31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Construction of Modular Novel Bioartificial Liver Support System

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Abstract—**A modular novel bioartificial liver support system was designed and constructed in order to simplify tedious operation of artificial liver treatment and to improve the applicability in the system. The design ideas, structure composition, system function, and etc, were described in detail. In this system, the variety of the therapy modes could be conveniently connected by the interface of modular structure. Industrial control computer was used as the main control platform, and physical of control parameters such as pressure, pump speed, dissolved oxygen, temperature, and etc, were transmitted into computer, then according to the instruction, process of the treatment was accomplished by the executing units implemented by main control system. Touch screen of human-computer interface was adopted, which made the system better operational and more comfortable. The system has passed the spot function test, and all indexes can meet requirements for the clinical treatment requested. It has the character such as modular design, systematic distribution, building-block structure, and etc, which supports a great novel operation platform for artificial therapy.**

Index Terms—**Bioartificial liver system, modular, medical equipment, therapy of artificial liver**

I. Introduction

Bioartificial liver support system (BALSS) is a new therapy that has just developed in recent years on a temporary substitute or support the main functions of liver, and its therapeutic effect has been affirmed by most experts [1,2]. BALSS working principle is to place the hepatocytes into an extracorporeal bioreactor to cultivate, through semi-permeable membrane with the plasma (or blood) of patients for Material exchange in order to achieve liver detoxification, synthesis and metabolism [3]. Because of the damage to hepatocytes which were caused by toxic substances in the patients' plasma, a novel bioartificial liver (NBAL) therapy has appeared in BAL Research areas in recent years [4] which can bring blood purification, plasma exchange and other non-biology-based BAL therapy aspect of the circulatory system into the novel BAL therapy. It could not only have the function of toxin removal, but also take the specific role of BAL, the detoxification, synthesis and metabolism.

As the requirement of hepatocyte culture in BAL, the BAL device has to take an environment which is similarly to cell culture laboratory [5,6]; it brought many disadvantage to BAL devices, such as bulky, inconvenient transportation, operation of complex, and so on. Furthermore, the introduction of non-biological treatment modalities allows the complex operation of BAL even more cumbersome. Those may not only increase the difficulty to the promotion of NBAL in clinical use, and proficiency of the operator will also be a direct impact on the treatment of artificial liver. It makes a lot of development restrictions for NBAL.

As to solve the problem that in view of the above-mentioned, we have designed a novel bioartificial liver support system (NBALSS) based on the construction of modular structure. By depth analysis of the major functions in NBAL and then use the idea of modular to divide the structure of system, a hardware platform of NBALSS was constructed from an engineering point of view. We have developed the software system and user interface too. The system could not only The system can not only achieve the necessary NBAL treatment for a variety of combinations, but also provide the function of a separate or several treatment modules by the basis of clinical need. The entire system has characteristics of modular design, systematic layout, and building-block structure. They can provide the necessary conditions for the further development of BAL.

II. Ideal of Design and System Function

According to the demand of BAL use, the construction features of NBALSS is necessary to build not only including the function of non-bioartificial liver devices (hemodialysis, hemofiltration, plasma exchange, plasma adsorption, and so on), but also to provide a appropriate physical environment for the growth of hepatocytes in bioartificial liver devices. Therefore, after depth analysis of the devices in non-bioarticifical and bioarticifical equipment [7,8], and research on the market of related products, we summarized the main features of NBAL, including the following aspects:

Manuscript received, June 20, 2009. This work was supported in part by the High Technology Research and Development Program of China under Grant 2006AA02A140.

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A. *Pump module in extracorporeal circle system*

This system is the power source of flow in NBALSS, basic flow-based peristaltic pumps were used as power source of liquid circulation. The regulation of pump speed feedback by other modules was implemented by computer through the control algorithms. It can maintain the control objectives by coping with other physical implementation control modules. At the same time, with a micro-injection pump, accurate quantitative slow delivery during the treatment process can be achieved.

B. *Physical Measurement and Control Module*

During the equipment running, a variety of physical can be send to the control system timely by the use of various types of sensing equipment. Based on past experience, a controller which has independent functions and perfect structure was build up through the selection fit to different control laws and control strategies. It can implement the control of important physical under different therapy mode, including: temperature, dissolved oxygen, pH, pressure, weight, air bubble detection, and so on.

C. *Rapid detection module of hepatocyte status*

A rapid detection system has been developed to get the hepatocyte status during hepatocyte culture. At the basis of the original work [9], we optimize the design of online detection, and make its function and structure modularly to access with the modular idea of the new system.

D. *Software operation module of Human-Computer Interaction*

A large amount of data should be saved by the system during the experiment, as the necessary basis for online optimize and offline process. Therefore, an operating system must be developed which should have the functions of data acquisition, analysis, processing and integration the control law of typical unit. At the mean time, the system should also meet the requirements of operability, ease of use and stability in practical use.

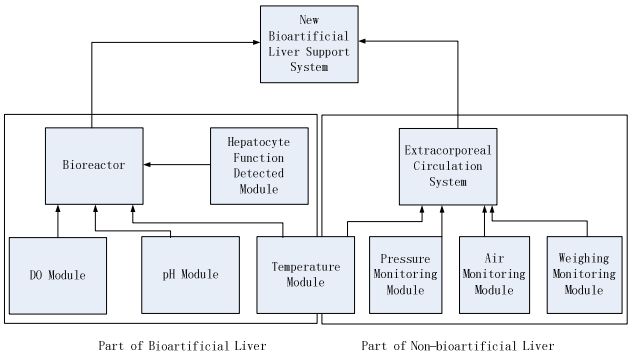

Fig. 1. Schematic diagram of modular structure in NBALSS

In accordance with the above design of the new system, as shown in Figure 1, every function of modules were implemented through a relatively independent structure. Construction of the modular system means a "building blocks" of the structure; it has many characters such as small volume, convenient operation, easy debugging, easy to carry, and so on. The data communication was implemented through the standard inter-module interfaces between every module and master computer. These can make the fault detection and processing more easy, simple and flexible during the therapy.

III. ENGINEERING IMPLEMENTATION OF THE SYSTEM

The entire hardware system was build up by four part include parameter measurement, data transmission, control regulation (master conditioning), and executing unit. As shown in Figure 2, parameters measurement system has a total of 15 points of measurement parameters that map with A-P in figure 2, including dissolved oxygen module, weighing module, temperature module, pressure module, bubble detect module, hepatocyte status module. Every point of measurement (sensors) data can be uploaded to master computer through the RS485 interface protocol after a data processing by data transmission system. Master computer can achieve precise control of every parameter and various open-end functions that the operating interface should have in accordance with the tasks set by operator. Eventually, operating instructions would be sent to executing units through the RS485 communication protocol, to implement the relevant executing unit. The executing units were map with 1-13 in figure 2, including extracorporeal pump circling systems, gas regulator valve, pipe valve adjust folder, temperature switches and of a total of 13 terminals.

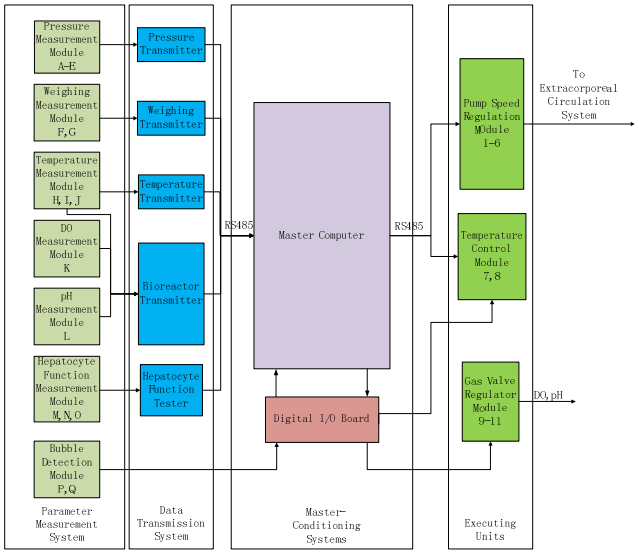

Fig. 2. Schematic diagram of hardware structure in NBALSS

During the therapy, a friendly human-computer interface (display module) has been designed in order to achieve interaction between operator and computer. It can display real-time status of every parameter in NBALSS and various tips to determine work status in current therapy mode. Operator can set expect parameters through a touch-interface software based on the display information and the needs of treatment. The software processes the input expectations data and monitored data, and then generates control information to adjust the executing units to be an expected status. As the

master computer is a common PC, it makes its software has a wealth of resources to facilitate the development of intelligent software and implementation. At programming technology, modular program is used to make the treatment function of system extend easily and debug conveniently. The software is build up with initialization module, display module, parameter setting module, control signals output module, and so on, the signal flow chart shown in figure 3.

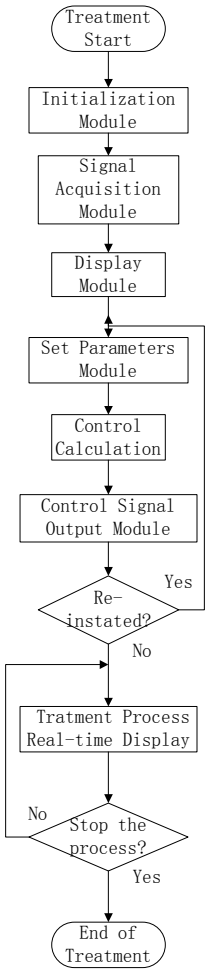

Fig. 3. Software of flow chart in NBALSS

IV. CLINICAL APPLICATION OF MODULAR NBALSS

The NBALSS that constructed in accordance with the idea of modular should through the corresponding functional tests to verify whether the experimental design objectives were achieved. The equipment was test in Zhejiang University School of Medicine, First Affiliated Hospital. In the experiment, connect the pipeline to the different treatment modalities, and select three typical ways that the pipeline connection will require more complex representative: plasma exchange (PE), Plasmapheresis combined perfusion bioreactor plasma exchange and continuous hemodiafiltration joint Dialysis filtration (CHDF) model, use the plasma of liver patients to circle about 4 to 6 hours. A pipeline pre-wash before each experimental treatment modalities verified the correctness of liquid circulation. And then the indicators and the treatment function were test by a plasma cycle. Figure 4 is a schematic diagram of clinical application in NBALSS for reference. As can be seen from the figure, the system can easily access a variety of cycle mode through the interface of each module. After application of the system, the staff no longer need to have a big headache about the Compatibility of the experimental equipment, which is no doubt has laid a solid foundation for the further development and exploration in the research of bioartificial liver. The picture of the application is shown in figure 5.

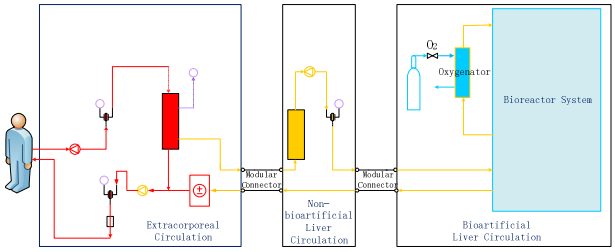

Fig. 4. Schematic diagram of clinical application in NBALSS

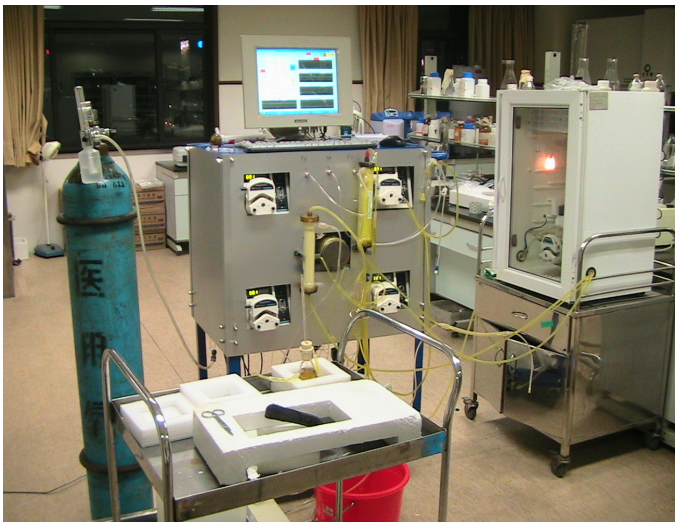

Fig. 5. Picture of the application of our modular NBALSS

V. RESULTS

After the actual test in site, we have built a modular NBALSS available: 5 pumps: 0 ~ 300rpm; 5 pressure monitoring: -300 ~ 500mmHg; heating temperature range: room temperature +5 ~ 60 ± 1 □; dissolved oxygen 0 ~ 500% ± 10%; 2 weigh monitoring: 0 ~ 10Kg ± 20g; precision injection pump accurate to trace μL class; bubbles can be detected in the air as low as 50μL; measurable albumin concentration 0.1 ~ 100g / L, urea/ urea nitrogen concentration 1 ~ 40mmol / L. Among them, field testing of dissolved oxygen response curve shown in Figure 6, and the pressure measurement is shown in Figure7.

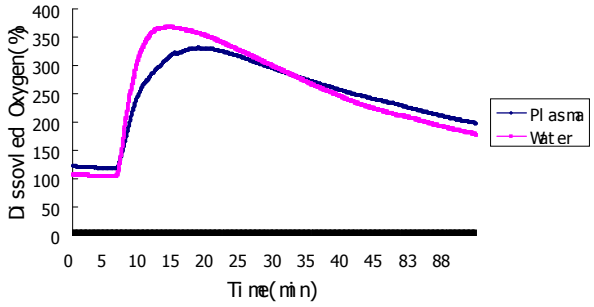

Fig. 6. Field testing of dissolved oxygen response curve

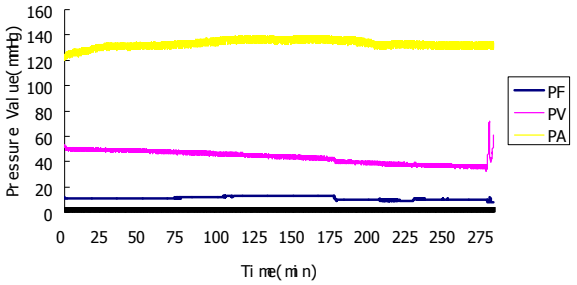

Fig. 7. Field testing of pressure measurement

The above test results show that the system can provide a variety of treatment modalities, including non-biological artificial liver, bioartificial artificial liver and Hybrid artificial liver. And the treatment function can be assembled arbitrarily in according with the clinical needs based on a variety of treatment modalities. In conclusion, the whole system is stable and reliable; ease of use, and easy to operate. NBALSS can meet the clinical needs, and the design has achieved the established objectives.

VI. CONCLUTION

Modular design, systematic layout, building-block structure make the system has features such as compact structure, convenient operation, easy debugging, and so on; the operating platform can be customized so that each function module can be connected through the standard connectors in according with the requirement in the therapy site, thus many types of treatment modalities can be achieved on the same equipment by any combination; human-computer interaction interface and intelligent computer control system can greatly simplify the operation of the flow and improve the efficiency of the operator; real-time data processing and analysis system can record the various situations during the whole treatment, which can take important basis to evaluate the treatment effect after BAL therapy.

Compared to the original BALSS, the new system will not only improve the level of process control and management, but also significantly enhance the usefulness of the system for the development of artificial liver technology provides a powerful guarantee.

ACKNOWLEDGE

Droctor Jiansheng Xu is thanked for contributing to and revising the paper.

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