RATING THE SEVERITY OF OPIOID-INDUCED ATAXIC BREATHING IN HEALTHY HUMANS

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OPIOID-INDUCED RESPIRATORY DEPRESSION

- 2015 Anesthesia Closed Claims Project database (1990-2009):
  - Majority of RD events (88%) occurred within 24 h of surgery
  - 97% were preventable with better monitoring and response

Lee LA, Caplan RA, Stephens LS, Posner KL, Terman GW, Voepel-Lewis T, Domino KB., Postoperative opioid-induced respiratory depression: a closed claims analysis., Anesthesiology. 2015 Mar;122(3):659-65
Quach JL, Downey AW, Haase M, Haase-Fielitz A, Jones D, Bellomo R. Characteristics and outcomes of patients receiving a medical emergency team review for respiratory distress or hypotension. J Crit Care. 2008;23(3):325-331.

OPIOID-INDUCED RESPIRATORY DEPRESSION

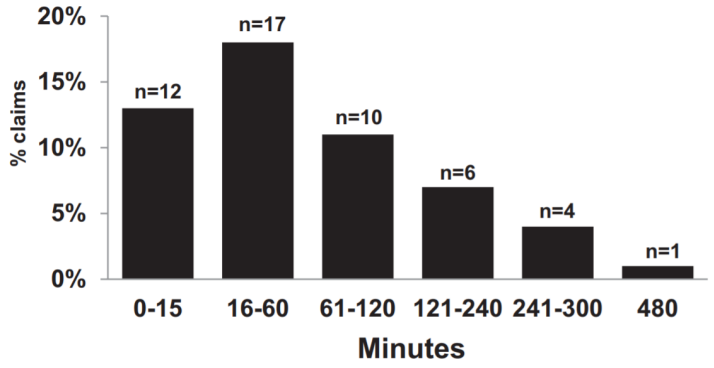

Fig. 1. Time between last nursing check and discovery of opioid-induced respiratory depression (RD). Claims with unknown timing (n = 39) and not applicable (at home, n = 3) not shown.

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OPIOID-INDUCED RESPIRATORY DEPRESSION

CO_2 Narcosis

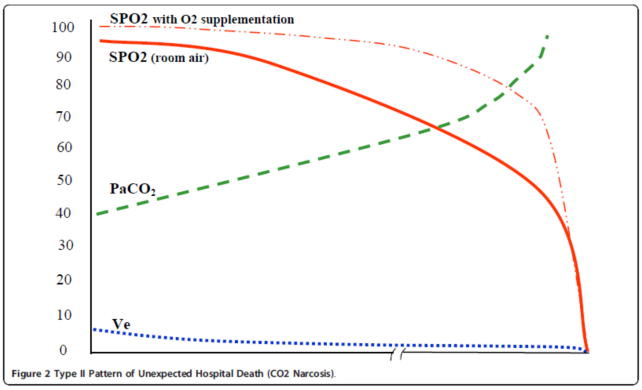

Figure 2 Type II Pattern of Unexpected Hospital Death (CO2 Narcosis).

Lynn, Lawrence A., and J. Paul Curry. "Patterns of unexpected in-hospital deaths: a root cause analysis." *Patient safety in surgery* 5.1 (2011): 3.

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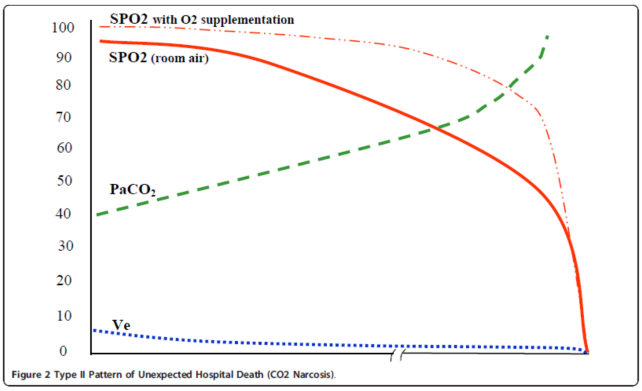
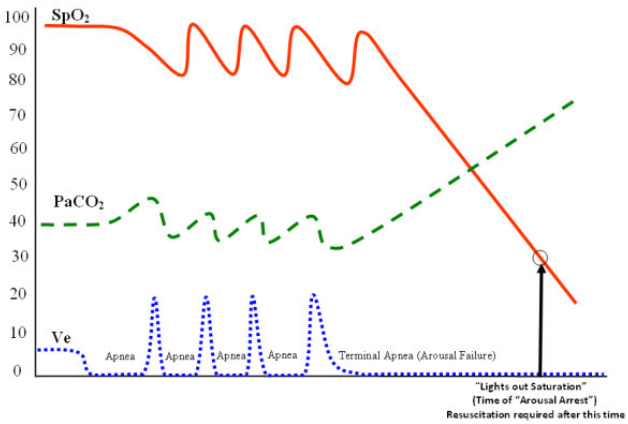


Figure 2 Type II Pattern of Unexpected Hospital Death (CO2 Narcosis).

Cyclic Apneas



Lynn, Lawrence A., and J. Paul Curry. "Patterns of unexpected in-hospital deaths: a root cause analysis." *Patient safety in surgery* 5.1 (2011): 3.

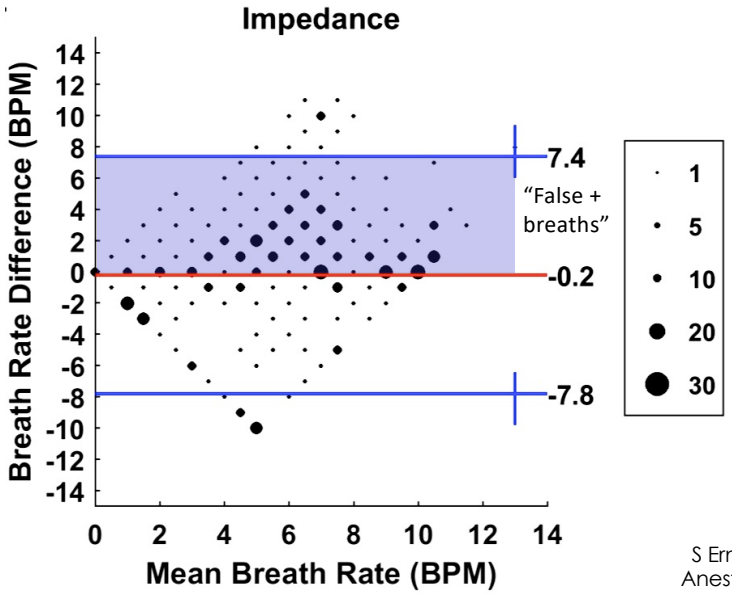
MONITORING STANDARDS

1. Respiratory Rate (< 8-10 bpm)
2. Oximetry (SpO_2 < 90-92%)
3. End-Tidal CO_2 ($ETCO_2$ > 50 mmHg)
4. Mental Status (Sedated)

Respiratory Rate is Unreliable for Detecting Opioid-Induced RD

1. RR obtained by physical examination is notoriously inaccurate (e.g. poor technique, patient arousal).
2. Most technologies are not validated for detecting slow respiratory rates.
3. Automated methods are insensitive to respiratory patterns (e.g. apneas) resulting in inaccurate RR.
4. RR does not equate to adequate ventilation.

Comparison of seven different sensors for detecting low respiratory rates using a single breath detection algorithm in non-intubated, sedated volunteers.



S Ermer, L Brewer, J Orr et al. Anesthesia & Analgesia (2018)

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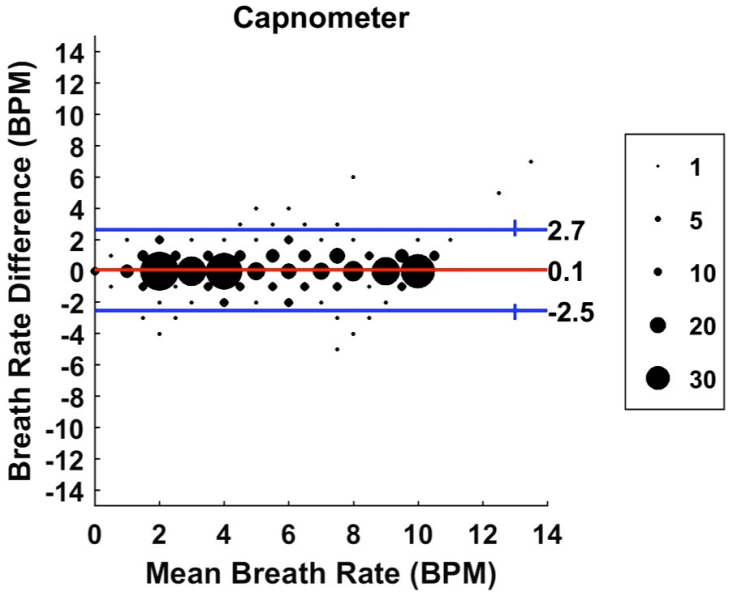
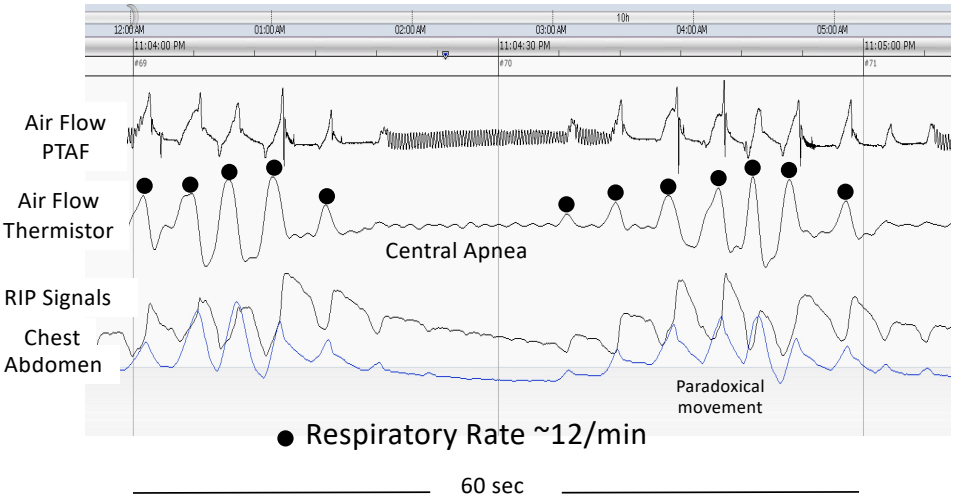
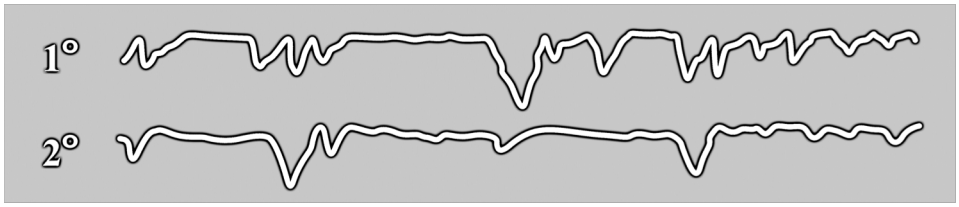


Respiratory Pattern versus Respiratory Rate



Contribution a l'ètude de phènomène respiratoire de Cheyne-Stokes.

MC Biot. Lyon Mèd 1876; 23: 517-528, 561-567

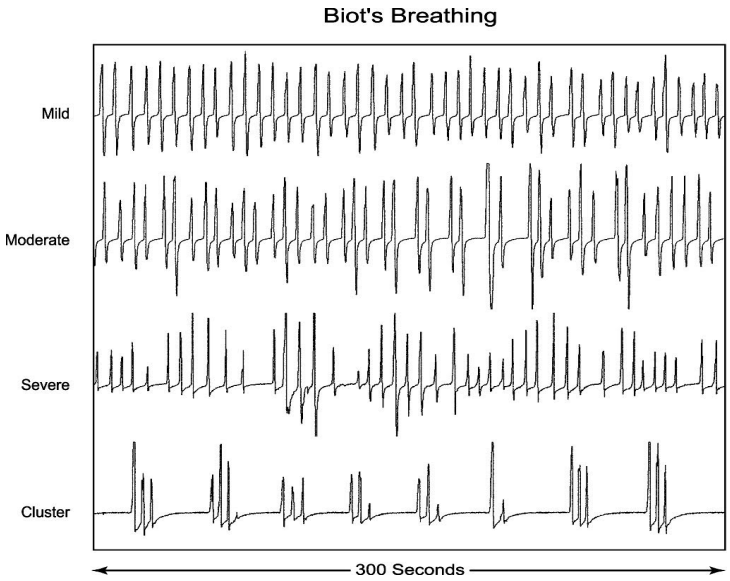


"Biot's" breathing in a 16 year old male with tuberculous meningitis.

Variations of Biot's (ataxic) breathing patterns

Major obstacle for monitoring a patient for Biot's (ataxic) breathing severity:

The need for ***manual offline analysis*** using a visual template



Farney, Robert J., et al. "Sleep disordered breathing in patients receiving therapy with buprenorphine/naloxone." *European Respiratory Journal* 42.2 (2013): 394-403.

PRIMARY HYPOTHESIS

For healthy volunteers receiving steady state infusion pairs of an opioid and a hypnotic to model light sleep with opioid-induced ventilatory depression:

The ataxic breathing severity scores from three domain experts and a machine learning algorithm classifier will be in agreement.

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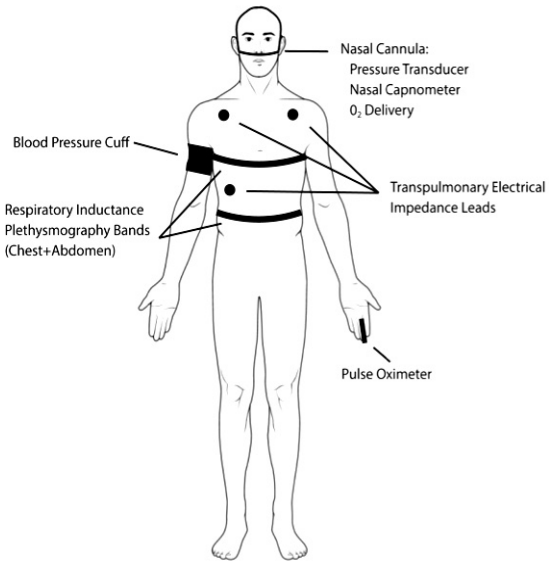
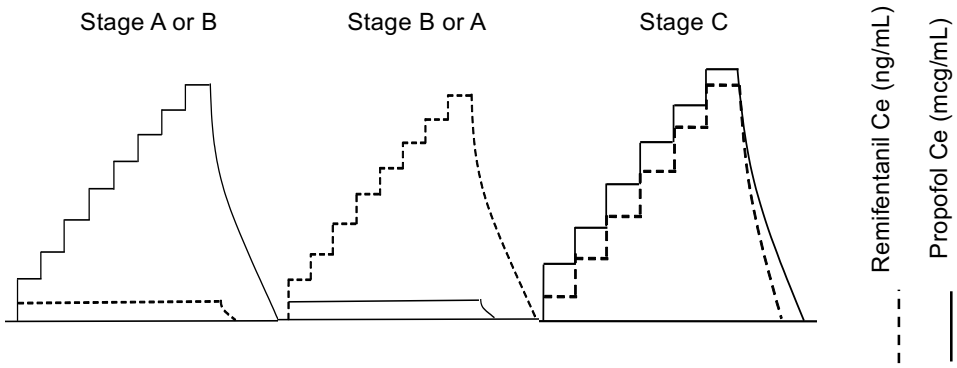
METHODS

26 Consenting Healthy Volunteers
- *Opioid naïve*
- *BMI 18-31,*
- *Age 18-41*



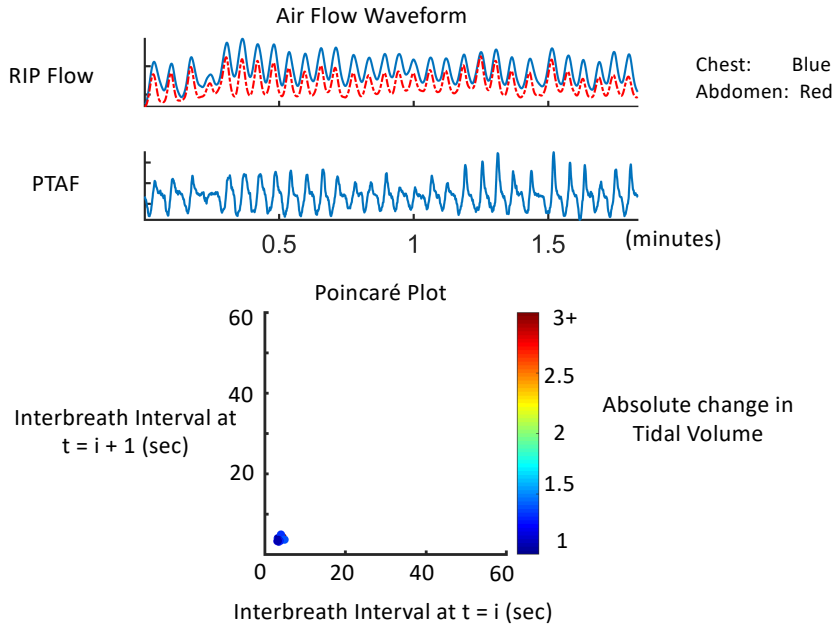
Target Controlled Infusion Drug Schemes



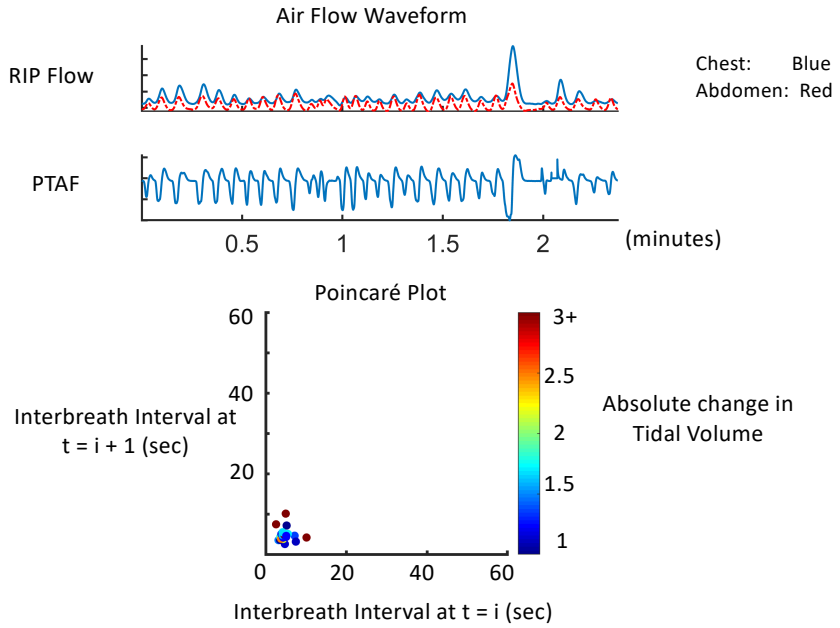
METHODS

- Three domain experts scored the severity of ataxic breathing on a scale of 0-4 in accordance with a visual scoring template. A machine learning algorithm was trained on 50% of the data.
- Krippendorff's alpha was used to rate agreement among all raters (machine and experts).
- Vanbelle's Kappa was used to assess the agreement between the machine learning algorithm and the three experts

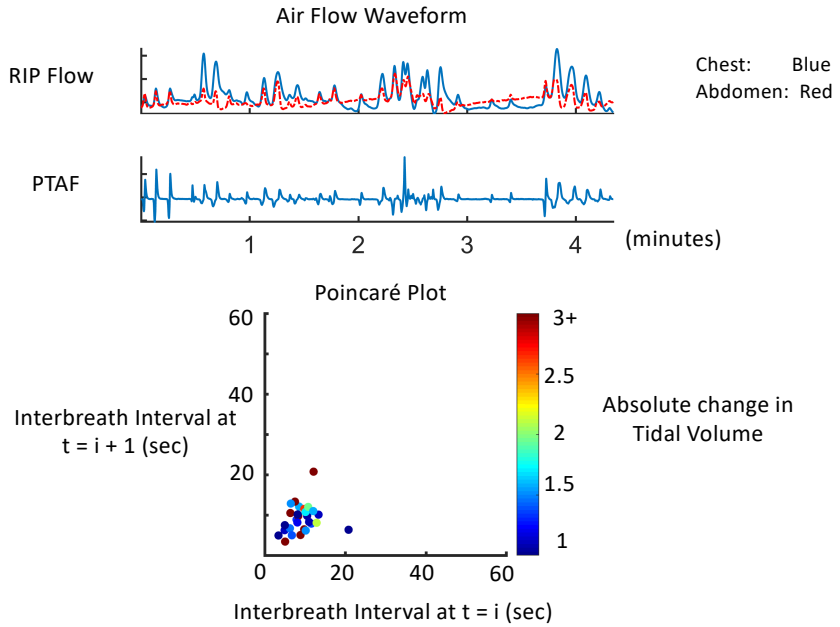
Ataxic Breathing Severity Score 0



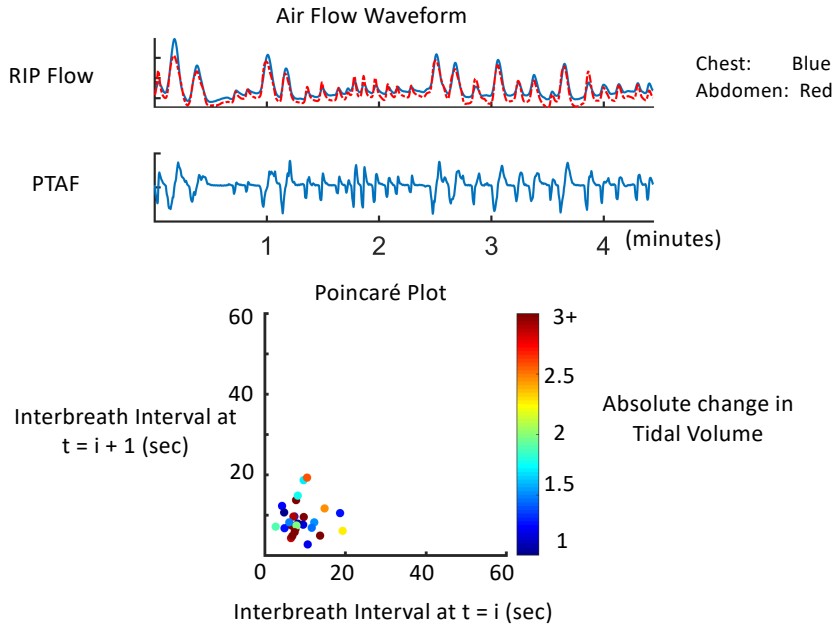
Ataxic Breathing Severity Score 1

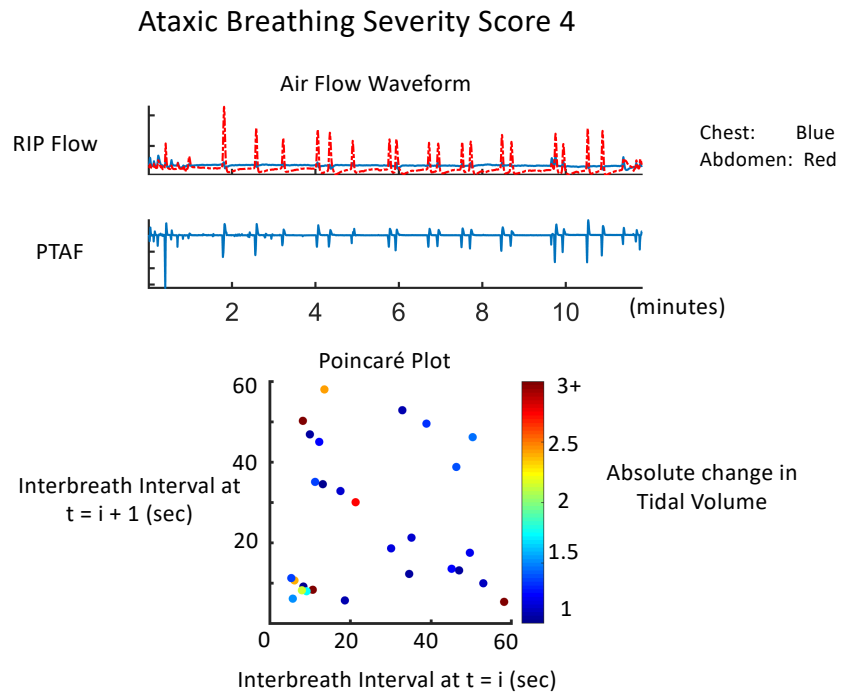


Ataxic Breathing Severity Score 2



Ataxic Breathing Severity Score 3

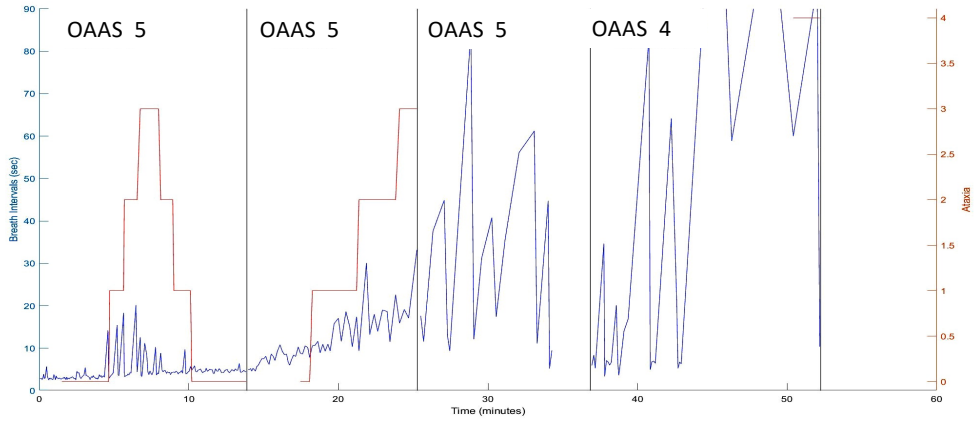




RESULTS

Rater Statistic	Basic Classifier: RIP Band Mean (95% CI)	Basic Classifier: Intranasal Pressure Mean (95% CI)
Krippendorff's Alpha	0.912 (0.852 - 0.949)	0.899 (0.819 - 0.941)
Vanbelle's Kappa	0.970 (0.951 - 0.983)	0.961 (0.921 - 0.979)

EXAMPLE PROGRESSION OF ATAXIC BREATHING



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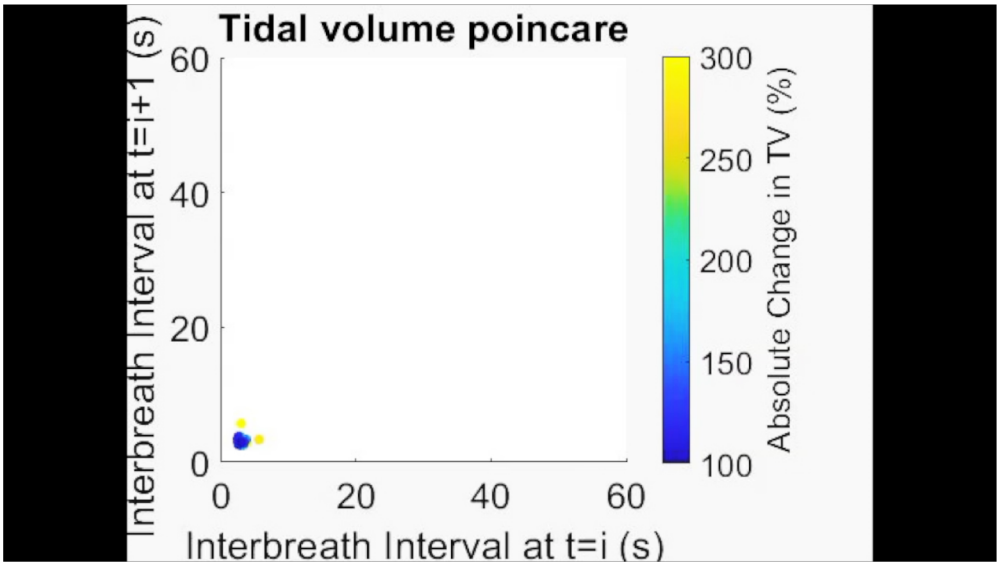

CONCLUSIONS

- A machine learning algorithm classified ataxic breathing severity in a manner consistent with a panel of domain experts.
- An ataxic breathing severity score may be helpful in conjunction with measures of respiratory rate and SpO2 to identify patients at risk for opioid-induced respiratory depression.
- Further work is needed to test the feasibility of this concept on clinical data.

THANK YOU

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