

Pulmonary embolism diagnostics from the driver function

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Introduction

Ventricular driver functions are not readily measured in the ICU, but can clearly indicate the development of pulmonary embolism (PE) otherwise difficult to diagnose, (for example, it is difficult to differentiate from cardiogenic shock, especially after right ventricular infarction). Recent work has developed accurate methods of measuring these driver functions from readily available ICU measurements. This research tests those methods by assessing the ability of these driver functions to diagnose the evolution of PE, based on a porcine trial.

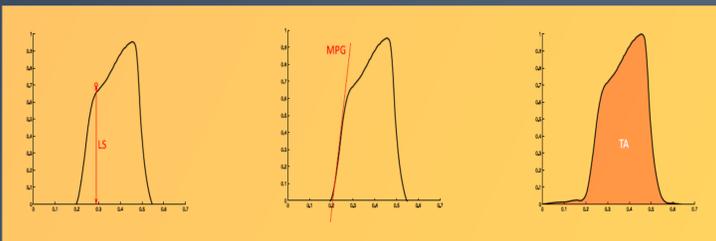
Methods

PE was induced in five pigs with cardiac measurements taken every 30 minutes. Pig-specific driver functions are estimated at each time point from the aortic artery pressure waveforms. Increases over time in two validated model-based metrics indicate PE:

- 1) Pulmonary artery resistance (R_{pul})
- 2) Right Ventricle Expansion Index (RVEI)

R_{pul} and RVEI at each time point were paired to specific points on the right driver function that change as PE is induced. The significant points of interest are:

- 1) Left-shoulder (LS) of the right driver function → correlated with the dead-space volume
- 2) Maximum pressure gradient (MPG) of the right driver function → related to compliance
- 3) Total area (TS) of the right driver function → analogous to work done by the ventricle



Correlations are calculated for each pig, and for measurements and driver functions averaged across all five pigs to see a general trend.

R_{pul} and LS were also normalised correlated after normalisations, which made it possible to achieve a good correlation without averaging. The normalisations were:

- R_{pul}: stroke volume
- LS: stroke volume and heart rate

Results

Correlation R values

| | Median | Range | Averaged | Non-averaged |
|--------------------------------------|--------|-----------|----------|--------------|
| RVEI to LS | 0.56 | 0.33-0.99 | 0.98 | |
| RVEI to MPG | 0.59 | 0.25-0.99 | 0.98 | |
| Rpul to TA | 0.53 | 0.04-0.85 | 0.96 | |
| Rpul ¹ to LS ² | | | | 0.89 |

¹ - normalised to stroke volume
² - normalised to stroke volume and heart rate

The results from the 5 pigs induced with PE are shown in the table to the right. Without averaging the 5 pigs, correlation levels were not consistent across the pigs or metrics, indicating inter-pig variability in the experimental response to PE. However, normalisations were found for R_{pul} and LS that produced a good correlation (R=0.89), showing that pig specific prediction of R_{pul} is possible with the right normalisation of the data.

Driver Function

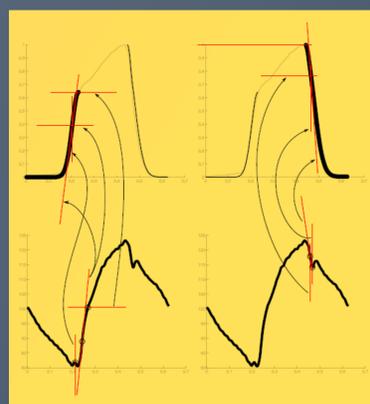
A patient specific function is constructed primarily from measurements that are readily available in the ICU. These measurements are:

- 1) The aortic pressure waveform
- 2) Timing from the pulmonary artery pressure
- 3) Global End Diastolic Volume (GEDV)

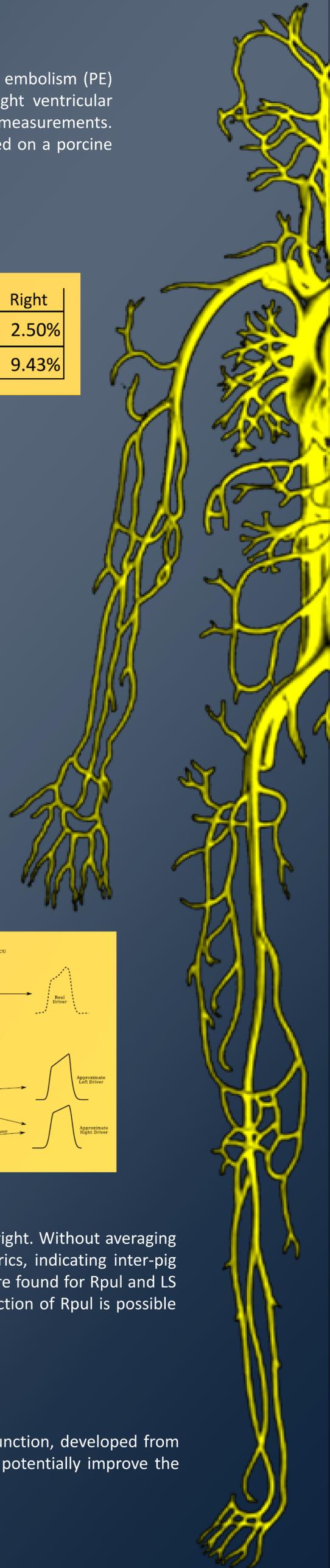
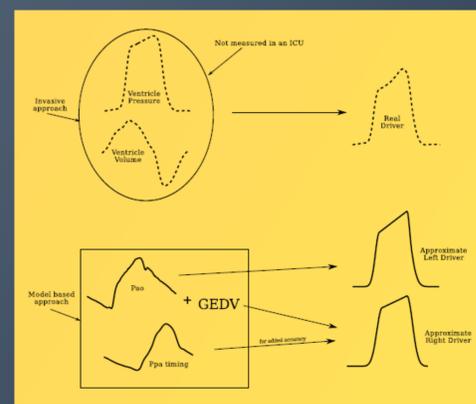
The left driver function only uses 1), while the right driver function uses all of them. The driver functions are calculated from population correlations derived from known driver functions and pressure waveforms.

This method has been shown to be very accurate for both PE and septic shock in porcine trials, achieving reconstructed driver functions with errors given in the table above (shown for PE, septic shock has comparable errors).

Each driver function is pieced together, using two exponential functions (the rise and decay) joined by a straight line. The two exponential sections are fitted by finding the inflection points and slope along the height which are calculated from pre-calculated correlations from the aortic pressure waveform, pulmonary artery pressure timing, and GEDV.



| | Left | Right |
|-----------|-------|-------|
| Mean | 1.32% | 2.50% |
| 90th Prct | 3.67% | 9.43% |



Conclusion

This research suggests that PE can be diagnosed and tracked from knowledge of a model-based patient specific driver function, developed from readily available ICU measurements. Further animal and human validation is required to confirm these results, and to potentially improve the correlations and normalisations.