Physiological Measurement

EDITORIAL

Continuous cardiorespiratory monitoring is a dominant source of predictive signal in machine learning for risk stratification and clinical decision support*

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Abstract

Beaulieu-Jones and coworkers propose a litmus test for the field of predictive analytics—performance improvements must be demonstrated to be the result of non-clinician-initiated data, otherwise, there should be caution in assuming that predictive models could improve clinical decision-making (Beaulieu-Jones et al 2021). They demonstrate substantial prognostic information in unsorted physician orders made before the first midnight of hospital admission, and we are persuaded that it is fair to ask—if the physician thought of it first, what exactly is machine learning for in-patient risk stratification learning about? While we want predictive analytics to represent the leading indicators of a patient’s illness, does it instead merely reflect the lagging indicators of clinicians’ actions? We propose that continuous cardiorespiratory monitoring—’routine telemetry data,’ in Beaulieu-Jones’ terms—represents the most valuable non-clinician-initiated predictive signal present in patient data, and the value added to patient care justifies the efforts and expense required. Here, we present a clinical and a physiological point of view to support our contention.

In a recent paper entitled ’Machine learning for patient risk stratification: standing on, or looking over, the shoulders of clinicians?’ (Beaulieu-Jones et al 2021), Beaulieu-Jones and coworkers make the provocative observation that a very great deal of the predictive information in the electronic medical record (EMR) resides in the hitherto uninteresting list of clinician-initiated orders before the first midnight of the admission. This brings into question the value of predictive models that are fashioned using the EMR alone—are they really predictive at all?

They observe, though, that ’routine telemetry data’ represents a non-clinician-initiated and unbiased readout of patient physiology. Such data—which we will call continuous cardiorespiratory monitoring—including ECG, chest impedance, and sometimes arterial waveform sampled at up to several hundred Hz, along with 0.5–1 Hz samples of the canonical vital signs of heart rate, respiratory rate, and invasively or non-invasively recorded blood pressure. These high-dimensional data, which are rarely used in illness scoring systems (Davis et al 2020), have proven value. They can both stand alone (Griffin and Moorman 2001, Tarassenko et al 2006, Saria et al 2010, Politano et al 2013, Moss et al 2016, Ruminski et al 2019) or add information to EMR data elements (Griffin et al 2005, 2007, Henry et al 2015, De Pasquale et al 2017, Moss et al 2017) in predictive analytics. A prominent example is the early detection of neonatal sepsis using heart rate characteristic analysis, a practice that improved survival in a large randomized clinical trial (Moorman et al 2011, Schelonka et al 2020).

In the past, continuous cardiorespiratory monitoring in hospitals is increasing, however, due to, for example, less obtrusive hardware, clinician preference, decreasing hardware costs, increasing capability to process, store, and analyze

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Table 1. Complexity of the physiological regulation of the sinus node and the heart rate.

| Variation in the relative abundance and kinetics of the ion channels making up the sarcolemmal membrane clock of the coupled clock system (Monfredi et al 2018) |
| Variation in the kinetics of calcium pumping into and out of the sinoatrial node cell’s main Ca store, the sarcoplasmic reticulum, making up the calcium clock of the coupled clock system (Kim et al 2018) |
| Variation in the mechanisms that regulate and synchronize the coupled clocks, including phosphorylation and dephosphorylation of critical clock components by protein kinase A and calcium/calmodulin-dependent protein kinase II (Yaniv et al 2015, Li et al 2016) |
| Variation in cellular processes that are known to affect coupled clock function, including mitochondrial function (Yaniv et al 2012), nitric oxide metabolism (Danson et al 2005), and reactive oxygen species metabolism (Yang et al 2020) |
| The presence of other comorbid conditions, leading to SAN electrophysiological remodeling consequent on aging, heart failure, obesity, athletic training, and other factors (D’Souza et al 2014, 2017, 2019, Yanni et al 2020) |
| Complex circadianicity of mechanisms involving automaticity in the SAN (Monfredi and Lakatta 2019, D’Souza et al 2020) |
| Newly discovered local oscillatory calcium signals that are highly heterogeneous in phase, amplitude, and frequency occurring within the infinitely complex and diverse meshwork of pacemaker cells (Bychkov et al 2020) |

A democratic shift of leading pacemaker sites through stochastic resonance (Clancy and Santana 2020)

the data, and increasing recognition by funding agencies of the potential of AI-based decision support (Bridge to Artificial Intelligence (Bridge2AI)|NIH Common Fun).

We contend that continuous cardiorespiratory monitoring represents the most valuable non-clinician-initiated predictive signal present in patient data based on clinical and physiological reasons.

First, consider the following clinical situation. Two identical patients with saddle pulmonary embolism are admitted to different hospitals and worked up by different care teams. If one team suspects the correct diagnosis but the other suspects heart failure, we can expect sizable differences in the recording of vital signs and the ordering of lab tests, and other elements in the EMR. Because the values available in the EMR differ, EMR-based predictive analytics would present different estimates of the illness severity and the risks. On the other hand, the ground truths found in the continuous cardiorespiratory monitoring would yield identical assessments of the illness severity and event trajectories of these patients. To be sure, patient physiology is interfered with by clinicians all the time, for example, through the administration of beta-blockers, or supplemental oxygen, or electronic cardiac pacing. In the majority of patients, though, clinicians would agree that there ought to be sufficient freely running physiology to allow for interpretation and analysis of current patient state and trajectory.

Second, human physiology is a networked enterprise (Bashan et al 2012, Bartsch et al 2015); good health teems with coordinated and synchronized signaling within and between cells and organs. Consider the dynamics of the heart rate, just one of the signals available from continuous cardiorespiratory monitoring. Analysis of respiratory sinus arrhythmia, the entrainment of the heartbeat by the lungs via the autonomic nervous system (Katona and Jih 1975), shows how the complex and adaptive nature of network physiology is disrupted by systemic illness (Godin et al 1996).

The dynamics of the heartbeat, moreover, report on physiology beyond the state of the autonomic nervous system. The sinoatrial node (SAN), the natural pacemaker of the heart, has a hierarchical system of coupled and highly regulated clocks including membrane ion channels and intracellular calcium release (Monfredi et al 2013, Tsutsui et al 2018). Many additional intracellular regulatory processes independent of autonomic nerves conspire together to time the next beat, several of which are modulated by gene expression. These processes are affected by the physiological status, including the severity of the present illness, of the patient on a range of time scales. These factors intrinsic to the SAN and its component cells are shown in the table 1.

Cardiac automaticity, that is the heart rate and rhythm, reflects complex synchronized signaling on multiple scales incorporating all of the above processes, each of which is affected by the prevailing physiological state of the organism. Thus, even the heart rate dynamics alone richly describe how well the patient is adapting to illness, and make continuous cardiorespiratory monitoring an obvious and appealing source of bedside data. Open source and benchmarked toolboxes are freely available for analysis of the complex yet interpretable physiology revealed in heart rate time series (Vest et al 2018).

There are, moreover, other available continuous signals that can report in non-clinician-initiated ways on clinical network physiology. An example is the well-known coincidence of bradycardia and oxygen desaturation in distressed premature infants. This phenomenon is associated with multiple illnesses (Sullivan et al 2018, Kumar et al 2020) and is robust across institutions (Zimmet et al 2021). It is an ideal candidate for at-home use and in low-resource countries, a growing field of application for continuous cardiorespiratory monitoring (Cakmak et al 2021). And, while the fundamental processes underlying each might be temporarily impacted by clinical care, they are not likely to be annulled by the acute decisions that physicians make.
Continuous cardiorespiratory monitoring offers an open window into the workings of what are, in health, finely-tuned, highly interdependent, and synchronized physiological networks. Illness and pathology cause shifts in these networks that are mostly invisible to the physician at the bedside, yet detectable in real-time using advanced analytics. These data directly and impartially report on the physiology of the heart and lungs and how they are controlled by the autonomic nervous system. While no two clinicians necessarily do anything the same way, the laws by which the autonomic nervous system and the complex network of sinoatrial nodal cells control the heart rate are not prone to such marked variability.

Continuous cardiorespiratory monitoring, when it is available, is a highly valuable source—we argue it is the predominant non-clinician-initiated source—of information for very early detection of fundamental changes in the true physiological state of the patient. If the goal of predictive analytics monitoring is the early detection of changes in illness trajectories that the clinician is not already aware of, continuous cardiorespiratory monitoring offers better insights than the EMR.

Data availability statement

N.A.

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