Imaging ischemic strokes: Correlating radiological findings with the pathophysiological evolution of an infarct

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Patient A: history

91 y.o. woman

Acute onset R sided weakness and aphasia

DDx

Stroke (Ischemic ~80% or Hemorrhagic ~20%)

Transient ischemic attack (TIA)

Seizure with post-ictal paralysis

Intracranial tumor (with secondary hemorrhage, seizure, or hydrocephalus)

Migraine

Metabolic encephalopathy

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Acute Stroke Management

Non-contrast head CT

Quickly identifies hemorrhagic strokes (fresh blood is bright on CT)

Ischemic stroke

Can administer tPA within 3 hrs (systemic) or 6 hrs (intra-arterial)

Identify source of ischemic stroke: Embolic, Thrombotic, Low-flow

Prevent secondary damage and expansion of infarct

Hemorrhagic stroke

DO NOT administer tPA

Mildly reduce blood pressure

Administer products to reduce interstitial fluid levels (eg. Mannitol)

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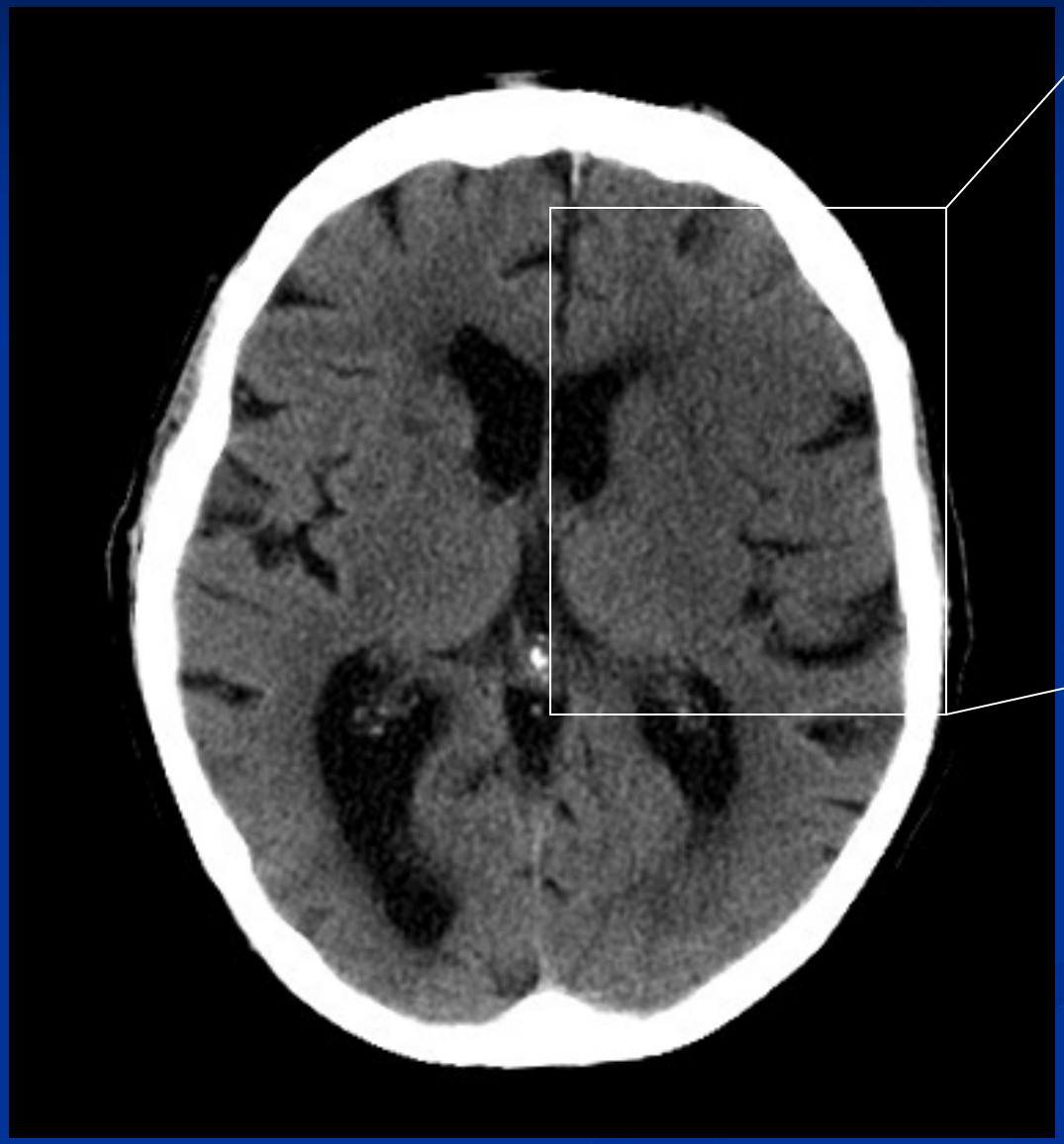
Patient A: Non-contrast CT



Findings

*** No evidence of hemorrhage***

Loss of gray-white matter distinction in L MCA territory

Sulcal effacement

Slight mass effect on L lateral ventricle

No midline shift

PACS, BIDMC

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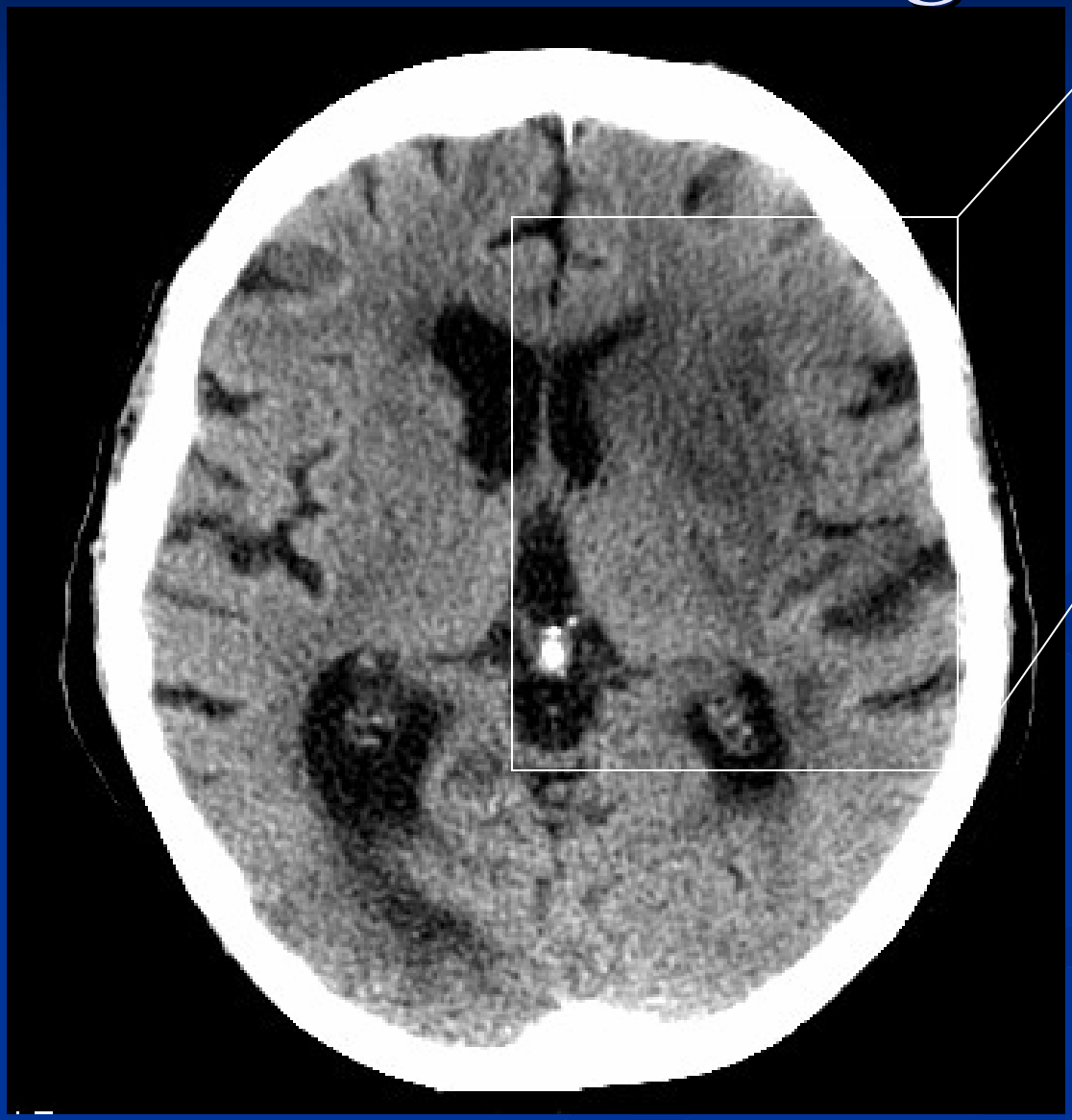
Patient A: Progression of Infarct



Findings

No evidence of hemorrhagic transformation

Hypodensity in region of L MCA infarct

Mass effect on L lateral ventricle with midline shift

Mechanisms of ischemic stroke injury

Event in Neurons	Time
Loss of blood supply	0
O_2 depletion	10 sec
Glucose depletion	2-4 min
Conversion to anaerobic respiration	2-4 min
Exhaustion of cellular ATP	4-5 min

NEURONS have very limited stores of energy in the forms of phosphocreatine and glycogen. In contrast, GLIAL cells have greater energy reserves and are less energy demanding.

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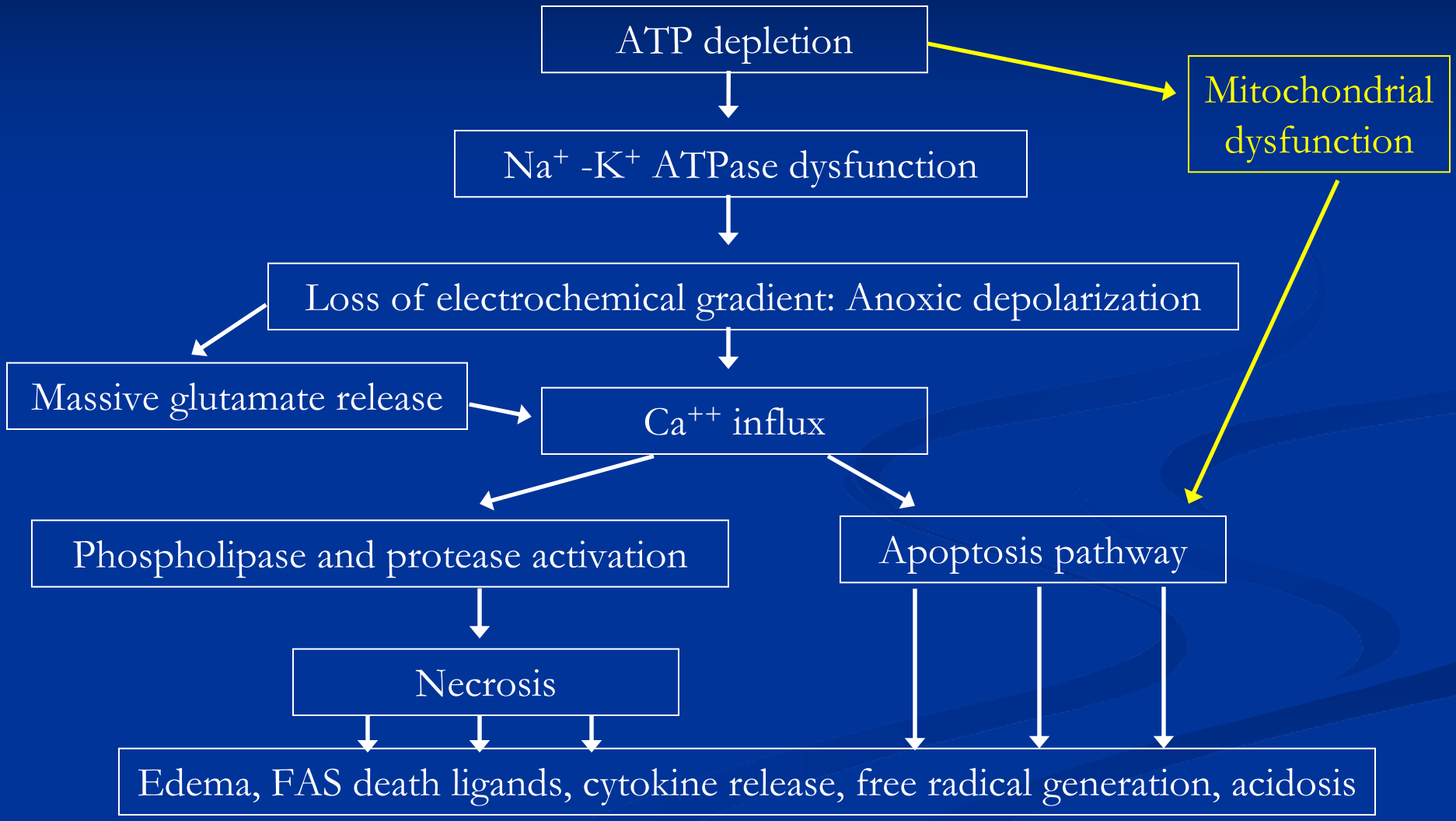
Mechanisms of ischemic stroke injury



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Early CT changes from intracranial edema

Loss of blood supply
↓
ATP depletion
↓
Cell death
↓
EDEMA

1. Effacement of gray-white matter distinction as edema reduces the small difference in gray and white matter attenuations
2. Effacement of sulci due to swelling within limited space
3. Mass effect on ventricles due to swelling within limited space

* Earliest CT changes seen several hours to days after initial loss of blood supply depending on size of infarct and volume of edema.

Edema: 0-20 HU; **Gray matter**: ~46 HU; **White matter**: ~40 HU

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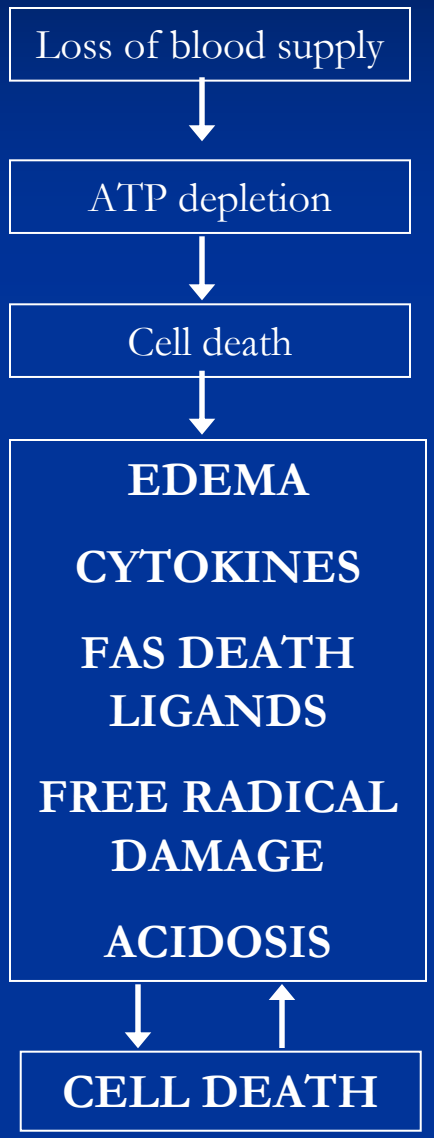
Progression of an ischemic infarct



Increase in infarct size over time is possible

Ischemic Penumbra - the region surrounding the infarcted tissue is subjected to numerous stresses:

- Decreased perfusion
- Abnormal cerebrovascular pressure autoregulation
- Compression by neighboring edema
- Active inflammation
- Free radical damage from infarcted region and neutrophils, astrocytes, microglia
- Induction of apoptosis by FAS death ligands

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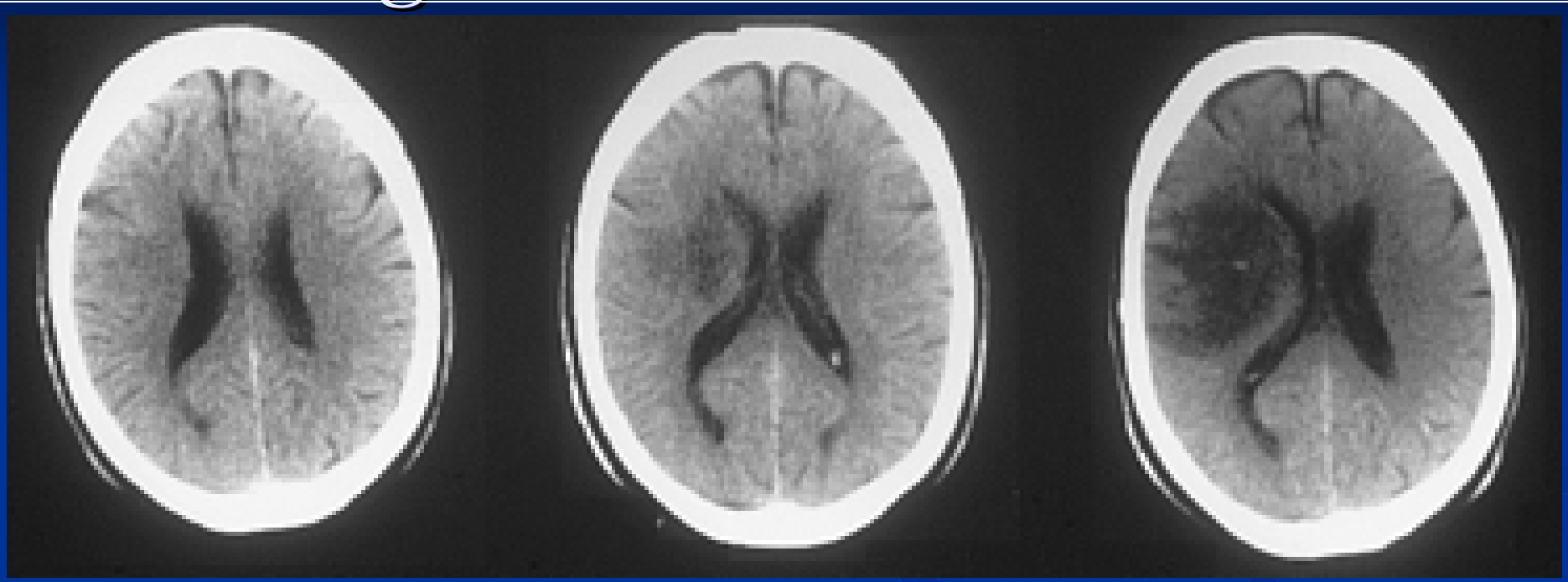
Pt B: Progression of an ischemic infarct



Time = 3.25 hr 30 hr 8 days

Late CT changes:

Increased infarction area, mass effect on ventricle, loss of sulci, hypodensity in infarcted tissue

* Hypodensity due to replacement of tissue by fluid

[Figure from Pantano et al. 1999. Stroke 30:502-507]

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Hemorrhagic transformation of ischemic stroke

Loss of blood supply

↓

ATP depletion

↓

Cell death

↓

FREE RADICAL DAMAGE:

METABOLIC BYPRODUCTS

NEUTROPHILS

O_2

↓

HEMORRHAGE

Hemorrhagic transformation of ischemic stroke results from **reperfusion injury**.

Reperfusion injury: Restoration of blood flow through a previously occluded intracranial vessel that results in vessel wall destruction and hemorrhage.

- Spontaneous or tPA-induced clot lysis
- O_2 combines with toxic metabolites to generate superoxide O_2^-
- Invading neutrophils convert O_2 to O_2^-
- Blood-brain barrier destruction from free radical damage to endothelial cells AND ischemic endothelial cell death (3-4 hrs)

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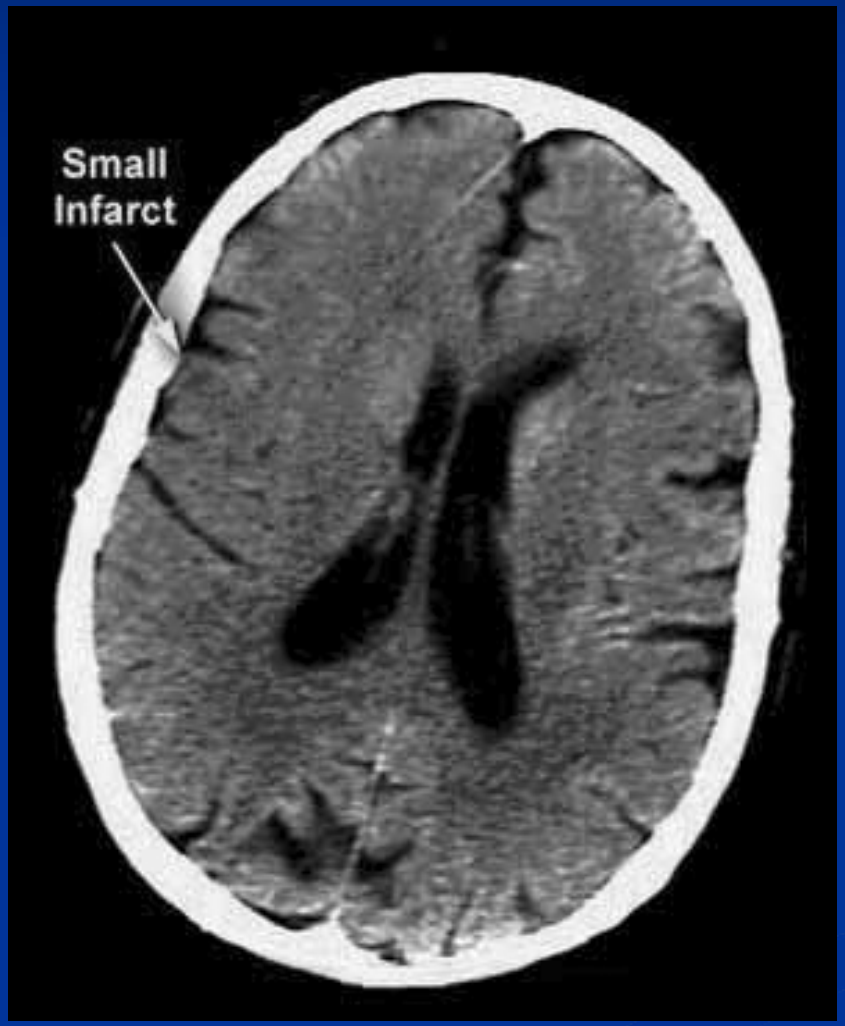
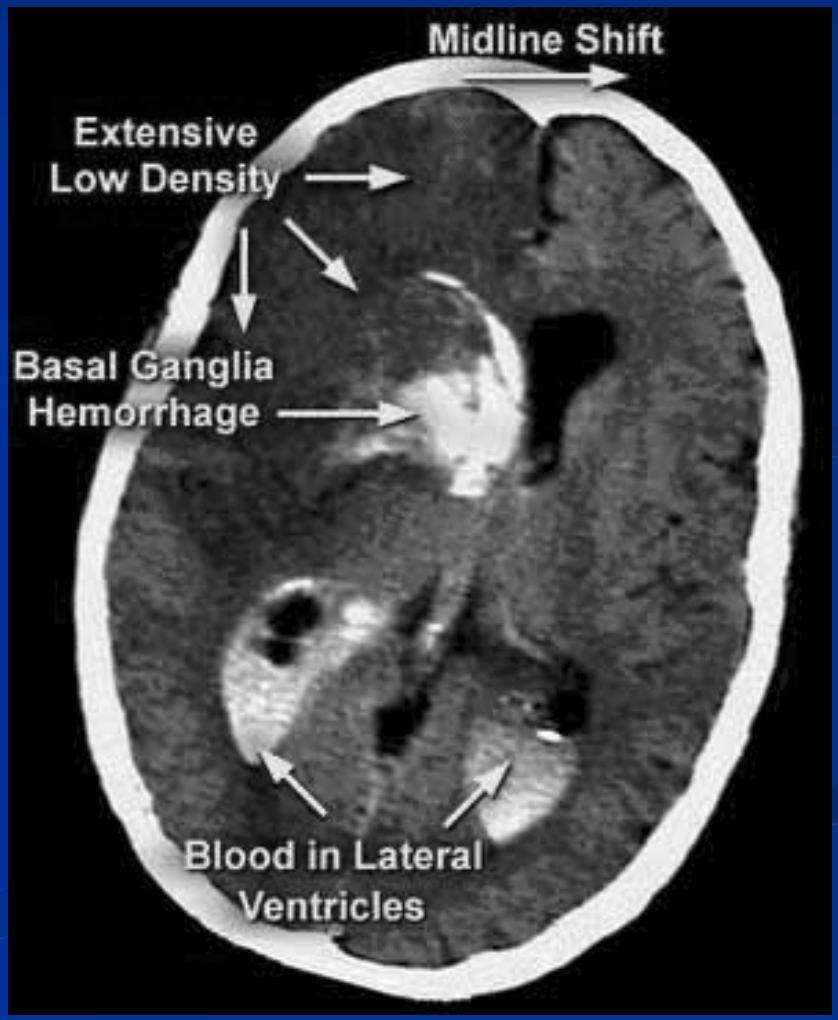
Patient C: Hemorrhagic transformation of an ischemic stroke





[Figure from http://www.strokecenter.org/education/ais_pathogenesis/16_hemorrhagic_conversion.htm]

tPA-induced hemorrhagic transformation: potential treatment

1. tPA treatment for ischemic stoke often leads to secondary hemorrhagic transformation due to reperfusion injury
2. Current models state that reperfusion injury occurs in large part from free radical damage following clot-lysis
3. Therefore, delivery of tPA WITH anti-oxidants should reduce the probability of hemorrhagic transformations

Animals models support co-administration of tPA with anti-oxidants in the prevention of secondary hemorrhagic transformation

- Lapchak and Zivin. 2003. STROKE 34(8):2013-8
- Lapchak et al. 2001. STROKE 32(1):147-153

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Ischemic strokes: imaging with MRI Diffusion-Weighted Imaging (DWI)

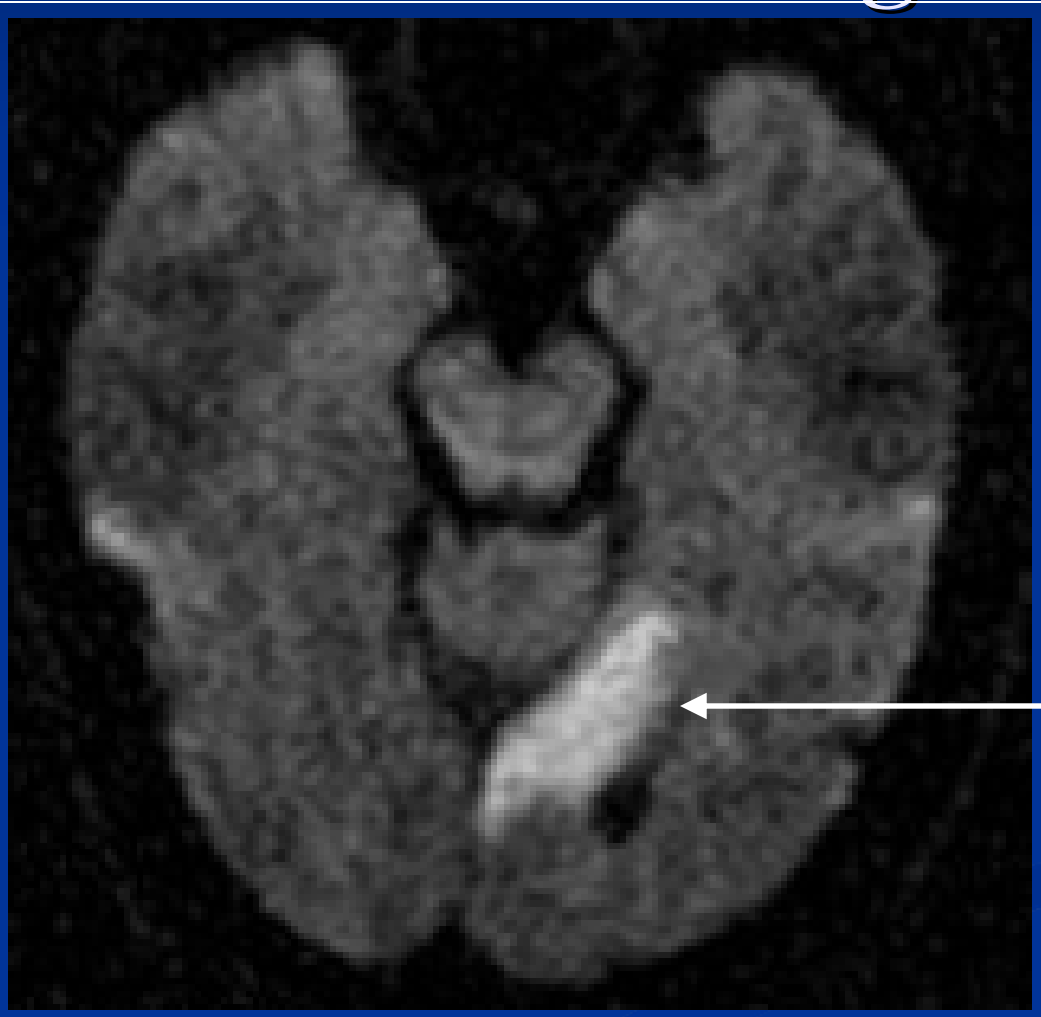
Loss of blood supply
↓
ATP depletion
↓
Massive depolarization
↓
↑ intracellular ions
↓
INTRACELLULAR EDEMA
↓
Cell death
↓
EXTRACELLULAR EDEMA

DWI signal intensity is related to the apparent diffusion coefficient (ADC) of water molecules (independent of the amount of water)

ADC(water) decreases by ~50% within 5-10 min of ischemic stroke due to intracellular edema and also possibly decreased temperature– recall that ATP is depleted from neurons within 4-5 min.

*** DWI changes can be seen within minutes of an ischemic stroke.

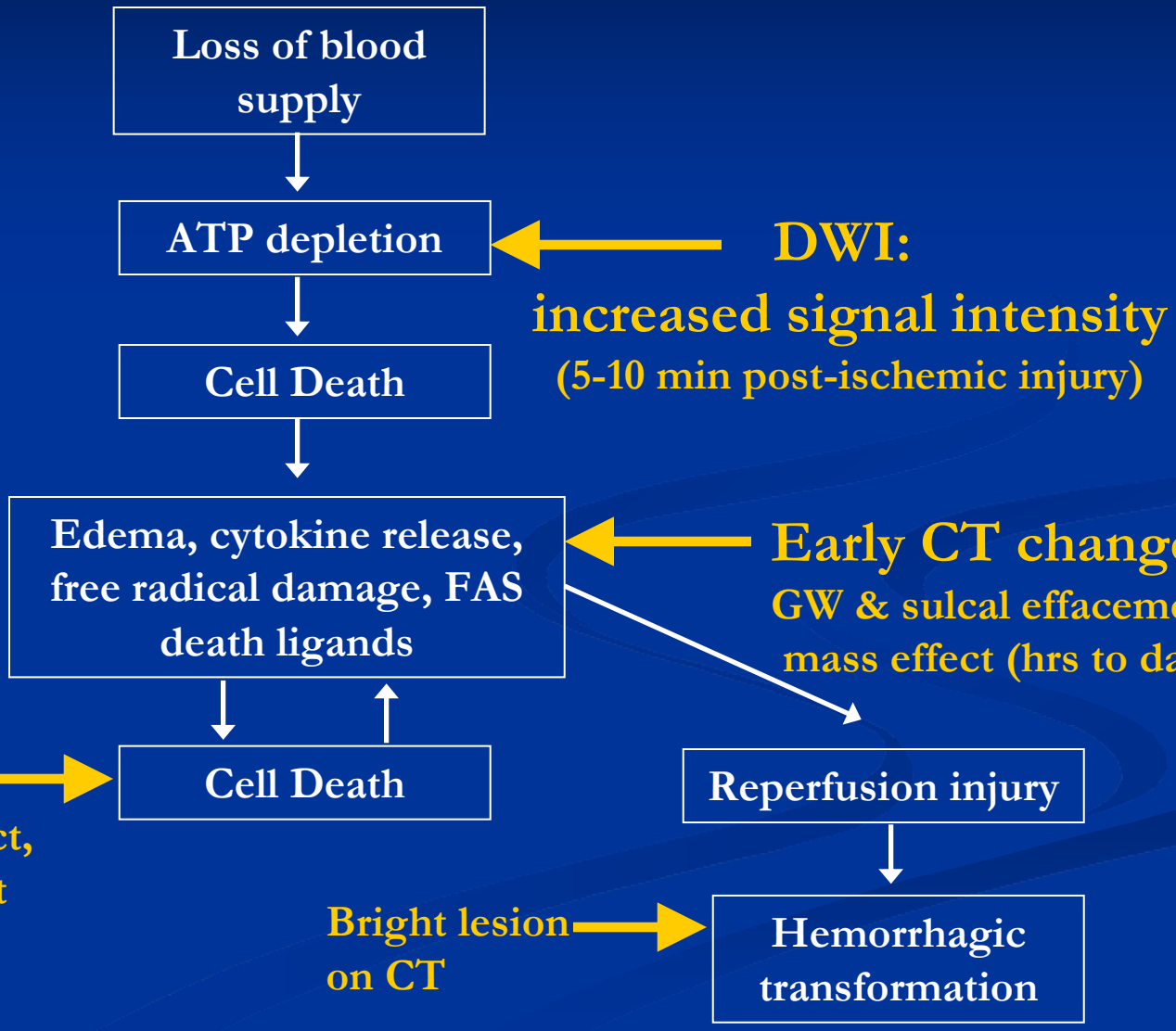
Pt D: Imaging ischemic strokes with MRI Diffusion-Weighted Imaging (DWI)



Left inferior temperal/occipital lobe ischemic infarct

PACS, BIDMC

Summary slide



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http://www.strokecenter.org/education/ais_pathogenesis/16_hemorrhagic_conversion.htm

All websites as of 9/20/04

Acknowledgements

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