs. 1.5-2.5 mSv
Technique

- CT perfusion data are analyzed at an imaging workstation
- Post-image-collection processing
Post-image-collection processing

- Place free-hand drawn ROI’s in an input artery and an input vein
  - Contrast-enhancement curves are then generated
Input artery and vein

- Artery: ACA or MCA
- Vein: large venous structure such as torcular herophili
Regions of Interest (ROI)

- Can be placed in the brain parenchyma to yield quantitative data
- 6 circular ROI’s placed along the periphery of each hemisphere
Clinical Applications

- Acute Stroke
- Cerebrovascular Reserve
- Temporary Balloon Occlusion
- Vasospasm
- Tumors
Normal Perfusion

CBF

CBV

MTT
Stroke

- Assist in selection of patients for thrombolytic Rx
- Identify potentially salvageable tissue at risk for infarction (ischemic penumbra)
- Identify those with extensive infarct
Recall

- Thrombolytics are most beneficial with cytotoxic edema involving 33% or less of the MCA territory.
- Those with conventional CT findings of cytotoxic edema involving >33% MCA territory will not benefit from thrombolytics.
Stroke Hypothesis

- Tissue at risk of infarction
  - Decreased CBF
  - Normal/elevated CBV
    - Secondary to activation of cerebral autoregulatory mechanisms
  - Elevated MTT

- Infarcted tissue
  - Decreased CBF
  - Decreased CBV
  - Elevated MTT
Acute Infarction

- Unresponsive 76yo F
- Subtle hypoattenuation in L insula, temporal lobe, and frontal lobe
Acute Infarction

- Decreased CBF in left ACA and anterior MCA territories
Acute Infarction

- Decreased CBV
Acute Infarction

- Slightly elevated MTT
Acute Infarction
Acute Infarction

- Follow-up
- Large infarct in left ACA and MCA territories
Ischemia without Infarction

- 47yo F, severe R ICA stenosis, episodes of L arm numbness
- Decreased CBF in R ACA and MCA territories
Ischemia without Infarction

- CBV is elevated
- Cerebral autoregulatory mechanisms
- Vasodilation in response to decreased perfusion
Ischemia without Infarction

- MTT is elevated
Reversible Ischemia
Interpretation Guidelines

- Evaluate CBF and MTT maps for abnormalities first.
- If abnormalities are present, use the CBV map to try to elucidate the underlying pathophysiology.
  - Ischemia vs. infarct
    - Keep in mind that CBV may be normal even in cases of infarction.
Pathophysiology

- Reversible paralysis: CBF < 20-23 (mL/100g/min)
- Irreversible infarction: CBF < 10-12
- Over time, infarction threshold increases to 17-18
Pathophysiology

- Upper threshold (reversible ischemia)
  - Failure of normal electric activity
- Lower threshold (infarction)
  - Energy and ion pump failures
- Potentially salvageable penumbra is between these 2 levels
Correlation with Head CT

- Areas of hypoattenuation on unenhanced head CT have a mean CBF of 13mL/110g/min
  - Irreversible infarction < 10-12mL???
Cerebrovascular Reserve

- Patients with known chronic cerebral ischemia
- Distinguish tissue in need of increased CBF
  - Tissue under hemodynamic stress
- From tissue with decreased CBF due to decreased metabolic demand
Cerebrovascular Reserve

- Acetazolamide administration in conjunction with quantitative measurement of CBF
- Normally causes vasodilatation of cerebral arterioles and increase in CBF
Cerebrovascular Reserve

- In patients with hemodynamic stress (tissues in need of increased CBF), are already maximally vasodilated
  - Due to utilization of cerebral autoregulatory mechanisms in response to decreased perfusion pressure
  - Cannot respond further to acetazolamide
Cerebrovascular Reserve

- These patients are considered to be at increased risk of stroke
- May benefit from interventions to increase CBF
Cerebrovascular Reserve: Guidelines

- Increase in CBF of 20-40% over baseline is normal
- Increase of less than 5% is indicative of relative hemodynamic insufficiency
- Decrease of 5% or greater (STEAL phenomenon) indicates tissue at higher risk of stroke
Cerebrovascular Reserve: Protocol

- Routine perfusion CT
- 1,000mg acetazolamide IV
- 20 minute delay
- Repeat perfusion CT
Pre-acetazolamide Perfusion CT

- 52yo M, 3wk h/o amaurosis fugax, L weakness/numbness and L facial droop
- Decreased CBF in R ACA and MCA regions
- Elevation of both CBV and MTT
Post-acetazolamide Perfusion CT

- Steal phenomenon in R ACA and MCA territories
- CBF decreased from baseline values
- Hemodynamic stress and tissue at high risk of infarction
Temporary Balloon Occlusion

- Patients in whom arterial sacrifice or prolonged temporary occlusion is considered part of the surgical or endovascular therapy
Temporary Balloon Occlusion

- Identify patients who clinically pass the temporary balloon occlusion test, but have low CBF or abnormal response to acetazolamide
  - May not tolerate sacrifice or prolonged occlusion
Protocol

- Angiography and balloon occlusion
  - Clinically evaluate the patient for 30 minutes
- If they pass, balloon is kept in place
- Perfusion CT with balloon inflated
- Perfusion CT with balloon deflated
- Re-inflate balloon, 1,000mg acetazolamide IV, and final perfusion CT obtained
Vasospasm

- Frequent early complication s/p aneurysmal SAH
- Angiographic evidence of vasospasm in 60-80% of patients with SAH
- 32% symptomatic
- May lead to infarction and/or death
Vasospasm

- Perfusion CT to monitor cerebral perfusion s/p SAH
- Measurement of CBF can help ID patients at risk for cerebral ischemia
  - Guide therapeutic decisions
  - Monitor response to therapy
Vasospasm

- Patients with delayed infarct after SAH have a lower mean CBF value than patients with early or no infarct
  - Presumably due to vasospasm
- In patients with moderate-severe vasospasm, CBF and CBV are significantly lower than in those with absent/mild vasospasm
Tumors

- Associated with increased angiogenic activity and neovascularization
- Results in increased blood volume and hyperpermeability related to immature vessels
Tumors

- Microvascular permeability increases with increasing biologic aggressiveness of tumors.
- Reduction in permeability (in response to anti-angiogenic Rx) c/w decreased tumor growth.
Tumors

- CBV and PS (measure of microvascular permeability) can be predictive of pathologic grade and to c/w tumor mitotic activity
Tumors
Summary Case #1
Summary Case #1
Summary Case #1
Summary Case #2
Summary Case #2
References