SUPPLEMENTARY MATERIAL

The following is supplementary material for:

An open-loop, physiological model based decision support system can reduce pressure support while acting to preserve respiratory muscle function.

Authors:

Savino Spadaro[a]; Dan Stieper Karbing[b]; Francesca Dalla Corte[a]; Tommaso Mauri[c]; Federico Moro[a]; Antonio Gioia[a]; Carlo Alberto Volta[a]; Stephen Edward Rees.[b]

[a]: Department of Morphology, Experimental Medicine and Surgery. Section of Anaesthesia and Intensive Care. Arcispedale Sant’ Anna. University of Ferrara. Ferrara, Italy.

[b]: Respiratory and Critical Care Group, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark

[c]:Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy.

Corresponding author:

S.E. Rees – sr@hst.aau.dk

The purpose of this supplementary material is to provide the reader with an understanding of the structure and function of the CDSS applied in this paper [1]. The material includes two sections, one describing the mathematical models included in the system and a second illustrating the presentation of advice to the clinician during the study. These examples illustrate the information that can be obtained from open-loop systems based on physiological models to enable understanding of the systems advice at the bedside.

Mathematical models included in the CDSS

Figure E1 illustrates the structure of the mathematical models with a full description of model formulation and evaluation published recently [2]. The system includes mathematical models of pulmonary gas exchange; respiratory mechanics; acid-base chemistry of blood, interstitial fluid, tissues and cerebral spinal fluid; respiratory drive and ventilation. All models are tuned to the individual patient's physiological status through measurement of respiratory gas flows and pressures; calorimetry and capnography measurements of respiratory gas fractions of O_2 and CO_2, and subsequent calculation of oxygen utilisation (VO_2) and carbon dioxide production (VCO_2); pulse oximetry measurement of arterial oxygen saturation; and arterial blood measurements of acid-base, oxygenation and haemoglobin fractions. The model of pulmonary gas exchange is tuned to the appropriate matching of ventilation and perfusion to account for O_2 and CO_2 differences between arterial and end tidal gas values. To do so an arterial blood gas (ABG) is required on system start up. In some patients, the system also requires modification of FIO_2 to two levels for 2-5 minutes at each level to tune the pulmonary gas exchange model to the patient [2,3].

The respiratory mechanics model is tuned to dynamic compliance. The model of acid-base chemistry of the blood is tuned to measured values of arterial pH, PCO_2, PO_2, and SO_2, and haemoglobin concentration, with the acid-base chemistry of the cerebrospinal fluid (CSF) regulated to arterial bicarbonate values to account for chemical changes in respiratory drive. The respiratory drive model is tuned to describe the relationship between alveolar ventilation (VA) and arterial acid-base and oxygenation status. The ventilation model is tuned to the measured serial dead space (V*ds*) to allow calculation of alveolar ventilation. A series of algorithms are present in the CDSS to re-tune the models as new measurements present, or if the patient condition changes. These models are used to simulate the effect of changes in ventilator settings, with the system generating advice based upon simulated values.

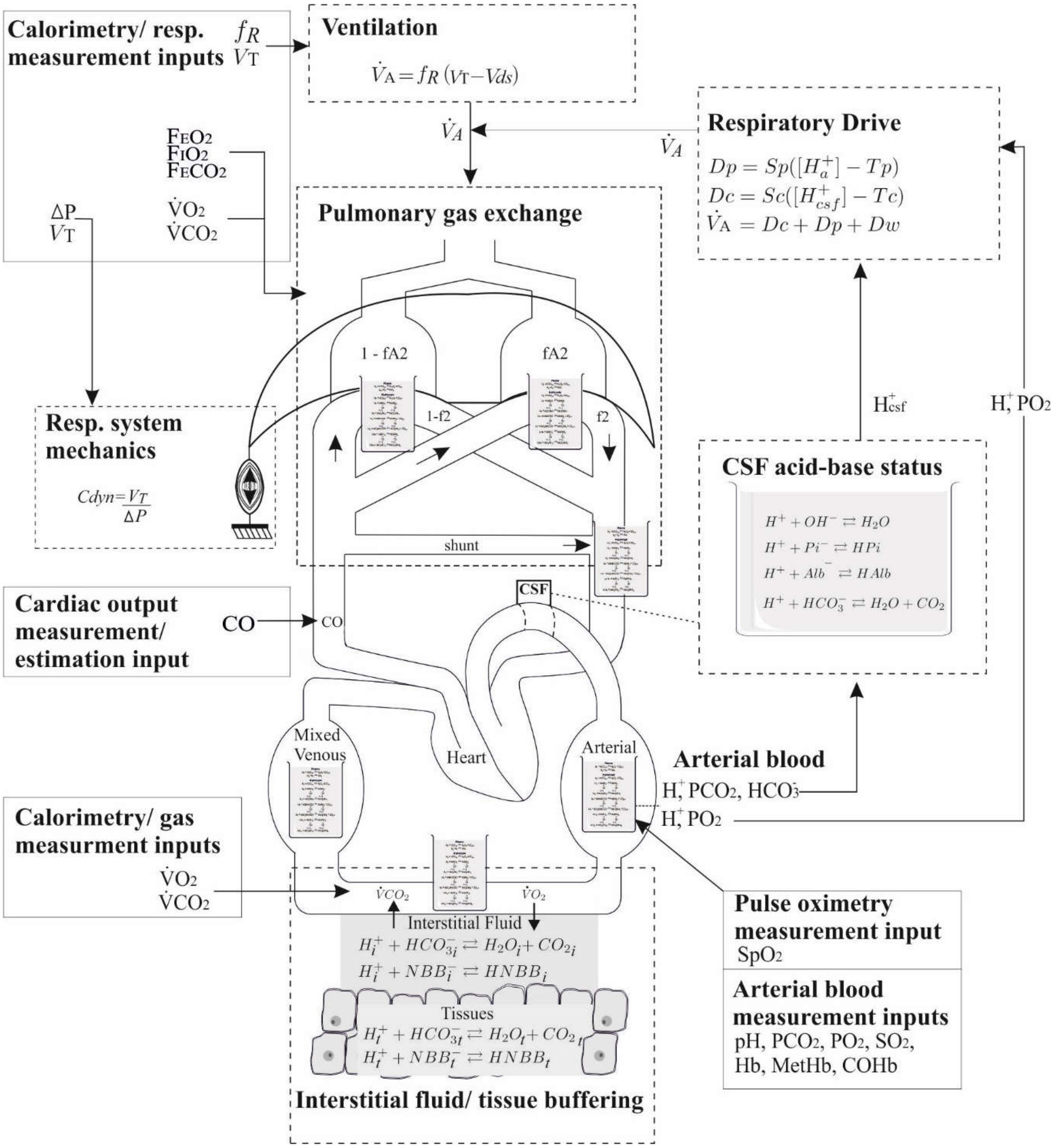

Figure E1: Mathematical models included in the CDSS. Modified from (1). Mathematical models are indicated by dashed boxes with the exception of the acid-base model of blood, which is illustrated in each blood compartment as used. Measured input values are indicated by solid boxes.

Use of the CDSS in this study.

The system can be used in two different modes, with or without generating advice for PEEP. For this study suggestions of pressure support was the focus of the study and PEEP advice was not enabled. The following text includes examples of advice generated by the CDSS in the study [1].

Figure E2 illustrates a typical screen of the CDSS with advice to reduce PS and FIO_2. The hexagon on the right hand side of the screen visualizes the patient state in terms of the balances described in the paper [1]. The three vertical axes on the hexagon present the three balances between over and under oxygenation (i.e. the compromise between the risks of oxygen toxicity and hypoxaemia, respectively); over and under ventilation (i.e. the compromise between the risks of ventilator induced lung trauma and acidosis, respectively); and the balance between over and under support (i.e. the balance between respiratory muscle atrophy due to over support, or patient stress due to under support). The blue symbol on the hexagon represents the patient's current state, and the grey symbol the simulated state according to the system's advice. The colour of the hexagon represents severity, with the most severe state represented as red, and the system automatically zooming in to yellow and green when possible. The left hand side of the screen shows both the current, simulated and advised settings. The white simulated blocks on the left are scroll wheels which allow the user to perform simulations of other levels of these ventilator settings.

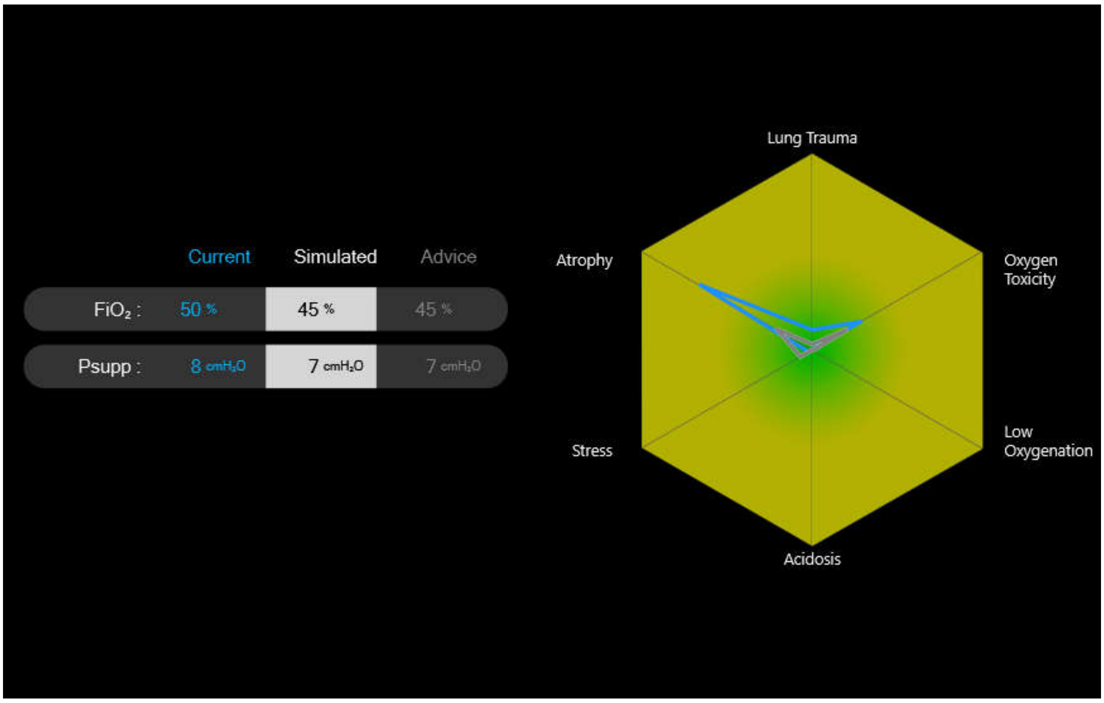

Figure E2 – User interface of the CDSS, with advice to reduce FIO_2 and PS.

Figure E3 illustrates the same screen as E2, but with the corners of the hexagon activated to show the current, simulated and advised values of variables simulated by the physiological models. In this patient, the current FIO_2 setting of 50 %, results in a SaO_2 value of 97.8 % and a current simulated SvO_2 of 77.1 %. The system illustrates that the current balance between over and under oxygenation may be inappropriate with the blue symbol on the hexagon pointing toward oxygen toxicity. The system therefore suggests reducing FIO_2. The system also illustrates an increased risk of respiratory muscle atrophy due to a low respiratory frequency, leading the system to suggest a reduction in PS from 8 to 7 cmH_2O.

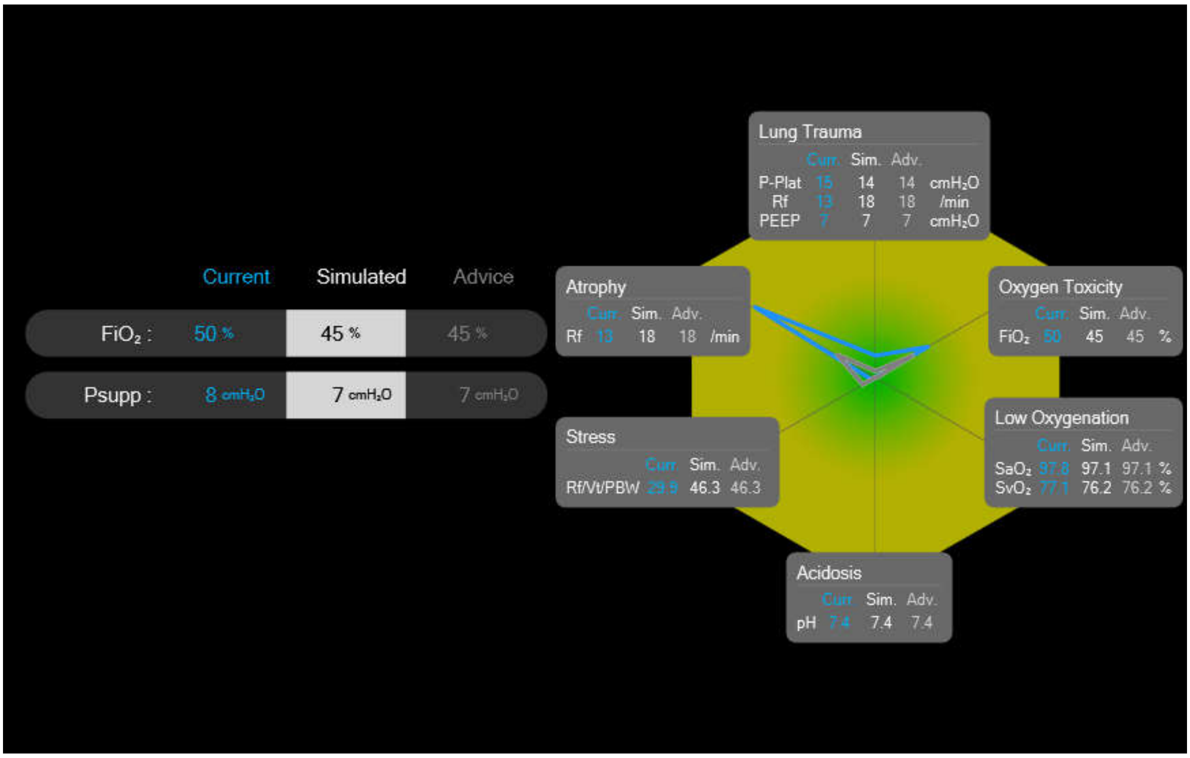

Figure E3 – User interface of the CDSS, with advice to reduce FIO_2 and PS and corners of the hexagon activated to show model simulated physiological variables associated with the different conflicting clinical goals of mechanical ventilation.

Figure E4 illustrates the result of following this advice and the subsequent advice provided by the system. The change in PS from 8 to 7 cmH2O increased respiratory frequency to 18 bpm, with this PS level being an appropriate compromise between respiratory muscle atrophy and stress according to simulations and as such, that PS should remain at this level. The system also calculates that it is possible to further reduce FIO_2 while maintaining reasonable arterial and simulated venous oxygen saturations. The system's subsequent function is to monitor the patient and, as the patient changes, re-tune the physiological models and calculate new advice.

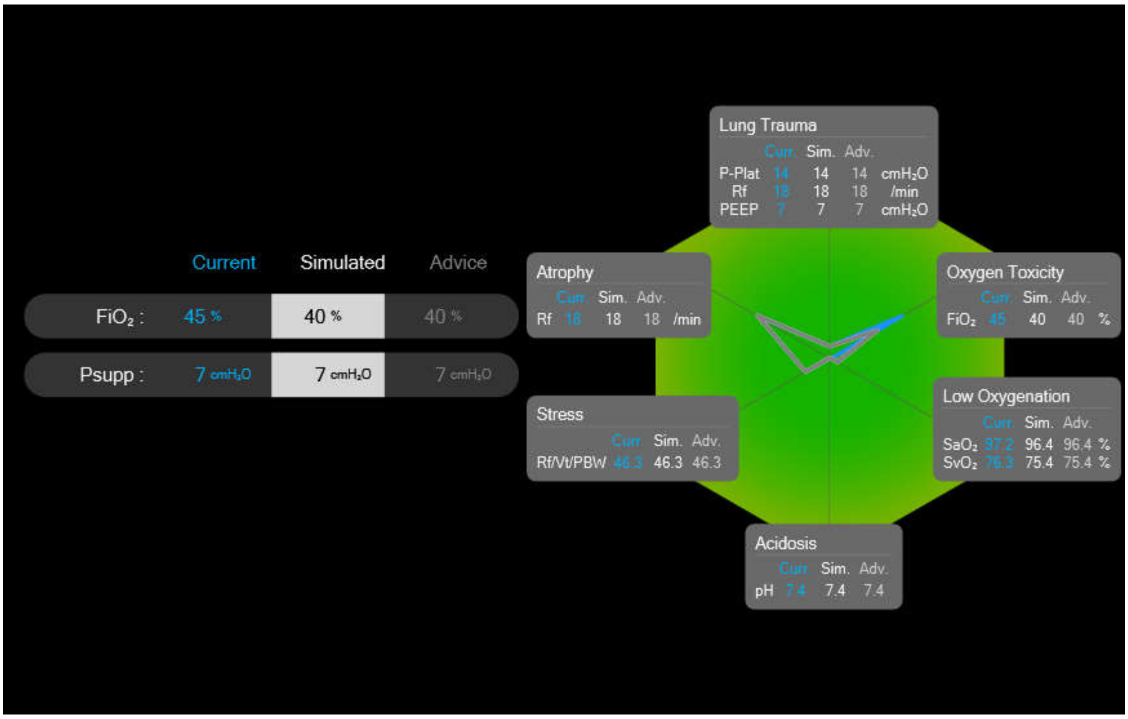

Figure E4 – User interface of the CDSS, with results of reducing FIO_2 and PS according to the advice in Figure 3, and the next advice, with corners of the hexagon activated.

Figure E5 illustrates a patient with advice to increase PS but reduce FIO_2. In this patient, the current FIO_2 setting of 40 %, results in a SaO_2 of 98.5 % and a simulated SvO_2 of 83.1 %. The system therefore suggests to reduce FIO_2. The system also illustrates an increased risk of patient stress due to a relatively high respiratory frequency to tidal volume ratio. The blue symbol on the hexagon points toward stress and the system suggests an increase in PS from 9 to 10 cmH_2O.

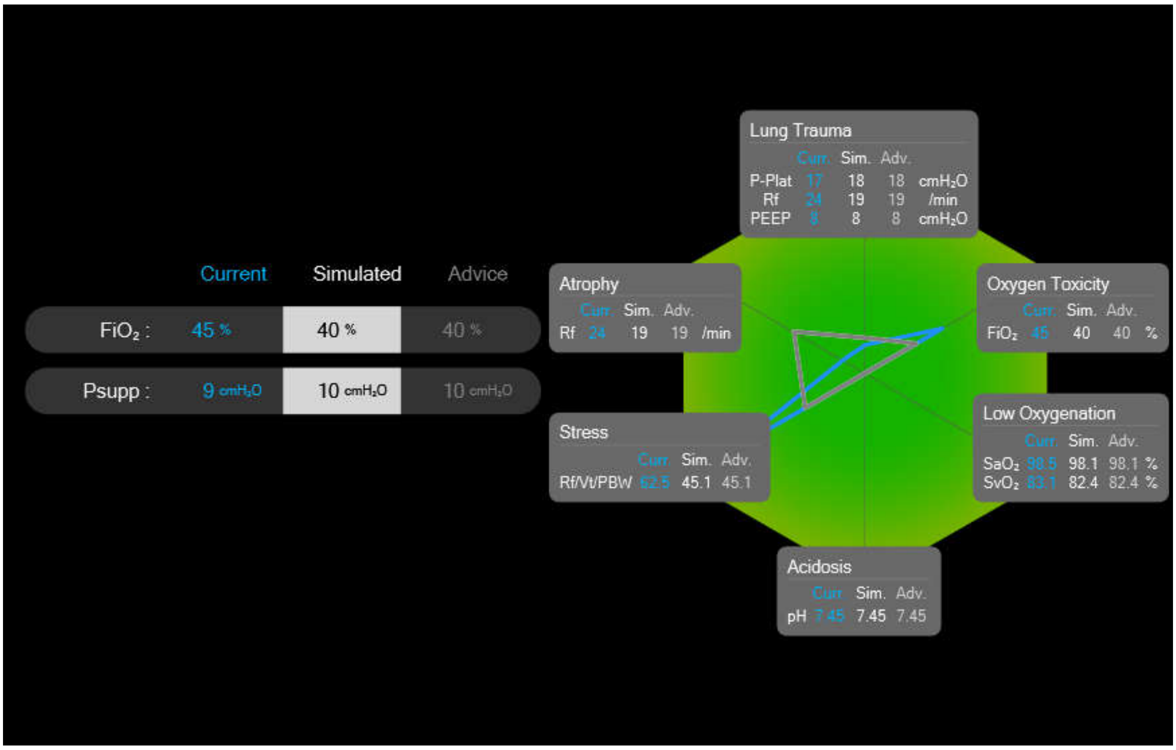

Figure E5 – User interface of the CDSS, with advice to reduce FIO_2 and increase PS, with corners of the hexagon activated.

Figure E6 illustrates the result of following this advice and the subsequent advice provided by the system. The system calculates that it is possible to further reduce FIO_2 while maintaining reasonable arterial and simulated venous oxygen saturation. The change in PS from 9 to 10 cmH_2O decreased respiratory frequency to 20 bpm, and the system calculates that a suitable compromise has been achieved between respiratory muscle atrophy and stress and that PS should remain at this level.

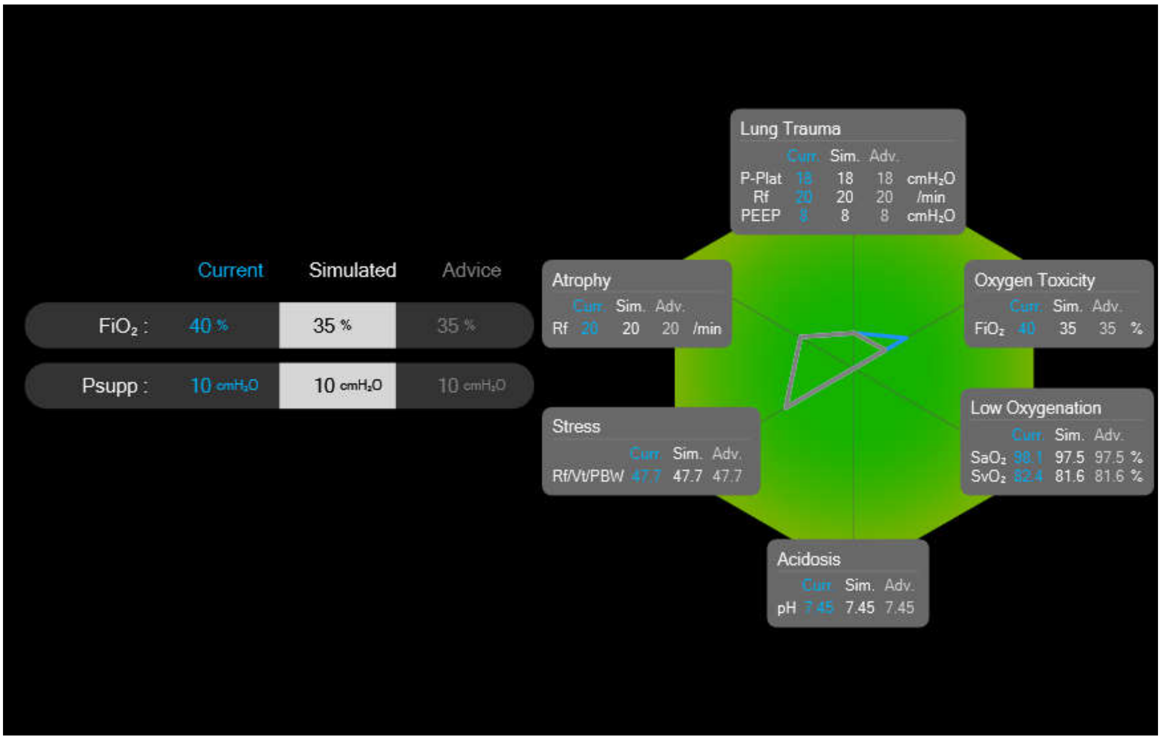

Figure E6 – User interface of the CDSS, with results of reducing FIO_2 and increasing PS, and the next advice, with corners of the hexagon activated.

Figure E7 illustrates advice of the CDSS system at the three phases of the protocol for a single patient. The left insert illustrates the optimal settings following advice from baseline. The middle insert illustrates the clinical picture of over support – risk of respiratory muscle trophy, risk of lung trauma, risk of over oxygenation – and the first advice to lower PS and FIO_2. The right insert illustrates the clinical picture of under support and over oxygenation – risk of respiratory muscle stress, risk of over oxygenation – and the first advice to increase PS and lower FIO_2.

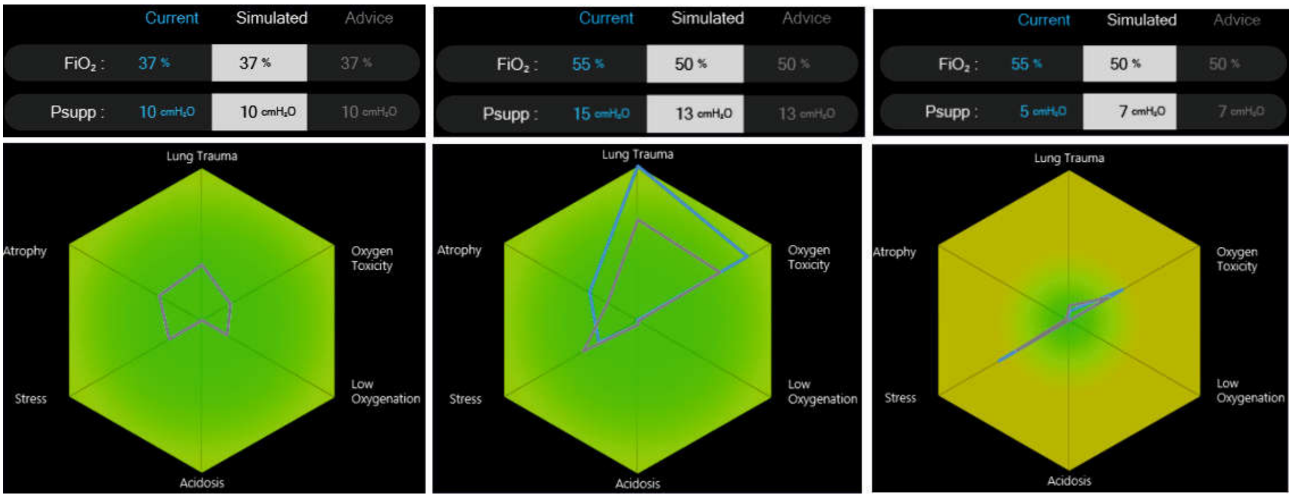

Figure E7 – Three hexagon graphics depicting Beacons suggestion for the optimal ventilator settings (left insert); advice following over support (middle insert) and advice following under support (right insert).

References

[1] Spadaro S, Karbing DS, Dalla Corte F, Mauri T, Moro F, Gioia A, Volta CA, Rees SE. Open-loop, physiological model based decision support systems can reduce pressure support while preserving respiratory muscle function. Journal of Critical Care, in submission.

[2] Rees SE, Karbing DS. Determining the appropriate model complexity for patient-specific advice on mechanical ventilation Biomed Tech (Berl). 201762(2):183-198.

[3] Thomsen LP, Karbing DS, Smith BW, Murley D, Weinreich UM, Kjærgaard S, et al. Clinical refinement of the automatic lung parameter estimator (ALPE). J Clin Monit Comput. 2013;27(3):341-50.