SUMMARY OF Ph.D. DISSERTATION

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Title

Study of burn monitoring by multiwavelength photoacoustic wave
and adhesion acceleration of transplanted skins with laser-based gene transfection

Abstract

Since severe burns affect not only local injured tissues but also the whole body, systemic management, as well as accurate assessment of burn depth and early wound closure, is required for treating severe burn patients. For systemic management, shock in the early stage and multiple organ dysfunction syndrome in the late stage are crucial, for which continuous, real-time monitoring of hemodynamics is of importance. For local wound management, continuous, careful attention should be paid to the status of wounds, because the wound depth might be increased by infection.

The goal of this dissertation is to develop new modalities for diagnosis and treatment of severe burn injuries; photoacoustic (PA) measurement has been applied to diagnosis of wound and systemic status of severe burns, and laser-based gene therapy has been applied for improving the outcome of skin transplantation, which is essential for treating full thickness burn injuries. PA measurement was used to provide two data sets: 1) time-dependent change in PA depth signal due to the recovery of blood perfusion and 2) time- and wavelength-dependent changes in PA amplitude signal which reflect the hyperdynamic state, which is an important symptom after severe burn injuries. PA measurement was also applied to the detection of dysfunctional hemoglobins in burned tissue, which might be produced due to the effect of thermal invasion. For skin transplantation, a therapeutic vector construct carrying human hepatocyte growth factor (hHGF) gene was delivered to grafts by use of laser-induced stress waves (LISWs), which was generated by irradiating a solid target with intense nanosecond laser pulses. It is shown that both reperfusion and reepithelialization in the grafted skins can be significantly enhanced, resulting in the efficacy of our LISW-mediated gene therapy in order to accelerate the adhesion of grafted skins.

This dissertation is composed of five chapters. Chapter 1 presents an overview of wound and systemic management of burn injuries. Fundamentals of PA measurement and LISW-mediated gene transfer are also described. In Chapter 2, the theory and research trend of medical application of PA measurement are described. PA measurement was used to monitor the local hemodynamics, which reflects systemic hemodynamics, for burns in rats as a function of time after injury. It is shown that PA measurement is useful for monitoring wound healing process and the hyperdynamic state after severe burn injuries. Chapter 3 presents the depth-resolved detection of hemoglobin derivatives, which might be produced due to the effect of thermal invasion, by PA spectroscopy. It is shown that methemoglobin can be detected in the thermally damaged tissue. Chapter 4 describes the experiment of skin transplantation, which was performed to demonstrate the efficacy of our LISW-mediated gene therapy for accelerating adhesion of grafted skins. Plasmid DNA coding for hHGF was transferred to skin grafts by the use of LISWs, autografting was performed with the grafts. It is shown that angiogenesis, blood flow, cell proliferation and reepithelialization after grafting can be significantly enhanced by gene transfer. It is demonstrated that our LISW-mediated gene therapy is effective for improving the outcome of skin transplantation. Finally, in Chapter 5, the results of this study are summarized, and the conclusion and future perspective are given.