現代生醫訊號分析於重症病患之應用

國泰醫院神經外科

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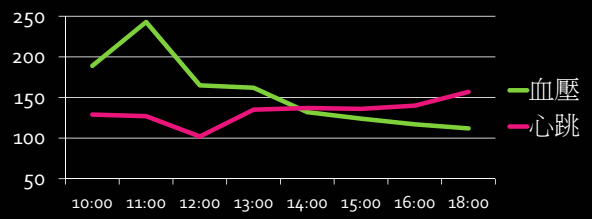
臨床實例

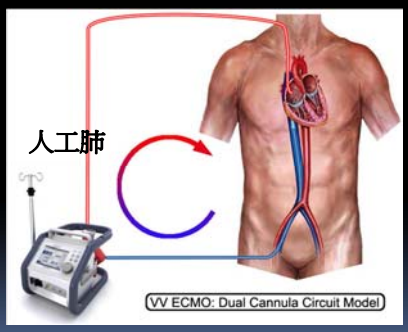
- 49歲男性嚴重車禍
- 救護車到現場時, 已無心跳呼吸, 瞳孔放大
- 到急診室以後給予急救，不到五分鐘，就有心跳了, 瞳孔也縮小了

臨床實例



- 急救成功後，在強心劑支持下, 血壓依舊不斷下滑，是否要不顧代價的搶救?
  - 否: 沒有任何活下來的機會
  - 是: 萬一救活了變成植物人，家屬無法接受，並成為家庭與社會的沉重負擔

葉克膜維生系統



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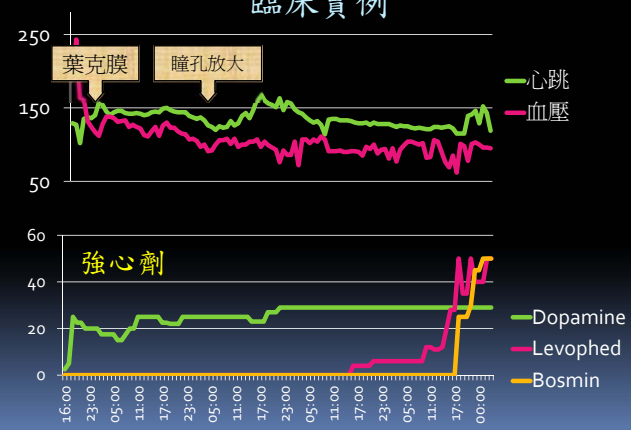

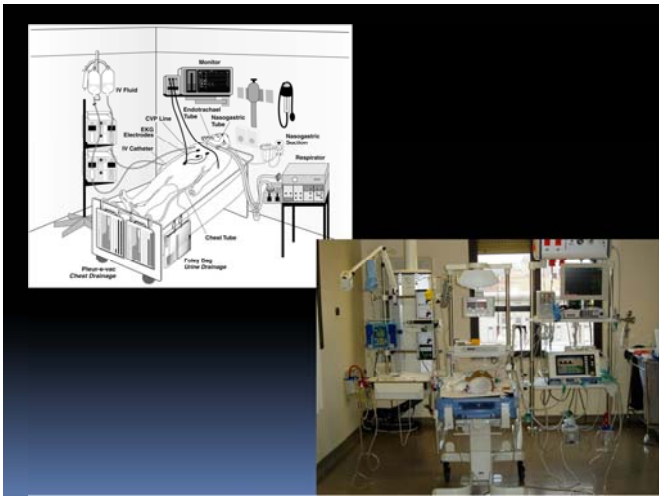

演講大綱

- 臨床常見之生物訊號
- 現代生醫訊號之兩大目標
  - Measure important physiological parameters
  - Disease/Severity classification
- 結論與展望

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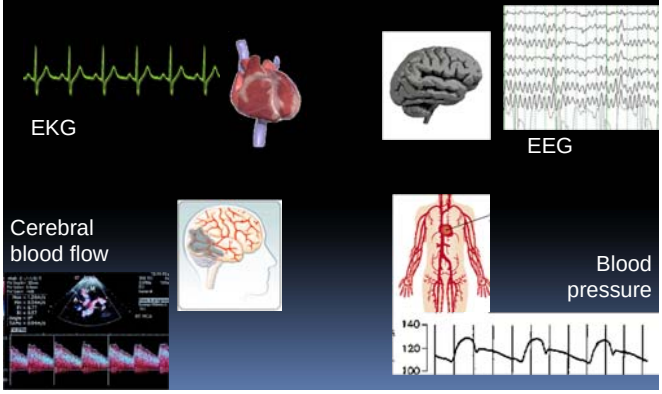

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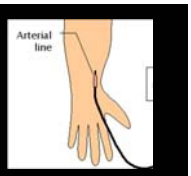
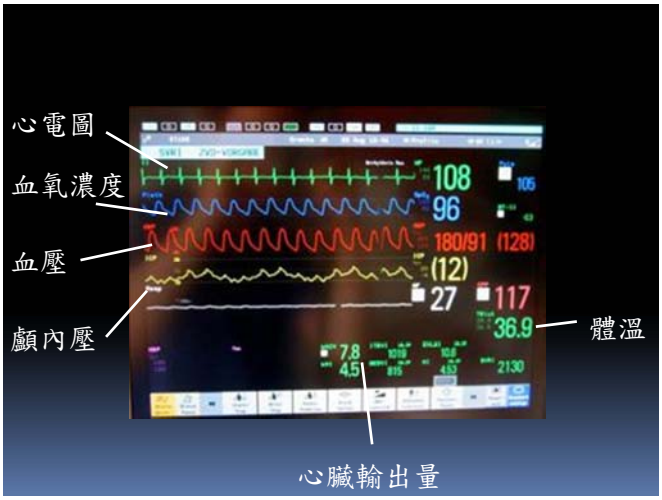
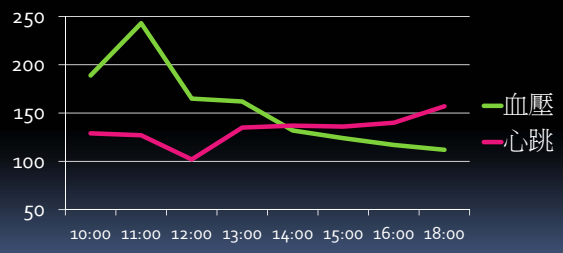


- Non-invasive
  - 心電圖，腦波，血氧濃度，體溫...
- Minimal invasive
  - 動脈壓，中心靜脈壓
- Invasive
  - 顱內壓，腦組織氧氣濃度，心臟輸出量



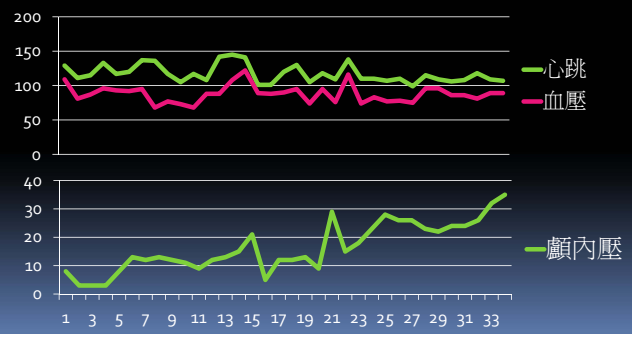
Usefulness of conventional biosignals

案例一



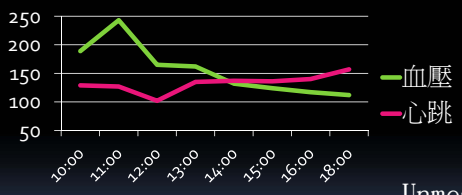
Usefulness of conventional biosignals

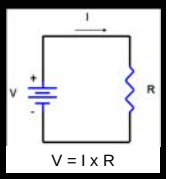
案例二



Limitations of conventional monitoring

案例一





Unmeasurable

Blood pressure
= Cardiac output X Vascular resistance
= (Heart rate X Stroke volume) X Vascular resistance

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Modern biosignal analysis

- Measure important physiological parameters
  - Many physiological parameters were still unmeasurable in human
  - Many physiological parameters were measured from invasive/risky procedures

Modern biosignal analysis

- Measure important physiological parameters
  - Traditionally unmeasurable
    - 腦血流自動控制、自主神經系統
  - Use non-invasive / minimal invasive to derive parameters
    - 心輸出量、顱內壓

Non - invasive
Minimal invasive
→ Invasive

Important physiological parameters

EKG → 自律神經系統 (Autonomic nervous activity)

EKG → 感壓反射 (Baroreceptor reflex)

BP → 感壓反射 (Baroreceptor reflex)

BP → 心臟輸出量 (Cardiac output)

BP → 腦血流自動控制 (Cerebral autoregulation)

Cerebral blood flow → 腦血流自動控制 (Cerebral autoregulation)

Cerebral blood flow → 顱內壓 (Intracranial pressure)

Important physiological parameters

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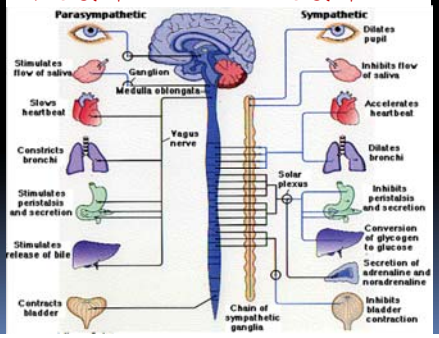
自律神經系統 (Autonomic nervous system)

副交感神經 交感神經

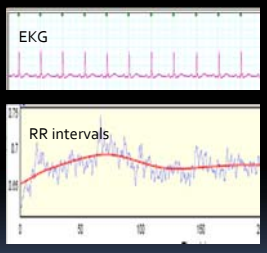


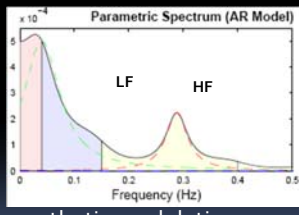
自律神經系統 (Autonomic nervous system)

- 傳統臨床上
  - 交感神經系統：Plasma catecholamine
  - 副交感神經系統：無法測量

自律神經系統 (Autonomic nervous system)

HRV analysis



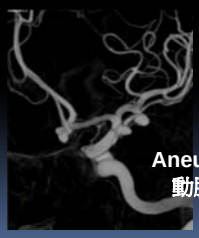


LF: sympathetic modulation
HF: Parasympathetic modulation

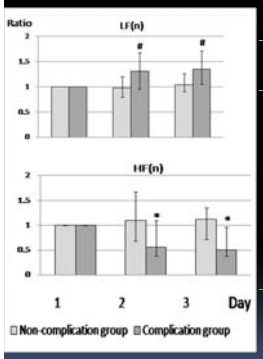
Eur Heart J 1996;354-81

自律神經系統 (Autonomic nervous system)

應用1: 腦部自發性出血



Acta Neurochir 2009;151:1631-7



Logistic regression

	Regression coefficient	Odds ratio*	P value
Age	0.003	1.00	0.96
Female gender	-1.52	0.22	0.19
Clinical severity	2.44	11.47	0.04
LF/HF increment	2.71	14.98	0.02

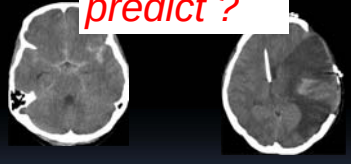
*Non-complication group as reference

Acta Neurochir 2009;151:1631-7

First insult Second insult

Neurogenic pulmonary edema
神經性肺水腫

Can we predict ?



Cerebral vasospasm related infarction
腦血管痙攣合併缺血性中風

Day 1 First insult → Sympathetic overactivity → Day 3 – 14 Second insult: early

Non-invasive Minimal invasive → Invasive or traditionally unmeasurable

EKG → 自律神經系統 (Autonomic nervous activity)

感壓反射 (Baroreceptor reflex)

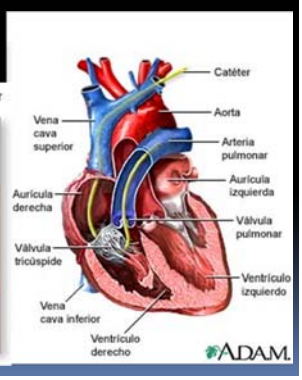
BP → 心臟輸出量 (Cardiac output)

腦血流自動控制 (Cerebral autoregulation)

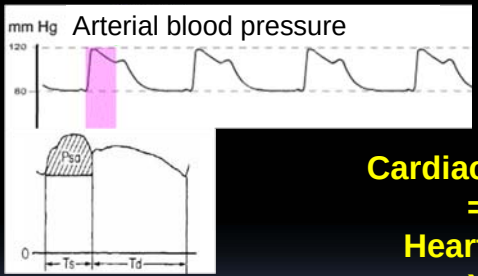
Cerebral blood flow → 顱內壓 (Intracranial pressure)

心臟輸出量 (Cardiac output)

- 傳統臨床上
  - Swan ganz catheter



心臟輸出量 (Cardiac output)

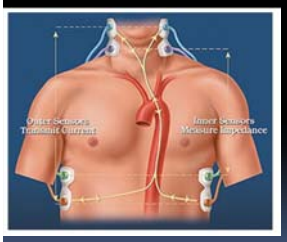


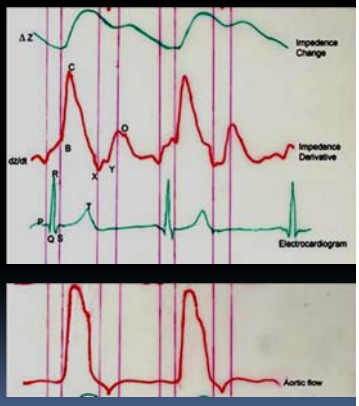
Cardiac output = Heart rate X Stroke volume

Pressure area during systole is proportional to stroke volume

Curr Opin Anaesthesiol 2009;22:71-77

Electrical impedance cardiography





Curr Opin Anaesthesiol 2009;22:71-77

CO technique	Invasiveness	Intermittent versus continuous	Limitations	Additional information
PAC BTCO	+++	Intermittent	PAC-related complications Arrhythmias Tricuspid regurgitation Intracardiac and extracardiac shunts Injected indicator volume	CVP, PAP, PCWP, SvO_2
PAC CCO	+++	Continuous	PAC-related complications Larger temperature shifts Intracardiac and extracardiac shunts Fast infusions	CVP, PAP, PCWP, SvO_2
TPCO	++	Intermittent	Arrhythmias Large temperature shifts Intracardiac and extracardiac shunts	GEDV, EVLW, PPV
LiDCO	++	Intermittent + continuous	Arterial signal quality Rapid changes in vascular motor tone	CBV
APCO	+	Continuous	Arterial signal quality Rapid changes in vascular motor tone IABP	SVV, SV, CI, SVI
PCCO-PulseCO	++	Continuous	Arterial signal quality Rapid changes in vascular motor tone	SVV
EDCO	+	Continuous	Esophageal disorder Turbulent flow Operator-dependent	Flow time
TTE/TEE	±	Intermittent	Esophageal disorder Operator-dependent	Anatomic and functional cardiac assessment
PDDCO	+	Continuous	Peripheral signal detection Allergy to indocyanin green	Intravascular blood volume
Bioimpedance	-	Continuous	Movement artefacts Thoracic fluid overload Abnormal thoracic anatomy Cardiac valve disease Intracardiac and extracardiac shunts Tachyarrhythmias	PEP, LVET

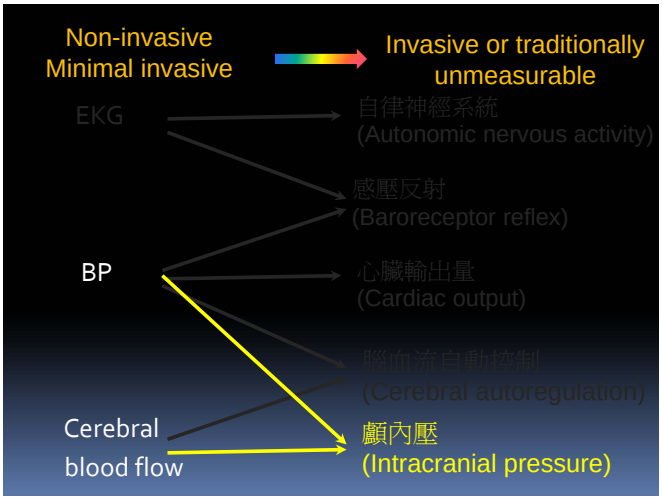
Curr Opin Anaesthesiol 2009;22:71-77

心臟輸出量 (Cardiac output)

- 應用1:

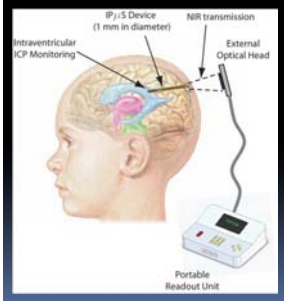
Blood pressure
= Cardiac output x
Vascular resistance
= (Heart rate x
Stroke volume) x
Vascular resistance

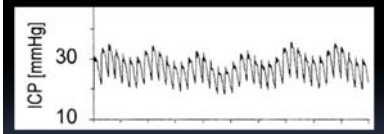
如何拉高血壓?
增加Stroke volume，適度降低Heart rate



顱內壓 (Intracerebral pressure, ICP)

- Need surgery to implant the monitor





顱內壓 (Intracerebral pressure, ICP)

Simulation

- Arterial blood pressure → Intracranial pressure

$$\mathrm{ICP}(t) = \int_0^\infty w(\tau) * \mathrm{ABP}(t-\tau)\, d\tau.$$

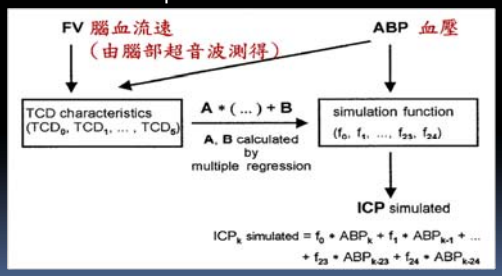
$$\mathrm{ICP}_k = w_0 * \mathrm{ABP}_k + w_1 * \mathrm{ABP}_{k-1} + \ldots + w_{23} * \mathrm{ABP}_{k-23} + w_{24} * \mathrm{ABP}_{k-24}.$$

- How to get ($w_0, w_1, w_2 \ldots\ldots w_{24}$) ?

*Comp Biomed Res*1998;31:231-43

顱內壓
(Intracerebral pressure, ICP)

- Arterial blood pressure ↔ Cerebral blood flow velocity



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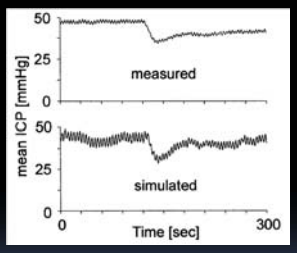
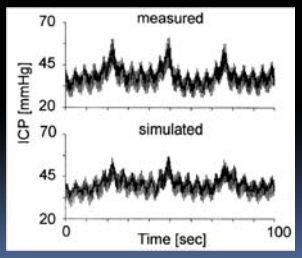
顱內壓
(Intracerebral pressure)





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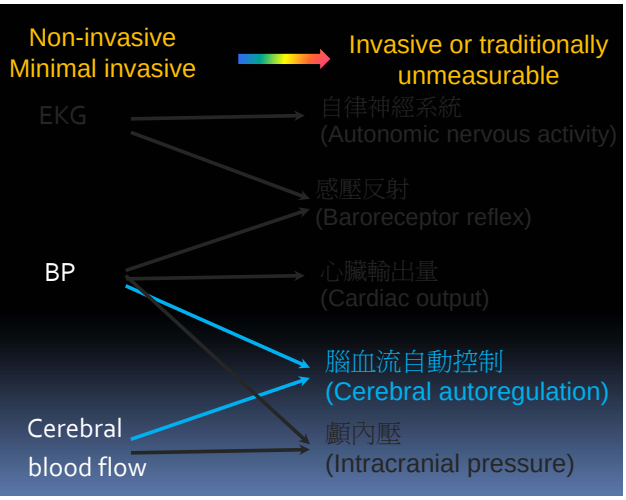
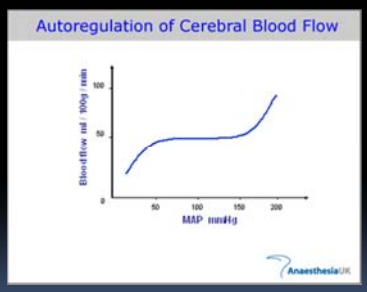


腦血流自動控制
(Cerebral autoregulation)



保持腦部血流恆定，不受血壓浮動影響

腦血流自動控制
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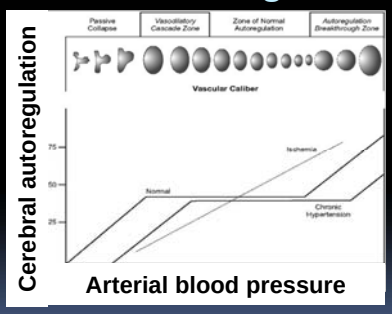

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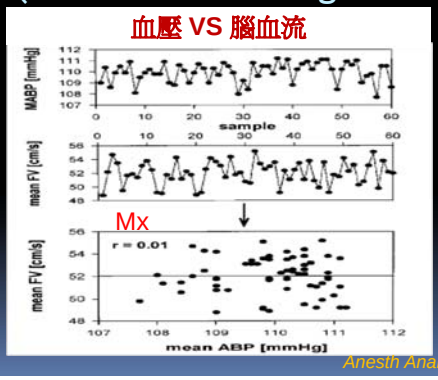

Anesth Analg 2004;98:1133-9

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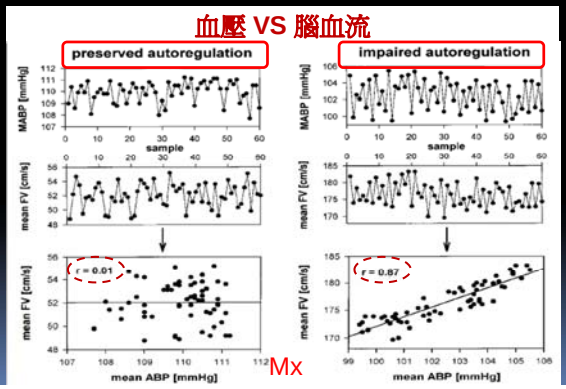

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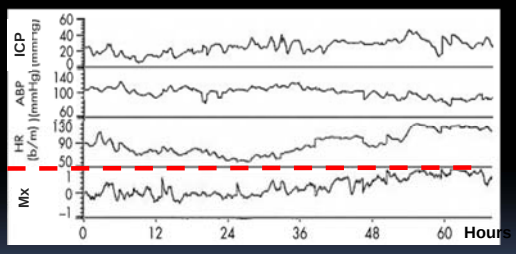

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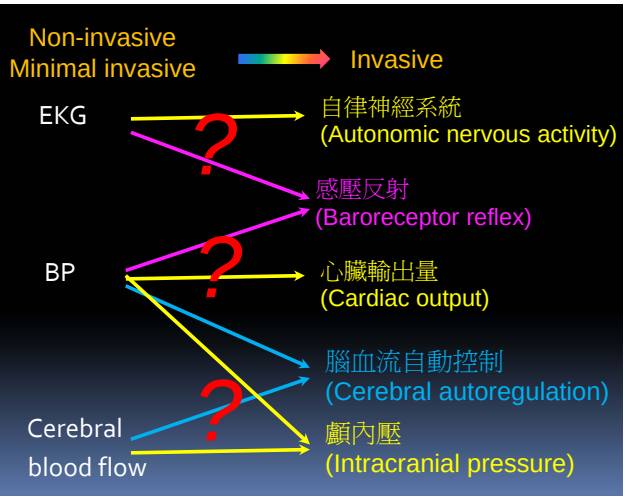

Are they clinically reliable ?

- All algorithms have basic assumptions:
  - It may apply to certain circumstances, but not necessarily others
- Is gold standard really standard?
- Same parameters simulated by different algorithms cannot be compared unless cross validation has been made
- Myth: Is invasive monitoring really should be abandoned?

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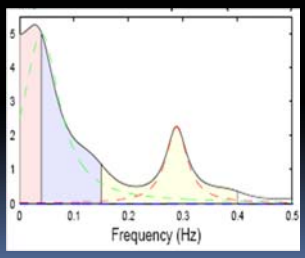

LF (0.04-0.14Hz): sympathetic modulation
HF(0.14-0.40Hz): Parasympathetic modulation

Problems
- RR tachograms are not absolutely linear system
- The definition of frequency band is artificial

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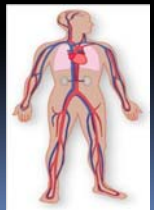
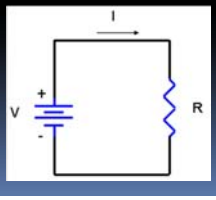
Voltage = Current x Resistance

Blood pressure = Cardiac output x Vascular resistance





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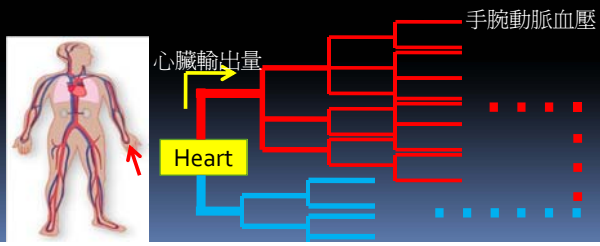
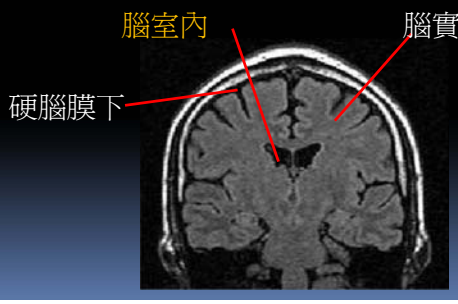


Are they clinically reliable ?

- Is gold standard really standard?
  - ICP can be inserted at different location of brain parenchyma



Are they clinically reliable ?

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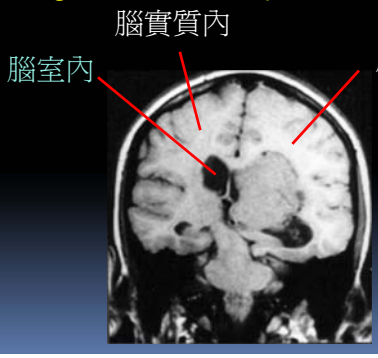
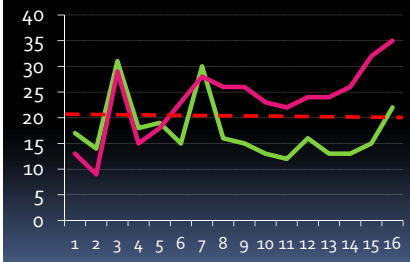


Are they clinically reliable ?

- Is gold standard really standard?



Are they clinically reliable ?

- Same parameters simulated by different algorithms cannot be compared unless cross validation has been made

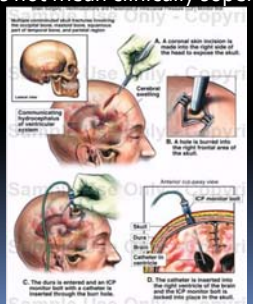
Table 2 Overview of the accuracy of different cardiac output monitoring techniques, compared with a reference technique

First author [reference]	Experimental technique	Reference technique	Setting: Location	Setting: Population	Bias	Precision (2 SD)	95% CI	ME (%)
Chakravarthy *et al.* [19]	PAC CCO	PAC BTCO	OR	Off-pump CABG	0.03	1.40	−1.37–1.43	NA
Bao and Wu [18]	PAC CCO	PAC BTCO	OR	Liver transplantation	−0.18	1.91	−2.09–1.73	22
Spöhr *et al.* [7]	TPCO	PAC CCO	ICU	Septic shock patients	0.20	2.20	−2.00–2.40	25
Costa *et al.* [21]	LiDCO	PAC BTCO	ICU	Liver transplantation	0.11	1.94	−1.84–2.05	24
De Waal *et al.* [31]	APCO	TPCO	OR and ICU	CABG	0	0.87	−1.71–1.71	33
Sakka *et al.* [35]	APCO	TPCO	ICU	Sepsis	0.50	4.60	−4.1–5.1	69
Button *et al.* [6]	APCO	PAC BTCO	OR and ICU	Cardiac surgery: several time points	0.10 to 0.60	1.8–2.6		43–48
de Waal [47•]	SVI-K	TPSVI	OR and ICU	CABG	1.0	10.8	−20.2–22.1	63
	SVI-SB	TPSVI	OR and ICU	CABG	9.8	11.4	−12.5–32.2	67
	SVI-W	TPSVI	OR and ICU	CABG	−15.7	8.2	−31.6–0.3	48
Gujjar *et al.* [48]	CO-K	PAC BTCO	ICU	Postcardiac surgery (± IABP)	−0.07	1.37	−1.44–1.30	26
Zoremba *et al.* [49]	EV-CO	PAC BTCO	ICU	Critically ill patients	−0.05	1.42	−1.47–1.37	27
Raval *et al.* [50•]	Bioreactance CO	PAC BTCO	CL	Cardiac catheterization laboratory	−0.18	2.04	−2.21–1.87	NA

Curr Opin Anaesthesiol 2009;22:71-77

Are they clinically reliable ?

- Myth: Is invasive monitoring really should be abandoned?
  - High-tech does not mean clinically superior



Are they clinically reliable ?

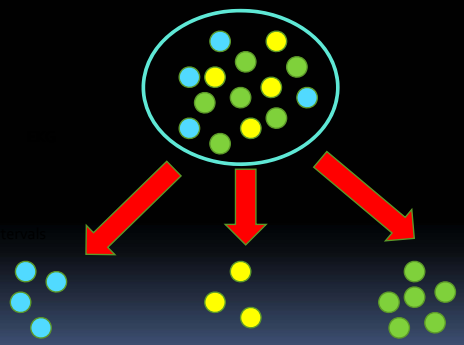
- All algorithms have basic assumptions:
  - It may apply to certain circumstances, but not necessarily others
- Is gold standard really standard?
- Same parameters simulated by different algorithms cannot be compared unless cross validation has been made
- Myth: Is invasive monitoring really should be abandoned?

➔ *商機無限*

演講大綱

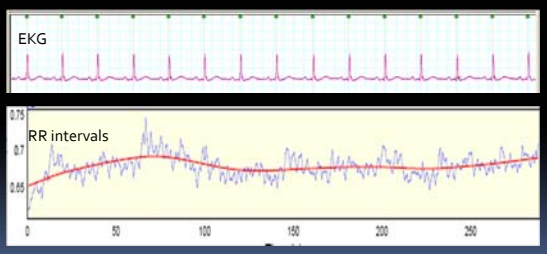
- 臨床常見之生物訊號
- 現代生醫訊號之兩大目標
  - Measure important physiological parameters
  - Disease/Severity classification
- 結論與展望

Disease/Severity Classification



Disease/Severity Classification

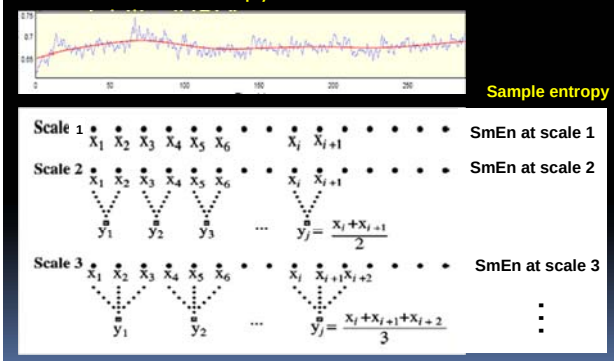
Multiscale entropy of heart rate variability(HRV)



Physical Review 2005;71:021906

Disease/Severity Classification

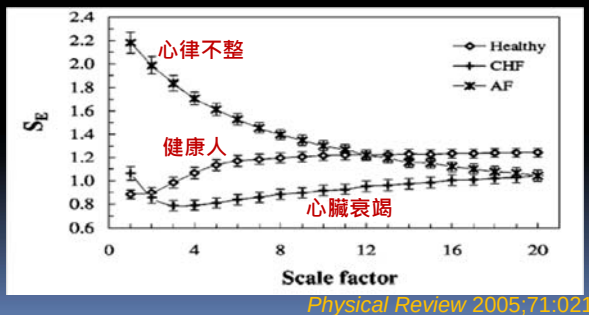
Multiscale entropy of heart rate



Physical Review 2005;71:021906

Disease/Severity Classification

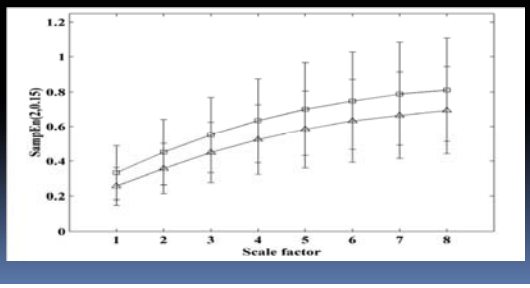
Multiscale entropy of HRV於心臟疾病之分類



Physical Review 2005;71:021906

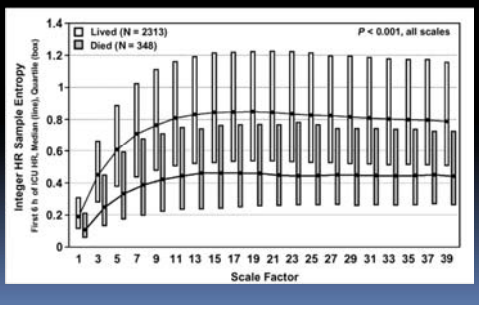
Disease/Severity Classification

- Fetal heart beat
  - Normal birth fetus *VS* distressed fetus at birth

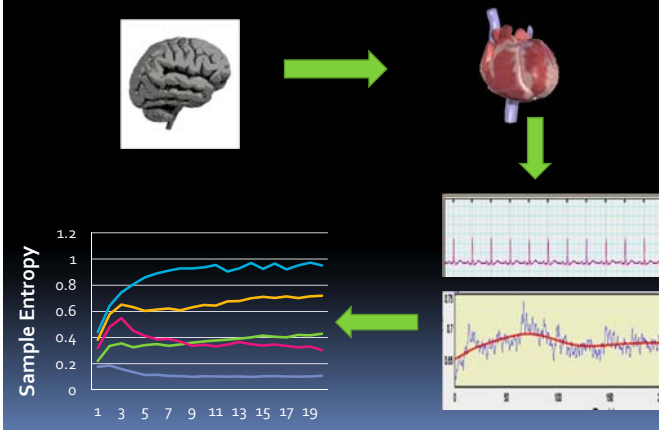


Disease/Severity Classification

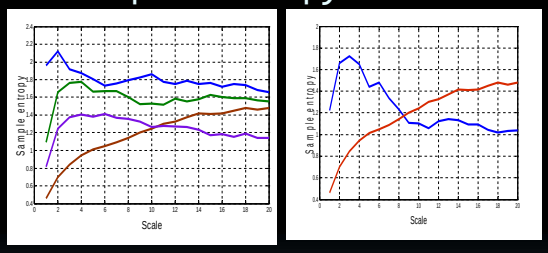
- Trauma pateints
  - Lived *VS* Died



Disease/Severity Classification



1. Sample entropy value



Complexity indicator

1. Area under curve (AUC)
2. Compare entropy between largest and lowest scale
   - △ S (=SmEn at scale 20 - scale 1)
   - Ratio_S (=SmEn at scale 20 / scale 1)

Complexity indicators of MSE

- Complexity indicators of MSE curve
  - AUC
  - △ S (=SmEn at scale 20 – scale
  - Ratio_S (=SmEn at scale 20 / scale 1)
- Different physiological condition has different effect on each indicator

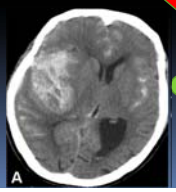
Complexity indicators of MSE

Two examples of classification

- Deep anesthesia VS. Deep coma
- Severity classification in patients with intracranial hemorrhage

Cardiac complexity in comatose individuals

昏迷病患



深度麻醉

腦部功能不足

麻醉對MSE之影響

麻醉前 — 清醒

誘導期

維持期

— 無意識

催醒期 — 半夢半醒

麻醉後 — 清醒

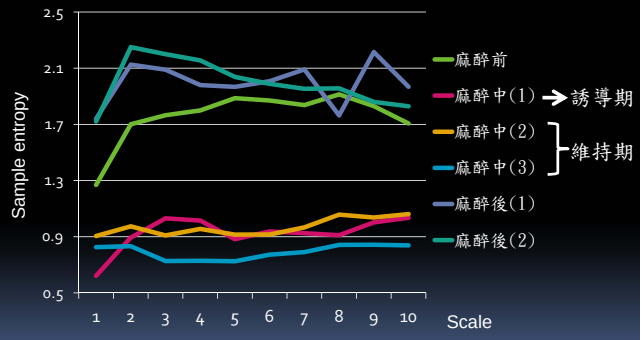
麻醉對MSE之影響

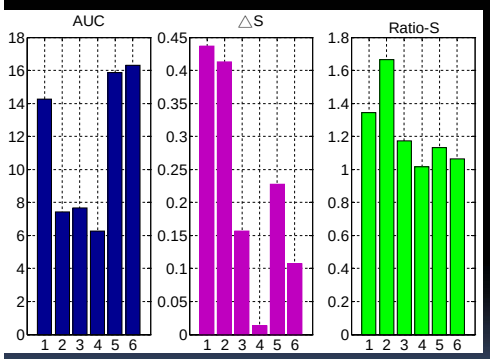
麻醉誘導期

麻醉維持期

麻醉催醒期

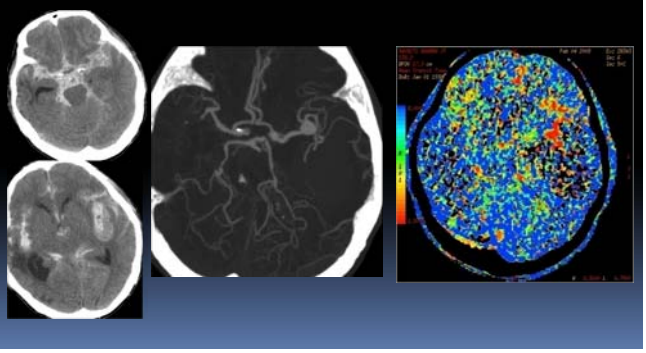
麻醉對MSE之影響



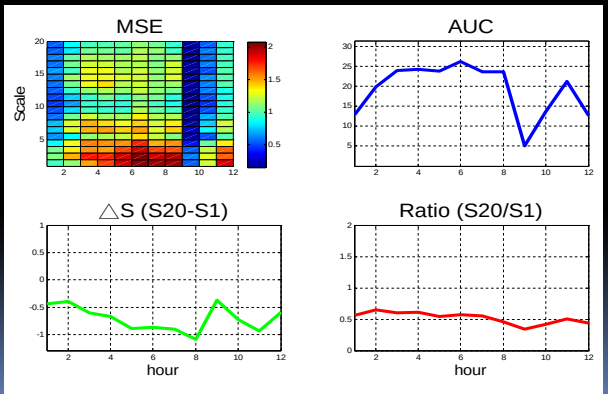


1: 麻醉前
2: 麻醉中(1)
3: 麻醉中(2)
4: 麻醉中(3)
5: 麻醉後 (1)
6: 麻醉後 (2)

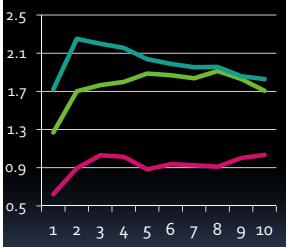
嚴重腦損傷對MSE之影響



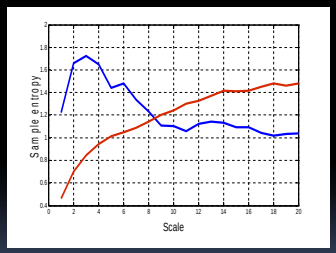
嚴重腦損傷對MSE之影響



麻醉和腦部損傷同樣會造成病患昏迷，但對MSE curve的effect是不同的



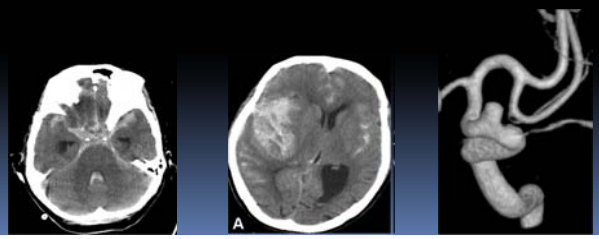
AUC改變，但Ratio_S變動不大



AUC變動不大，但Ratio_S由>1 → <1

蜘蛛膜下腔出血(SAH)對MSE之影響

- **SAH: 1-7% of all strokes**
- **Up to half of all cases are fatal and 10-15% die before reaching a hospital**

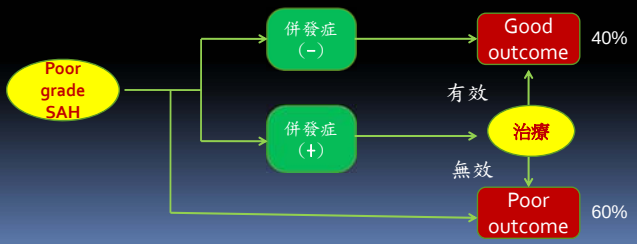


蜘蛛膜下腔出血之臨床嚴重度分級

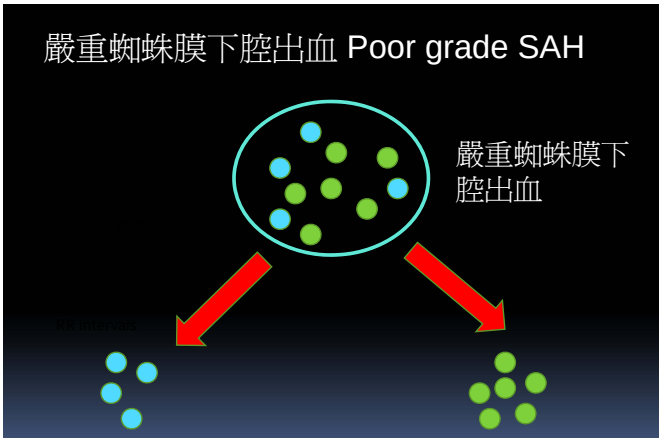
Grade	Signs and symptoms	Survival
1	Asymptomatic or minimal headache	70%
2	Moderate to severe headache; no neurologic deficit except cranial nerve palsy	60%
3	Drowsy; minimal neurologic deficit	50%
4	Stuporous; possibly early decerebrate rigidity and vegetative disturbances	20%
5	Deep coma; decerebrate rigidity; moribund	10%

嚴重蜘蛛膜下腔出血 Poor grade SAH

- The greatest issue is to find out a reliable way to early predict possible outcomes of the poor-grade patients after treatment

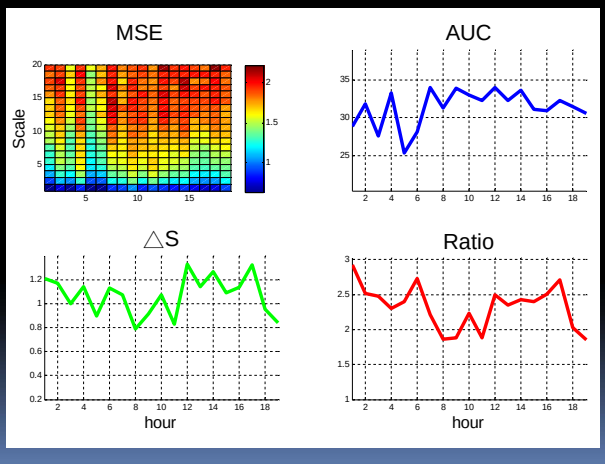


嚴重蜘蛛膜下腔出血 Poor grade SAH



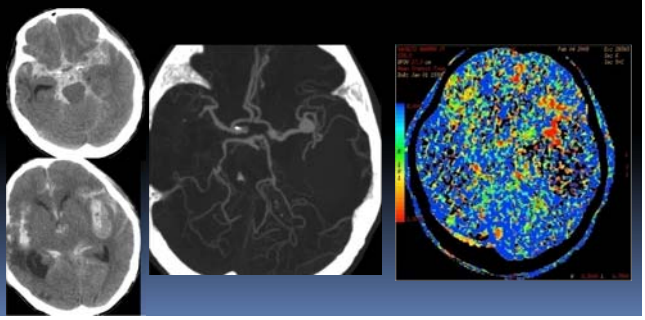
Case illustration

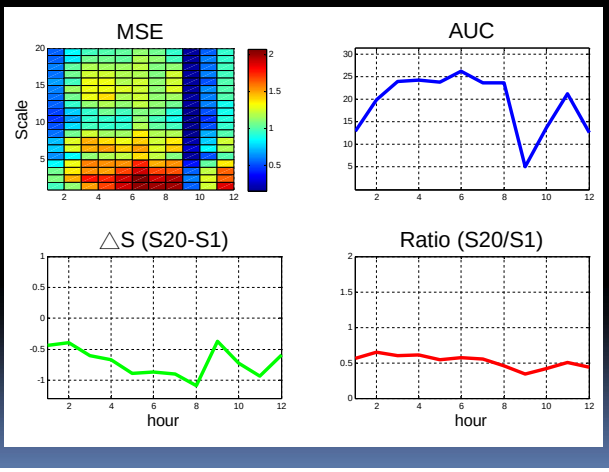
Case 2: 61 year-old female, E1M5Vt
No surgery ➔Good outcome



Case illustration

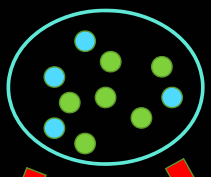
Case 40: 52 year-old female, E1M1Vt
No surgery





嚴重蜘蛛膜下腔出血 Poor grade SAH

MSE analysis of HRV

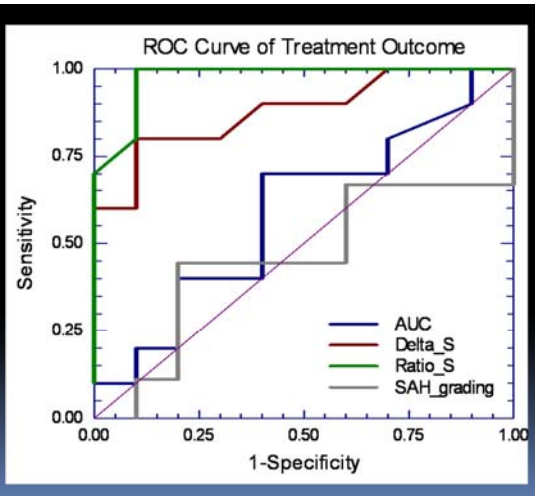


嚴重蜘蛛膜下腔出血

Treatment outcome

Good

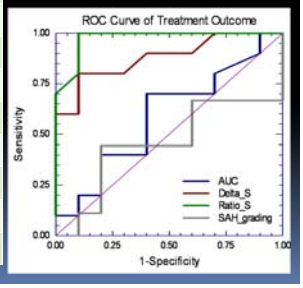
Poor

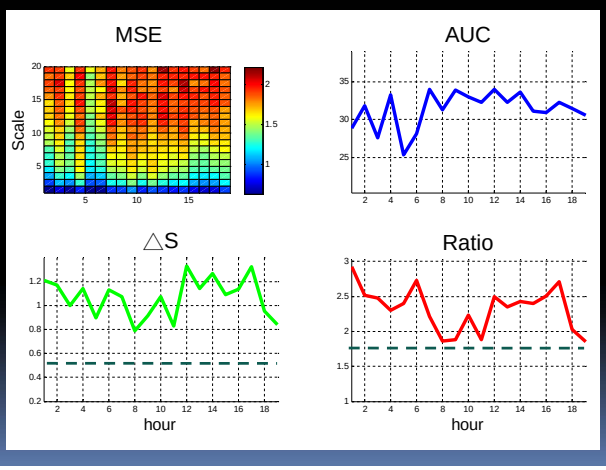


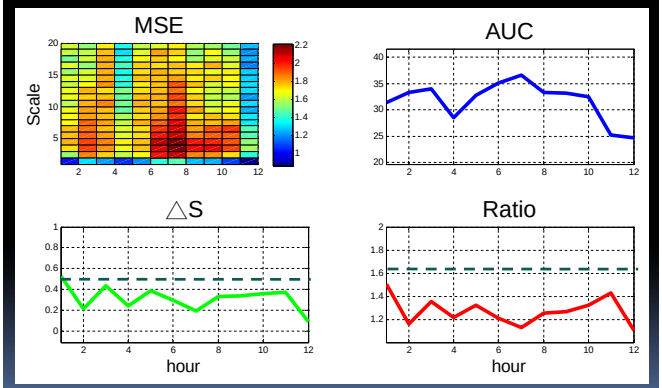
Prognostic values of each index

		Area-under-curve of ROC	95% confidence interval	one-sided P value
SAH grading		0.46	0.12-0.70	0.38
MSE related indicator	AUC	0.60	0.28-0.80	0.30
	△S (S20-S1)	0.87	0.57-0.96	<0.01
	Ratio_S (S20/S1)	0.98	0.80-0.99	<0.01

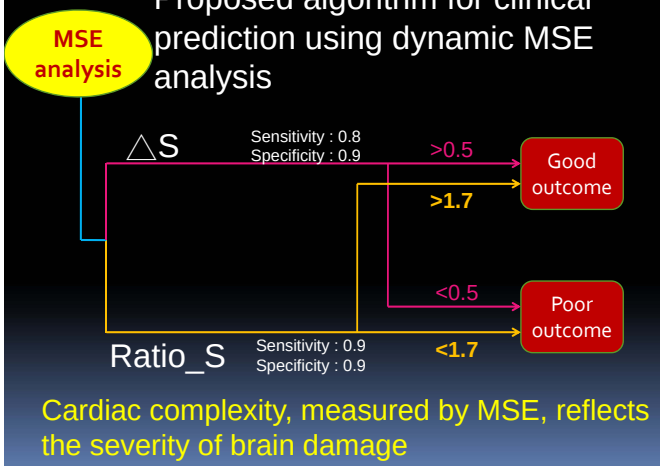
Cut-off value	Sensitivity	Specificity
△S (S20-S1)		
0.45	0.7	0.9
0.49	0.8	0.9
0.53	0.8	0.9
0.57	0.8	0.8
0.61	0.8	0.8
0.65	0.8	0.7
Ratio_S (S20/S1)		
1.52	0.7	1
1.66	0.9	0.9
1.81	0.9	0.9
1.96	1	0.7
2.11	1	0.5







Proposed algorithm for clinical prediction using dynamic MSE analysis



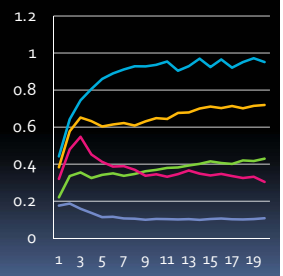
Cardiac complexity, measured by MSE, reflects the severity of brain damage

Complexity indicators of MSE

- Complexity indicators of MSE curve
  - AUC
  - △ S (=SmEn at scale 20 – scale
  - Ratio_S (=SmEn at largest scale/ smallest scale)
- Different physiological condition has different effect on each indicator

Complexity indicators of MSE

- Complexity indicators of MSE curve
  - (AUC)
  - △S
  - Ratio_S
- Hypothesis: Ratio_S is the most deterministic complexity parameter

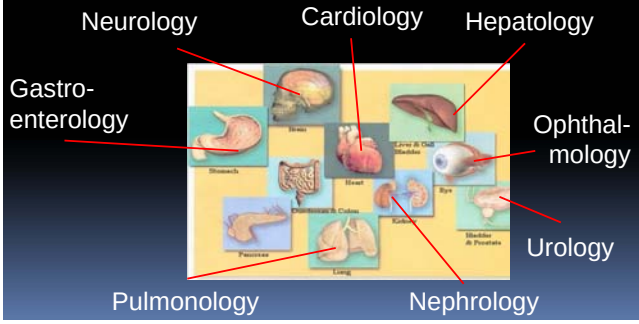


演講大綱

- 臨床常見之生物訊號
- 現代生醫訊號之兩大目標
  - Measure important physiological parameters
  - Disease/Severity classification
- 結論與展望

結論與展望

- 適當的生理訊號分析可以在某種程度上反映某器官系統的表現



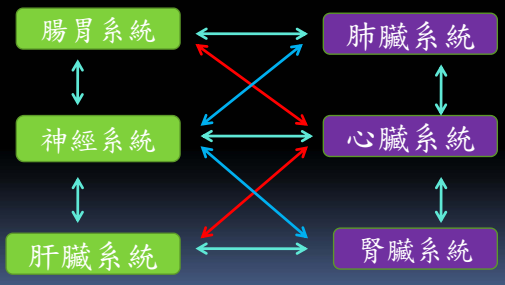
結論與展望

- Measure important physiological parameters

Non - invasive → Invasive

Minimal invasive → Invasive

- Disease/Severity classification



結論與展望

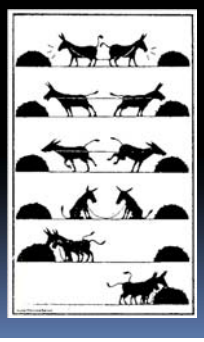
Future challenges

- More clinical applications
- Real time monitoring
- Multimodality monitoring and analyses
- Cloud computing

Ultimate goal

電腦資訊專家

訊號分析專家



生物醫學專家

Thanks for your attention