An example of machine integration

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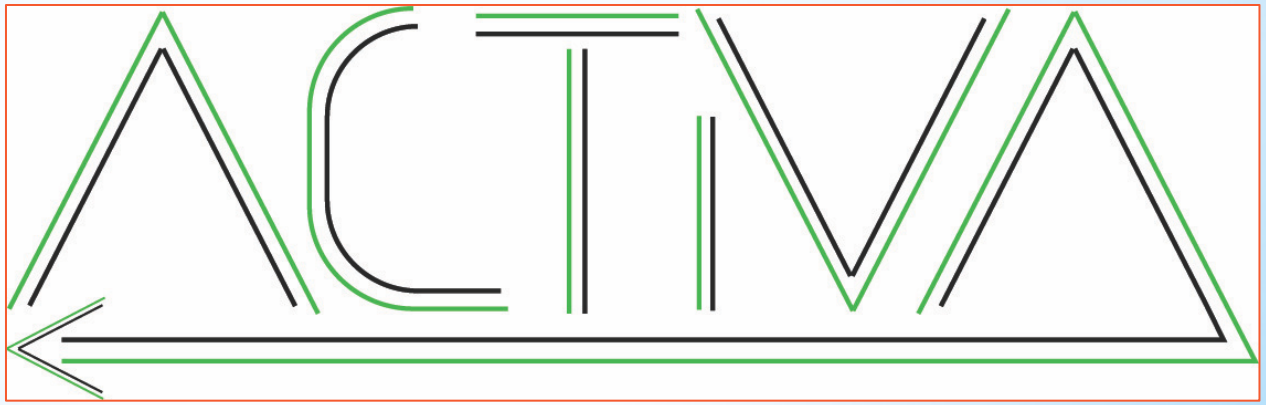
ACTIVA: Automatic Control in Total Intra Venous Anesthesia

Outline

- Take a look at the system's components
  - System Set-Up
- Explanation of GUI (Graphic User Interface)
- Simulator mode
  - Ready to go
  - Induction phase
  - Maintenance phase (surgical phase)
  - Patient waking up
- Clinical Case(s)
- Competitors
- Conclusions



System components

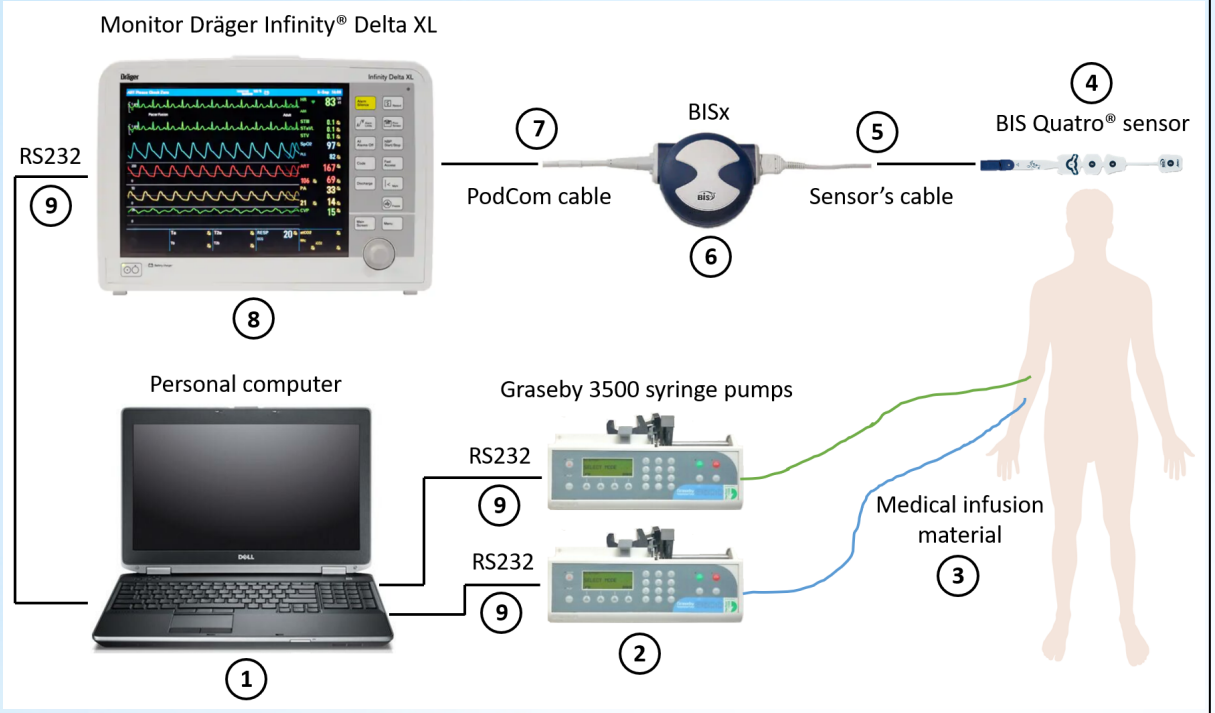


Figure 4.1: *Diagram of the control system instrumentation.*

1. **Personal computer** with **ACTIVA software**
2. **Syringe pumps** (Graseby 3500 - Smiths Medical, London, UK).
    1. Syringe pumps represent the control system's actuators.
    2. They are driven by the control algorithm.
    3. Two pumps are required, one for propofol and one for remifentanil.
3. **Venous Line Access** for drug's infusion (should be dedicated, or if not possible must be as close as possible the venous catheter to avoid boluses)
4. **BIS Quatro sensor** is the control system's sensor. It is composed by 4 electrodes placed on the patient's forehead that read EEG waves.
5. **Sensor's cable** is used to connect the BIS Quatro sensor to the BISx device.
6. **BISx** is the device that performs the required calculations in order to obtain the BIS index from the raw EEG waves read by the sensor
7. **PodCom cable** is used to connect the BISx device to the monitor
8. **Monitor** Drager Infinity Delta (Dragerwerk,Lübeck,DE) provides the BIS signal and other patient's parameters to the control algorithm.
9. **Three USB to RS232 DB9 serial adapter** cables are required in order to allow the communication of the personal computer with monitor and syringe pumps.

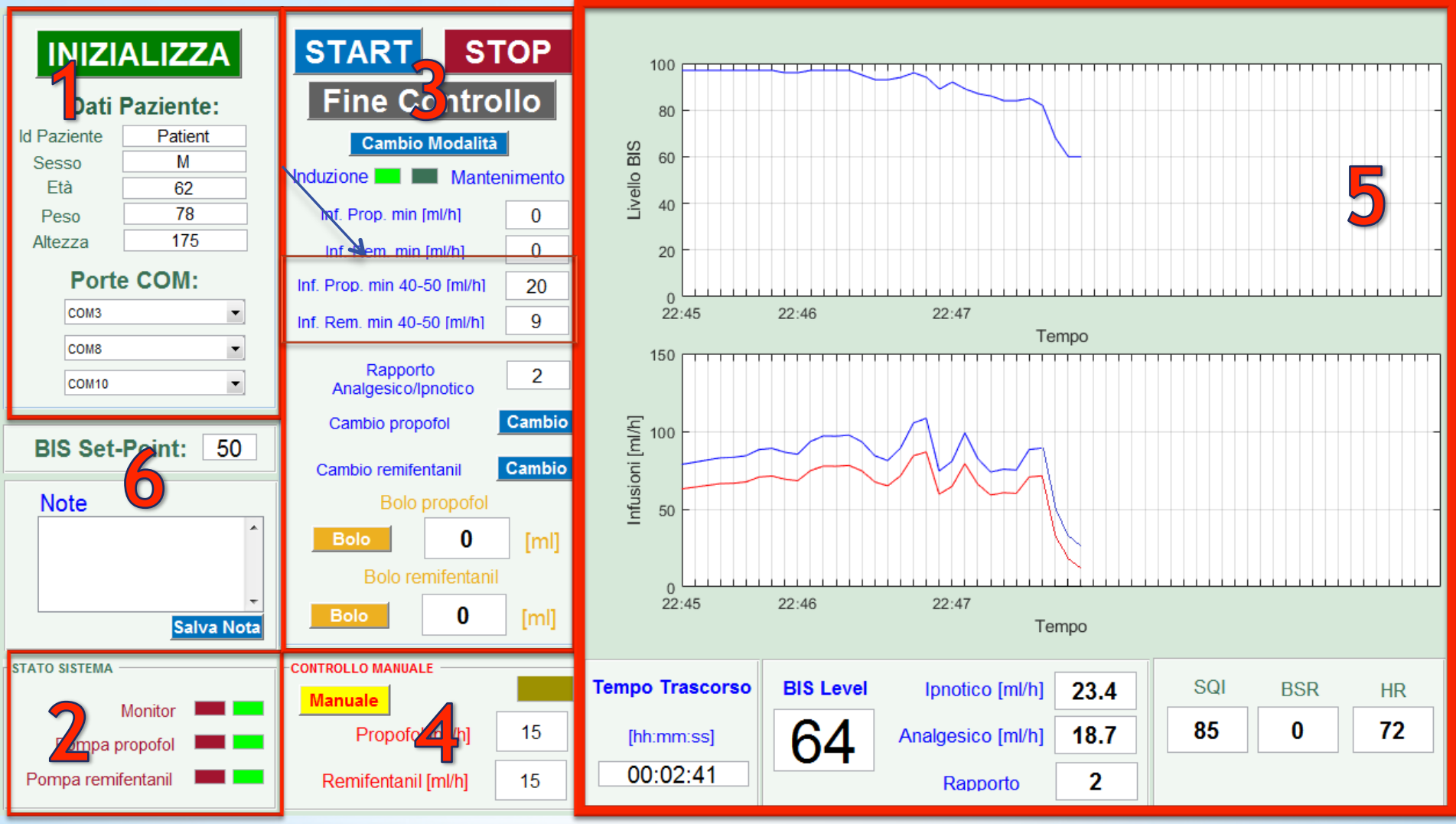
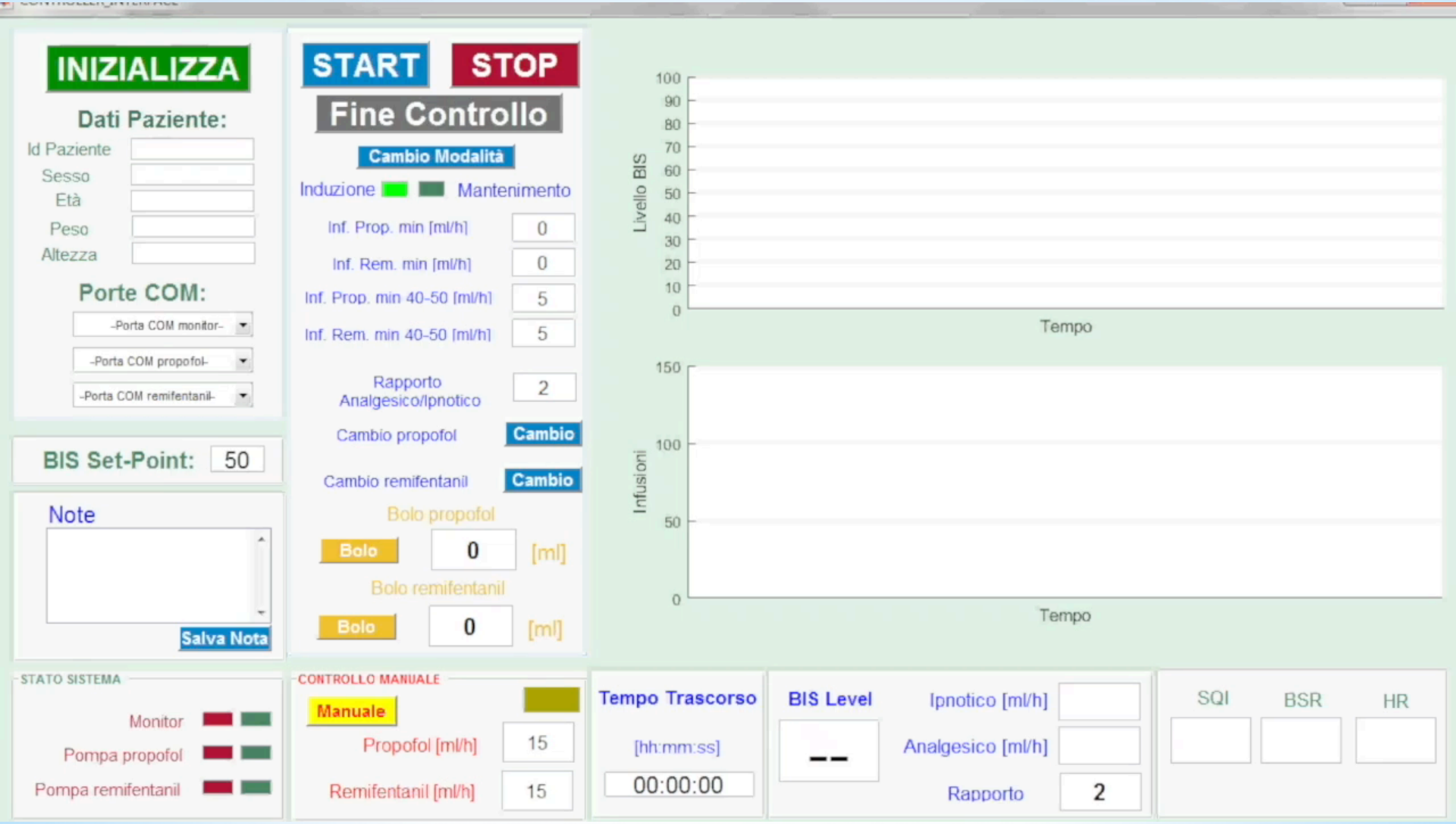


Figure 4.10: *Screen shot of the ACTIVA GUI during runtime operation.*

Here is ACTIVA GUI

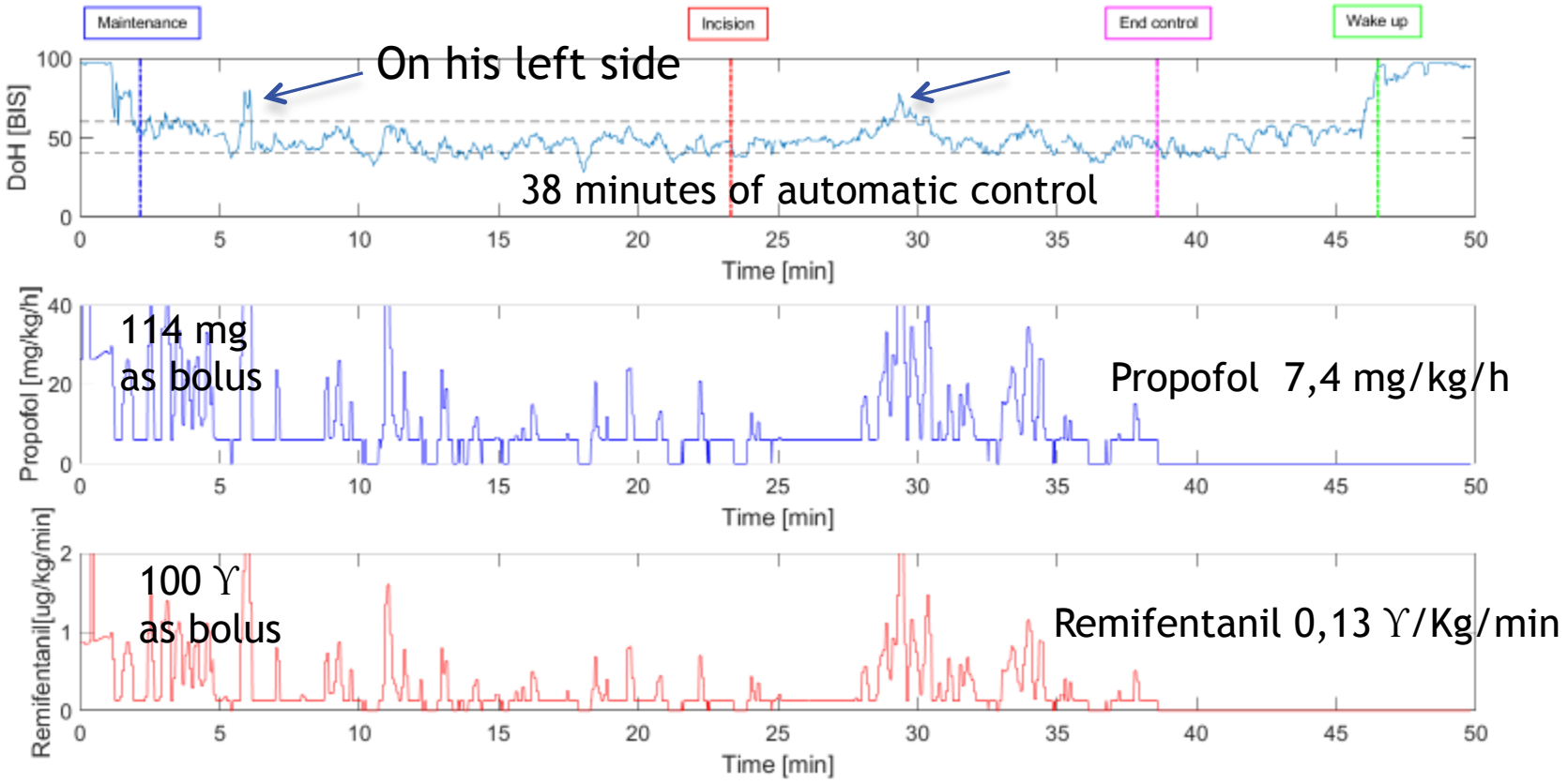
Simulator mode (for training use)

Real life


INIZIALIZZA
Dati Paziente:
Id Paziente
Sesso
Età
Peso
Altezza
Porte COM:
-Porta COM monitor-
-Porta COM propofol-
-Porta COM remifentanil-
BIS Set-Point: 50
Note
Salva Nota
START
STOP
Fine Controllo
Cambio Modalità
Induzione
Mantenimento
Inf. Prop. min [ml/h] 0
Inf. Rem. min [ml/h] 0
Inf. Prop. min 40-50 [ml/h] 5
Inf. Rem. min 40-50 [ml/h] 5
Rapporto Analgesico/Ipnotico 2
Cambio propofol Cambio
Cambio remifentanil Cambio
Bolo propofol
Bolo 0 [ml]
Bolo remifentanil
Bolo 0 [ml]
Livello BIS
100
90
80
70
60
50
40
30
20
10
0
Tempo
Infusioni
150
100
50
0
Tempo
STATO SISTEMA
Monitor
Pompa propofol
Pompa remifentanil
CONTROLLO MANUALE
Manuale
Propofol [ml/h] 15
Remifentanil [ml/h] 15
Tempo Trascorso
[hh:mm:ss]
00:00:00
BIS Level
--
Ipnotico [ml/h]
Analgesico [ml/h]
Rapporto 2
SQI
BSR
HR

Giancarlo (scheduled for electrochemoterapy) ***Case 1***

Age: 74 Weight: 71 [kg] Height: 170 [cm] ASA: 3



TT: 123 [sec]

min BIS (after incision): 35

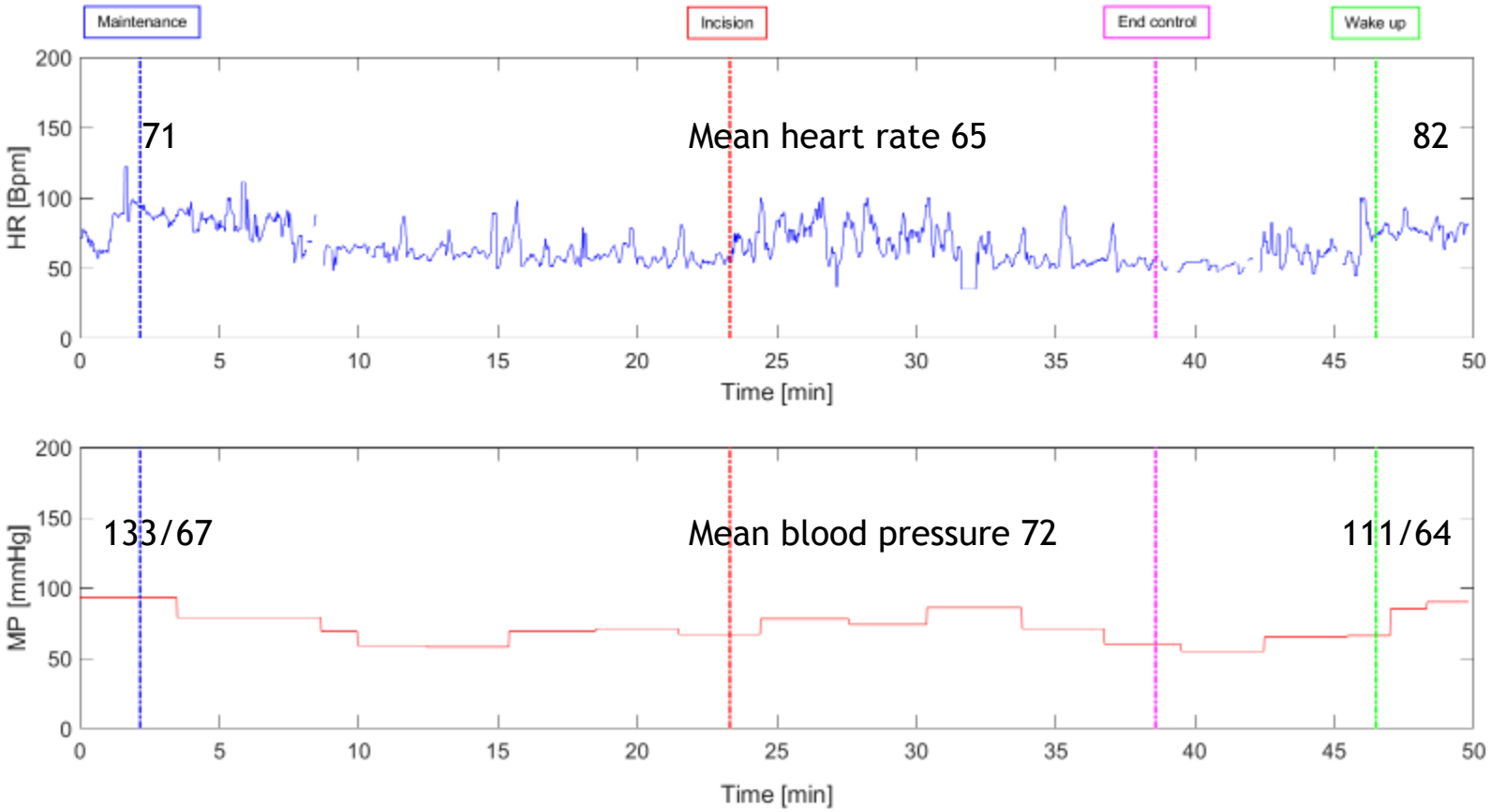
BIS 40-60: 82.94 [%]

BIS NADIR (before incision): 30

max BIS: 78

wake up Time : 7 min 30 sec

Heart rate & Blood pressure

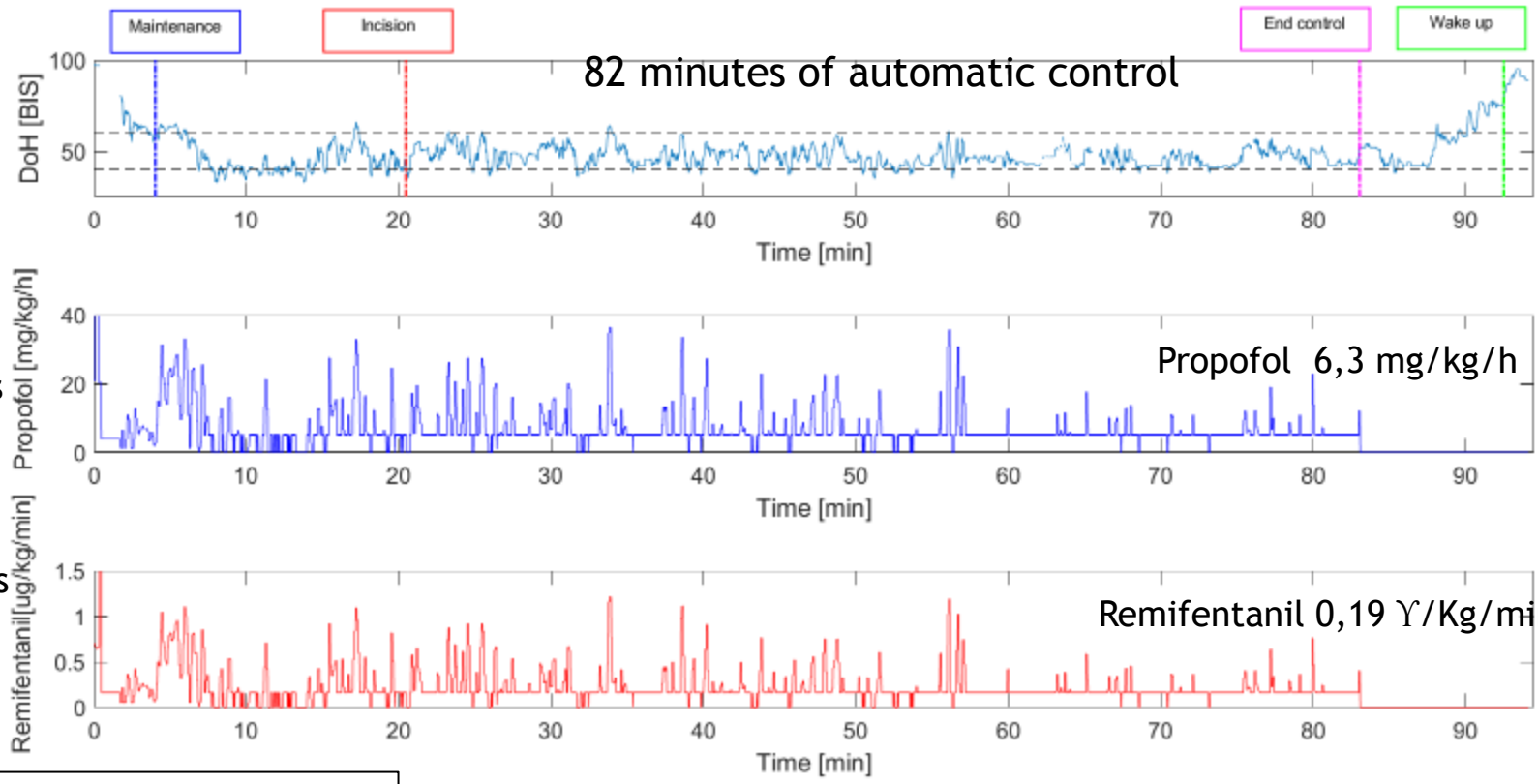


No vasopressor administered
No pre-medication

Mean BIS:48

Annamaria (scheduled for skin cancer melanoma and sentinel limph node biopsy) ***Case 2***

Age: 65 Weight: 77 [kg] Height: 169 [cm] ASA: 2



100 mg as bolus

100 ϒ as bolus

Fentanyl 100 ϒ pre-med

TT: 4 [min]

min BIS (after incision): 35

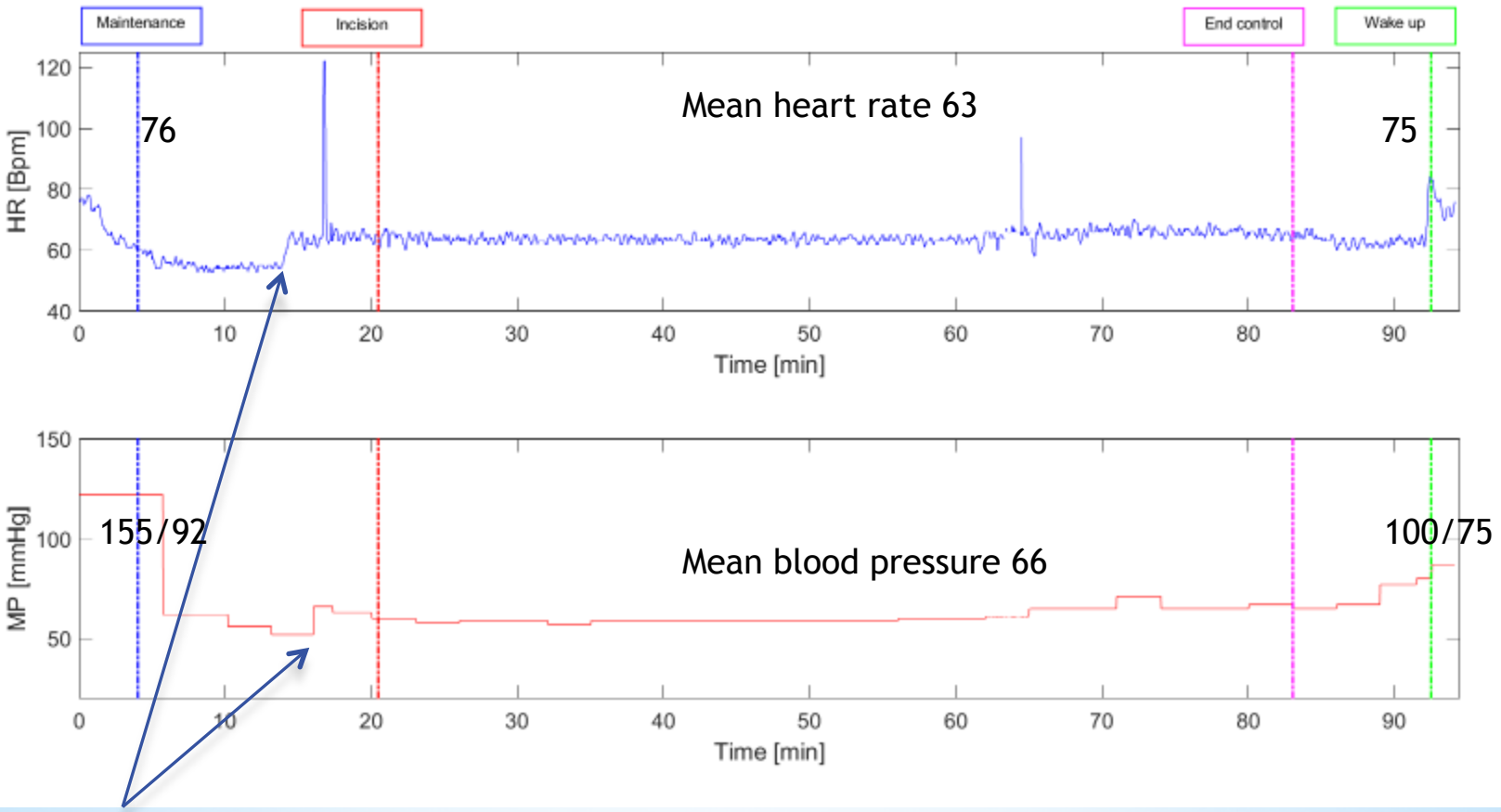
BIS 40-60: 88.62 [%]

BIS NADIR (before incision): 38

max BIS: 64

wake up Time: 9 min and 24 sec

Heart rate & Blood pressure

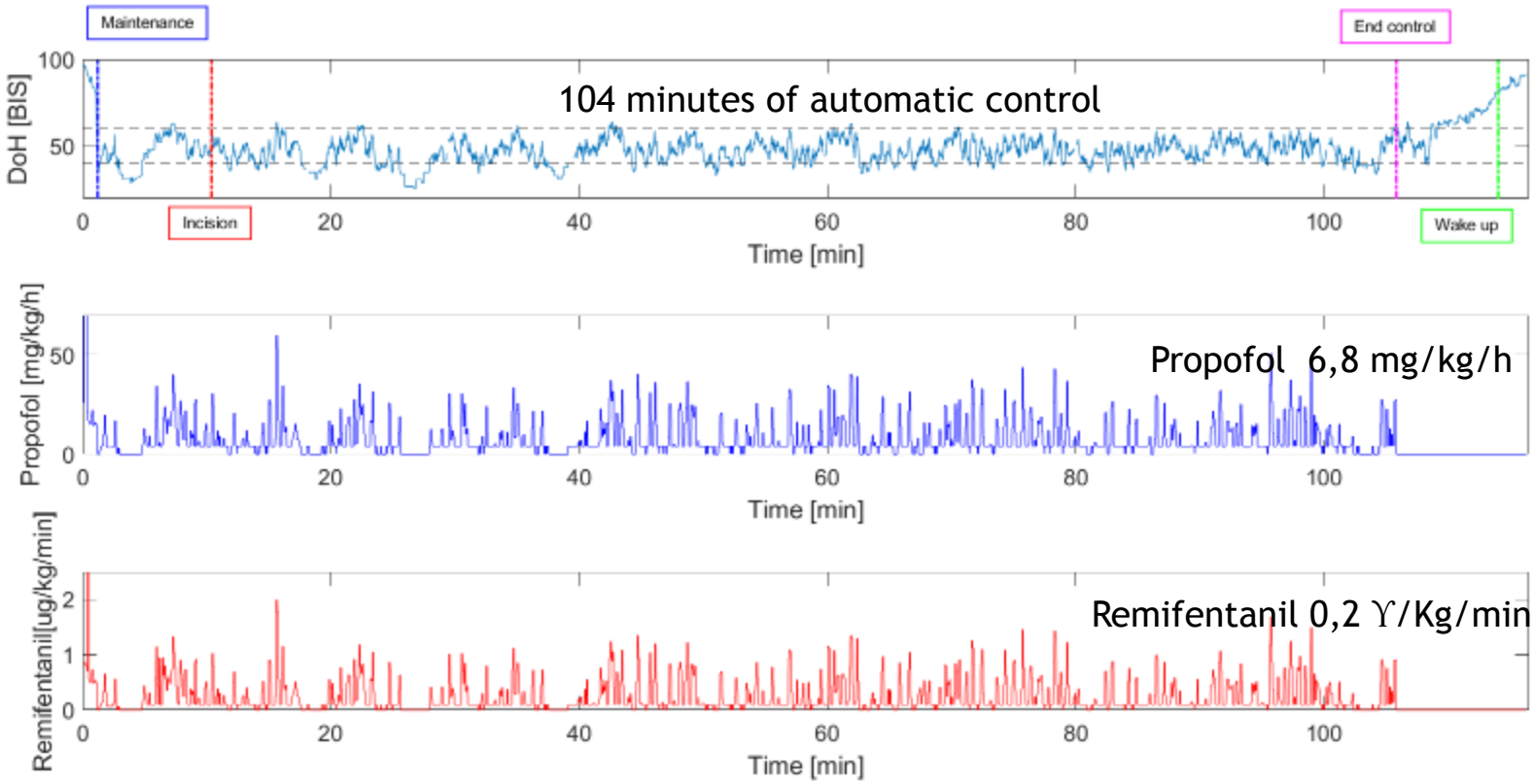


Ephedrine 10 mg

Mean BIS:47

Elisabetta (scheduled for toe skin cancer melanoma and sentinel limph node biopsy) ***Case 3***

Age: 60 Weight: 60 [kg] Height: 162 [cm] ASA: 2



94 mg as bolus

85 ϒ as bolus

TT: 68 sec

min BIS (after incision): 26

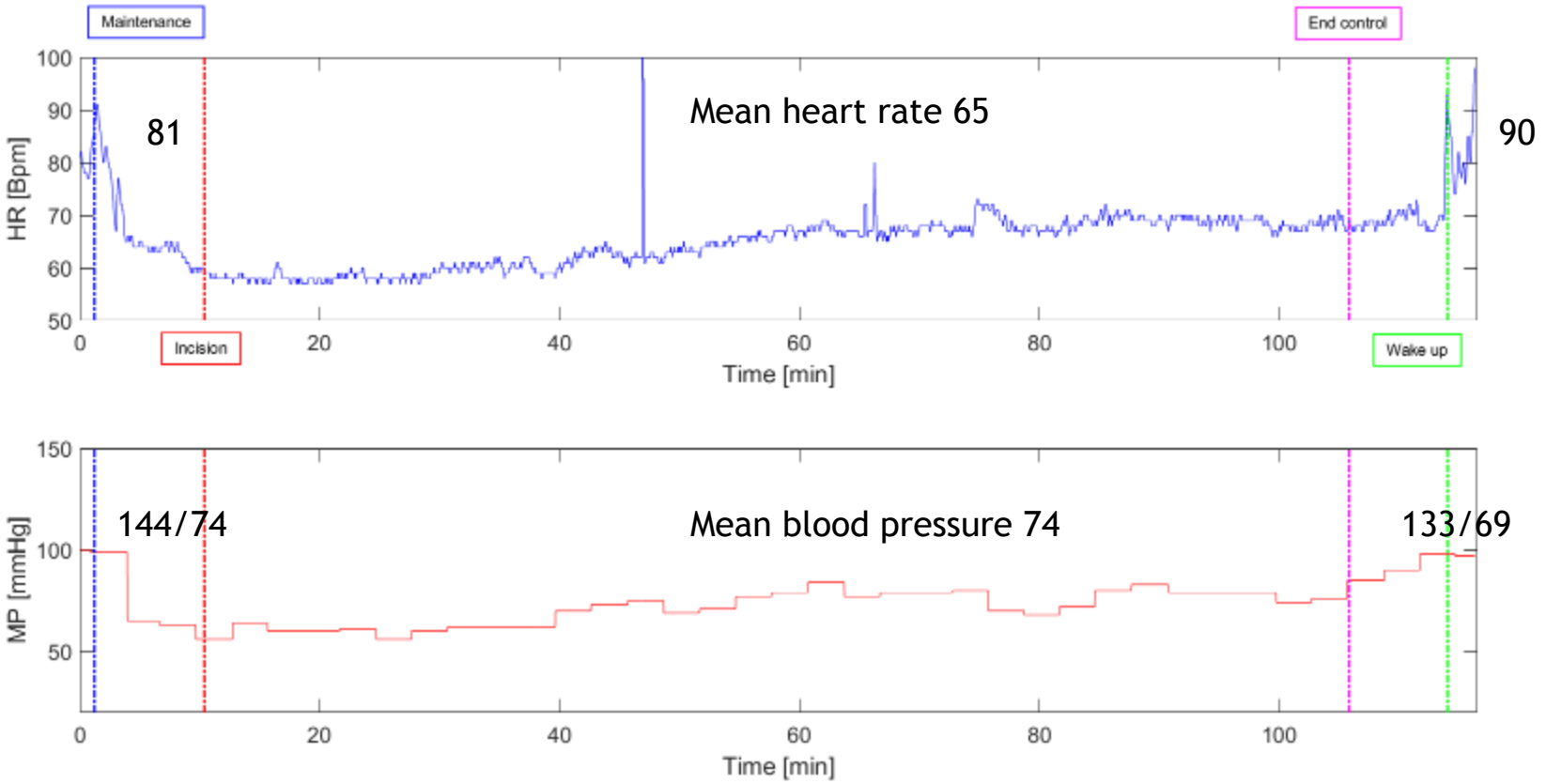
BIS 40-60: 82.7 [%]

BIS NADIR (before incision): 29

max BIS: 64

wake up Time: 8 min and 12 sec

Heart rate & Blood pressure

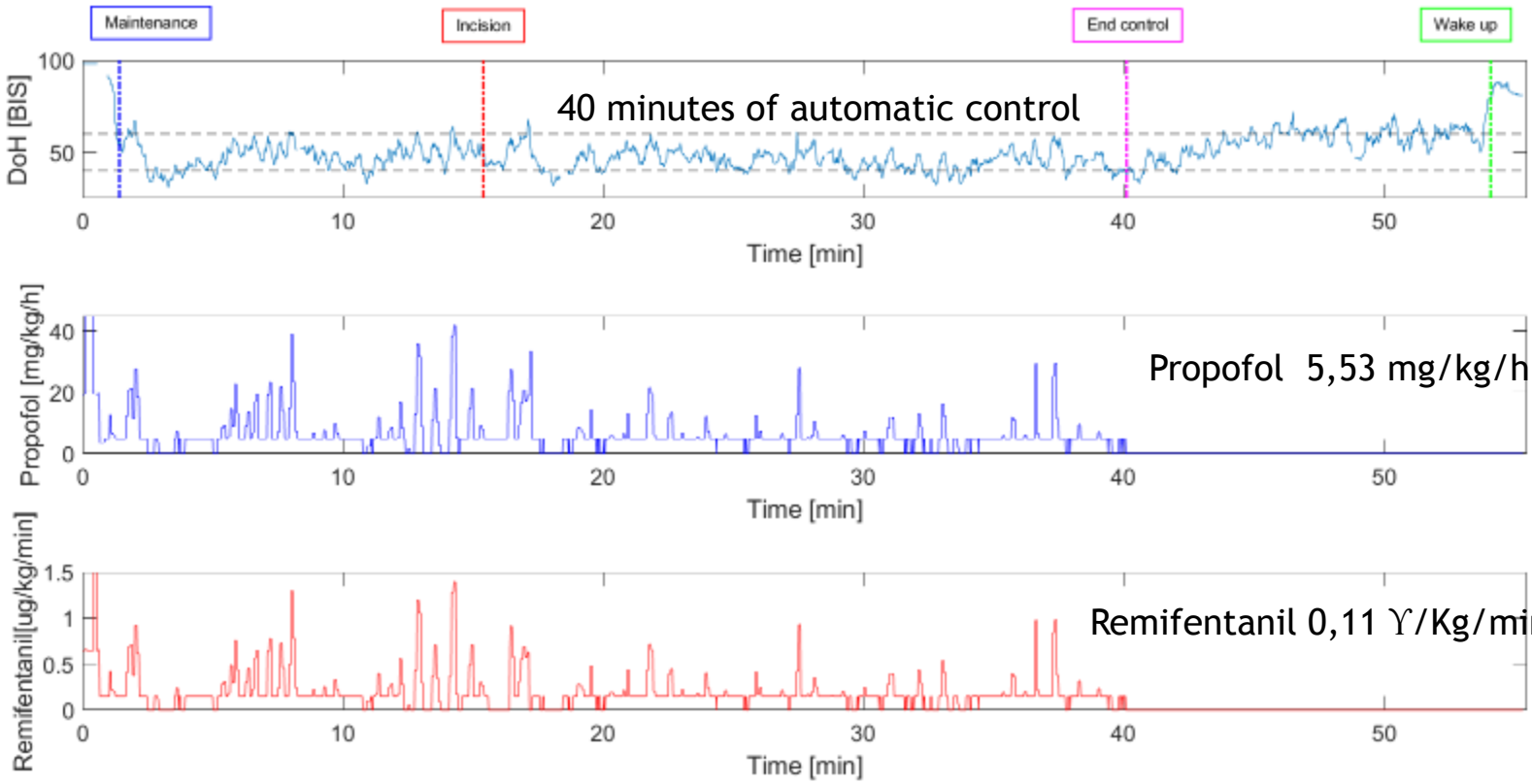


No vasopressor administered
No pre-med

Mean BIS:47

Giuseppe (scheduled for dorsal skin cancer melanoma and sentinel limph node biopsy) ***Case 4***

Age: 67 Weight: 83 [kg] Height: 173 [cm] ASA: 2



114 mg as bolus

100 ϒ as bolus

TT: 82 sec

min BIS (after incision): 32

BIS 40-60: 84.92 [%]

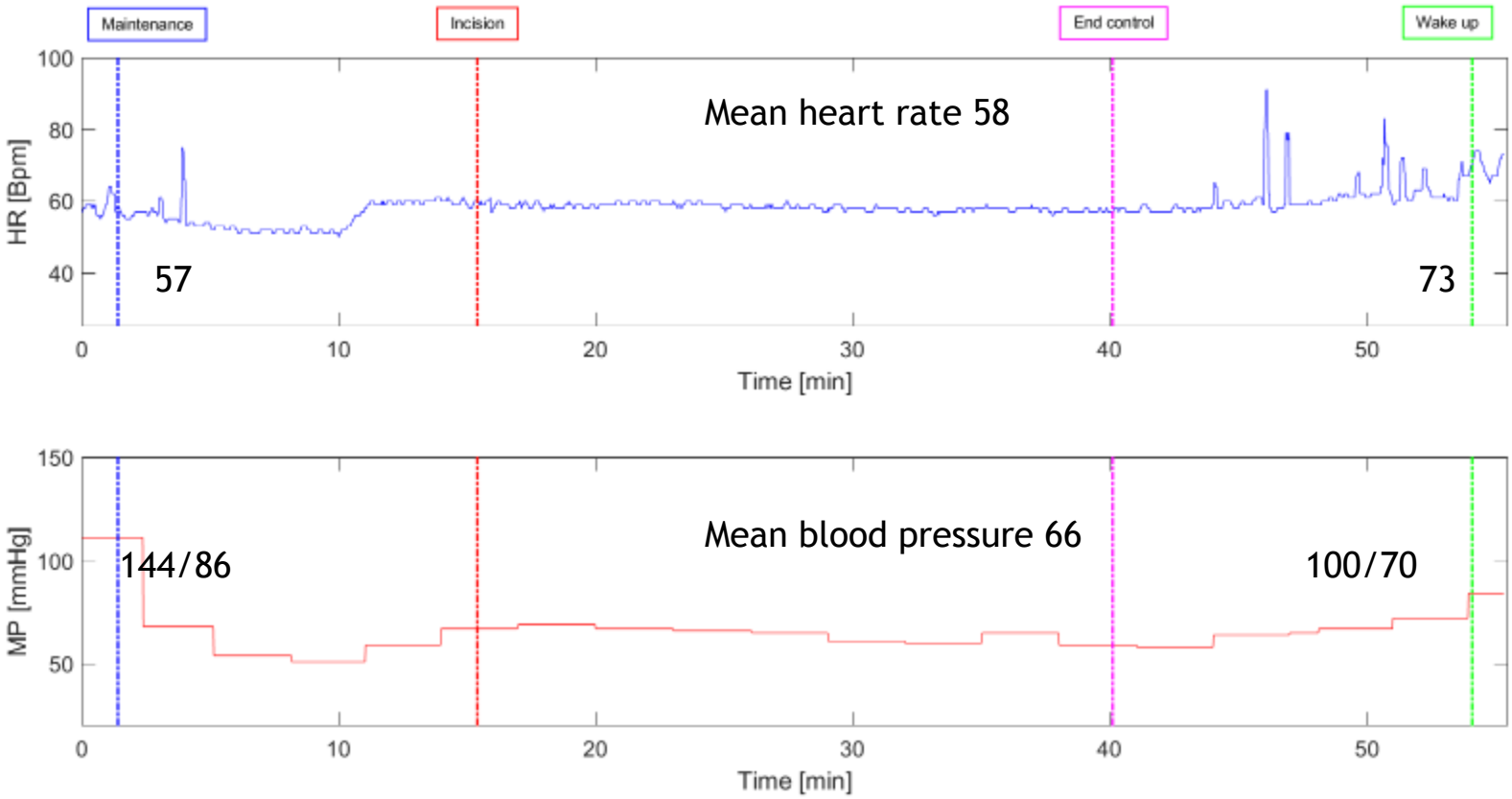
BIS NADIR (before incision): 31

max BIS: 68

wake up Time: 14 [min]

Pre-med with:
100 Y fentanil
1 mg midazolam

Heart rate & Blood pressure

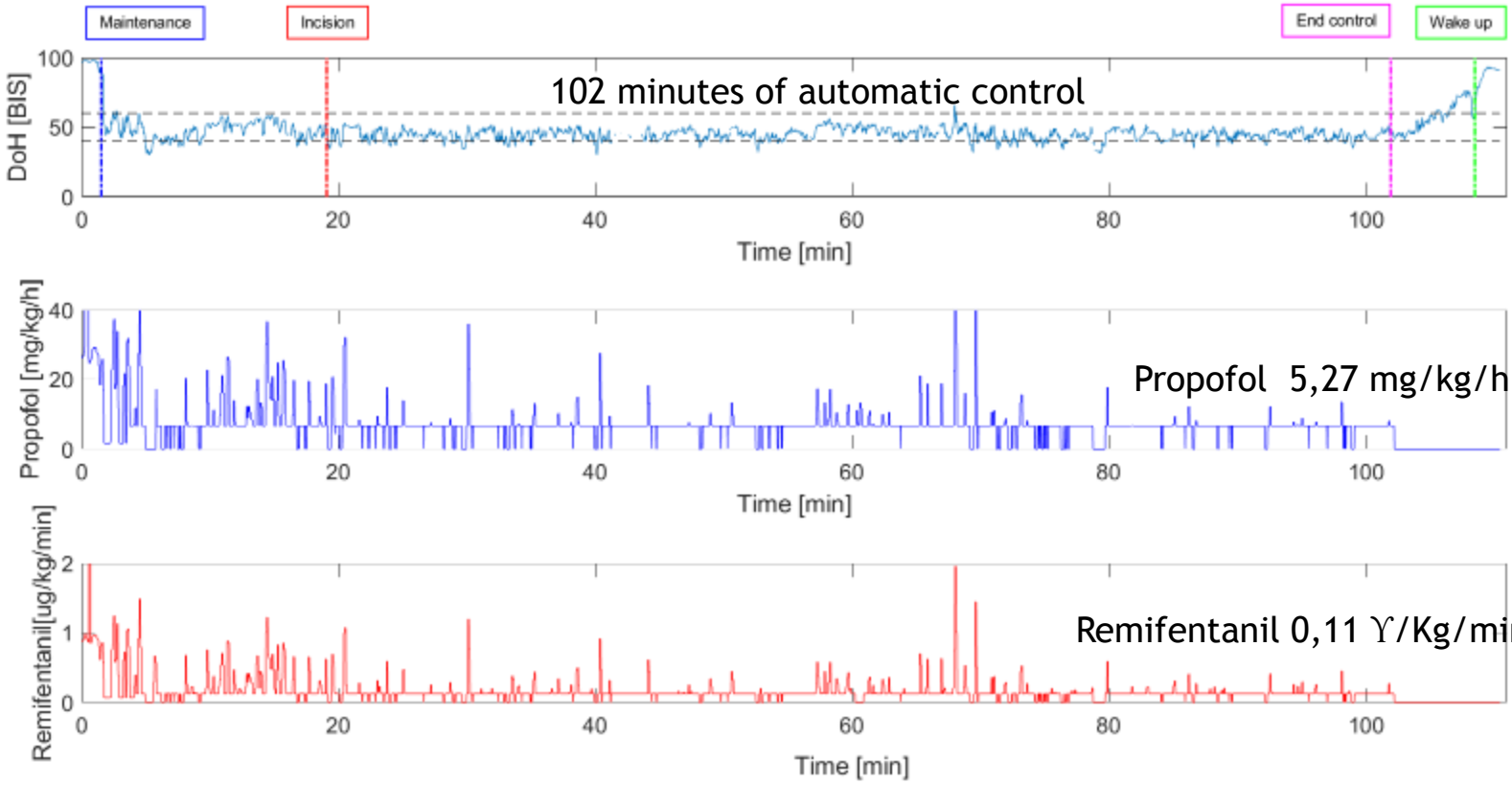


No vasopressor administered

Mean BIS:46

Rosario (scheduled for torax skin cancer melanoma and axillary sentinel limph node biopsy) ***Case 5***

Age: 50 Weight: 78 [kg] Height: 178 [cm] ASA: 2



114 mg as bolus

115 ϒ as bolus

TT: 108 sec

min BIS (after incision): 30

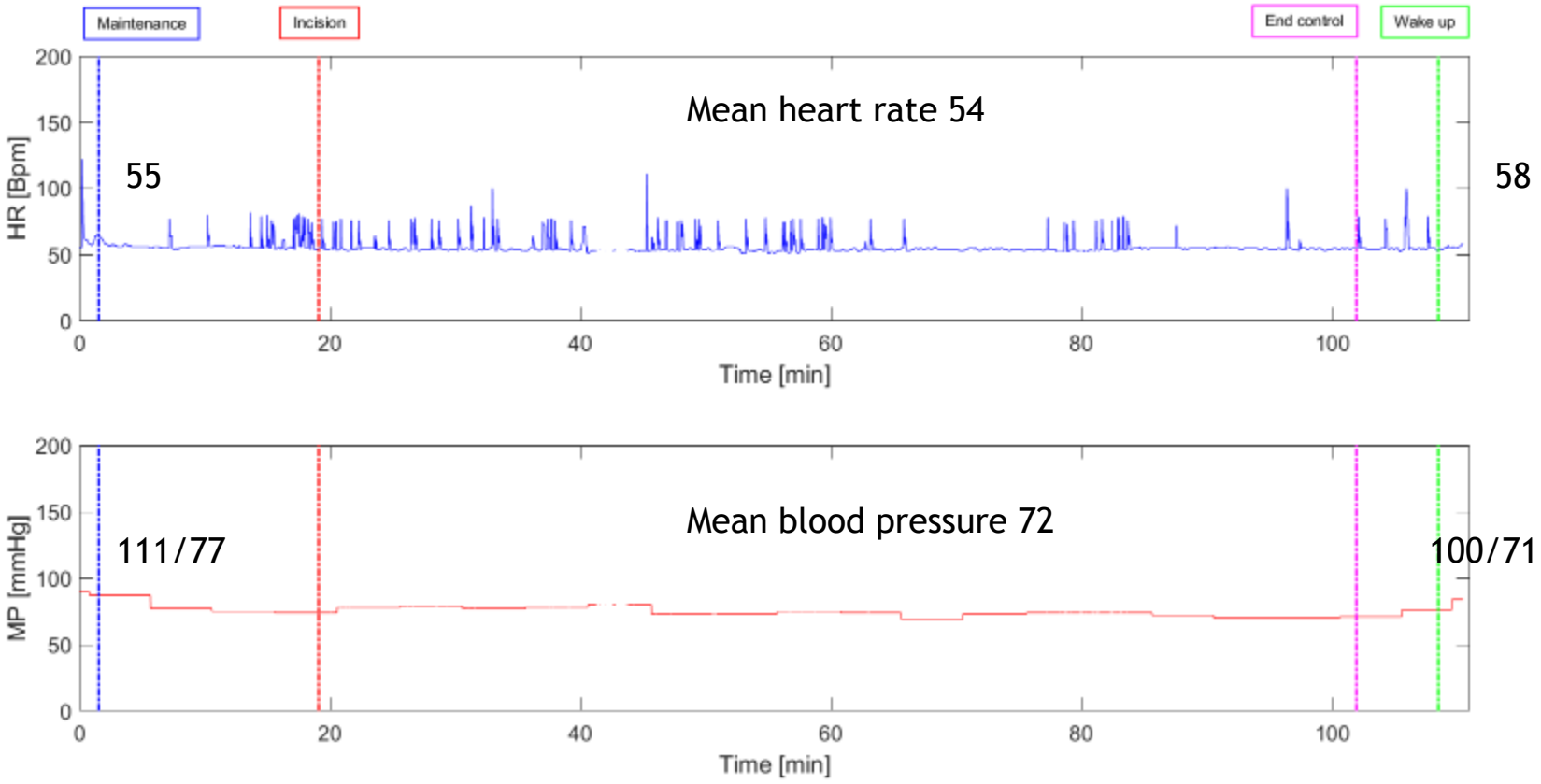
BIS 40-60: 84.93 [%]

BIS NADIR (before incision): 30

max BIS: 66

Wake up Time: 6 min and 36 sec

Heart rate & Blood pressure



No vasopressor administered
No pre-med

Mean BIS:45

Competitors: BIS on target (%)

SYSTEMATIC REVIEW ARTICLE

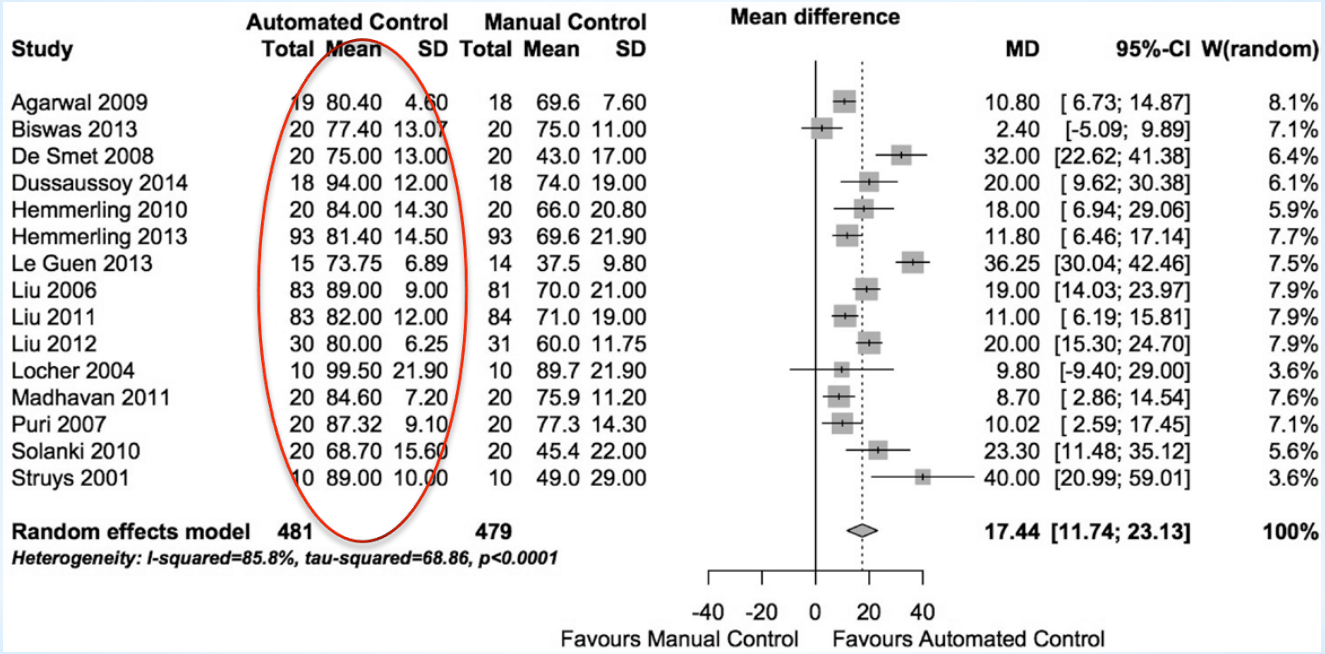


Figure 2. Forest plot presenting the percentage of time a given target (bispectral index or SE) was maintained within the desired range in closed-loop delivery systems (automated control) in comparison with manual control. The diamond represents the pooled results while the horizontal line represents the 95% confidence interval (CI).

February 2017 Volume 124 Number 2 on Anesthetic Clinical Pharmacology (www.anesthesia-analgesia.org) Brogi et al.

ACTIVA is 85% in the desired range

Competitors: Propofol and remifentanil doses

Table 3 Dose and modifications of drugs and extubation time. *Significant difference at 0.05 level (two-tailed). Data are presented as mean (SD) (95% confidence interval), analysed using the Mann–Whitney *U*-test

	McSleepy group ($n=93$)	Control group ($n=93$)	*P*-value
Mean propofol dose (μg kg^{-1} min^{-1})	115 (30) (109/121)	108 (25) (103/113)	0.0801
Modifications of propofol doses (times h^{-1})	67 (18) (63/71)	6 (8) (4/8)	<0.0001*
Mean remifentanil dose (μg kg^{-1} min^{-1})	0.21 (0.11) (0.19/0.24)	0.19 (0.09) (0.17/0.20)	0.0742
Modifications of remifentanil doses (times h^{-1})	28 (8) (26/29)	4 (5) (3/5)	<0.0001*
Total rocuronium dose (mg kg^{-1})	1.1 (0.5) (1.0/1.2)	1.1 (0.6) (1.0/1.2)	0.6230
Time to extubation (min)	10.1 (4.7) (9.2/11.1)	13.7 (8.8) (11.9/15.4)	0.0013*

6,9

0,21

Hemmerling
McSleepy

Table 3. Comparison of anesthetic procedures between the two groups during the maintenance phase.

		Closed-loop (n = 89)	Opened-loop (n = 86)	P
Maintenance time	(min)	199.3±96.2	202.5±101.0	0.832
Propofol				
Mean dose	(mg/kg·h)	5.28±1.32	5.52±1.29	0.230
Mean target concentration	(μg/ml)	2.32±0.58	2.56±0.57	0.006
Adjusted times	(/h)	31.55±9.46	6.84±6.21	0.000
Remifentanil				
Mean dose	(μg/kg·h)	11.14±3.08	11.05±3.30	0.848
Mean target concentration	(ng/ml)	5.01±1.25	4.87±1.22	0.465
Adjusted times	(/h)	2.62±2.06	3.61±2.68	0.007

5,3

0,19

Liu
Concert CL

ACTIVA:
Propofol 6,3 mg/Kg/h
Remifentanil 0,15 ϒ/Kg/min

Why Automatic Control in TIVA?

- AC *can* decrease the anesthesiologist's workload
  C. Dussaussoy et al. J Clin Monit Comput (2014) (28:35–40)

- BIS on target *may* decrease postoperative delirium and cognitive decline
  Matthew T.V. Chan et al. (J Neurosurg Anesthesiol 2013;25:33–42)

- AC is clinically feasible in pediatric patients
  G. A. Orliaguet et al. (Anesthesiology 2015; 122:759-67)

- AC is clinically feasible in obese patients
  N. Liu et al. British Journal of Anaesthesia 114 (4): 605–14 (2015)

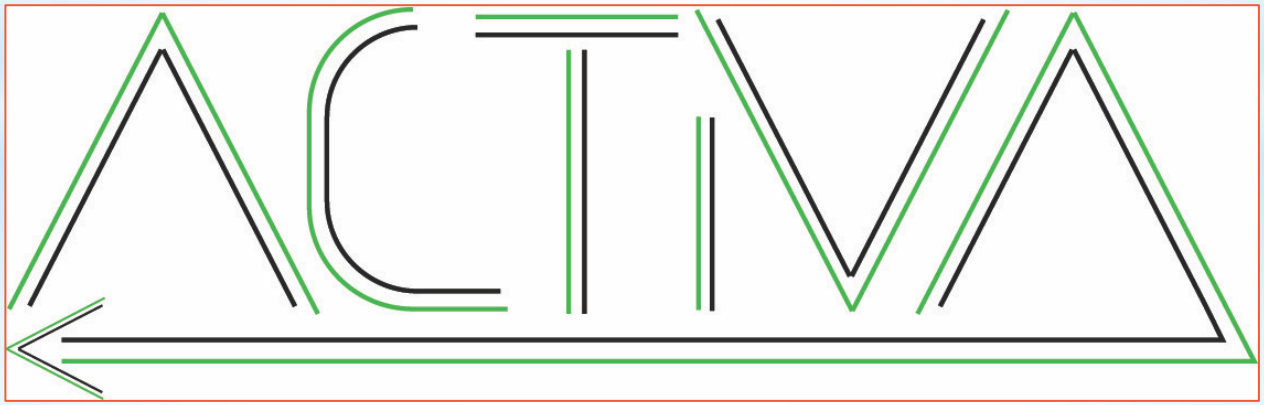
- AC *may* outperform manual administration of propofol and remifentanil in critically ill patients with deep sedation
  Morgan Le Guen et al. Intensive Care Med (2013) 39:454–462

- AC *can* avoid unnecessary deep anesthesia
  Monk T et al. Anesth Analg 2005;100:4 –10
  Lindholm M et al. Anesth Analg 2009;108:508 –12
  Leslie K et al. Anesth Analg 2010;110:816 –22
  Kertai M et al. Anesthesiology 2010;112:1116–27

ACTIVA: **A**utomatic **C**ontrol in **T**otal **I**ntra **V**enous **A**nesthesia

Conclusion

- Simulator Mode can be usefull to understand the system and for training
- Clinical study is approved by ethics committee and by Italian Health Department:
  - Primary outcome is safety
- First clinical data are encouraging



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Prof. A. Visioli, Prof. N. Latronico
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Please contact us at massimiliano.paltenghi@asst-spedalicivili.it

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8. L. Merigo, F. Padula, A. Pawlowski, S. Dormido, J. L. Guzmán Sánchez, **N. Latronico, M. Paltenghi**, and A. Visioli, *A model-based control scheme for depth of hypnosis in anesthesia* Biomedical Signal Processing and Control, 42:216-229, 2018.
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FRIDAYS FOR FUTURE

SEE YOU NEXT YEAR…
MAYBE
HANDS ON SESSION:
ACTIVA!!??