Evolution and update of neurointervention in patients with acute ischemic stroke

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- Female 46
- RHD without treatment for 20 years
- 09/28 0:00 Dizziness, 4 limbs weakness (can walk), 署立台 北 ER.
- 09/28 8:00 Dizziness & vomiting admission 署立台北.
- 09/29 12:30 In hospital attack of loss of sensation in left extremity, sudden 4 limbs palsy, speaking disability

#### MRA 09/29 15:14

### 09/29 15:14 (40 hrs) 署立台北 Emergent MRA

• occlusion of right distal VA & proximal basilar artery with acute infarctions in medulla & pons.





# **Clinical information**

- At ER: Alert
  - Speech: aphonia, aphasia
  - CN: Ophthalmoplegia, OU; Screw nystagmus with Bobbing sign, OU
  - Babinskin sign: present bilateral
  - Saliva drooling
  - EKG: AF
  - Motor: quadriplegia (Gr 0/4 of bilateral U/L limbs with pain withdraw)
  - NIHSS 26

Admission diagnosis:

1. Acute brain stem infarction with quadriplegia and locked-insyndrome

2. RHD

# CT & CTA MRA 09/29 21:30



• CT 21:30 showed no hemorrhage

CTA confirmed

 5cm occlusion
 of basilar artery
 and right distal
 vertebral artery.







#### Groin puncture 09/29 on 22:26 (46 hrs after onset)

- > Timing points: Received telephone consultation 20:23, CTA on 21:30, leaving CT room after CTA for angiography suite, on Foley's catheter, and groin preparation.
- > Data input for angiography on 22:09; Groin puncture on 22:26; First AP fluoroangio confirmed occlusion of the proximal basilar artery on 22:36;Second AP fluoroangio after position set of the guiding catheter on 22:38;
- > A Marksman Catheter combined a SliverSpeed -16 wire was advanced and passed the thombosed basilar artery. Fluoro angio confirmed microcatheter location at the distal basilar artery & patency of distal artery on 22:55
- > Then were was removed, and changed with a Solitare SRD-6-30, which was ready to expansion & fluoroscopic image taken on 22:59
- > The Solitare was removed after about 8 minutes and the first fluoro angio showed patency of right vertebrobasilar system on lateral view on 23:15.
- > The final angiogram was taken on 33:27. Then the catheter was removed. The sheath remained in the groin and removed on the next day morning.



- Groin puncture 09/29 on 22:26
- Stent in place 22:55
- Basilar artery patent and normal 23:15

\*\* Interval from femoral puncture to regain patency: 49'

# Clinical follow up

- D1: 能發聲音, 部分聽懂", 左手可動, 左腳可動, 無 法抵抗 gravity. 石手: normal, 右腳: 稍微無力
- D2: 可言語, 慢慢講, ,"眼睛痛", 聽懂, nystagmus
- D3: 轉出 CU
- D7: Speech 流利; "怕鬥雞眼".
  - motor: 右側正常, 左手肘 antigravity, fingers 可動; 左 腳 hip joint 可antigravity.
  - eyes: limitation of lateral gaze OS (VI palsy)
- D29: NIHSS= 8 (Improved from 26 before revascularization)

Motor: right upper 5/5, lower 4/5 left upper 4/5, lower 3/5

# MRI 2014/10/01 10:54





• Basilar artery regained patency





**Before treatment** 



After treatment

Sudden aphasia, and right hemiparesis for 2 hours IA urokinase 600,000 IU infusion

Recovered immediately after treatment.

#### 2848261-3 林\*\* F/85

**2011/8/20** 9:00 AM found to be weakness of right extremities & aphasia.



11:00 AM 1<sup>st</sup> CT
13:01 notified by CR, and I recommended CTA & CTP
13:36 CTA & CTP
14:20 call anesthesiologist - available at 15:00
14:58 MR began
15:30 Arrival in Angiogram



15:48 Anesthesia done and ready (84') 16:37 (7.5 hrs after onset) Penumbra device - Reperfusion catheter in 16:55 2<sup>nd</sup> Reperfusion catheter in 16:58 Begin reperfusion procedure in M1 17:12 Finished procedure 9/9 出院 (d20) with mRS: 2











Puncture – patency 84'



- F/57. Acute onset left hemiplegia at 4:00.
- ER 4:56 motor (1/5), NIHSS 10, CT 5:07 (-)
- CTP + CTA 6:30 large penumbra
- 7:52 9:12 (onset 4 hrs) IA revascularization 500,000 IU urokinase
- NIHSS 1 on next day





oligemia penumbra

## dead core



Penumbra could be further damaged by: hypoperfusion, hyperglycemia, fever, seizure

shok Srinivasan, Radiographi<mark>cs; 2006 )</mark>

## **ISCHEMIC PENUMBRA**

## **PATHOPHYSIOLOGY OF THERAPEUTIC WINDOW**





stroke confirm and exclusion

**Patient selection** 

detection of penumbra

Emergent intervention

Outcome prediction complication management



- Clinical s/s not correlate with images findings
- Hemorrhage at any degree (ICH, SAH, IVH, etc.)
- Brain tumor, aneurysm or vascular malformation
- Mass effect with resultant midline shifting
- Cortical sulci effacement > 1/3 M.C.A territory

patient selection Inclusive Criteria

- Within Golden Time ( < 6-8 hours for ant. circulations; post. circulation may be could up to 12-24 hours )
- Clinical s/s consistent with occlusive level
- 4< NIHSS<30 (except isolated aphasia or hemianopia)
- Complete modern neuro-radiological studies: MR diffusion/perfusion images, MRA or

CT, perfusion CT and CTA

Emergent thrombolysis/ thrombectomy for acute ischemic stroke

## **Facts:**

- nature history of ischemic stroke are heterogeneous and varies
- narrow therapeutic window
- risk of post-treatment hemorrhage
- remains controversial and poses many treatment challenges



- Types of strokes, any acute hemorrhage ?
- Large or small vessels occlusion ?
- Severity of the stroke ?
- Complications of the ischemic stroke ?
- Irreversible infarction or salvageable penumbra ?
- Stroke mimics ?

## Detect and differentiate infarction and salvageable penumbra

#### **CT studies:**

- **1.** Non-contrast CT
- 2. CT Angiography
- 3. CT Perfusion

#### **MRI** studies

- 1. T1WI, T2WI, FLAIR,
- 2. Diffusion Weighted Imaging & ADC maps
- 3. MR Perfusion Imaging
- 4. 3D TOF MRA or contrast enhancement MRA
- 5. Susceptibility weighted images (SWI)
- 6. Single voxel MRS & CSI multi voxel MRS

## **CT Findings of Acute Infarct**

- Normal (25% to 40% within 6 hours)
- Hyperdense artery sign ( 25% to 50% )
- loss of insular ribbon sign, partial disappearance of basal ganglia
- Cortical effacement, sulcal effacement
- Slight decrease in tissue density, low density in CTA source images



## **Source images of CTA**

### **Follow up CT**



the degree of leptomeningeal collaterals contrast enhancement in arterial branches beyond the occlusion occurs as an estimate of the collateral blood flow

(Wildermuth et al. 1998)

# **CT Angiography**

- Provide information of vascular stenosis or occlusion, other possible vascular lesions ( aneurysm, dissection or malformation)
- Parenchyma slight low density change in source imag es of CTA are compatible with acute infarct
- **Potential to deliver information about quality of the collateral circulation** (*Knauth et al. 1996*)



# **CT Perfusion**

## distinguishing infarct tissues from the penumbra

Entity	MTT	CBF	CBV	Non-enhanced CT
Penumbra	Elevated (>145%)	Decreased	Normal or mildly increased	Normal findings or brain swelling
Infarct core	Elevated	Markedly decreased	Markedly decreased (<2mL/100g)	Hypoattenuating parenchyma

(Wintermark M. Stroke, 2006) (De Lucas EM. RadioGraphics, 2008)

# CT Perfusion: distinguishing infarct tissues from the penumbra



## **MRI and MRA**

Confirm the insulted brain tissues
Confirm the obstructive level
Evaluation patient's outcome
Treatment planning
Exclude the possibility of emboli autolysis before thrombolysis

(20% of cases could not identify the occlusive level)



# MR perfusion

After thrombolysis Day 2

Criteria for acute fibrinolysis

PWI/DWI > 1.2

(Schellinger et al. Stroke, 2000)

DWI PWI (rMTT) MRA

Onset

1 hour

# Evolution of IA thrombolysis and thrombectomy

- IA thrombolysis (chemical thrombolysis)
- Mechanical thrombolysis
  - guidewire, catheter, snare
  - stent: Wingspan, Enterprise
- Mechanical thrombectomy
  - Merci
  - Penumbra
  - stent-Retrievers
    - \* Solitaire, Trevo.
- Aspiration: new Penumbra

**Intra-Arterial Thrombolysis** (chemical thrombolysis) **History Review:** 1.Special Writing Group of AHA (1996) considered investigational and only used in the clinical trial setting 2.PROACT I (1994-1998) the first randomized, multicenter, controlled trial 3.PROACT II (1996-1999) the only randomized, controlled, multicenter clinical trial to show the efficacy of IA thrombolysis in patients with acute ischemic stork of less six hours duration and caused by MCA occlusion

# Local Intra-arterial thrombolysis

- technically easy, sometimes ineffective and usually time consuming.
- it could take up to two hours to achieve recanalization after the procedure begins.
- only thrombolytic agent alone rarely achieve recanalization in fewer than 30 minutes, improve efficacy with adjunctive devices.
- recanalization is often incomplete
- may induce acute or delayed I.C.H

**Intra-arterial Thrombolysis** (General Technique : procedure )

- 1.direct intra-thrombus injection of thrombolytic agent (limit the agent use and prevent hemorrhage)2.progressively advance the microcatheter after partial clot dissolution
- 3.possible mechanical manipulation, clot disruption4.heparin (-/+)

# Local intra-arterial thrombolysis

Study	(n)	Drug/Dose	Window	Symptomatic ICH		Recanalization		ABSOLUTE
				drug	control	drug	control	benefit
Early trails	174	2ml UK/ 80mg tPA	6hrs	4%	-	39%	-	-
PROACT-I	46	бmg proUK	6hrs	15%	7%	58%	14%	10-12%
PROACT-II	180	9mg proUK	6hrs	10%	2%	66%	18%	15%

# Case study (1) What is the real golden time ? F/69

C.C: Slurred speech and Rt limb weakness on 7pm
P.H: HTN(+). DM(+). Drug allergy(-)
P.E: GCS:E3M5V2 pupils: 3.0mm, O.U. Bil. Eyes deviated to Lt side. Babinski's sign: R/L +/Impression: CVA. Acute Lt MCA infarction

- 0800pm to 1<sup>st</sup> hospital, complete CT study no IV TPA
- On 2<sup>nd</sup> day 0100 am: transfer to our ER (NIHSSS: 25)
- On 2<sup>nd</sup> day 0200am: MRI
- Acute I.A thrombolysis (7 hrs after onset) : total 720.000 units U.K
- On 2<sup>nd</sup> day 0400 am: finished procedure
- On 4<sup>th</sup> day : NIHSSS:25>>>4 GCS: 15 Clinical Outcome: MRS: 2 BI: 55
   Discharge on the 5<sup>th</sup> day without neurological deficit but mild memory impairment

### 95-3-11 0800 PM: non-contrast CT after symptom onset one hour


#### 95-3-12 0200 AM brain MRI and MRA : after onset 7 hours







## 0400 AM acute I.A thrombolysis: after onset 9 hours



## the next day post-procedure follow up brain CT



# Case study (2) Why IA thrombolysis is important for vertebrobasilar thromboembolic stroke ?

#### F/62

C.C: unsteady gait, dizziness and consciousness change for days, become slurred speech and drowsy

- P.H: HTN(+). DM(+).
- P.E: GCS:E3M6V3 NIHSSS:18
- Impression: CVA. Acute brain stem infarction

- 1046 am: complete CT study
- 1134 am : complete MRI study
- Acute I.A thrombolysis (> 48 hrs ): total 420.000 units U.K PTA ( 3.5x10mm balloon) for five times Aggrastat IV for conjunctive treatment
- 1440pm finished procedure
- Discharged day: NIHSSS:18>>>10 BI: 10 MRS: 4











Case study (3) common etiology: cardiogenic embolic stroke

- M/43
- Acute onset global aphasia, mild consciousness change, decrease Rt upper limb muscle power (4/5)
- Onset time: around 5am Initial GCS 15, NIHSS 11
- Procedure finished at 1200 pm, s/p 180,000 I.U urokinase infusion and clot maceration
- Compact stony hard emboli with Lt M.C.A middle third M1 segment total occlusion
- Only reopen of the Lt temporal branch, non-open of the Lt frontal branch

# Initial ER non-contrast brain CT



## **Diagnostic MRI:** three hours after onset



# **Diagnostic MRA**



## **Diagnostic D.S.A: the meniscus filling defect**



**Thrombectomy and thrombolysis** (five hours after onset)



## Partial re-open of the Lt M.C.A, good pial collaterals from A.C.A



Original techniques and devices used in the mechanical thrombolysis

- Catheter and/or wire disrupt the clot/thrombus.
- Thrombus aspiration by syringe
- Direct balloon angioplasty and/or stenting to disrupt/compress the clot and plaque.
- Snare or basket devices for thromboembolic retrieval.

## Mechanical clot removal with thrombolysis

#### Pro

- Longer time window (<8 hrs )
- Rapid re-open of occluded artery
- Less dosage or no need of thrombolytic agents, reducing the risk of ICH.

#### Con

- Limits to larger intra-cranial artery
- More invasive procedure than IAT because of larger guiding catheter, more stiffer of wire and retriever/ basket
- Potential complications: vascular spasm, dissection, perforation with intracranial hemorrhage.



Recanalization by mechanical embolus disruption during IAT in the carotid territory (AJNR 2004;25:1391-1402)



Technique of microcatheter and guide-wires disrupt the clot



Balloon disruption (BD, angioplasty) of embolism Goto et al, 1998

- 61 patients.
- Recanalization in BD vs IAT: 76.7% vs 41.9%
- Ambulatory in BD vs IAT: 70% vs 41.9%.
- Significant lower dose of urokinase was used.
- Relative less ICH in BD.



#### M/59, Gr3 SAH























## Self-expanding stents

- Advantage: more flexibility, less radial force exerted during deployment with increasing safety. Stent revascularization is immediate.
- Disadvantage: need anti-platelet therapy, only for large arterials only, cannot use for long thrombi and at bifurcation.



Neuroform - Semi-open Cell Design

#### EVOLUTION OF THROMBECTOMY TECHNOLOGY (courtesy of Penumbra, Inc)







PENUMBRA (2009) 2ND CENERATION The penumbra aspiration system involves maceration of the thrombus with a separator under direct aspiration to prevent showering of fragments. Once the catheter system is delivered to the target vessel, ongoing clot maceration is performed without the need to re-access.



SOLUMBRA (late 2012) To minimize the distance the stent retriever must travel while engaging the thrombus and mitigate the possibility of losing purchase of the dot, the stent retriever is then pulled directly into a large bore intermediate catheter while maintaining aspiration.

#### ADAPT (2013)

A large caliber aspiral on catheter that is advan :ed up to the thrombus. Direct a spiration is employed to engag and then remove the thrombus.

Spiotta AM, Chaudry MI, Hui FK, Turner RD, Kellogg RT, Turk AS. Evolution of thrombectomy approaches and devices for acute stroke: a technical review (published online ahead of print 2 January, 2014). J NeuroIntervent Surg doi:10.1136/neurintsurg-2013-011022



#### Courtesy of Pneumbra INC

The perfect device of thrombectomy should have the capacity

- Opens artery quickly
- Removes thrombus intact and completely
- Safe and simple procedure
- Economical

## NEED FOR SPEED

## Final Multivariable Model Risk Ratios

Variable	Risk Ratio	95% Confidence Interval	p-value
Time to Reperfusion (every 30 minute delay)	0.90	0.82-0.99	0.02
Baseline ASPECTS 5-10	3.70	1.25-11.00	0.01
Lack of Premorbid Disability	2.61	1.05-6.50	0.01
NIHSS =19 (vs /=20)	1.64	1.07-2.51	0.01

Every 30 minute delay in reperfusion is associated with a 10% relative reduction in probability of good clinical outcome (mRS 0-2).



<sup>1</sup> Khatri P, Yeatts SD Conference; February 6-8, 2013 NEED FOR QUALITY REVASCULARIZATION

## Revascularization Predicts Good Outcome For ICA, M1 Occlusion

	TICI=0	TICI=1	TICI=2a	TICI=2b	TICI=3	
	n= 32	n= 16	n= 67	n= 80	n= 5	
% 90 Day mRS 0-2	3.1%	12.5%	19.4%	46.3%	80%	
	6.3%			35.5%	p < .0001	
	13.9%		48.	p < .0001		

<sup>1</sup> Tomsick T. Comparison of outcome by IA approach and interpretation in light of comparative trials. Paper presented at: International Stroke Conference; February 6-8, 2013; Honolulu, HI, USA.

# NEED TO REMOVE CLOT INTACT

## Significance of New Emboli? 90-day mRS Outcome by Presence of New Emboli (ICA, M1 Occlusion)

New Emboli	N	mR		
(Core Lab)	IN	Ν	(%)	
No	172	52	30.23%	<i>12% differen<mark>c</mark></i>
Yes	28	5	17.86%	е

<sup>1</sup> Tomsick T. Comparison of outcome by IA approach and interpretation in light of comparative trials. Paper presented at: International Stroke Conference; February 6-8, 2013; Honolulu, HI, USA.

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Clots are very organized and removed intact

Clot deformed from 5MAX<sup>™</sup> tip

Courtesy of Pneumbra

# **REMOVES CLOT INTACT**





Courtesy of Penumbra

#### MERCY (Stroke 2005)









## The MERCI and multi MERCI trials results

	Pts 7	Time	Hemorrhage	Recanaliz ation	Mortality		Good outcome	
		Time		Recanaliza tion	Recanal ized	non- recanal ized	Recanalized	non- recanali zed
MERCI	141	8hrs	7.8%	48% 60%	32%	53%	46%	10%
Multi MERCI	164	8hrs	10%	54% 69%	34%		50%	
## **Outcomes of Intracranial ICA Occlusion in MERCI & Multi-MERCI I**



### 80 patients, NIHSS $20 \pm 5$ , SICH 10%

(Presented by Dr. Flint AC, International Stroke Conference 2007, San Francisco)



#### Penumbra device, courtesy of Penumbra

### The Penumbra System: A Mechanical Device for the Treatment of Acute Stroke due to Thromboembolism (Am J Neuroradiol 2008;29:1409 –13)

- Twenty-three subjects were enrolled, and 21 target vessels were treated in 20 subjects by the PS. At baseline, mean age was 60 years, mean mRS score was 4.6, and mean NIHSS score was 21.
- Postprocedure, all 21 of the treated vessels (100%) were successfully revascularized by the PS to TIMI 2 or 3. At 30-day follow-up, 9 subjects (45%) had a 4-point or more NIHSS improvement or an mRS of 2 or less. The all-cause mortality rate was 45% (9 of 20), which is lower than expected in this severe stroke cohort, where 70% of the subjects at baseline had either an NIHSS score of more than 20 or a basilar occlusion.

## Stent-retrievers (2012)

- Clinical trials (SWIFT, TREVO) showed better revascularization and better outcomes compare to MRECI.
- Works as a temporary endovascular bypass
- Less time to recanalization (<60 mins)
- Recanalization (TICI2b/3: 68-80%), good clinical outcomes (40-50%)
- Major problem: distal embolism (7-9%)
- Solution: combined aspiration and thrombectomy (Sol-umbra, Tre-Numbra)



### Solitaire<sup>™</sup> FR revascularization device Overview



Solitaire <sup>™</sup> FR Revascularization Device Ordering Information												
Reference Number	Recommended Vessel Diameter (mm)	(A) Total Length (mm)	(B) Retrieval Zone (mm)	(C) Device Diameter (mm)	(D) Push Wire Length (cm)	(E) Distal Markers	(F) Proximal Markers	Minimum Micro Catheter ID (in)				
SFR-4-15	2.0 - 4.0	26	15	4	180	3	1	0.021				
SFR-4-20	2.0 - 4.0	31	20	4	180	3	1	0.021				
SFR-6-20	3.0 - 5.5	31	20	6	180	4	1	0.027				
SFR-6-30	3.0 - 5.5	42	30	6	180	4	1	0.027				

The Solitaire<sup>™</sup> FR device's unique over-lapping Parametric<sup>™</sup> design







The Solitaire<sup>™</sup> FR device with Parametric<sup>™</sup> Design provides multiple planes of clot contact to

capture thrombus.<sup>3</sup>

\*Simplicity claims based on devices required per Instructions Per Use.

## Parametric <sup>™</sup> Design on Cell

- Overlaps stent walls allowing the device to unfurl in larger vessels and refold in smaller.
- Maintains cell size regardless of vessel size.
- Automatically resizes for simple deployment and continuous clot adhesion upon retrieval.
- Provides a **double layer of clot adhesion** in smaller vessels.







### Courtesy of Covidien



## FIRST GENERATION DEVICES: LONG PROCEDURE

97 mi<u>n<sup>1</sup></u>

### $79 - 120 \min^{2,3}$

7% Solitaire Trevo<sup>2</sup> Proximal aspiration has limited effect at the site of occlusion Trevo and **Solitaire**<sup>™</sup>

1. The Penumbra Pivotal Stroke Trial Investigators. The Penumbra Pivotal Stroke Trial: Safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease. Stroke. 2009;40:2761-2768. 2. Kass-Hout O, Sun C-H J, et al. Clinical, angiographic and radiographic outcome differences among mechanical thrombectomy devices: initial experience of a large-volume center (published online ahead of print March 21, 2014). J NeuroIntervent Surg. doi:10.1136/neurintsurg-2013-011037.

3. Nguyen T, Malisch T, Castonguay AC, et al. Balloon guide catheter improves revascularization and clinical outcomes with the Solitaire device. Analysis of the North American Solitaire Acute Stroke Registry (published online ahead of print December 3, 2013). Stroke. doi:10.1161/STROKEAHA.113.002407.



Spiotta AM, Chaudry MI, Hui FK, Turner RD, Kellogg RT, Turk AS. Evolution of thrombectomy approaches and devices for acute stroke: a technical review (published online ahead of print 2 January, 2014). J NeuroIntervent Surg. doi:10.1136/neurintsurg-2013-011022.

## Outcome summary (courtesy of Penumbra, Inc)

	Merci	Original Penumbra System™	Stent Retriever	"Solumbra"	5MAX	ACE
Author	Kass-Hout (JNIS 2014)			Humphries (JNIS 2014)	Turk (JNIS 2014)	
n	81	91	115	105	44	44
TICI 2b/3	70%	78%	86%	88%	96%	98%
TICI 3	14%	9%	37%	44%	41%	61%
Puncture to Revas	91 min	75 min	79 min	57 min	38 min	36 min
sICH	7%	6%	7%	5%	0%	0%
mRS ≤ 2 at 90 days	25%	41%	36%	44%	34%	50%

Kass-Hout T, Kass-Hout O, Sun C-H J, et al. Clinical, angiographic and radiographic outcome differences among mechanical thrombectomy devices: initial experience of a large-volume center (published online ahead of print 21 March, 2014). J NeuroIntervent Surg. doi:10.1136/neurintsurg-2013-011037.

Humphries 🛞 Joit D, Doss VT, et al. Distal aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke (published online ahead of print 2 January, 2014). J NeuroIntervent Surg. doi:10.1136/neurintsurg-2013-010986.

Turk AS, Frei D, Fiorella D, et al. ADAPT FAST study: a direct aspiration first pass technique for acute stroke thrombectomy (published online ahead of print 25 February, 2014). J NeuroIntervent Surg. doi:10.1136/neurintsurg-2014-011125.

# Conclusions

- Team work: EMS, ER, neurologist, interventional neuroradiologist, anesthetist, NCU, neurosurgeon.
- Short interval between onset & treatment correlate with higher rate of re-canalization and improved outcome.
- Trans-IA thrombectomy with recanalization of occluded artery is one of important role in managing acute ischemic stroke with good clinical outcomes in selected patients.
- New device associating with good quality of recanalization, shortening of procedural timing may have better clinical outcomes.

- F/70 years old
- Adenocarcinoma of left lower lobe of lung, patient underwent LLL lobectomy on 2015/04/29.
- Acute ischemic stroke at the 2015/05/01, 1640pm.



Brain CT (onset <60 mins DSA onset <3 hrs















### Onset 5 hrs

### 2015/05/03



### 2015/05/18



## **Thank You for Your Attention**

