J. Biomed. Eng. Res : 187-193, 2010

# Design and Experiment of a Micro Electronic System for Prediction of Alveolar-Gas Partial Pressures

Da-Jung Kim[1], Keun-Shik Chang[1], Saji Kim[1], Hye-Yun Park[2] and Gee-Young Suh[2]

[1]*School of Mechanical, Aerospace and Systems Engineering, Korea Advanced Institute of Science and Technology, 373-1 Guseong-dong, Yuseong-gu, Daejeon 305-701, Republic of Korea*

[2]*Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea*

*(Received January 27, 2010. Accepted April 12, 2010)*

**Abstract**

In this study we have designed and fabricated an inexpensive micro electronic system that we call Alvitek. It can indirectly but accurately predict and display the partial pressures of alveolar oxygen and carbon dioxide for the patients in the ICU of a hospital. Alvitek consists of both hardware part and software part. Performance of the system is tested by animal experiment with pigs for various $F_IO_2$ and RR(Respiratory Rate) values under the mechanical ventilation. The predicted alveolar gas partial pressures are cprpared with the approximate alveolar oxygen partial pressures easily calculated by the physician's bedside formula. As a result, we have concluded that the relative error of A-a$DO_2$ calculated by the bedside formula grows seriously for lower $F_IO_2$ values. The present prediction method of Alvitek is henceforth believed very meaningful to the physicians. The system hardware and software are described in the text.

**Key words :** Alveolar gas, Digital signal processor, Mechanical ventilation, Computational blood gas analysis, CO2 sensor

## Ⅰ. INTRODUCTION

According to the data from the Statistics Korea, the fifth greatest cause of death is the respiratory disease. The number of patients who die from respiratory diseases steadily increases every year. Henceforth the more accurate methods and standards for diagnosis and treatment of the respiratory patients seem very urgent.

The oxygen partial pressure of alveoli ($P_AO_2$) is used to determine whether a patient has serious gas exchange disorder in the alveolar-capillary unit of the lung during the mechanical ventilation. In addition, A-a$DO_2$ (difference of oxygen gas partial pressures between the alveoli and arterial blood) is used to judge whether a patient has serious oxygen diffusion impairment. Unfortunately, partial pressures of the alveolar gas cannot be directly measured because the average size of alveoli is as small as 0.1~0.2mm in diameter. We can predict instead the alveolar gas data, $P_AO_2$ and $P_ACO_2$, by solving the mass balance equations. Because computing of the mass balance equations is complicated and time-consuming, physicians prefer a simple bedside formula to check with $P_AO_2$ that is only a very approximate solution to the complete mass balance equations.

The computing algorithm introduced in the reference[1] can solve the mass balance equations in a faster and easier manner than before. However, these algorithms are at present based on a desktop computer that has absolutely no mobility. Also the algorithm is big in the program size and computing is too slow to be used on the bedside of the intensive-care patients. To overcome these drawbacks, we have done several measures. First, we had the computing algorithm to solve the mass balance equations modified and embedded in a DSP (Digital Signal Processor, TMS320F28335, Texas Instruments). Second, we built a hardware system in which DSP is interfaced with the NDIR(Non Dispersive Infra Red) $CO_2$ gas sensor and other I/O devices. Third, we developed a software system that controls the functions of DSP.

**Corresponding Author** : Keun-Shik Chang
School of Mechanical, Aerospace and Systems Engineering,
Korea Advanced Institute of Science and Technology
Daejeon 305-701, Republic of Korea
Tel : +82-42-869-3711 / Fax : +82-42-350-3710
E-mail : kschang@kaist.ac.kr

## II. Computational Blood Gas Analysis[1]

### A. Respiratory gas exchange model

Alveoli are the micro air sacs of the lung where oxygen and carbon dioxide molecules are exchanged by diffusion through the alveolar membrane, between the ventilation gas and the pulmonary end-capillary blood. The basic gas-exchange model considered in this study is the three-compartment lung model depicted in Fig. 1. It takes account of the dead space gas and the shunted blood by which the alveolar ventilation and arterial blood gas is affected. We can numerically compute the alveolar partial pressures of $O_2$ and $CO_2$ using the CFD(computational fluid dynamics) techniques that are well developed in the mechanical and aerospace engineering.

### B. Mass Balance Equations

1) Mass balance equation

Based on the three-compartment lung model, we calculate accurately the alveolar partial pressures, $P_AO_2$ and $P_ACO_2$, by solving the boundary value problem consisting of the mass balance equations and four terminal boundary conditions. Two out of the four boundary conditions come from the external respiration: they are the inspirational gas data $P_IO_2$ and the end-tidal gas data $P_{ET}CO_2$. The other two come from the internal respiration: they are the mixed-venous blood gas data, $P_VO_2$ and $P_VCO_2$, and the arterial blood gas data, $P_aO_2$ and $P_aCO_2$.

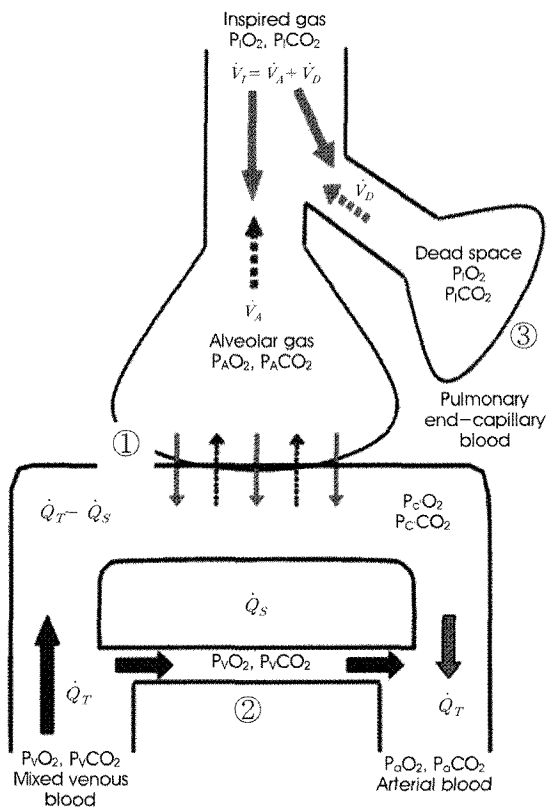


**Fig. 1.** The three-compartment lung model

These boundary conditions are used in the following mass balance equations to determine the unknown $P_AO_2$ and $P_ACO_2$.

$$\left(\dot{V}_I/\dot{Q}\right)_1 P_I O_2 - \left(\dot{V}_A/\dot{Q}\right)_1 P_A O_2 = k\left(C_{C'}O_2 - C_{\bar{V}}O_2\right) \quad (1)$$

$$\left(\dot{V}_A/\dot{Q}\right)_2 P_A CO_2 = k\left(C_{\bar{V}}CO_2 - C_{C'}CO_2\right) \quad (2)$$

$$\left(\dot{V}_I/\dot{Q}\right)_3 P_I N_2 - \left(\dot{V}_A/\dot{Q}\right)_3 P_A N_2 = \lambda_{N_2}\left(P_{C'}N_2 - P_{\bar{V}}N_2\right) \quad (3)$$

$$P_A O_2 + P_A CO_2 + P_A N_2 = P_B - P_{H_2O} \quad (4)$$

The subscripts in the above mean follows. I: inspiration air, A: alveolar gas, C': end-capillary blood, and $\bar{V}$: mixed venous blood. The constant $\lambda$ (= 0.0017) is the blood-to-gas partition coefficient for the nitrogen gas. The constant $k$ is a conversion factor between the two different unit conventions: the STPD (standard temperature and pressure, dry) convention used for the gas content C and the BTPS (body temperature and pressure saturated with water vapor) convention used for the ventilation rate $\dot{V}$. Equations (1) ~ (3) state that a volume of oxygen, carbon dioxide or nitrogen disappeared from one breathing agent reappears in the other agent by diffusion, between the ventilation gas and the circulation blood. Equation (4) states that partial pressures of all these gases are added to be a barometric pressure minus the vapor pressure. The gas partial pressures $P$ in the ventilation and the gas contents $C$ in the circulation can be inter-converted by means of the oxygen and carbon dioxide dissociation curves of the hemoglobin in the blood[5,8].

The mass balance equations (1)-(3) have two parameters, the inspired ventilation-to-perfusion ratio, $\dot{V}_I/\dot{Q}$, and the alveolar ventilation-to-perfusion ratio, $\dot{V}_A/\dot{Q}$. We put a tag to each of these ventilation-to-perfusion ratios in order to distinguish what equations they belong to: subscript 1 to those in equation (1), subscript 2 to those in equation (2) and subscript 3 to those in equation (3). Since computation is started with some initial guesses for the unknown variables, these subscripted parameters are naturally discrepant during the iterative computation. However, when the computation is converged to a solution, they all become single-valued within a tolerance as an exit is made from the multiple do-loops of the computation.

2) Shunt Ratio Equations

The shunt ratio is defined by equation (5) below. It is a ratio

of the oxygen content diminished in the arterial blood because of mixing with the shunt blood, to the oxygen content escalated by diffusion between the mixed venous blood and the end-capillary blood. The shunt ratio can be equally determined by considering either the oxygen content in equation (5) or the carbon dioxide content in equation (6). These two shunt ratios are also discrepant during the iterative computation but converge to a single-valued function as the numerical solution is converged.

$$Y_{O_2} = (C_{c'}O_2 - C_aO_2)/(C_{c'}O_2 - C_{\bar{V}}O_2) \quad (5)$$

$$Y_{CO_2} = (C_aCO_2 - C_{c'}CO_2)/(C_{\bar{V}}CO_2 - C_{c'}CO_2) \quad (6)$$

3) Bedside formula

The physician in the ICU(Intensive Care Unit) of a hospital would use a conventional bedside formula given by equation (7) below to obtain the alveolar oxygen partial pressure, $P_AO_2$. We can, in fact, show that this formula is a reduced form of the mass balance equations by introducing a few very bold approximations.

$$P_AO_2 = F_IO_2 \times (P_B - P_{H_2O}) - P_aCO_2/RQ \quad (7)$$

In the above, $RQ$ is the respiratory quotient defined as a ratio of the carbon dioxide output to the oxygen uptake in the respiration. Physicians usually take the value 0.8 for $RQ$.

### C. Computing Algorithms

Following are the computational steps to solve for the alveolar partial pressures.

1. Input the four boundary conditions:
   $P_IO_2$, $P_{ET}CO_2$, ($P_VO_2$, $P_VCO_2$) pair and ($P_aO_2$, $P_aCO_2$) pair
2. Start FOR loops
   ① Put an arbitrary $P_AO_2$ and set the dead space ratio X equal to zero.
   ② Set $P_ACO_2 = P_{ET}CO_2 / (1-X)$
   ③ Solve the mass balance equations to find new iterative $P_AO_2$.
   ④ Solve the shunt equations using the above $P_AO_2$ and $P_ACO_2$
   ⑤ Check if the two shunt ratios are equal, namely, $Y_{O_2} = Y_{CO_2}$.
   Elseif go to step ① to reassume the trial values, $P_AO_2$ and X.
3. End FOR loop.
4. Determine $P_AO_2$, $P_ACO_2$, X and Y

## Ⅲ. SYSTEM DESIGN

### A. Hardware system

Hardware system is showed in the conceptual block diagram in Fig. 2. Inside the box outlined by the dashed line is the hardware system fabricated in this research. Terminal boundary conditions obtained by ABGA (Arterial Blood Gas Analysis), VBGA (Venous Blood Gas Analysis) and from the mechanical ventilator are typed into the DSP through a keypad. The analog voltage output from the NDIR $CO_2$ sensor (maximum measurement error ± 30 ppm) is transmitted to the ADC(Analog to Digital Converter). After digitized, it is passed to a digital filter to get rid of noise and calibrated with respect to the temperature. Then the DSP picks up the partial pressure of end-tidal $CO_2$. These data are real-time to measure the changing physical state of the patient. To be truly real-time, however, we need to wait until the blood gas analysis becomes fully real time with a sensor attached to the catheter as has recently been demonstrated in Europe and North America. As the computer determines $P_AO_2$ and $P_ACO_2$ through computational algorithms, the DSP transmits the result to a display device.

The functions of the DSP in this system are multiple: 1) digitizing the analog voltage output from the sensor, 2) receiving through the key pad the input values of the terminal boundary conditions, 3) computing alveolar-gas partial pressures and 4) sending results to the display panel. The high-precision ADC is therefore included with the I/O port and UART(Universal Asynchronous Receiver/Transmitter).

In addition, to handle the real-time and floating- point unit computing of large number of mathematical operations, the DSP particularly designed for digital signal processing is employed. It responds quickly and repetitively to a set of data

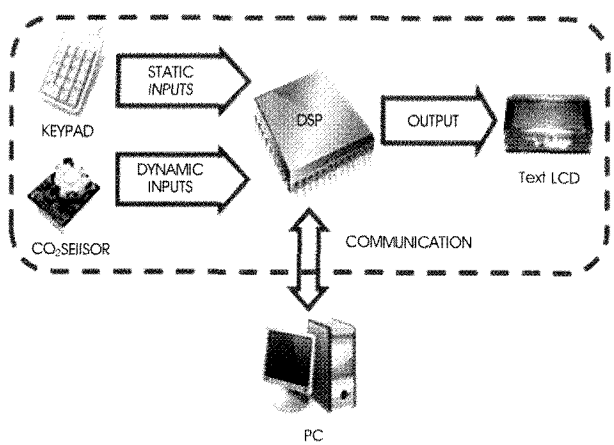


Fig. 2. Block diagram of the hardware system

having wide dynamic range[4].

In order to measure the partial pressure of $CO_2$ in the expired gas and in the end-tidal $CO_2$, the NDIR $CO_2$ gas sensor is implemented to the experimental system. It has a low power, reduced size, five-year warrant and needs no calibration.

### B. Software system

Software system is divided into two parts. One part is the software system for operating a hardware platform. The other part is the subroutines to calculate the mass balance equations. Considering portability of the system and handling of dynamic I/O, we have changed the programming language from Fortran to C language. The flow chart is given in Fig. 3.

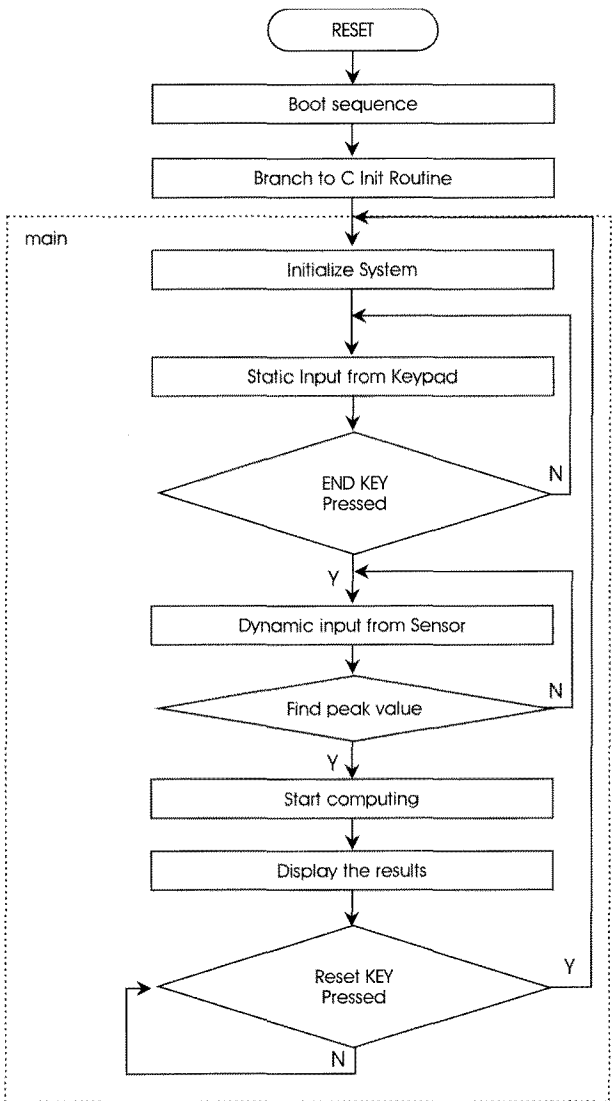


Fig. 3. Flow chart of the software system for operating hardware platform.

## Ⅳ. EXPERIMENTS & RESULTS

### A. Preprocessing for experiment

Healthy pigs (8 to 10 weeks of age) weighing around 30kg are anesthetized with 6mg/kg/hr of pento-barbital and 0.1mg/kg/hr of vecuronium during the animal experiment. A modified volume-preset ventilator (GALILEO; Hamilton Medical, Switzerland) is operated as the inhalational anesthesia is replaced by intravenous anesthesia. Initial settings of the ventilator are as follows. Tidal volume, 8ml/kg; respiratory rate, 20 breaths/min; PEEP(Positive End Expiratory Pressure), 5 $cmH_2O$; $F_IO_2$, 1.0; the ratio of exhalation to inhalation, 1:2, that is later adjusted according to

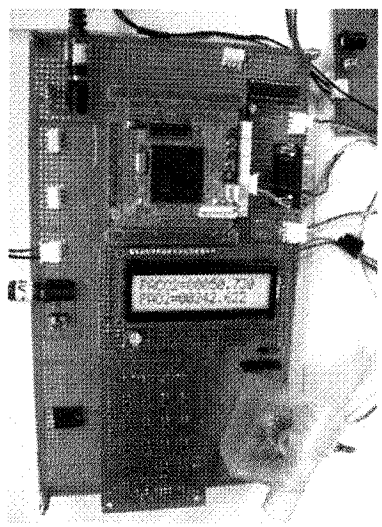

Fig. 4. The Alvitek

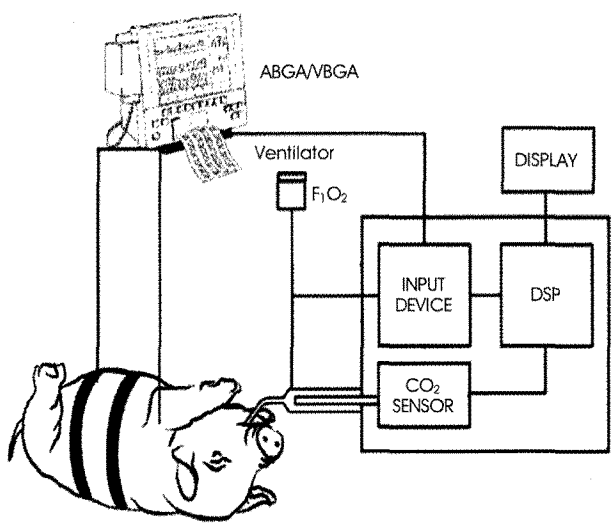


Fig. 5. A schematic of the animal experiment.

the experimental protocol[4].

For measurement of the arterial breath gas contents, extraction of blood was first made by a 20G catheter inserted to the right femoral artery of a pig. For multiple purposes like extraction of the mixed venous blood and others, a catheter was inserted from the right jugular vein into the right atrium of the heart. Saline solution was injected to the lung with a speed of 4ml/kg/hr when artificial lung impairment was desired. A 7 Fr Swan-Ganz catheter (balloon-tripped flow-detecting thermo- dilution catheter, Baxter inc, USA) was inserted to the pulmonary artery through the left jugular vein to check the pressure waveform. Throughout the procedure, the arterial and the pulmonary arterial pressures were monitored with Hewlett-Packard Component Monitoring[5].

The blood samples from the femoral and the pulmonary arteries were analyzed by 288 Blood Gas Analyzer (CIBA-Coring, USA). These procedures are respectively called ABGA and VBGA.

**Table 1.** Experimental condition (32 kg pig, body temperature 37.3 C)

| Case \ Condition | Ventilator Setting | | |
|---|---|---|---|
| | RR [b/min] | $V_{control}$ [ml] | $F_IO_2$ [%] |
| Case 1 | 15 | 300 | 40 |
| Case 2 | 15 | 300 | 60 |
| Case 3 | 15 | 300 | 80 |
| Case 4 | 25 | 300 | 40 |
| Case 5 | 25 | 300 | 60 |
| Case 6 | 25 | 300 | 80 |

**Table 2.** Clinical data obtained by ABGA and VBGA

| | | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 |
|---|---|---|---|---|---|---|---|
| ABGA | Hb [g/dL] ** | 8.9 | 8.2 | 8.2 | 8.1 | 8.6 | 7.9 |
| | Hcrit [%] ** | 26 | 24 | 24 | 24 | 25 | 23 |
| | pHa | 7.334 | 7.308 | 7.306 | 7.421 | 7.426 | 7.418 |
| | $P_aCO_2$ [mmHg] ** | 51.3 | 50.9 | 51.3 | 36.4 | 35.9 | 36.3 |
| | $P_aO_2$ [mmHg] ** | 193.3 | 321.7 | 422.7 | 225.7 | 349.3 | 413.5 |
| | A-a$DO_2$ [mmHg] | 37.5 | 57.1 | 103.3 | 22.3 | 46.1 | 128.1 |
| VBGA | pHv | 7.227 | 7.247 | 7.224 | 7.332 | 7.322 | 7.287 |
| | $P_vCO_2$ [mmHg] ** | 65.1 | 59.0 | 52.5 | 46.6 | 49.4 | 48.4 |
| | $P_vO_2$ [mmHg] ** | 35.5 | 44.0 | 48.1 | 30.7 | 33.6 | 39.9 |

**Table 3.** Comparison of the Alvitek results with the bedside formula

| case | Predicted Solution (PS) by Alvitek | | Bedside Formula (BF) | | Error (\|BF-PS\|/PS) | |
|---|---|---|---|---|---|---|
| | $P_ACO_2$ : $PAO_2$ [mmHg] | A-a$DO_2$ | $P_AO_2$ [mmHg] | A-a$DO_2$ | $P_AO_2$ [%] | A-a$DO_2$[%] |
| 1 | 50.73 : 242.63 | 49.32 | 220.57 | 27.27 | 9.09 | 44.7 |
| 2 | 50.40 : 379.76 | 58.06 | 363.41 | 41.71 | 4.31 | 28.16 |
| 3 | 51.07 : 503.56 | 80.86 | 505.26 | 82.56 | 0.34 | 2.10 |
| 4 | 36.18 : 252.96 | 27.26 | 239.19 | 13.49 | 5.44 | 50.5 |
| 5 | 35.49 : 396.01 | 46.80 | 382.16 | 32.86 | 3.50 | 29.79 |
| 6 | 35.12 : 537.01 | 123.51 | 524.01 | 110.51 | 2.42 | 10.53 |

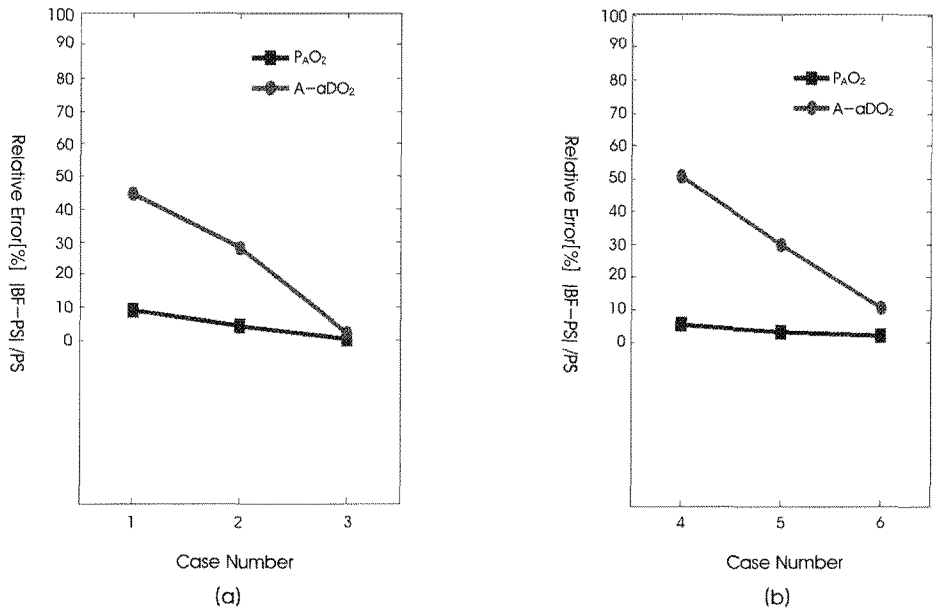


**Fig. 6.** *The errors of the bedside formula relative to the results predicted by the Alvitek: (a) RR=15, (b) RR=25*

## V. EXPERIMENTAL CONDITION

Table 1 shows the six different conditions of the mechanical ventilator for the animal experiment. They are some of the data base that shows the typical trend of correct measurement. Due to the limited physical range of the relatively-inexpensive NDIR $CO_2$ sensor, we had the end-tidal $CO_2$ sensor operated under 50,000 ppm. Two groups are distinguished by assigning RR with 15 and 25. The inspired gas volume was fixed with 300ml in the two groups. Concentration of the inspired oxygen was varied with 40%, 60%, and 80% in each group. Body temperature of the animal was 37.3℃: it was used for calibration of the sensor and for calculation of the vapor pressure $P_{H2O}$.

Experimental data obtained by ABGA and VBGA are shown in Table 2. The data marked with superscript ** are the four terminal boundary conditions and the two basic blood data obtained by ABGA and VBGA; the rest variables are the calculated data.

## VI. RESULTS & DISCUSSION

As mentioned earlier, the alveolar gas partial pressures for $O_2$ and $CO_2$ cannot be directly measured with the current technology. However, the alveolar-gas partial pressures predicted by solving the mass balance equations are believed considerably accurate as far as we implement the computer algorithm with correct blood chemistry and supply accurate terminal boundary data.

It is interesting at this point to compare the $P_AO_2$ values obtained by the bedside formula with the present results. In Table 1, $F_IO_2$ is increased from 40% to 80% in the first group ( Cases 1~3) as well as in the second group (Cases 4~6). In Table 3, the error of the bedside formula for $P_AO_2$ relative to the Alvitek results is evidently increased for lower $F_IO_2$ values. For example, the relative error increases from 0.34% in the Case 3 to 9.09% in the Case 1 in the first group, and from 2.42% in the Case 6 to 5.44% in the Case 4 in the second group. The relative error of A-a$DO_2$ for the bedside formula is

**Table 4.** Specification of the Alvitek

| Case | Device Size [cm] | Device Weight [kg] | Calculation time [s] |
|---|---|---|---|
| 1 | 15*20 | 1.5 | 3.41 |
| 2 | | | 3.97 |
| 3 | | | 5.72 |
| 4 | | | 3.41 |
| 5 | | | 3.41 |
| 6 | | | 6.32 |

even more serious: we note that it is increased from 2.10% in the Case 3 to 44.7% in the Case 1 in the first group, and from 10.53% in the Case 6 to 50.5% in the Case 4 in the second group. One of the reason is because the bedside formula has been derived from the mass balance equations by applying the ideal lung model and the steady state assumption.

The results show a problem of the bedside formula because A-a$DO_2$ is the medical index more useful and desired by the physicians in charge of the ICU of a hospital. In short, since the bedside formula can give as much as 50% error in the A-a$DO_2$ prediction when lower oxygen concentration is used in the mechanical ventilators, it is necessary to invent some reliable methods to predict the true alveolar gas pressures. The present Alvitek should be a nice substitute.

## Ⅶ. CONCLUSION

In this work, we designed and developed an inexpensive, fast and compact micro-electronic system to predict oxygen and carbon dioxide partial pressures of the alveolar gas. The system is based on the software with CBGA (Computational blood gas analysis) algorithm, NDIR(Non-Dispersive Infra-Red) $CO_2$ sensor and a DSP(Digital Signal Processor) with peripheral devices having user-friendly interface.

In order to validate the efficiency and accuracy of the developed system, animal experiment has been carried on pigs with varying $F_IO_2$ and RR(Respiratory Rate) values. It was possible to compare the physician's bedside formula with the present Alvitek results to assess how much relative error exists between the two.

The present Alvitek system has its own weakness since it relies on the invasive method for acquisition of the terminal boundary data of the blood such as the mixed-venous and the arterial blood data. Nevertheless it uses a compact electronic system of a pocket calculator size for CBGA and ourput display with minimum data input. The Alvitek has academic and clinical importance as it has a potential for further advancement like continuous blood data measurement and development of less invasive method: it would ultimately lower the clinical risk existing with the present methods.

## ACKNOWLEDGEMENT

This work has been financed by the National Research Foundation of Korea Grant funded by the Korean Government (NRF-2009-R01-0083698). The authors are deeply grateful to NRF for this support.

## REFERENCES

[1] Hwang. Bae, *A minimally invasive Prediction Method for Respiratory Gas Partial Pressure of Alveoli and Mixed Venous Blood*, Daejeon, Korea: Ph.D. thesis, KAIST, 2008.

[2] Robert E. St. John, RN, RRT, MSN, "End-Tidal Carbon Dioxide Monitoring," *Critical Care nurse.*, vol. 23, no 4, pp83-88, 2003.

[3] *TMS320F28335, TMS320F28334, TMS320F28332 Digital Signal Controller Data Manual*: Texas Instruments, 2007.

[4] T. H. Clutton-Brock, "The evaluation of a new intravascular blood gas monitoring system in the pig," *Journal of clinical monitoring.*, vol, 10, no 6, pp.387-391, 1994.

[5] D. G. Markhorst, "A system for integrated measurement of ventilator settings, lung volume change and blood gases during high-frequency oscillatory ventilation," *Journal of medical engineering & Technology.*, vol. 27, no.3, pp.128-132, 2003.