Influence of Size and Placement of Electrodes on the Efficiency of Transscleral Ocular Iontophoresis

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Abstract – *The transscleral ocular iontophoresis is used to increase the amount of particulate drug delivered to sclera by transmitting weak direct current. In this study, we investigated the influence of the size and placement of electrodes on the efficiency of drug delivery using computational simulations. For the numerical simulations, finite element model of a human head and eye was constructed and Nernst-Planck equation was used for the calculation of the drug concentration in the sclera. The results showed that reducing the sizes of both anode and cathode was effective for more efficient drug delivery. Increasing the distance between the anode and the eyebrow and locating the cathode right above the drug injection site contributed to the improvement of the drug permeation.*

Keywords: Ocular iontophoresis, Nernst-Planck equation, finite element method, numerical simulation

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1 Introduction

Transscleral ocular iontophoresis is a non-invasive drug delivery system that transmits weak direct current to the eye through two electrode pads on the skin for enhancing the delivery of charged drug particles into the eye sclera [1]. Traditionally, the electrode with the same polarity as the particulate drug was attached near the drug injection site and the other electrode was placed over the forehead. Since electric field is the main force acting on the particulate drug penetrating into tissues, the properties of electrodes are important factors influencing the overall efficiency of the ocular iontophoresis. In this study, we investigated the influence of electrode properties, such as size and location of electrodes, on drug penetration based on numerical simulations. We assumed PLGA (poly lactic-co-glycolic acid) nanoparticles as the target drug particles, which were injected into lower cul-de-sac of the left eye. Finite element method (FEM) was used for calculating the electric field and the concentration of drugs in the sclera.

2 Methods

Human head model was constructed from a T1-weighted magnetic resonance (MR) image with 1 mm resolution. Five tissues including scalp, skull, cerebrospinal fluid (CSF), gray matter and white matter were segmented using ITK-SNAP. The eyes were segmented into six tissues: sclera, vitreous body, retina, lens, ciliary body, and iris region and anterior chamber. We combined the head and eye models to create FE model consisting of 600,609 nodes and 4,102,984 tetrahedral elements.

Since PLGA nanoparticles are negatively charged, the cathode was placed over the skin directly above the drug injection site and the anode was attached to the left eyebrow. The shape of the electrodes was assumed to be circular. We called this montage the base location. Then, the anode was moved from its base location to superior direction. Similarly, the cathode was moved from its base location to inferior direction. In both cases, the electrode was moved up to 3 cm with a constant step size of 1 cm, while the other electrode was fixed at the base location. The size of electrodes was also changed: the diameter of either the anode or cathode varied from 0.5 cm to 2 cm in increment of 0.5 cm at the base location while the diameter of the other electrode was fixed to 1 cm.

Nernst-Planck equation without electroosmosis was used for the calculation of the drug concentration:

$$\frac{\partial c}{\partial t} = D\nabla c - \frac{DzFc}{RT}\nabla\left(c\vec{E}\right) \quad (1)$$

where c (mol/cm^3) is the drug concentration, t (sec) is the time, D (cm^2/s) is the diffusion coefficient, F (C/mol) is the Faraday's constant, R (J/mol·K) is the gas constant, T (K) is the absolute temperature, and $\vec{E}$ (V/m) is the electric field calculated using Laplace equation given as

$$\nabla(\sigma\nabla V) = 0 \quad (2)$$

where V (V) is the electrical potential and σ (S/m) is electrical conductivity. Injection current was assumed to be 2 mA. The diffusion coefficient and electrical conductivity of each tissues were determined according to the previous studies [2, 3].

For each simulation condition, the drug concentration in the sclera was derived at every time sample. Then, the

concentration at 30 minutes was used to calculate the rate of increase relative to initial concentration (C_R). Figure 1 shows the initial drug concentration and electric field distribution when two electrodes with diameters of 1 cm are attached at base locations.

3 Results and discussion

Our simulation showed that movement of the anode location 2 cm upward from the base location resulted in the most effective drug delivery to the sclera (see Figure 2). On the contrary, the highest C_R was obtained when the cathode was placed on the base location. Results also showed that the higher the electric field flowed into the eye, the more drug penetrated into the sclera. As for the electrode sizes, reducing the size of electrode was effective to increase the drug penetration into the sclera, in both anode and cathode (see Figure 3). Reducing the cathode size made much clearer difference than adjusting the anode size. However, the size of electrodes should be carefully decided because the electrodes smaller than a certain size may cause potential side-effects in skin such as tingle, itching and burn. Considering all these, the optimal electrode condition was determined as the anode placed over 2 cm above the eyebrow and the cathode attached at base location with minimum diameter guaranteeing the safety.

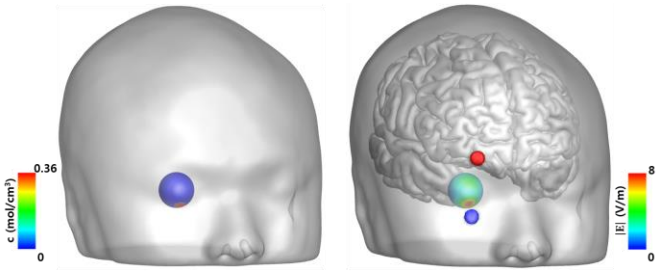

Figure 1. Initial drug concentration (left). Electric field distribution when the electrodes are attached at the base locations (electrode diameter: 1 cm) (right)

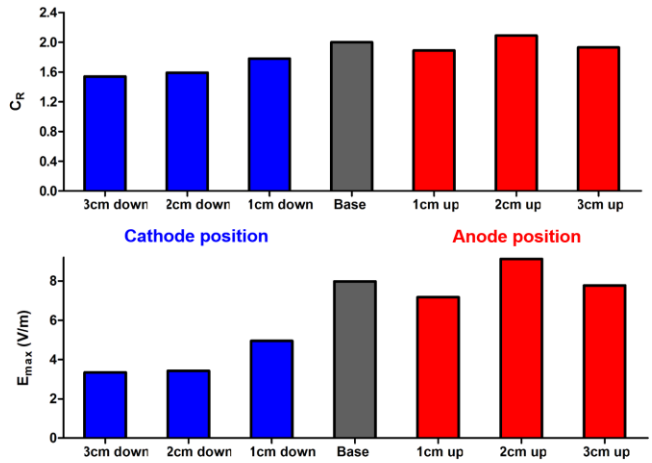

Figure 2. Increase rate of drug concentration (up) and peak value of electric field in the eye (down) for different electrode location conditions

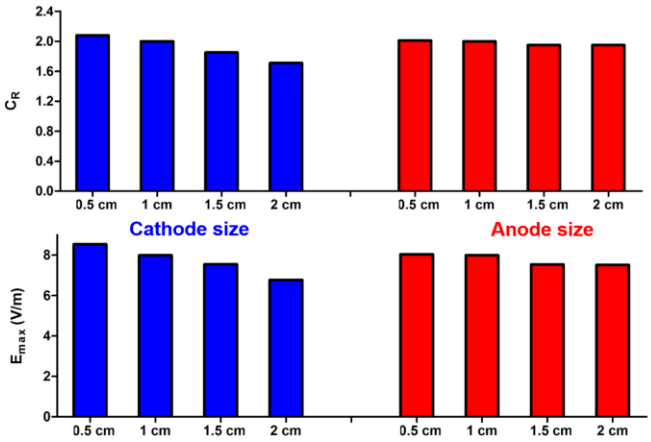

Figure 3. Increase rate of drug concentration (up) and peak value of electric field in the eye (down) for different electrode size conditions

4 References

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