In vivo evaluation of fine needle type glucose sensors implanted in rabbit blood vessel

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There is no doubt that blood glucose management is essential for diabetes patient, while it is also importance in variety of medical treatment, since drugs and stresses may cause insulin resistance, which lead to an acute hyperglycemia state even in non-diabetes patient [1]. In order to prevent hyperglycemia, excess amount of insulin are injected to the patient. However, insulin resistance can be a passing phenomenon, which continue for a certain time and it can suddenly reduce its effect to provide hypoglycemia. When the hypoglycemic state of less than 30 mg/dl remain for a while, damage of the brain can be presented and may also lose one's life. Therefore, rapid recognition of hypoglycemia is essential for effective treatment.

Several continuous glucose monitoring system (CGMS) in the market, while their designs are to measure the interstitial fluid glucose concentration in subcutaneous tissue. They provide valuable information correlated with blood glucose behavior. However, it is well known that the glucose level of interstitial fluid in subcutaneous tissue differ significantly with blood glucose, when glucose concentration change rapidly. Therefore, direct blood glucose monitoring can be profitable in the case of serious insulin resistance.

In this study, fine needle type glucose sensors were prepared and implanted in rabbit blood vessel for in vivo evaluation.

The schematic illustration of the glucose sensor is shown in Fig. 1. Pt-Ir wire and Ag/AgCl were used as working (a sensing region) and counter/reference electrode, respectively. The sensor fabrication consisted of three main steps: permselective inner layer preparation, enzyme immobilization and biocompatible external layer construction. The fine needle sensor produced was detained using a cannula after sterilization (Fig. 2). The amperometric measurement were performed with a Potentiostat (Model 3104) or wireless Potentiostat (Model 3100 RX) and examined at a potential of 0.6 V (vs. Ag/AgCl).

Evaluation of the sensor: After steady-state response was confirmed, blood glucose value was measured using commercially available glucose meter and was used for one-point calibration. [2] Then glucose was injected and also periodic blood glucose measurements were performed to compare with sensor response. Insulin injection was also performed to obtain hypoglycemic state.

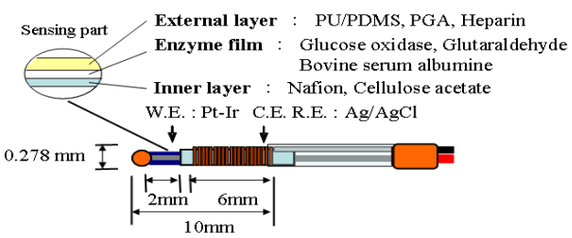

Fig. 1 Schematic illustration of the glucose sensor.

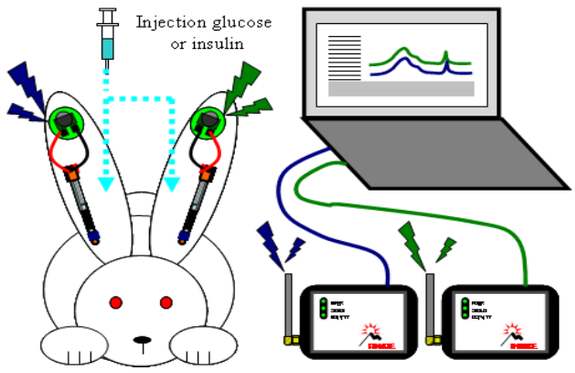

Fig. 2 In vivo measurement of fine needle type glucose sensors in rabbit ear blood vessel.

Glucose sensor with polyurethane/polydimethylsiloxane outer film showed response to glucose on the day of implantation, while clear glucose response was not obtained after 18 hours. Adsorption of the thrombus was observed on the surface of the sensor after the removal from blood vessel. On the other hand, the sensors with heparin outer membrane provided satisfactory glucose response also in the second day (Fig. 3). Although, response to glucose was confirmed in the implanted sensors, different trend was obtained with the sensor implanted in blood vessels of right ear and left ear. Difference on blood flow between two blood vessels can be one reason for this phenomenon.

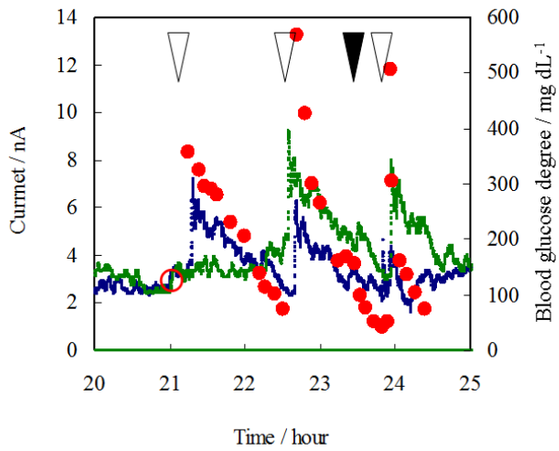

Fig. 3 Comparison of the glucose sensors response (solid line) and blood glucose measured using commercial glucose meter (solid circle) with time. Glucose sensors were inserted in blood vessel for 2 days at the time of measurement. White and black arrows indicate the injection of glucose and insulin, respectively.

References

[1] Dellinger RP, Levy MM, Carlet JM, et al, Crit Care Med 36, 296-327(2008)

[2] Choleau C, Klein JC, Reach G, Aussedat B, Demaria-Pesce V, Wilson GS, Gifford R, Ward WK, Biosens Bioelectron 17, 647-54(2002)