ELECTRODE COMBINATION AND SPECIFICITY IN SPINAL CORD STIMULATION

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ABSTRACT

Because of its beneficial effects on disturbed motor functions, spinal cord stimulation (SCS) may contribute significantly to the restoration of motor coordination and control in patients with spinal cord injury and other motor disorders. However, SCS is still a non-specific therapy for a variety of neurological disorders. The neurophysiological mechanisms underlying the effects of SCS, as well as the neuronal fibre systems that have to be activated, are unknown. Since the excitation of a nerve fibre by electrical stimulation depends on the value of the second derivative of the imposed field potential along the fibre (activating function), we have got a clue for the further investigation of the effects of SCS. With this knowledge and a realistic model of the passive electrical properties of the spinal cord and surrounding tissues we are able to predict which electrode combinations favour the activation of nerve fibres with a specific position and orientation in the cord.

Our first aim was to investigate the differences between activating functions with different electrode combinations from a four-electrode epidural probe. Therefore we modelled a simple 3-dimensional, isotropic, uniform, resistive medium and represented the electrodes by equidistant point sources. It was shown that different electrode configurations favour activation functions with different orientations. This result led us to continue the investigation by the design of a more realistic volume conductor model, including the geometry, inhomogeneities and anisotropy of the spinal cord and surrounding tissues.

Keywords: spinal cord stimulation - electrode combination - potential field - volume conductor model - selective activation.

INTRODUCTION

Since the first stimulation of the spinal cord for pain relief, reported by Shealy et al. in 1967 (1), this method has been applied to large numbers of patients with a variety of neurological disorders like spasticity, cerebral palsy, torticollis, dystonia, bladder dysfunction, chronic intractable pain and peripheral vascular disease. Except for the treatment of intractable pain, based on the gate control theory of pain mechanisms (2,3), no detailed theories exist which cover the neuro-

physiological mechanisms underlying the effects of spinal cord stimulation (SCS) on these disorders (4).

Because of its beneficial effects on motor coordination and control, SCS may contribute significantly to the restoration of motor functions in patients with spinal cord injury and other motor disorders. SCS should be considered as a method complementary to functional electrical stimulation (FES), because it facilitates the use of motor functions preserved in these patients. However, there is a large variation in the therapeutic effects of SCS on motor disorders as reported in literature by different medical centres. These divergent results can partly be due to differences in patient selection criteria and varying stimulation parameters. However, we were not able to establish any relationship between clinical effects of SCS and stimulation parameters - like the location and configuration of the stimulating electrodes, the stimulus frequency, etc. - from a large number of published results. Application of SCS is still mainly based on trial and error, although several authors reported that a midline placement over the dorsal columns gives the optimal results (5).

Usually an array of (four) electrodes is placed medially over the dorsal columns in the epidural space at a cervical or thoracic level. It is assumed that the recruitment of nerve fibres takes place close to the cathodal electrode(s) (6) and that in all neurological disorders where SCS is applied, a single anatomical structure is directly activated: the ascending fibres in the dorsal columns (7). Therefore SCS is often called dorsal column stimulation. It is also supposed that stimulation of the dorsal columns activates fibres - directly or by synaptic transmission - in many spinal pathways located in both the dorsal and ventral parts of the cord (6,8). It is assumed that - by inhibitory and facilitatory effects - SCS influences the activity in segmental networks and suprasegmental long-loop reflexes involved in a variety of effector mechanisms (7), and is able to normalize more or less their function. Moreover, prolonged electrical stimulation may cause changes in synaptic morphology and accumulation of specific neurotransmitters, and may thereby change the input-output relation of spinal networks.

It can be concluded that SCS is still a nonspecific method which produces a more or less beneficial effect on several specific effector mechanisms and pain. A more precise determination of the pathway(s) which must be activated may result in a more selective and effective utilization of SCS. This problem can be tackled by different approaches, which should be considered complementary. In a basic, neurophysiological approach one would like to be able to specify, for any particular configuration of epidural electrodes, which neuronal elements will be recruited - directly or indirectly - by stimulation. Direct evidence of the stimulation of particular spinal pathways, and of the facilitatory and inhibitory effects on specific segmental and suprasegmental neuronal circuits can only be obtained by electrical recordings from brain and cord in animal experiments. At this level of neuronal complexity the question arises whether SCS on animals can be an appropriate model for SCS on

man.

In a second approach one would analyse carefully the role of electrode placement and other stimulation parameters in the application of SCS on man. The relationship between electrode placement and fibre systems in the spinal cord recruited directly by stimulation can be estimated by a theoretical approach, in which biophysical properties of the cord and the neuronal elements are modelled (9,10). The location and orientation of the neuronal elements in the cord that will be recruited selectively by a specific placement of anodal and cathodal electrodes, can be predicted if a realistic volume conductor model is used. If then patients are stimulated with different epidural electrode combinations, it may be possible to conclude whether stimulation of specific pathways has any effect on specific symptoms. In addition, clinical neurophysiological methods have to be used for the identification of the activated pathways. We started this second approach in order to increase the selectivity of SCS and to improve the benefit for patients with specific neurological disorders.

VOLUME CONDUCTOR MODELS

For the investigation of the role of electrode placement on the recruitment of spinal nerve fibres, the following axonal characteristics have to be considered. (a) The diameter of the nerve fibres, which is correlated with their recruitment threshold. In myelinated fibres the probability of excitation also depends on the position of the nodes of Ranvier with respect to the stimulation electrodes (11). (b) The position and orientation in the spinal cord. Not only the distance of a fibre from the electrodes, but also its spatial orientation determines the probability of excitation, because the activation of a nerve fibre is a function of the second derivative of the field potential along the fibre (12,13). Generally the potential gradient in some small volume within the spinal cord, due to a stimulus current, will vary in different directions. Therefore the activation of a nerve fibre in that volume will depend on the orientation of the fibre. Beside the ascending and descending fibre bundles close to the dorsolateral and ventral surface of the cord, various fibre systems have different orientations, like the dorsal and ventral roots and their continuation in the spinal cord. Therefore, selective activation of specific fibre bundles in and around the spinal cord, which depends on the characteristics of the potential field, can be achieved in principle by the right choice of the positions of cathodal and anodal electrodes and their currents. Of course the clinical practice will impose restrictions to the locations where electrodes can be placed.

We started to investigate the selectivity of different anode-cathode combinations of the epidural SCS electrode with four equidistant metal contacts. Computer models were made of the resistive medium of the spinal cord and surrounding tissues, and the potential field arising from current injection at specific sites was calculated. From the 3-dimensional potential

field the spatial second derivative, or activating function was calculated at different sites and for different orientations.

The homogeneous, isotropic model.

Our first aim was to investigate the differences between activating functions with different electrode combinations from the four-electrode epidural probe. Therefore we started to model the spinal cord and surrounding tissues as a simple homogeneous, isotropic, infinite, resistive medium with conductivity σ, in which the electrodes were represented by equidistant point sources.

Analytical model

In case of a single point source with current I at the position (x_1,y_1,z_1) in a cartesian coordinate system the potential V at a position (x,y,z) will be (14):

$$V(x,y,z) = \frac{1}{4\pi\sigma} \cdot \frac{I}{((x-x_1)^2+(y-y_1)^2+(z-z_1)^2)^{1/2}} \qquad [1]$$

The four point sources with current I_i (i = 1,2,3,4) are located at the positions (0,0,z) along the Z-axis of the coordinate system. See Fig. 1.

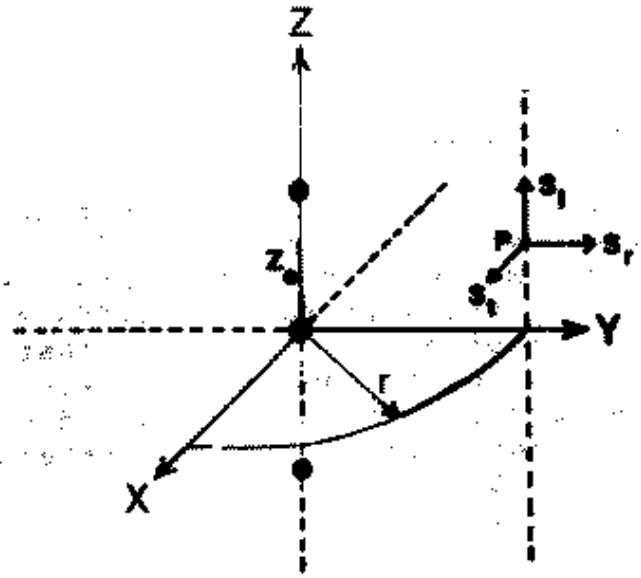


Figure 1. The homogeneous, isotropic model.

In case of several point sources, as indicated in Fig. 1, the potential V(x,y,z) follows from the superposition of the fields due to single current sources, according to [1]:

$$V(x,y,z) = \frac{1}{4\pi\sigma} \sum_{i=1}^{4} \frac{I_i}{((x^2+y^2+(z-z_1)^2)^{1/2}} \qquad [2]$$

Because the potential V, and therefore also the activating function S, has a cylindrical symmetry with respect to the Z-axis, we only need to calculate the second spatial derivative at positions P=(0,y,z) to know the value of the activating function at any position. As is shown in Fig. 1, the activating function S is calculated in three orthogonal directions in the longitudinal (S_l), the radial (S_r) and the tangential direction (S_t). These activating functions at the position P=(0,x,y) are calculated as follows:

$$S_l(o,y,z) = -\frac{1}{4\pi\sigma}\sum_{i=1}^{4} I_i \frac{y^2-2(z-z_i)^2}{(y^2+(z-z_i)^2)^{5/2}} \qquad [3]$$

$$S_r(o,y,z) = -\frac{1}{4\pi\sigma}\sum_{i=1}^{4} I_i \frac{(z-z_i)^2-2y^2}{(y^2+(z-z_i)^2)^{5/2}} \qquad [4]$$

$$S_t(o,y,z) = -\frac{1}{4\pi\sigma}\sum_{i=1}^{4} I_i \frac{1}{(y^2+(z-z_i)^2)^{3/2}} \qquad [5]$$

All three activating functions are proportional to $1/y^3$, e.g. their values decrease with the third power of the distance to the Z-axis (= the array of current sources). Because the orthogonal activating functions at position P are the second spatial derivatives of the field potential, they meet the Laplace equation for a homogeneous medium (14):

$$\frac{\partial^2 V}{\partial l^2} + \frac{\partial^2 V}{\partial r^2} + \frac{\partial^2 V}{\partial t^2} = 0 \qquad [6]$$

According to the model of McNeal (12) a positive value of the activating function parallel to a nerve fibre at P=(0,y,z) corresponds with a depolarization of the nerve fibre membrane at the level of P. A negative value of S(0,y,z) corresponds with a membrane hyperpolarization. With increasing value of S depolarization will increase. When a threshold depolarization is reached an action potential will be generated locally (in a myelinated fibre at a node of Ranvier) and will propagate along the fibre in two directions. In contrast, local hyperpolarization of the nerve fibre membrane may block the propagation of action potentials recruited artificially or by physiological mechanisms at a distant site of the fibre.

Results.

With formulas [3], [4] and [5] we calculated the activating

functions at positions P=(0,r,z) for a number of electrode combinations of the four-electrode array. (The radial coordinate r=y.) These combinations are shown schematically in Fig. 2. "c" is a (negative) cathode and "a" a (positive) anode.

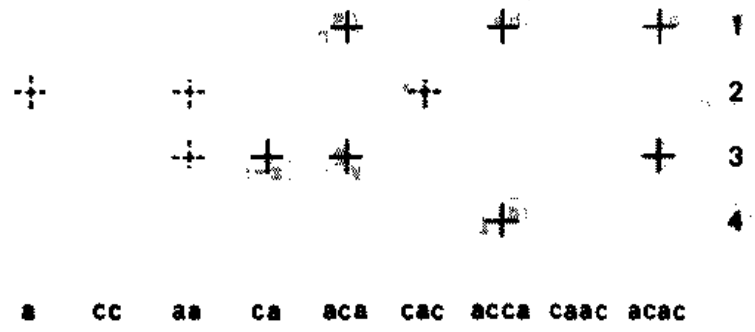
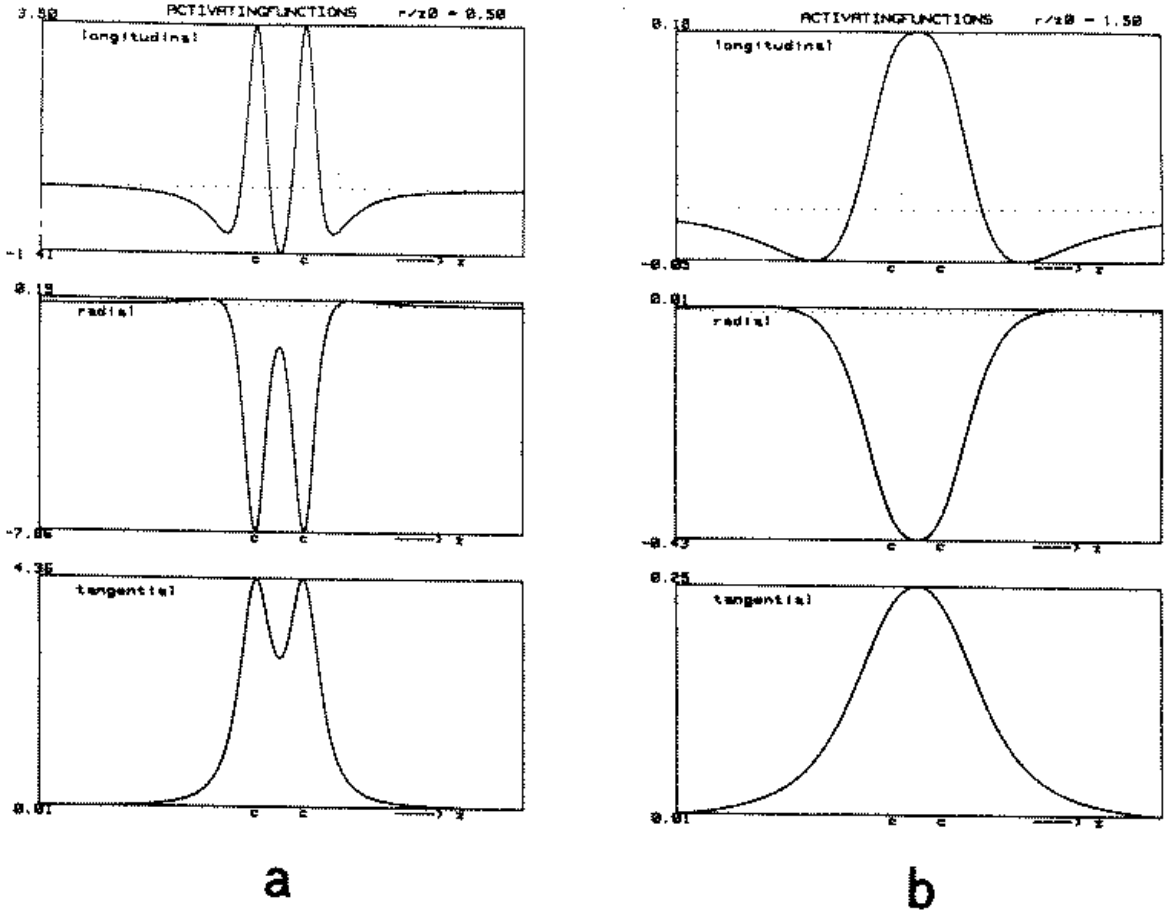


Figure 2. Electrode combinations

We only calculated the activating functions S(0,y,z) for the combinations shown by solid lines. The values of S for the combinations shown by interrupted lines simply follow from other combinations having cathodes at the positions of anodes and vice-versa. We only had to substitute I_i by $-I_i$ in [3], [4] and [5]. In combinations with only a single anode (or cathode) the current injected by this source had a value I (or -I). If two anodes (or cathodes) were present, each one injected a current of 0.5 I (or -0.5 I). With combinations having only anodes (or cathodes) the cathode (or anode) was considered to be at an infinite position.

In Fig. 3 and 4 the results of the calculations for the electrode combinations cc and aca are shown. In a and b the longitudinal, radial and tangential activating functions are shown for positions P=(0,r,z) parallel to the Z-axis with $r=0.5z_o$ (a) and $r=1.5z_o$ (b). z_o is the interelectrode distance (Fig. 1). In Fig. c the maxima of the three activating functions are plotted at all values of r from $r=z_o/8$ to $r=2z_o$. The radial (S_r) and tangential (S_t) activating function are expressed as a percentage of the longitudinal (S_l) function (=100%). In this way the maximal values of the three functions S_l, S_r and S_t can be compared at several radial distances from the electrode array. The real maximum values of S_l are also plotted in Fig. c (solid line). These values are proportional to $1/r^3$. In Fig. 3c it can be seen that for the double cathode the maximum of S_t is higher than S_l, with a maximum of 174% at about $r=z_o$. The maximum of S_r is only 6% of S_l, but its (nega-



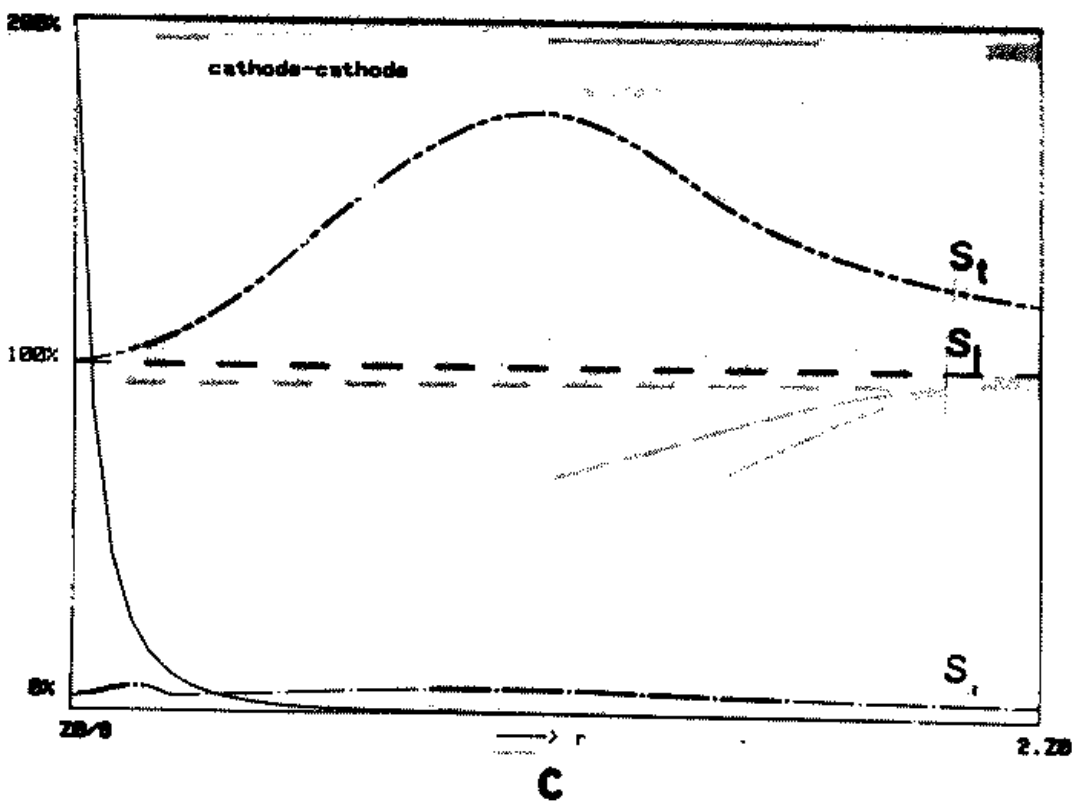
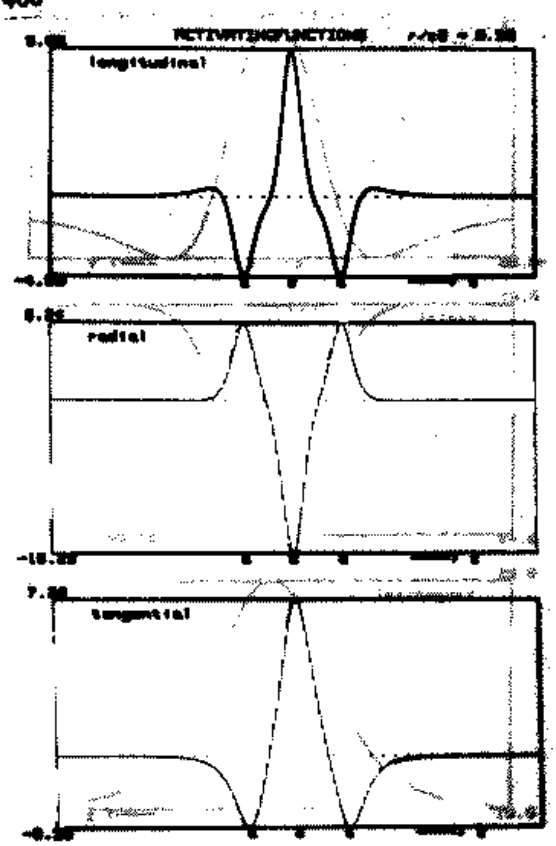
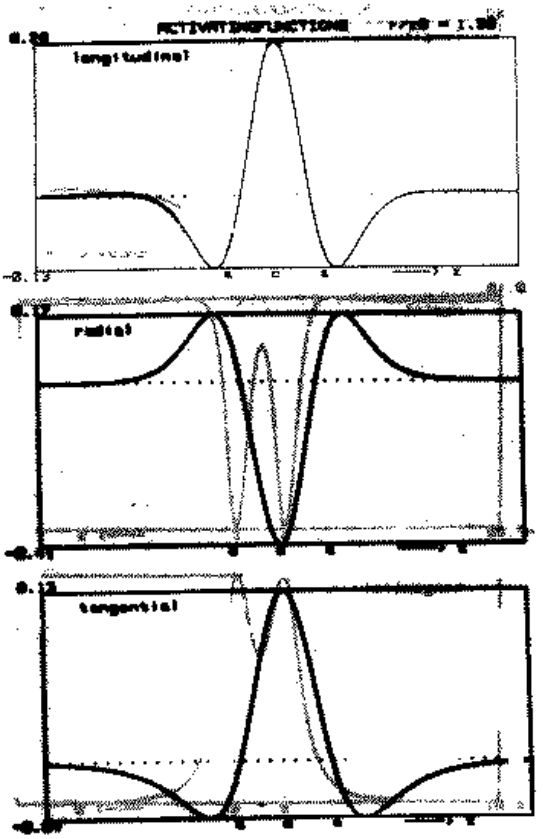


Fig. 3. Activating functions of cathode - cathode



a



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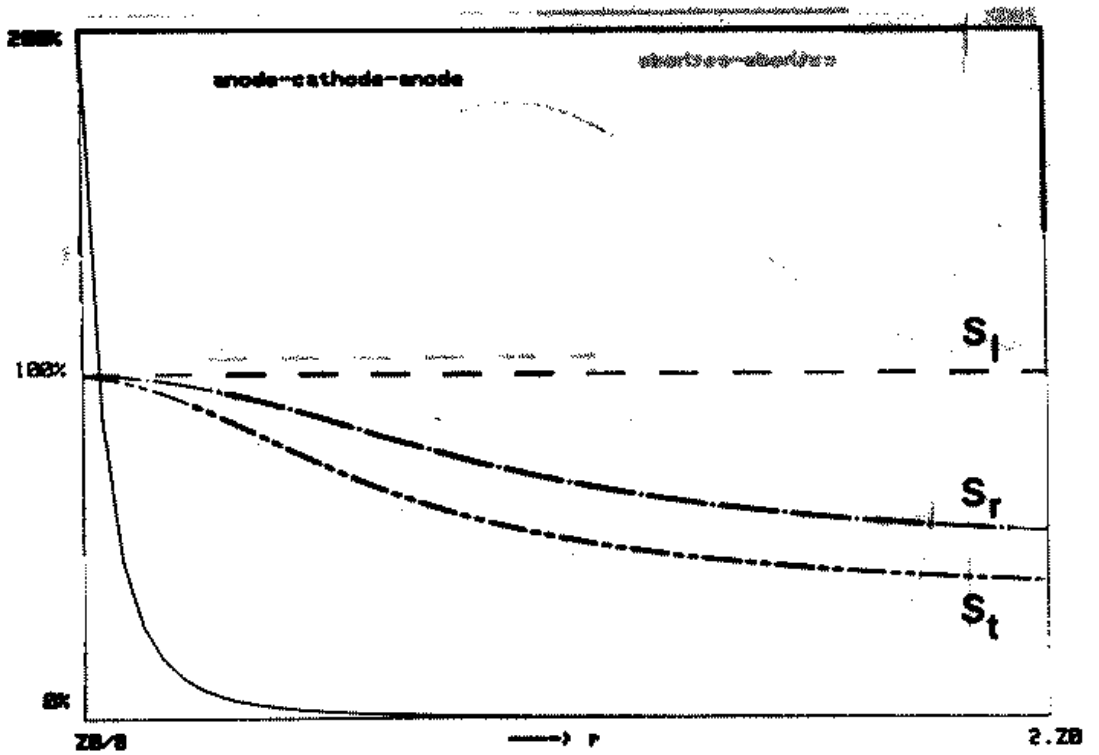

c

Fig. 4. Activating functions of anode - cathode-

tive) minimum has a value of 225% of the maximum of S_l at $r=0.5z_o$ (Fig. 3a). Therefore it can be stated that - under the assumptions of this simple model - a cathode-cathode combination will activate (depolarize) nerve fibres in a longitudinal and a tangential direction, but will block (hyperpolarize) fibres with a radial orientation. As can also be seen from Fig. 3a-b these effects strongly depend on the longitudinal position with respect to the electrodes. If the signs of the activating functions in Fig. 3a-b are inverted, we have got the results from the anode-anode combination. Now nerve fibres with a radial orientation will be activated and fibres in the other two directions will be blocked (if the local value of S is sufficiently high). The results from the anode-cathode-anode combination, shown in Fig. 4, are different in some respects. From Fig. 4c it can be seen that S_l has a higher maximum than S_r and S_t at almost all radial distances r. The (negative) minimum of S_r is 181% of the maximum of S_l at $r=0.5z_o$ (Fig. 4a). Activation of longitudinal and tangential fibres will occur at the level of the cathode, but radial fibres will be blocked at this level. Activation of radial fibres will occur at the level of the anode.

Conclusions

Regarding the effects of SCS with different combinations of an epidural four-electrode array, conclusions with a quantitative character cannot be drawn from this simple model. However, some results will also be relevant beyond this model and may help to improve the notion about the effects of SCS and the role of electrode combinations.

1. Sites of maximum value of S. The longitudinal and tangential activating functions have their maximum at the (longitudinal) level of the cathode and their minimum at the anodal level; the radial activating functions have the opposite characteristics with respect to the electrodes. With increasing radial distance (r) the peak values of the activating functions shift somewhat away from the centre of the electrode array (Figs. 3b and 4b) and decrease proportionally to $1/r^3$.
2. Selectivity regarding the activation/inhibition of fibres. With most electrode combinations the three activating functions are almost symmetrical: positive and negative peak values at the same distance from the electrode array do not differ by more than a factor 2. Therefore these combinations are expected to recruit and inhibit nerve fibres at the same time, but at different segmental levels of the spinal cord. The only exceptions are the combinations with only one type of electrodes. The combinations c and cc will only recruit fibres with a longitudinal and a tangential orientation, and only block fibres with a radial orientation. The combinations a and aa have the opposite characteristics.

3. Selectivity regarding the orientation of fibres. Selective activation of radial fibres and simultaneous blocking of longitudinal and tangential fibres at the same distance from the electrodes will be possible with the combinations a and aa. The inverse effects are expected with the combinations c and cc.
4. Selectivity of activation and inhibition of nerve fibres with different positions and orientations in the spinal cord has to be investigated with a more realistic model. Not only the effects of the four-electrode array, but also of other electrode combinations have to be examined.

The inhomogeneous, anisotropic model.

In this approach the properties regarding the geometry and electrical conductivity of the anatomical structures within and around the spinal cord will be modelled. The question of how much detail is necessary in order to obtain a realistic model with respect to the potential field, can best be approximated in the following way. After starting with a relatively simple, inhomogeneous model consisting of concentric layers, more details regarding geometry and conductivity will be added until significant changes in the potential distribution do not occur any more. Because the variability of the anatomical structures among individuals has to be taken into account, the sensibility of the model for variations in geometry will also be investigated. The electrodes in this model are not point sources, but will have finite dimensions. The model will be implemented on a DEC 2010 computer.

Principles of the calculation

Any method for the calculation of the potential V in a conducting medium has to meet the Laplace equation. For an inhomogeneous medium this equation can be written as

$$\mathrm{div}\ (\sigma\ \mathrm{grad}\ V) = 0 \qquad [7]$$

with σ being the conductivity tensor.
The following conditions apply to the model:
1. V=0 at the outer surface of the conducting volume under consideration, and
2. V≠0 and constant at the surface of an electrode.

The potential field will be calculated by way of the variational method (15) and will include a number of iterations in order to minimize the error in [7]. For the calculation of the field resulting from stimulation with several electrodes, superposition of the fields due to single electrodes can be used. At selected locations activating functions with specific orientations will be calculated from the local potential distribution. Because the conducting medium is assumed to be resistive, we can calculate the potentials under (quasi-) stationary conditions (e.g. the electrode potential is kept constant).

For the discretization of the 3-dimensional medium we use

identical volume-elements instead of finite elements with varying geometry (9). The advantages of our method are: (a) the implementation of the model is relatively simple, (b) the geometry of the model can easily be changed and (c) the spatial resolution can easily be adapted. In a rostro-caudal direction the model of the spinal cord is divided into slices and in a transverse plane into equilateral triangles. In this way wedge-shaped volume elements are obtained. If the model is symmetrical with respect to the mid-saggital plane or the transverse plane, the volume in which potentials have to be calculated can be reduced to 50% if the electrode is also positioned symmetrically with respect to that plane. In this situation the potential gradient perpendicular to the plane of symmetry has to be zero.

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