

가

가

2000 12



恩師

가

가

가

가

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| ----- | | | | | | | 21 |

| | | | |
|-----|---|-------|----|
| 1. | | ADC | |
| | | ----- | 16 |
| 2.1 | 가 | ADC | |
| | | ----- | 18 |
| 3.1 | 가 | TTP | |
| | | ----- | 20 |
| 4.1 | 가 | rCBV | |
| | | ----- | 23 |

가

가 , (apparent diffusion coefficient: ADC)

가
가

가 ADC

ADC

가

24

ADC

가

3-3.5kg

19

30 (4), 1 (7), 3 (4)

(4) . 1 , 3 , 6 24

(diffusion-weighted imaging: DWI), ADC, time to peak(TTP)

regional cerebral

blood volume(rCBV)

. DWI

가

, ADC

24

triphenyl

tetrazolium chloride(TTC)

. DWI

가

. 가

1

DWI

24

DWI

가

TTC

ADC, TTP

rCBV

가

ADC

5

60

ADC

24

TTC

가

< >

.

(hyperacute ischemic stroke) 3
(ischemic penumbra)가

activator: rtPA) .¹⁻⁴
(urokinase recombinant tissue plasminogen

가
가 .⁵⁻⁸

rCBV(regional cerebral blood volume)가 가

rCBV TTP(time to peak)가 가 rCBF(regional cerebral blood flow)가
가 .⁹
가 .¹⁰

(perfusion-weighted MR imaging: PWI)
가 (bolus tracking method)

T₂* (R₂*)가

가 ,^{9,11,12} PWI rCBF
가 ,¹³⁻¹⁵

. , rCBF
 . PWI TTP rCBV 2
 (perfusion parametric imaging) 가
 . TTP - (time-relaxation curve)
 .
 rMTT(regional mean transit time) ,
 TTP rMTT .¹⁶
 TTP 가
 . rCBV R₂*
 .¹⁷
 (diffusion-
 weighted imaging: DWI) 14-60
 , DWI 가
 .¹⁸⁻²⁰ DWI Brownian
 . DWI
 (post-image processing) (apparent diffusion coefficient:
 ADC) DWI ADC
 .¹⁸⁻²¹
 ADC 6
 , 3
 가 24 가
 .²⁰ Loubinoux
 24 , 15
 ADC가 18% , 2 35% , 24, 48 ADC 35%
 .²²
 ADC
 , Hoehn-Berlage 2
 ADC가 ,
 ACD가 60% ADC가 ,
 86-94% .²³

가 , 30

ADC가 .²⁴ Kastrup 180

5 PWI

(post-ischemic hyperperfusion) , gadopentetate dimeglumine

BBB(blood-brain barrier)가 ,

60 5 2 BBB ,

BBB 4.5-6 .²⁵

60

60

24 120

.²⁶ Muller 45 DWI

24.2% 9.9% 120

24.4% 29.1% 가 ,²⁷ 120

가

ADC

ADC ADC TTP rCBV

가 , 3

가 ,⁴ 가

가 가

가 , Kastrup

가 가

,²⁵ 24 PWI

Tc^{99m}-ECD SPECT 2

CT

30 , 1 , 3

가 (reversible ischemia)가 가

가

ADC

,

가

ADC

ADC

24

ADC

가

,

.

1.

가.

3-3.5kg / 15
 . 30 , 1 , 3 3 ,
 30 4 , 1 7 , 3 4 .
 1 , 3 , 6 24 DWI, ADC, TTP rCBV .
 DWI 가 , ADC가 24
 triphenyl tetrazolium chloride(TTC)

4 . 1 , 3 , 6 24 DWI,
 ADC, TTP rCBV .

2.

Ketamine HCL(Ketara[®] ,) 1mg/kg

transorbital approach .
 , venous clip ,
 acryl holder
 ketamine HCL
 pulse oximeter
 PaO₂ PaO₂가 92%

3.

EPI(echo planar imaging)가 1.5T MR (Horizon, GE medical system,

Milwaukee, Wisconsin, USA) DWI PWI .

가.

DWI single shot spin-echo EPI 180°
 , b-factor 0, 500, 1000s/mm
 3 . EPI
 TR 2000ms, TE , / 5mm/1mm, 1,
 12x12cm, 128x128 . ADC DWI
 , IDL(interactive data language) (Research
 System Inc., Boulder, CA, USA) SUN (SUN Microsystem,
 Palo Alto, CA, USA) . b-factor 가

DWI

(S) Stejskal Tanner [1] ADC(D)

28

$$S(TE,b) = S_0 e^{-TE/T_2} e^{-bD} \quad [1]$$

$$\ln S(TE,b) = \ln S_0 - \frac{TE}{T_2} - bD$$

$$D = -\ln \left[\frac{S(TE, b)}{S(TE,0)} \right] \cdot \frac{1}{b}$$

[2] Stejskal Tanner ADC D
 b gradient attenuation factor b-factor

$$b = (\gamma G_D \delta)^2 (-\delta/3) \quad [2]$$

γ gyromagnetic ratio, G_D , δ
 180° , $-\delta/3$ diffusion time

DWI ADC

, Y, Z ADC IDL SUN ADC
 trace, ADC
 ADC (Dxx, Dyy, Dzz)
 [3] trace Trace{D}
 trace, trace

$$\text{Trace}\{D\} = (D_{xx} + D_{yy} + D_{zz}) \quad [3]$$

Trace NIH, / trace
 trace ADC, trace ADC

PWI gradient-echo EPI 12x12cm, TR
 1500ms, TE 40ms, flip angle 90°, / 5mm/lmm, 128x128,
 1kg 0.2mmol gadopentetate dimeglumine(Magnevist,
 Shering AG, Germany) 5 2ml 1.5
 60 IDL
 SUN
 rCBV TTP

(time-signal intensity curve) echo time(TE)

$$T_2^*(t)$$

$$S(t) = S(0)e^{-TE/T_2^*(t)} \quad [4]$$

S(t) t, S(0) 가 가
 가 T₂*가
 가 1/T₂* (R₂*)
 [4]

$$\Delta R_{2^*} = \frac{1}{T_{2^*}} = \frac{\ln[S(t)/S(0)]}{TE} \quad [5]$$

[5] R_{2^*} R_{2^*}
r-variate fitting 1 , rCBV
 rCBV rCBV
 $R_{2^*}(t)$
 TTP $R_{2^*}(t)$ TTP
 ,
 .²⁹

4. DWI

24
 2% TTC³⁰
 37-42°C 15
 15 TTC , 10%
 formalin 2

5. MRI - 가

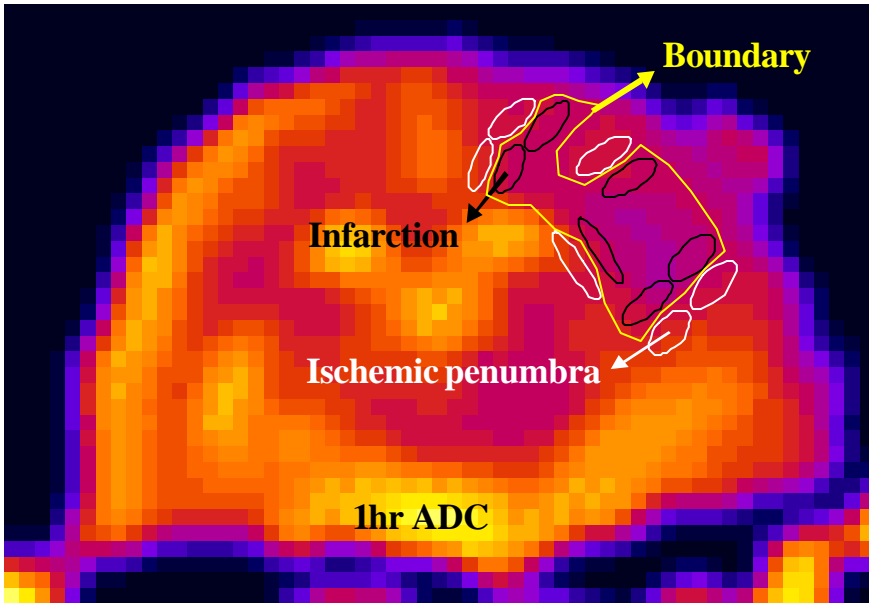
30 , 1 3 . DWI
 가
 1, 3, 6, 24 DWI
 ,
 , 가 24 DWI
 . 가 1
 DWI 24 DWI 가
 , TTC

6. ROC

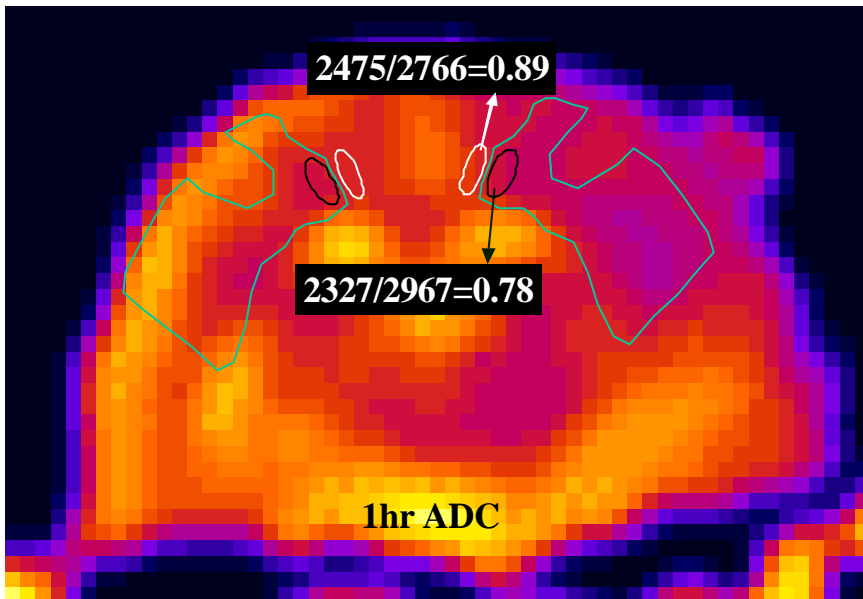
1 가 가 5 DWI ADC

24 DWI TTC ,
 1 ADC 가
 . 1 pixel 가
 (region of interest: ROI) . 가
 6 , 12 (1), 5 60 ROI .
 ROI 10 pixels 3 ADC
 . / ADC (2). 24
 ROC
 ADC .

7. ADC, TTP rCBV - 가
 ADC, TTP rCBV 가 ADC, TTP
 rCBV .
 , / ADC, TTP rCBV
 . ROI 20pixels . ROI 3
 . ± . Mann-Whitney
 Test , p < .05 .



1. 가 ADC ROI



2. 가 ADC

1.

가.30

30 T2WI 가 . TTP 1 24 MRI 가 DWI (3). ,

.1

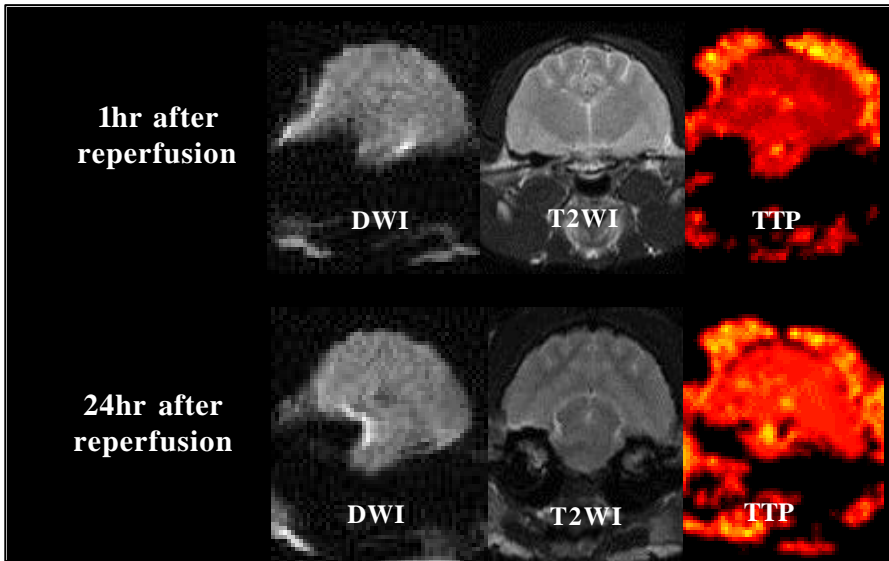
1 7 5 가 , 3, 6 1 24 DWI TTC (4). , 1 DWI 7 2 1 DWI 가 TTC 24 DWI

.3

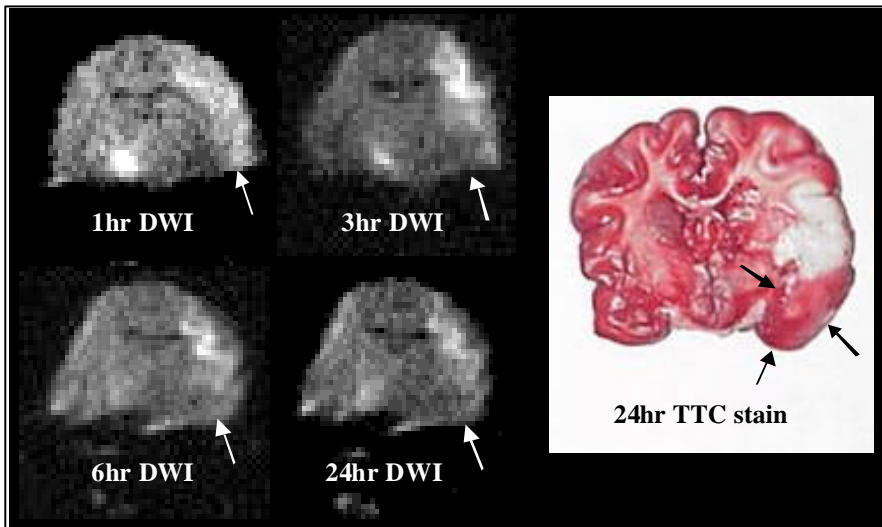
3 가 , 1 DWI TTC DWI (5). 24 DWI

6

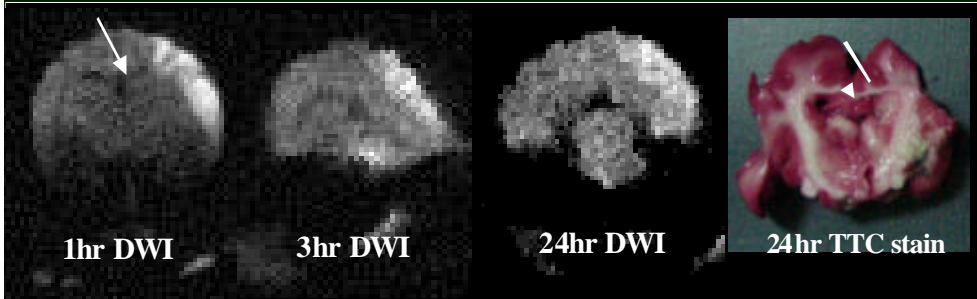
. 24 . 24 DWI TTC (6).



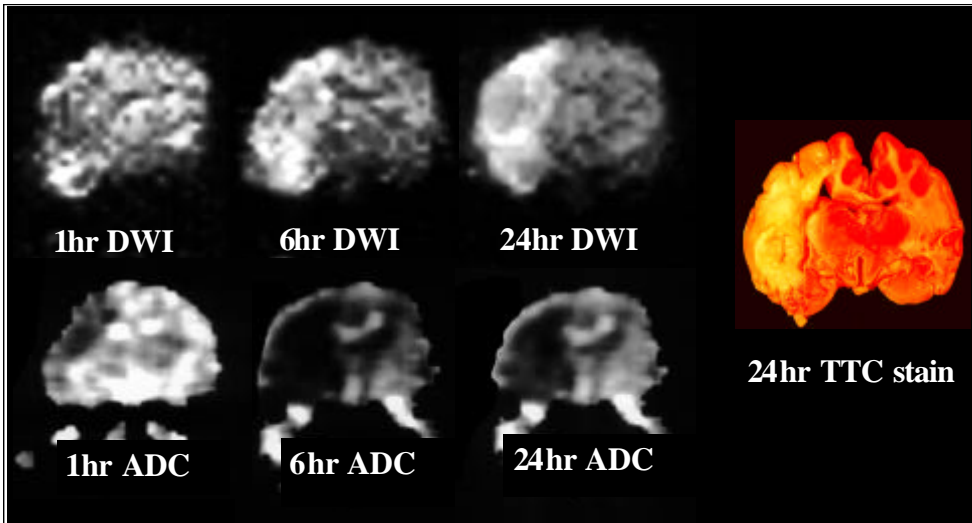
3. 30 1, 24 DWI, T2WI TTP . DWI, T2WI TTP .



4. 1 1, 3, 6 24 DWI TTC .
 1 DWI 가
 (arrows) TTC .



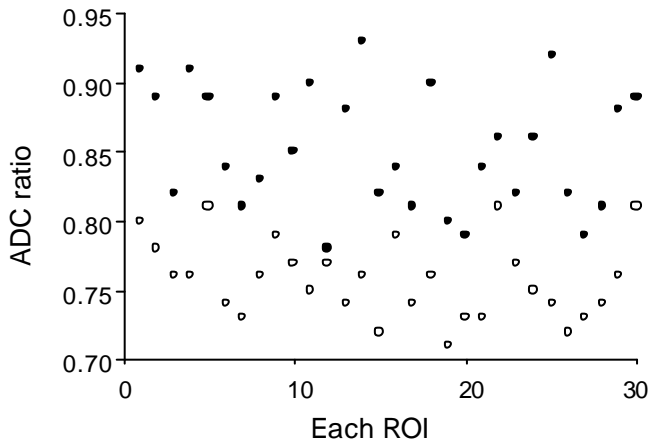
5. 3 1, 3 24 DWI TTC . DWI
 가 .
 (arrows) DWI TTC



6. 1, 6 24 DWI, ADC TTC . DWI
 ADC가 가 .
 TTC 24 DWI

2 가 ADC

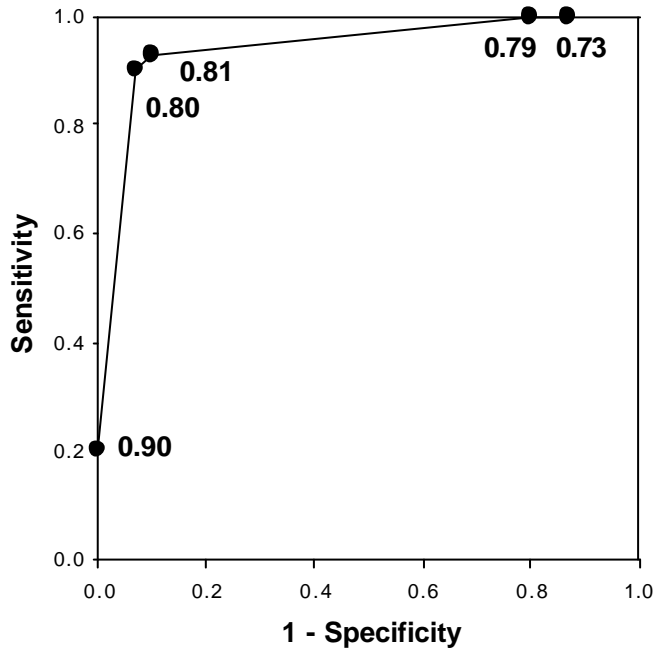
1 ADC TTC
 가 ADC 0.71
 ~ 0.81 가 ADC
 0.79 ~ 0.93 (7). ADC 0.80 가
 93%, 90% (1, 8).
 가 golden time



7. 가 ADC . 5 60
 ROI ADC 가 (●) 0.79 ~ 0.93
 , (○) 0.71 ~ 0.81

1. ADC (n=60)

| ADC ratio | Sensitivity | Specificity |
|-----------|--------------|--------------|
| 0.73 | 1 (30/30) | 0.13 (4/30) |
| 0.79 | 1 (30/30) | 0.20 (6/30) |
| 0.80 | 0.93 (28/30) | 0.90 (27/30) |
| 0.81 | 0.90 (27/30) | 0.93 (28/30) |
| 0.90 | 0.20 (6/30) | 1 (30/30) |



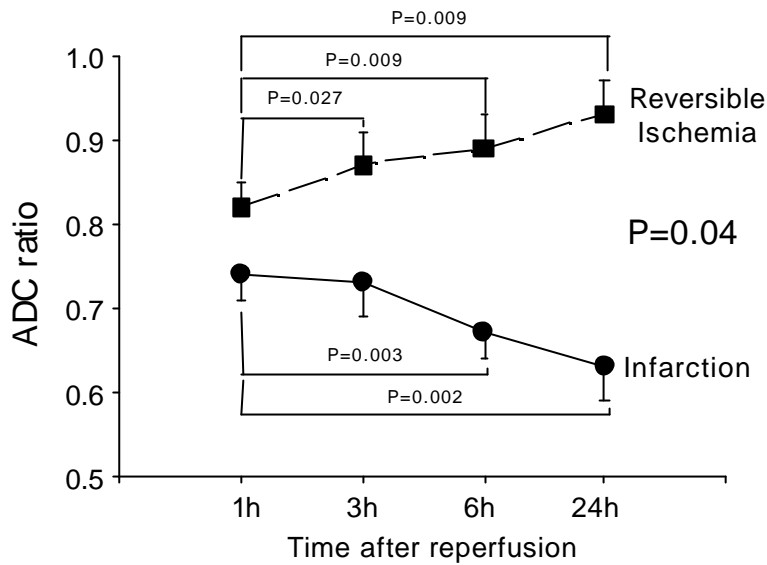
8. ADC 가 ROC
 . ADC 0.80 가 93%,
 90%

3. 24 ADC, TTP rCBV - 가

1. ADC

1 가 ADC
 가 (p=0.04). 가 1 ~ 3
 ADC (p=0.027). 가
 1 ADC 0.82 ± 0.03 , 24
 0.98 ± 0.04 가 . 1 ~ 6
 ADC (p=0.003). 1
 ADC 0.74 ± 0.03 24 0.64 ± 0.04
 (2, 9).

| 2. 1 | 가 | | | | ADC | | | |
|------|---------------------|------|--------|------|---------|------|-------|------|
| | reversible ischemia | | | | infarct | | | |
| | 1hr | 3hr | 6hr | 24hr | 1hr | 3hr | 6hr | 24hr |
| Mean | 0.82 | 0.87 | 0.89 | 0.93 | 0.74 | 0.73 | 0.67 | 0.64 |
| Max | 0.85 | 0.90 | 0.93 | 0.96 | 0.78 | 0.76 | 0.71 | 0.67 |
| Min | 0.79 | 0.84 | 0.86 | 0.89 | 0.70 | 0.69 | 0.65 | 0.59 |
| SD | 0.03 | 0.04 | 0.04 | 0.04 | 0.03 | 0.04 | 0.03 | 0.04 |
| | Mean: | | , Max: | | , Min: | | , SD: | |



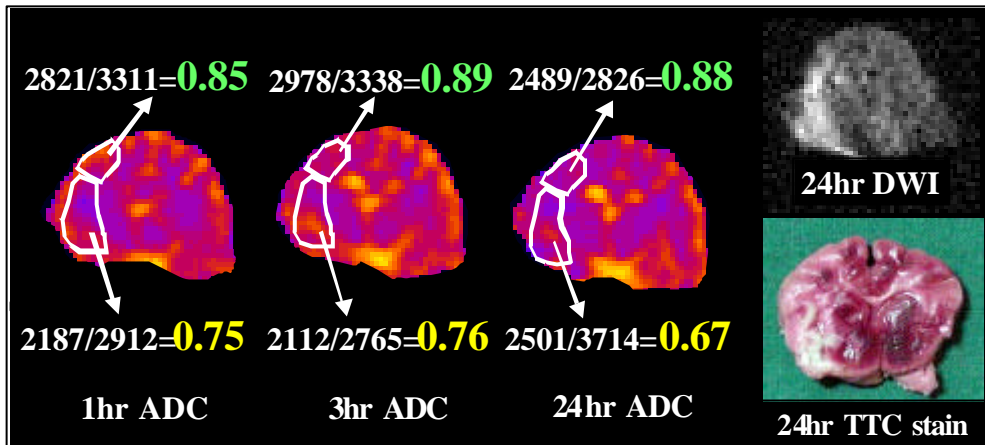
9-1. 1 가 ADC . 가

(■) (●) ADC

가 (p=0.04). 가 1 ~ 3

ADC (p=0.027). 1 ~ 6

ADC (p=0.003).



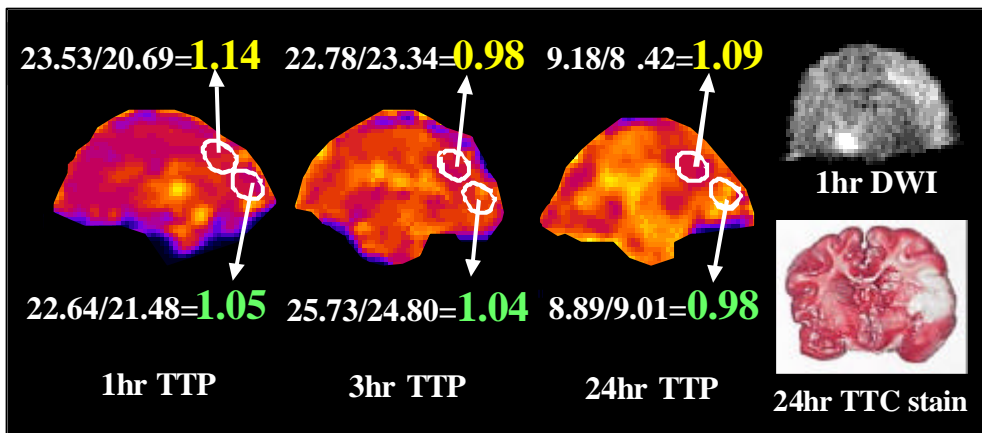
9-2. 1 가 ADC 가

(green) ADC 1 0.85 ,

(yellow) 1 0.75 24 0.67

. 24 DWI 가 가

TTC



10-1. 1 가 TTP 가

TTP 24 가 (green)

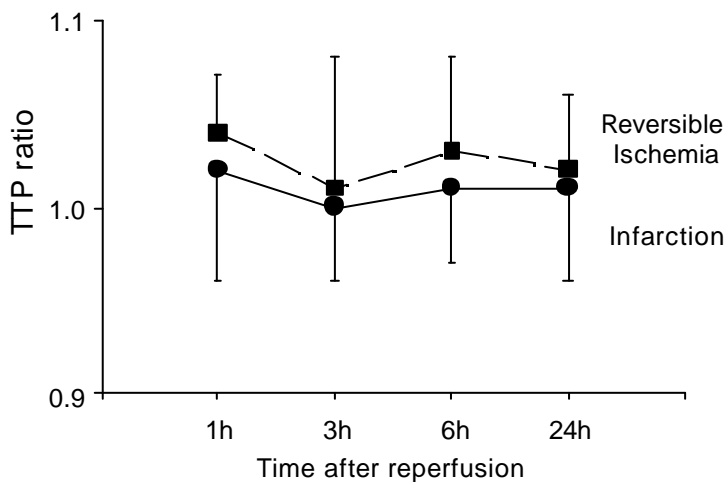
(yellow)

. TTP

1 TTP 1, 3, 6 24 가
 가 , 24
 TTP
 , 가 1.02 ± 0.05, 1.01 ±
 0.05 (3, 10). TTP

| | 가 | | | | TTP | | | |
|------|---------------------|------|------|------|---------|------|------|------|
| | reversible ischemia | | | | infarct | | | |
| | 1hr | 3hr | 6hr | 24hr | 1hr | 3hr | 6hr | 24hr |
| Mean | 1.04 | 1.01 | 1.03 | 1.02 | 1.02 | 1.00 | 1.01 | 1.01 |
| Max | 1.07 | 1.06 | 1.12 | 1.08 | 1.14 | 1.04 | 1.07 | 1.09 |
| Min | 0.99 | 0.90 | 0.97 | 0.98 | 0.97 | 0.93 | 0.97 | 0.91 |
| SD | 0.03 | 0.07 | 0.05 | 0.04 | 0.06 | 0.04 | 0.04 | 0.05 |

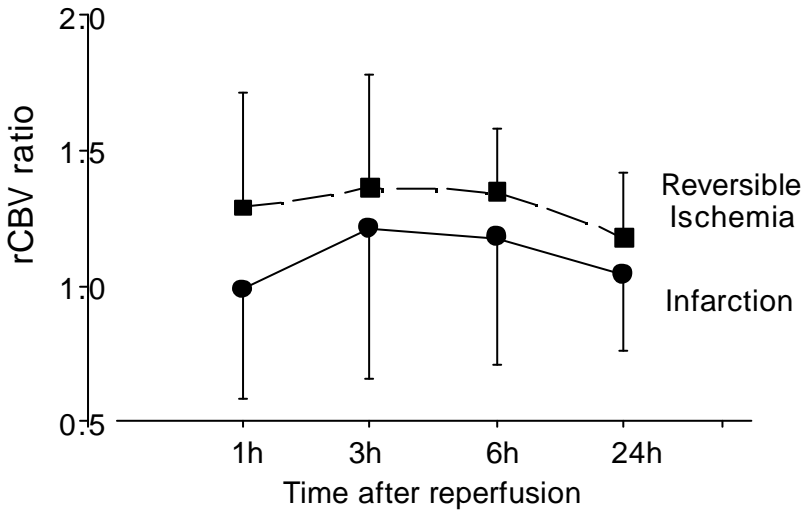
Mean: , Max: , Min: , SD:



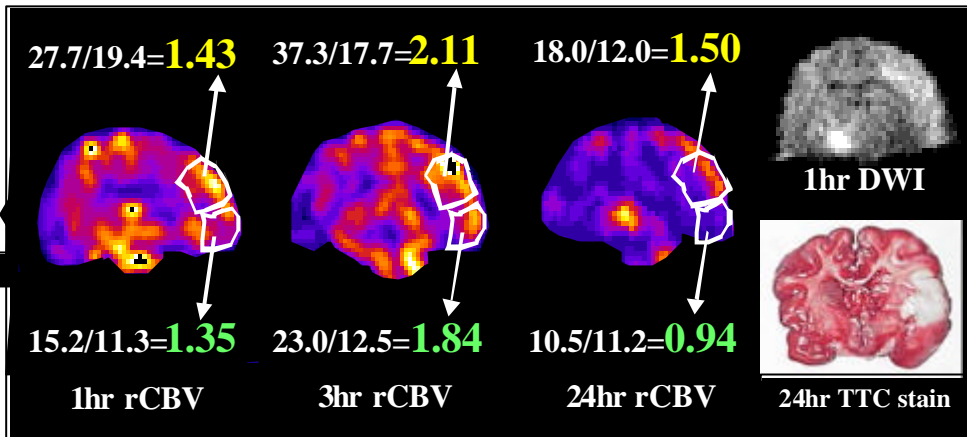
10-2. 1 가 TTP
 TTP 24 , 가 (■) 1.02
 ± 0.05, (●) 1.01 ± 0.05 가

.rCBV

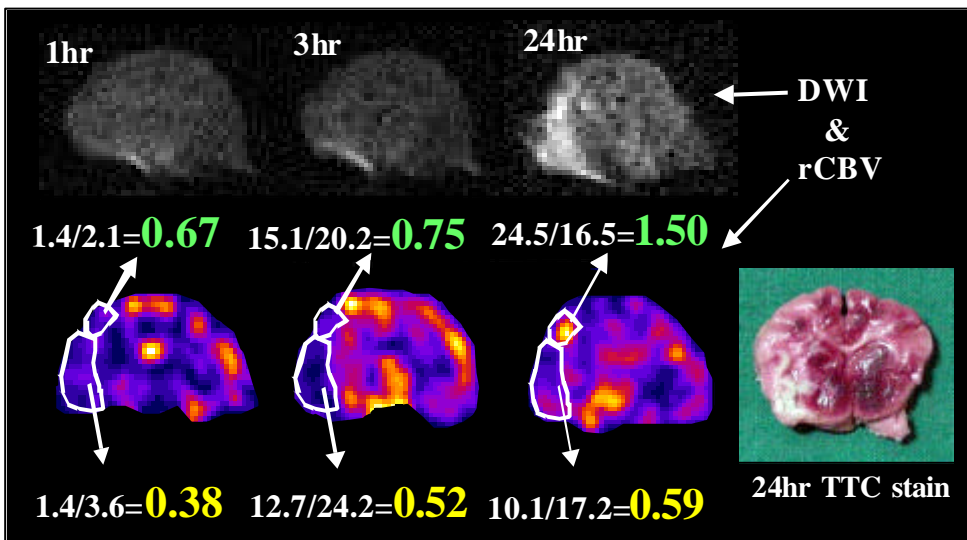
1 가 rCBV 가 가 , 가 가
 가 . rCBV 가 가 , 가 ,
 24 rCBV가 가 가 ,
 24 가 rCBV 1.29 ± 0.32 가
 (4, 11).
 rCBV가
 . , 24 rCBV 1.11 ± 0.42
 . rCBV가 가 , 2 3
 , 2 6 rCBV 가 가 .
 24 rCBV가 가 가 가
 1 (11-2). rCBV
 가 .



11-1. 1 가 rCBV .
 가 (■) (●) rCBV
 . 24 가 rCBV 1.29 ± 0.32 가
 1.11 ± 0.42 . rCBV
 가 .



11-2 1 가 rCBV
 rCBV 1, 3 가 (green) (yellow)
 가 가 가 24 rCBV
 가 , 가 24



11-3. 1 가 rCBV
 1, 3 가 (green) (yellow) rCBV
 , 24 가
 DWI rCBV

| 4.1 | 가 | | | | rCBV | | | |
|------|---------------------|------|------------------|------|------------------|------|-----------------|------|
| | reversible ischemia | | | | infarct | | | |
| | 1hr | 3hr | 6hr | 24hr | 1hr | 3hr | 6hr | 24hr |
| Mean | 1.29 | 1.36 | 1.35 | 1.18 | 0.99 | 1.21 | 1.18 | 1.04 |
| Max | 1.77 | 1.84 | 1.72 | 1.50 | 1.48 | 2.11 | 1.81 | 1.50 |
| Min | 0.67 | 0.75 | 1.17 | 0.94 | 0.38 | 0.52 | 0.55 | 0.59 |
| SD | 0.42 | 0.42 | 0.23 | 0.24 | 0.41 | 0.55 | 0.47 | 0.28 |
| | Mean: , | | Max: , | | Min: , | | SD: , | |

IV.

1 ADC 0.80 가 ADC '0.80' .

, , . ADC 0.81 , ADC 0.80 가 90% 가 93% , ADC 가 가 93% 가 90% 가

ADC 0.80 .

1 pixel 0.94mm 가

1 ROI 2.82mm . Co-registration H&E 가

, 1 pixel ROI .

ROC ADC

, ADC . Mancuso ADC 가

가 , ADC가 45% 가 72 가

. 30 , ADC가 , 30 ADC 가

가 , 30 . 1 가

, 가

Hoehn-Berlage 2 .³¹ rCBF

가 31 ± 11 ml/100g/m in 가

ACD 86-94% .²³ Robert

가 6

ADC 10-20% .³⁰ ADC ADC
0.80 ADC

30 24
DWI, T2WI PWI . Li 8, 15, 30
ADC가
, 72 15 30
가 가 , 8 가
.²³ .³⁴ 가
ADC, 가
ADC , ADC 가
72
1 가
1 가
가 1 DWI ADC
TTC ADC

.^{35,36} ADC ‘spontaneous electrical activity’
.⁵ 가
가
.³⁷ TTC
, 가
가 Robert TTC 1

ADC 가 TTC , ADC가 87.5
 ADC가 $97.8 \pm 7.9\%$,
 $\pm 10.7\%$,³⁰
 (selective neuronal damage) (apoptosis)가 ,
 가 ,³⁸
 Ketamine N-methyl-D-aspartate receptor(NMDA)
 , (cerebral metabolic rate for oxygen: CMRO₂)
 가 . Ketamine 가 1)
 , 2)
 CMRO₂가 가 가
 가 , Ca⁺⁺ channel
 Ca⁺⁺ Mg⁺⁺
 가 ,³⁹⁻⁴¹ Ketamine
^{42,43}
 ketamine HCL .
 가 , ketamine HCL
 S(+)-ketamine ketamine racemate
 가 ,
 ketamine HCL .
 3kg
 rCBV 가
⁴⁴
 $41.4 \pm 3.8 \sim 21.3 \pm 4.0$
 ml/100g/min 가 ,⁴⁵
 가 ,
 가 ,⁴⁶
 Shimosegawa 6 Tc^{99m}-
 HMPAO SPECT 30 3 CBF가 가

CT

(reperfusion injury)

가

⁴⁷

5

4

, 4

1

24

가 가

(11-2),

Shimosegawa

(positron emission tomography: PET)

3

CMRO₂

(oxygen extraction fraction: OEF)

⁴⁸

1

3

가

가

3

가

, 가

5

가

가

⁴⁹

^{5,37,38,50}

DWI, ADC

PWI

PET

⁵⁰

TUNEL (terminal deoxynucleotidyl

transferase – mediated deoxyuridine triphosphate nick – end labeling)

⁵¹

MRI

가

DWI/PWI

^{52,53,54}

ADC

0.80

가

10

가 ,
ADC
ADC
32,33
가
“
가?”
가

V.

| | 가 | 24 | DWI | PWI | TTC |
|-------|-----------------|------|-----------------|-----------------|-------|
| | , | | ADC | | . |
| 1. 30 | | 24 | DWI, T2WI | TTP | . |
| 2. 1 | | | 가 | | , TTC |
| 3. 3 | | DWI | | | . |
| | 가 | | , | | . |
| 4. 1 | | 가 | | 1 | ADC |
| | 0.82 ± 0.03 | | | | . ADC |
| | 가 | 24 | 0.93 ± 0.04 | | 가 |
| 5. | 1 | ADC | ADC | 0.80 | 가 |
| | | 93%, | 90% | | . |
| 6. 1 | | | | | 24 |
| | ADC가 | | 24 | 0.64 ± 0.04 | . |
| 7. 1 | | 가 | | TTP | 24 |
| | | | , | 24 | . |
| | TTP가 | | 가 | | . |
| 8. 1 | | 가 | | | 24 |
| | rCBV | 가 | | | rCBV |
| | | , | | 가 | 가 |
| | 가 | | | | . |
| | | 1 | | | . |
| | 가 | 가 | | . ADC | 0.80 |
| | | | | , | . |

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Abstract

Reversal of apparent diffusion coefficient(ADC) and cerebral perfusion in magnetic resonance imaging(MRI) following transient focal cerebral ischemia in cats

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Hyperacute ischemic stroke needs early diagnosis and active treatment for the recovery of the ischemic penumbra. The Ischemic penumbra is the ischemic tissue of decreased perfusion which, although still structurally intact, is functionally impaired. Early reperfusion can minimize the area of tissue injury. Although permanent and temporary animal models of middle cerebral artery occlusion(MCAO) have shown the pathophysiology of the ischemic penumbra, reports on the reversal of the apparent diffusion coefficient(ADC) and on cerebral perfusion following transient focal cerebral ischemia have not provided sufficient information.

The temporary model of MCAO was used in this study to evaluate the pathophysiology of reperfused hyperacute ischemic stroke and to ascertain the time independent criteria for early recanalization and other active treatment modalities for hyperacute stroke. The MR images of the reversible ischemic tissue, possibly representing the ischemic penumbra, were obtained. The distribution of ADC ratios was evaluated in the periphery of the infarct and reversible ischemic tissue. The threshold ADC ratio suggesting reversible ischemia was obtained. Nineteen adult Korean cats weighing 3-3.5kg were used. Temporary occlusion groups of 30 min(4 cats), 1 hour(7 cats), 3 hour(4 cats) duration and a permanent occlusion group(4 cats) were made. Diffusion-weighted imaging (DWI), ADC, time to peak(TTP) and regional cerebral blood volume(rCBV) maps were obtained at 1, 3, 6 and 24 hours after reperfusion. Cats with high signal intensity on DWI or decreased ADC were

killed after 24 hour imaging. Brain slices were obtained and triphenyl tetrazolium chloride(TTC) staining of brain slices was done. DWI and TTC stained brain slices were compared with the naked eye. Reversible ischemia was defined as occurring in the area of normalized high signal intensity on follow-up DWI and normal staining on TTC stain. The changes of ADC, TTP and rCBV after reperfusion were evaluated in the reversible ischemia and infarct. For the threshold ADC ratio suggesting the existence of the reversible ischemia, 60 ADC ratios were obtained in the periphery of the infarct and reversible ischemia. Tissue survival showing normal TTC stain was used as final determination. The sensitivity and specificity of each ROI was obtained and an ROC curve was made.

The 1 hour temporary occlusion group showed the reversible ischemia with almost normal TTC stain in the periphery of the infarct core. The ADC ratio of the reversible ischemia was 0.82 ± 0.03 at 1 hour after reperfusion and this was higher than that of the infarct to a statistically significant degree. The ADC ratio of the reversible ischemia gradually improved over time and increased to 0.98 ± 0.04 at 24 hours after reperfusion. This suggests that improvement of cytotoxic edema occurs in the reversible ischemia after reperfusion. The ADC ratio of 0.80 obtained in the 1hour after reperfusion predicted the survival of the ischemic tissue with 93% sensitivity and 90% specificity. In the presumed infarct, although reperused, the ADC ratio progressively deteriorated to 0.64 ± 0.04 at 24 hours after reperfusion. The TTP ratio improved and became almost normalized in both the reversible ischemia and infarct. The TTP ratio was relatively stable without fluctuation during the first 24 hours after reperfusion. The CBV ratio increased in both the reversible ischemia and infarct during the first 24 hours after reperfusion. Although the magnitude and the period of increased rCBV varied, probably due to diverse collateral circulation, the post-ischemic hyperemia seen in the region of the reversible ischemia of all cats might suggest a good prognosis for ischemic tissue in some cases.

In conclusion, the 1 hour temporary occlusion group showed the reversible ischemia with reversal of ADC and cerebral perfusion. The ADC ratio 0.80 may be considered a time independent criterion for assessing the effectiveness of candidates for active treatment such as early recanalization or neuroprotective drugs or hypothermia in the case of hyperacute ischemic stroke.

Key words: hyperacute ischemic stroke, ischemic penumbra, magnetic resonance imaging, diffusion-weightedimaging,apparentdiffusioncoefficient, perfusion - weightedimaging, reperfusion