EXPERIMENTS ON THE ELECTRODE NERVE CONNECTION [x)]

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Summary

For functional electric stimulation the electrode can be connected either to muscle or nerve fibres. According to our concept which was presented at the last meeting (1978) we prefer nerve stimulation for control of extremities in paraplegic patients. Electrode nerve connection causes multifarious problems. Therefore we analysed this problems in different experimental studies.

1. Direct current influence (less than 1 uA)
   A self developed DC-generator was implanted in 50 rats. The electrodes were positioned around the ischiatic nerve and fixed with a suprimed 9-0 suture. Examinations were done in different periods up to 55 weeks.
2. Influence of different pulse amplitudes (2, 4 and 8 Volts)
   A 3-channel stimulation unit was developed and implanted in up to now 6 sheep. The implanted battery guarantees a 3 month period of 4 second stimulation intervalls with 50 % ratio.
3. Variation of pulse parameters
   To optimize the durability of the electrode extensive in vitro tests were done by variation of polarity, duration, amplitude and frequency of the pulse. This experiments were carried out in physiological saline solution with constant current conditions.

Studies were done with an electrode of stainless steel standardized since 5 years. This electrode (Eticon EH 612 P) consists on 17 monofiles with a diameter of 0,05 mm. The electrode is isolated with silicon rubber.

1. Introduction, state of the project "Mobilisation after Paraplegia"

On the occation of the last ETAN-meeting we introduced our concept for mobilisation after paraplegia /1, 2/. Different to some other investigator teams we are stimulating nerves to achieve functional movement of extremities. Nerve stimulation is done by means of a new method, developed in 1973 and protected by patent meanwhile, using a "round about electrode" /3/. The main advantages of this method, which was tested even in clinical applications, up to 5 months, are twofold /4/: On the one hand smooth movements are obtainable, on the other hand fatigue of the nerve-muscle-connex can be avoided. Current problems, which are goal of our research work at present, concern:
./. function and stability of electrode-nerve-connection and

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./. management of movement (identification of the motionsystem). The former problem is topic of this article, but first some remarks on the current state of the project:

As far as technology is concerned, without doubt the most essential progress is the development of a thinfilm hybrid circuit for an implantable 8-channel-stimulation-unit /5/. This stimulator can be controlled with a time multiplex code in parameters by means of an extracorporal driving unit. First experiences with this new technology revealed problems, not important before, for example efficiency of stimulation units with even more channels /6/.

First attempts of a solution of the problem "management of movement" failed. So we changed our aim and are developing a training system for paraplegic patients which will help to learn controlling movements of stimulated extremities with fingers.

Point of our animal experiments are examinations on the reaction of electrodes described in the following /7/. Additionally we gained several results in technological as well experimental point of view in the field of electrotherapy of scoliosis /8/. Findings of these examinations are presented in a separate paper of this congress /9/.

Original ideas aimed at a collection of results on the long term implantation of electrodes and stimulation units. As the problematic nature is rather complex and multivariant we split solution of the problems into three steps:

./. Behaviour of the electrode in low DC-currents
./. Behaviour on high voltages
./. Development of appropriate impulse design for optimal long-term-stability.

By means of the splitting into three sub-problems, precise description of reaction of electrode and nerve is possible without violating laws concerning prevention of cruelty to animals.

2. Pilotstudies on rabbits

2.1. The electrode

Our electrode is made of stranded wire (17 x 0,05 mm, ETHICON type EH 6129). This gives a diameter of the wire of 0.2 mm or 0.6 mm when isolated respectively. The end of the electrode wire is wound to a small loop (diameter 1 mm). This loop prevents concentration of the electric field and helps to fasten the electrode by m-ans of a thin suture (fig. 1). All examinations were done with the same electrode material (stainless steel). The same electrode is also used in clinical applications (up to 5 months), in animal experiments they were even tested more than one year. There are some reasons to believe that this type of electrode, which is much cheaper than those made of precious metal (platinum-iridium), can be used for routine. This electrode is not optimal as far as mechanical properties are concerned, but electrical properties are good, especially if stimulation current is low or moderat. If stimulation current or voltage is high (corresponding to the

Fig. 1: Stainless steel electrode, size 1 mm Ø,
8 weeks implanted ·

surface of the electrode), the electrode becomes instable and desintegrates within a short time.

It is evident that we had to develop implantable generators for some electrode tests. Expenditures are rather high but are unavoidable for clinical applications.

Precious metal electrodes are offered by industry especially for the application of nerve stimulation for treatment of cronical pains. These electrodes are fixed to a small sheet made of silicon rubber. According to the conception of the producer this sheet should be wrapped around the nerve. This technique is easy to apply but risk of compression of the nerve because of reaction of the surrounding tissue is rather high. Because there is no possibility for the nerve to give way demage of the nerve is likely. Consequently these electrodes are forbidden in our applications.

2.2. Experiments on rabbits

In a first series on 6 rabbits our electrodes described above were connected to the nervus ischiaticus. The electrodes were supplied by miniture implantable one-channel-stimulation-units, which were powered transcutanously by battery-operated driving unit. Fig. 2 shows situs of operation and the stimulation unit (diameter 18-20 mm). Fig. 3 shows stretching of the hind leg when the transmitter is switched on. This series was interrupted because of high rate of dislocation of the electrode. Because of the high mobility of the animal it would not have been wise to

Fig. 2 Experiments on rabbits, implantation of a one channel stimulation device

use rabbits any longer. Beside this cronical stimulation would not have been possible because of legal considerations (sensitivity of the mixed nerve). Despite these negative results full function of stimulation could be profed one year after implantation.

3. Studies with DC-currents on rats

We implanted DC-current generators, developed in our own laboratory in 60 rats in the region of the neck. Our standarized electrodes were tied to the nervus ischiaticus. Currents were extremely low, (1 uA on an average) and did not cause any depolarisation. In the electrolytical point of view this DC-current simulated the worst circumstances possible, when an impulse train is applied to the electrode. Aims of this experiments were twofold:
./. examination of the stability of the electrode
./. effects on electrode and nerve.
In couse of extensive follow-up examinations hystological sections of the nerve tissue in the distal and proximal region were done to point out demages caused by the surgical application and the cronical implantation. Fig. 4 shows the implantable DC-generator, powered by a mercury-cell (diameter 12 mm), fig. 5 shows the situs of the follow-up examination. The DC-generator was disconnected and by means of an external stimulation unit the following data was measured: stimulation current necessary for minimal and maximal movement, smoothness and strenght of movement (subjectively) and electrode resistance. Condition of the electrode and the DC-generator as well as positioning of the electrode was recorded too.

3a

3b

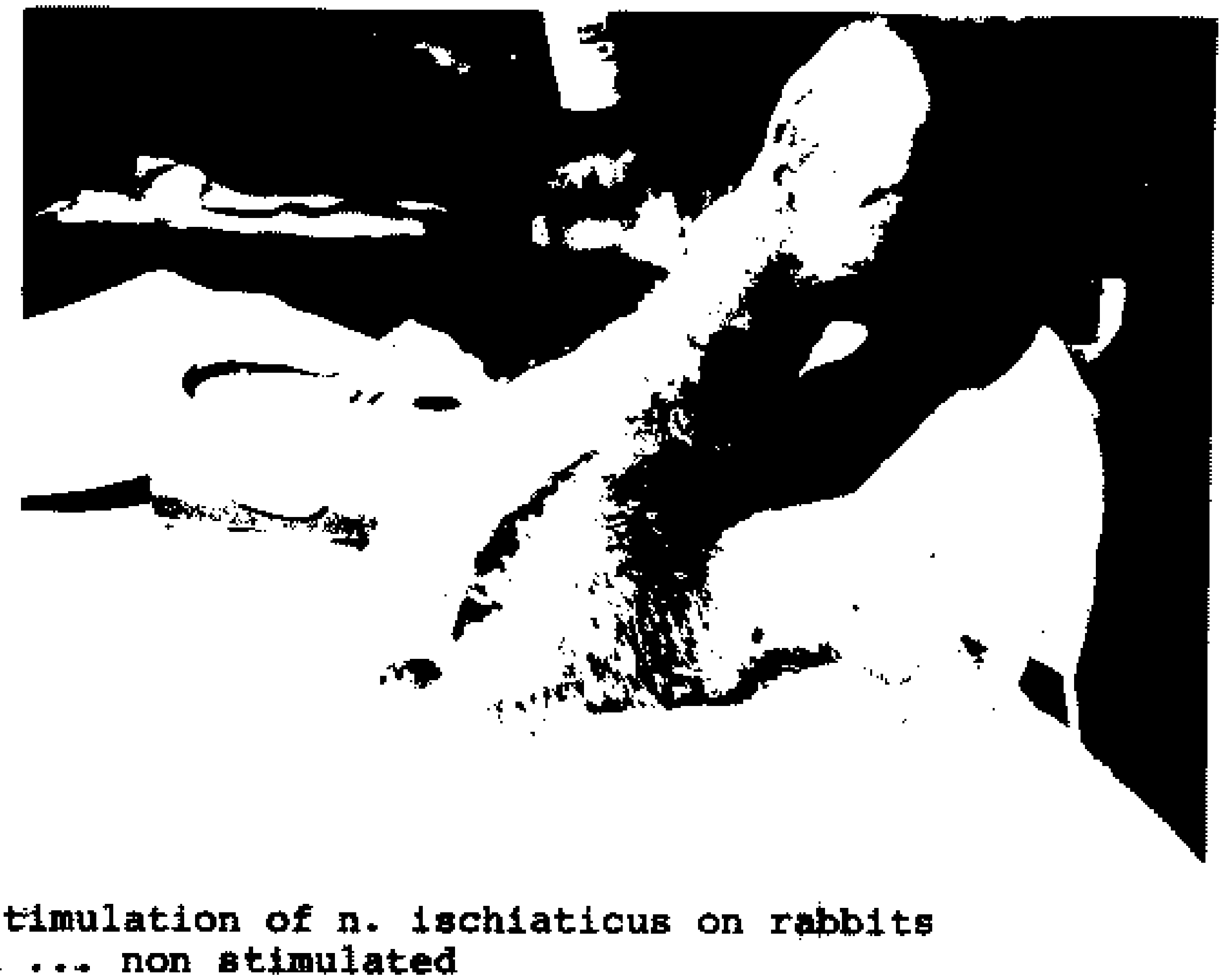


Fig. 3: Stimulation of n. ischiaticus on rabbits
a ... non stimulated
b ... stimulated

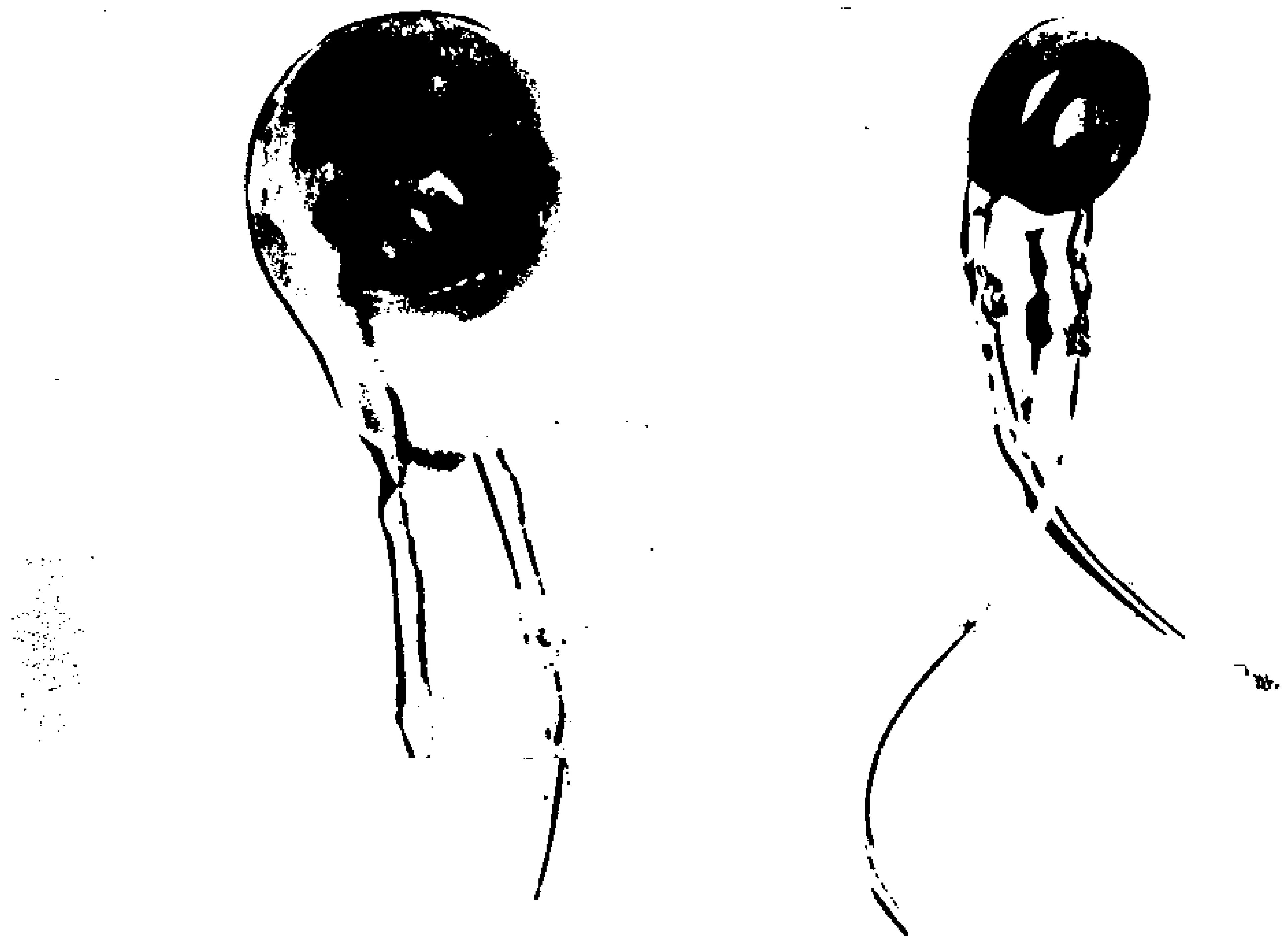


Fig. 4: Implantable DC generators
left covered with Hysol and silicon rubber

Fig. 5: Implantation of a DC generator, follow up examination

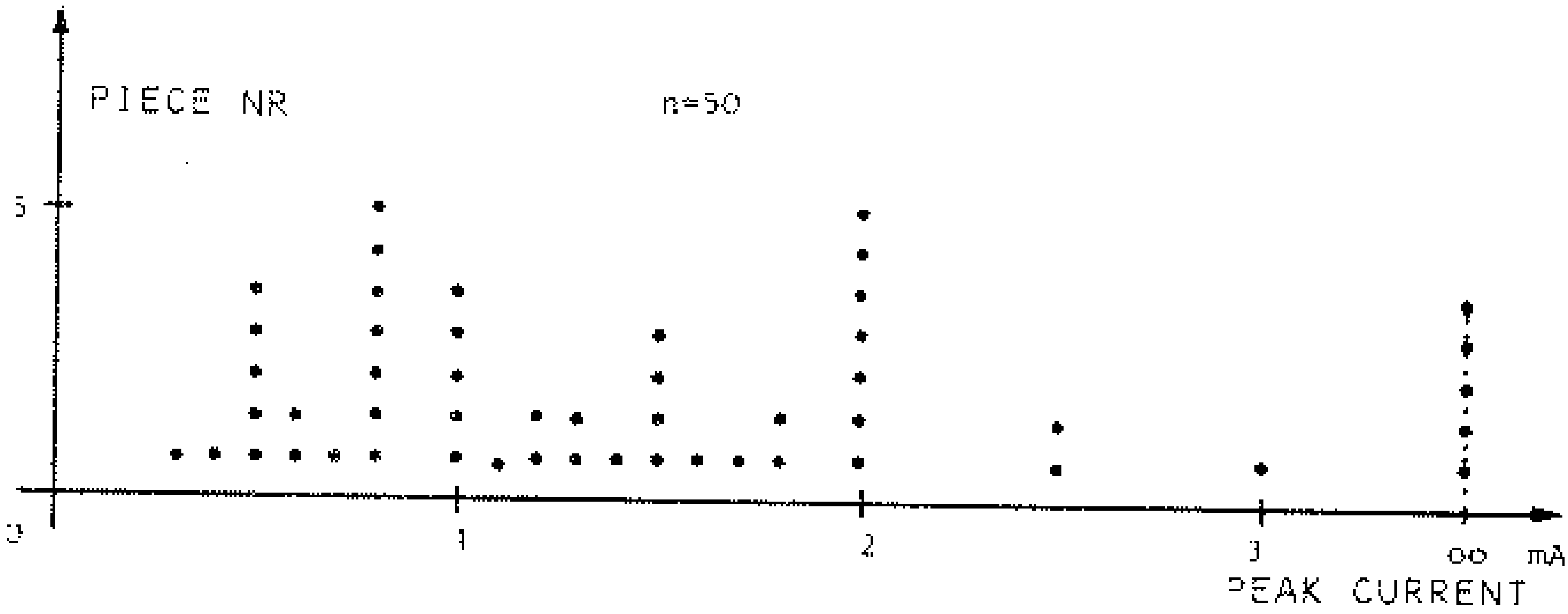


Fig. 6: Distribution of current amplitudes during follow up study

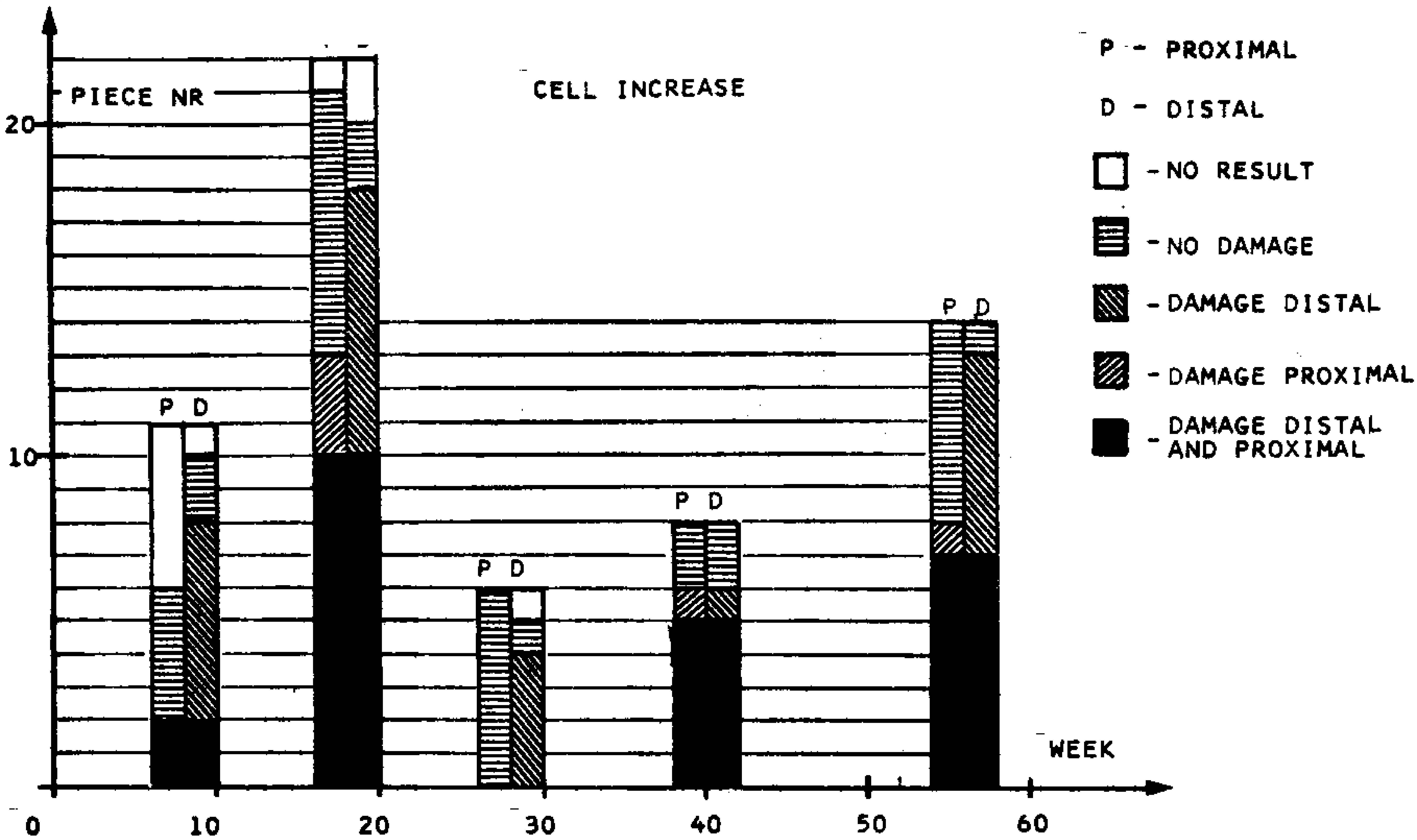
Electrical parameters

Data found in the follow up examinations can be judged to be quite good as far as electrical parameters and function is concerned. 80 % of the animals could be stimulated functionally with smoth movement, using a current less than 3 mA. Impedences of the electrodes were between 500 and 2000 Ohms. Fig. 6 shows distribution of current amplitudes of 50 animals. Half of the 20 % failurerate was caused by surgical imperfection. So only 10 % of electrodes were out of function because of dislocation of the electrodes or damage of the nerve. It has to be pointed out that - disregarding the usual brown layer of oxidation - no corrosion could be recorded. Unfortunately these positive results could not be confirmed by histological examinations.

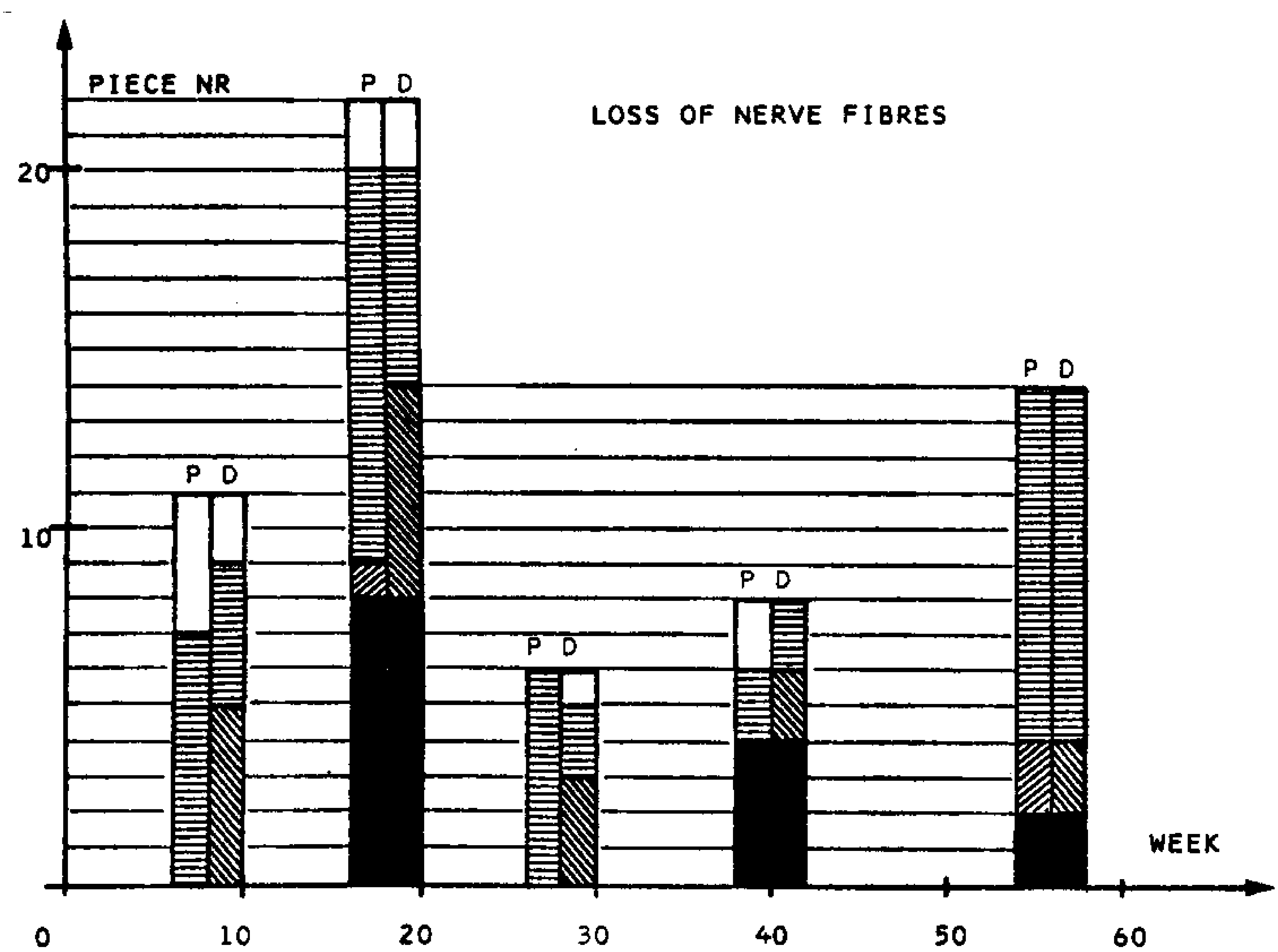
Histological examinations

In the histological point of view we had to notice a high amount of damage of the nerve distal as well as proximal. Using dyeing methods
./. increase of quantity of cells
./. loss of nerve-fibres
./. growth of connective tissue
became visible. It has to be considered that an increase of quantity of cells does not cause functional loss in any case. In the following histograms damages are classified in 5 groups chronologically (Fig. 7, 8, 9). Especially interesting is the dynamic nature of damage. Probably there are different reasons for the damages, so we have to discuss generation and regeneration of defects depending on the duration of the experiment. So it is interesting that there is a maximum of number of defects in the 20th week, while there is a minimum in the 30th week. Also the last group (55 weeks) shows less loss of function than group No. 4 (40 weeks).

Contradiction between the good results in the electrical and functional point of view to the damages found histologically, can be explaines: In our statistics each visible damage, even



7: Histologic results during DC application on the rats nerve



8: Histologic results during DC application on the rats nerve

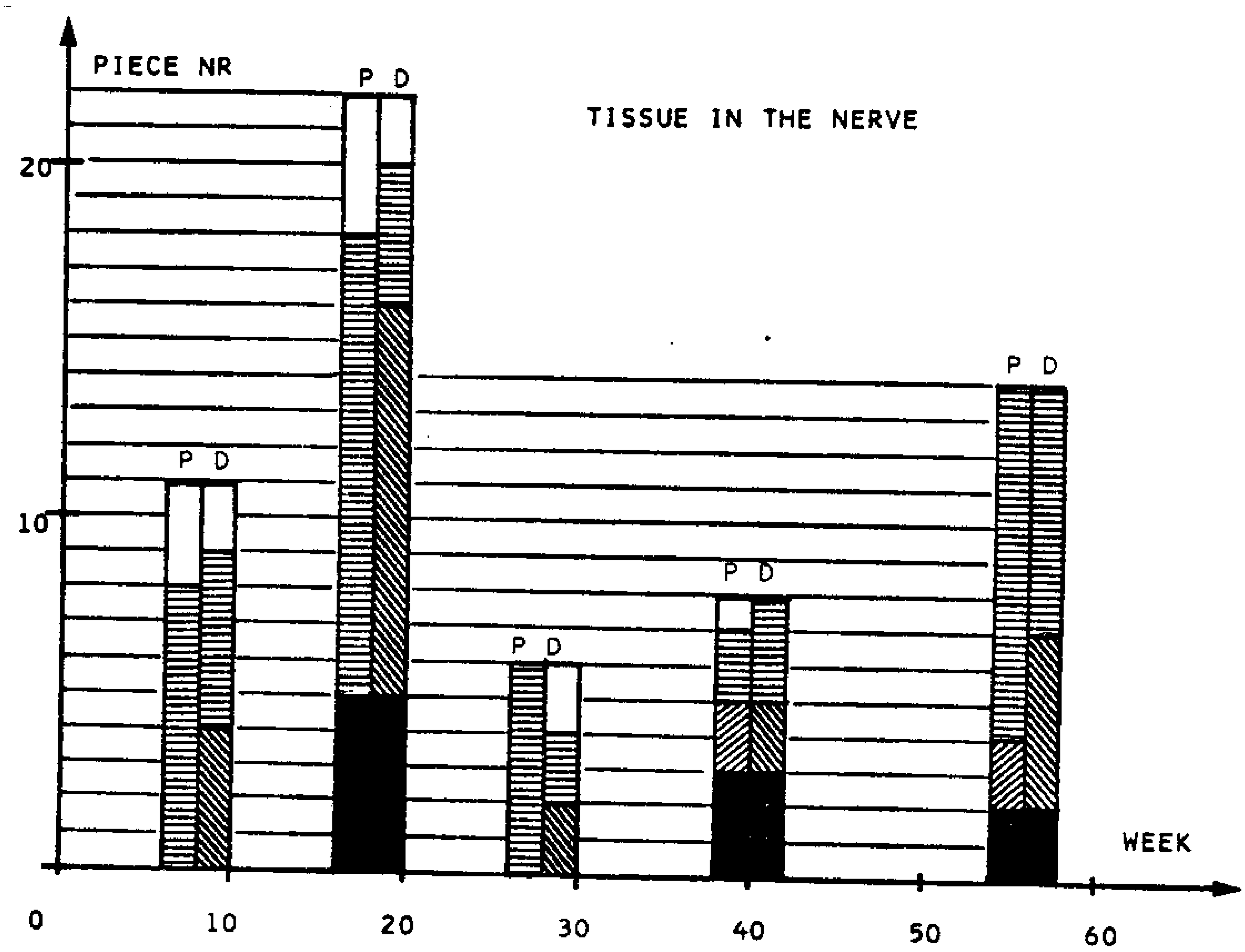


Fig. 9: Histologic results during DC application on the rats nerve

those below 5 % refered to the whole area was considered. Compering electrical and histological results we can conclude, that damages below 10 % do not cause any considerable loss of function. Concluding it must be considered, that our arrangement corresponds to worst case conditions because the rat is a very mobile animal and relation between nerve and electrode is very disadvantageous.

4. Studies with stimulation voltages on sheep

We developed a completely implantable and battery-powered stimulation-unit delivering three constant impulse-amplitudes (2, 4 and 8 Volts). The electrical parameters are adjustable, usually we use 1 ms impulse duration at a frequency of 25 Hz. Stimulation is switched on for 2 seconds, followed by a 2 second break. The 3 output channels are separated inductively and electrodes are decoupled by capacitous (3,3 uF). Efficience of the whole unit is 60 %, allowing function up to 3 month (fig. 10 shows the stimulation unit and the outlines). Two series on sheep were carried out (twice 6 animals). After the first series some improvements on electrode wire and connector to the stimulation unit were necessary. Because of legal considerations the 8-Volt-electrode was not implanted in stimulatable area. Results of the first series is shown in fig. 11. Because of management reasons it was not possible to check function of stimulation very often, so that durations of stimulation given in the table have to be considered as minimum values. We assumed that the 8 Volt-electrode should corrode first. Despite this opinion corrosion was only visible in one animal. After at least 6 weeks of stimulation the 8-Volt-electrodes

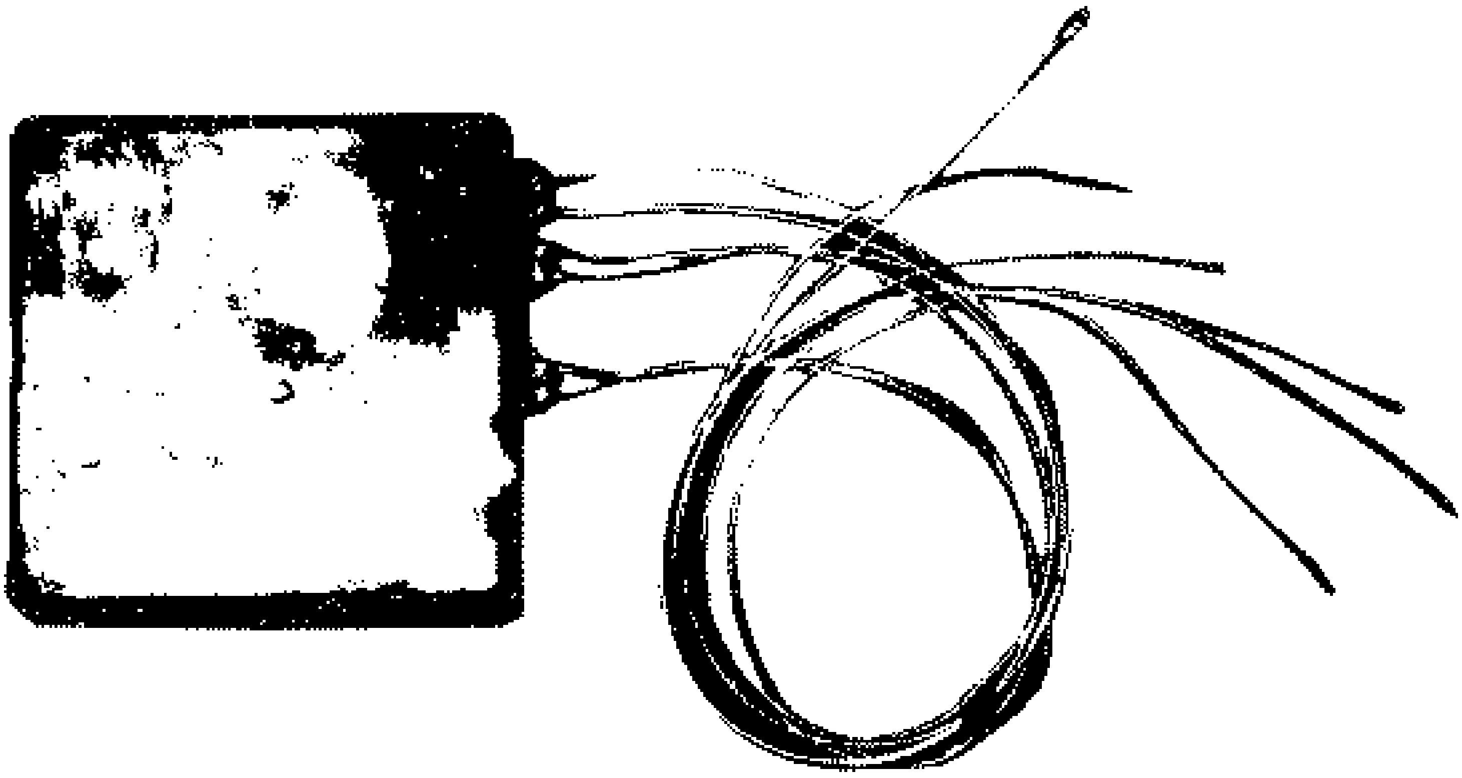


Fig. 10: Battery powered 3-channel stimulation unit

ANIMAL'S NR.			1 ♀	10 ♀	[illegible] ♂	[illegible] ♂	2 ♀	75 ♀
DAY OF IMPLANTATION			10. 9.80	19. 9.80	16.10.80	16.10.80	17.11.80	21.11.80
DAY OF EXPLANTATION			9. 1.81	8. 1.81	14. 1.81	16. 1.81	24. 2.81	24. 2.81
IMPLANTATION TIME			17 weeks	16 weeks	13 weeks	13 weeks	14 weeks	13 weeks
LEAST STIMULATION TIME			6 weeks	6 weeks	7 weeks	8 weeks	3 weeks	6 weeks
ELECTRODE'S POSITION im = intramusc., sc = subcutanous, distance (cm)		2 Volt	im, 1,5	im, 1,5	im, 3,0	im, 3,0	im, 3,0	im, 3,0
		4 Volt	sc, 1,5	im, 1,5	im, 3,0	im, 3,0	im, 3,0	im, 3,0
		8 Volt	sc, 2,0	im, 1,5	im, 3,0	im, 3,0	im, 3,0	im, 3,0
INVESTIGATION DURING EXPLANTATION FUNCTIONAL ELECTROSTIMULATION WITH 20 Hz/1ms, starts with .mA	2 Volt	Current (mA)	2,2	3,5	wire break	wire break	wire break	wire break
		Voltage (V)	3,6	6				
		Impedance (kOhm)	1,6	1,7				
	4 Volt	Current (mA)	2,4	0,9	wire break	0,6	10,5	1,5
		Voltage (V)	5	2		4,5	26	2,5
		Impedance (kOhm)	2,1	2,2		7,5	2,5	1,7
	8 Volt	Current (mA)	1	0,9	1,6	1,7	10,8	wire break
		Voltage (V)	50	2	3	3,6	12	
		Impedance (kOhm)	50	2,2	1,9	2,1	1,1	

Fig. 11: Electrode tests in animal: Results of a serie of 6 sheep

of 3 sheep showed an electrode resistance of 2,5 kOhms. Stimulation unit of animal 4 had a malfunction after 3 weeks, no corrosion occured and animal 6 had broken electrode wires. Hypothesis, that high voltages consequently result in corroded electrodes cannot be maintained. Summerizing results gained in the first series are too inhomogenious to come to a final conclusion. The second series is still in progress.

5. Optimization of impulsedesign

To gain objectiveness concerning impulse design we tested our electrodes in NaCl-solution. Application of a microcomputer makes possible a standarized recording of electrode corrosion. Fig. 12 shows the blockdiagram of the whole measurement equipment.

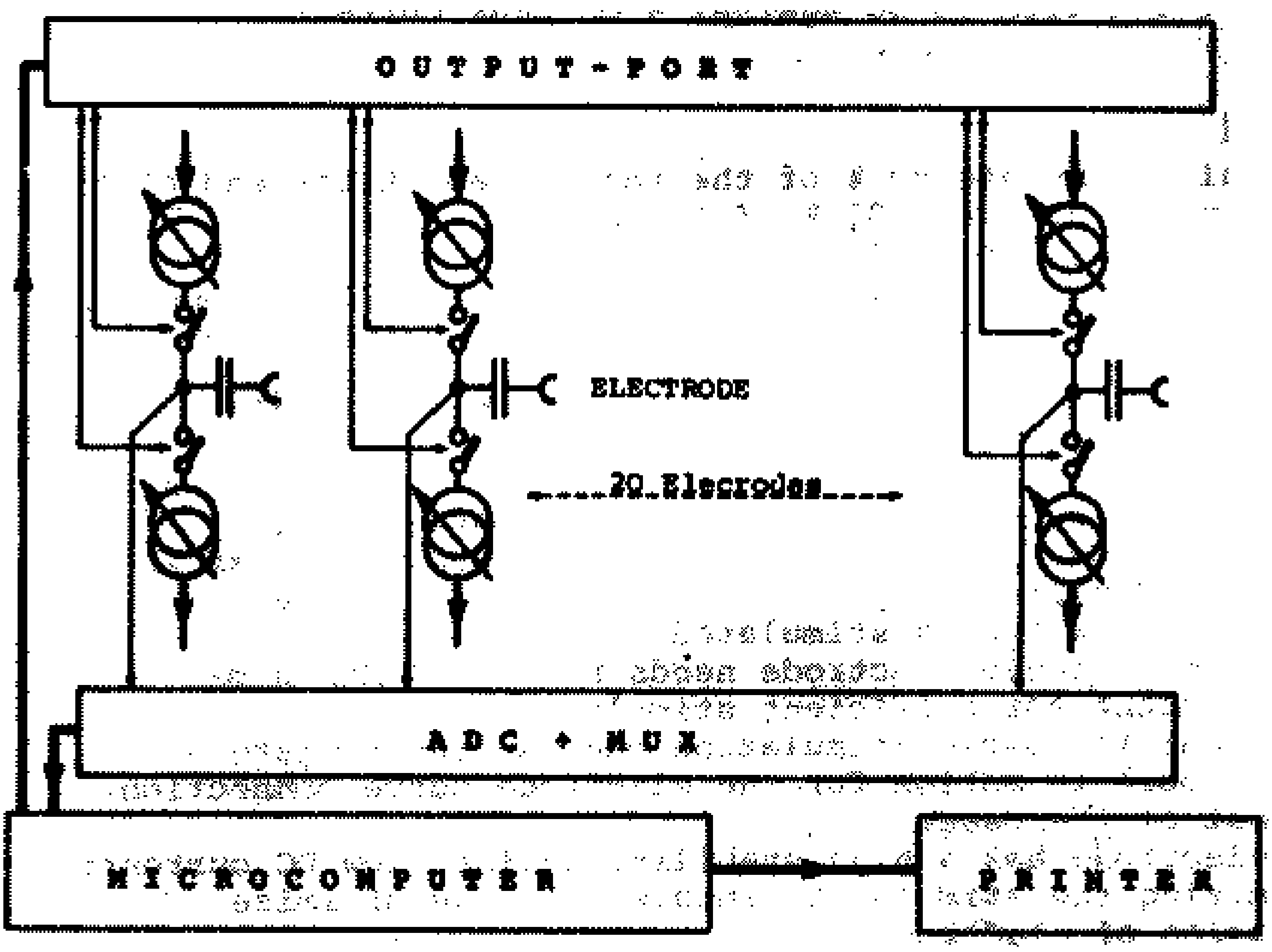


Fig. 12: Blockdiagram of the computerized in vitro electrode test with different impulsdesign

Alltogether 10 pairs of electrodes are tested simutaneously. Various impulse trains, different in shape, polarity and amplitudes are used for stimulation. A capacitor for electrode decoupling prevents a continous DC-fraction. In periodical intervals (e.g. all 4 hours) continous stimulation is interrupted for measurement. Each pair of electrodes is adressed separately and 250 us after current is switched on voltage at the electrode is measured. After analog digital conversion voltage is normalized and printed. Trend of voltage corresponds to the stability of the electrode. Voltage increases when electrode resistance increases. Fig. 13 shows an example of a stable electrode (nr. 9) and a corroded electrode (nr. 6). The example shows the relevance of the statement that an electrode with slowly increasing resistance is lost within short time (4 days). At present we are examinating 4 different shapes of impulses (fig. 14).

Stimulation current, frequency and impulsduration are changed alternately. Stimulation is done without any interruption to stimulate worst case conditions. Fig. 14 shows some results including visual judgement 100 hours after switching on. At this moment 4 electrodes stimulated with 8 mA are already disintegrated. The remaining electrodes nr. 3 and 4 are stimulated with special impulseshapes. Electrode nr. 2 with an increase of voltage of only 7 % probably will remain stable. Electrode nr. 8 and 9 are stimulated with impulseshapes nr. 2 and 4 and seem to be against 4 mA peak current.

6. Results

./. We could stimulate 90 % of the rat nerves at the end of the experiment, however, 85 % of the animals showed histological changes (!).
./. Even by selective stimulation with 4 or more electrodes an additional stimulation of other muscles sometimes cannot be avoided.
./. There are some technologic problems with very smale multiple electrodes.
./. We can achive a smooth motion of extremities implanting 4 or more electrodes close around the nerve. It is possible to avoid fatigue caused by transmitter loss in the nerves end plate by cyclic changing the electrode combination which is stimulated.
./. A well positioned electrode needs not more than 3 mA peak current for sufficient stimulation.
./. Different to muscle stimulation one can investigate a region pure in motion for the electrode nerve connection in most of the cases.
./. The electrode has a high stability against low DC currents.
./. Optimizing the stimulation impulse one can minimize corrosion of electrodes.
./. There is up to now no imperative reason to reject the stainless steel electrode.

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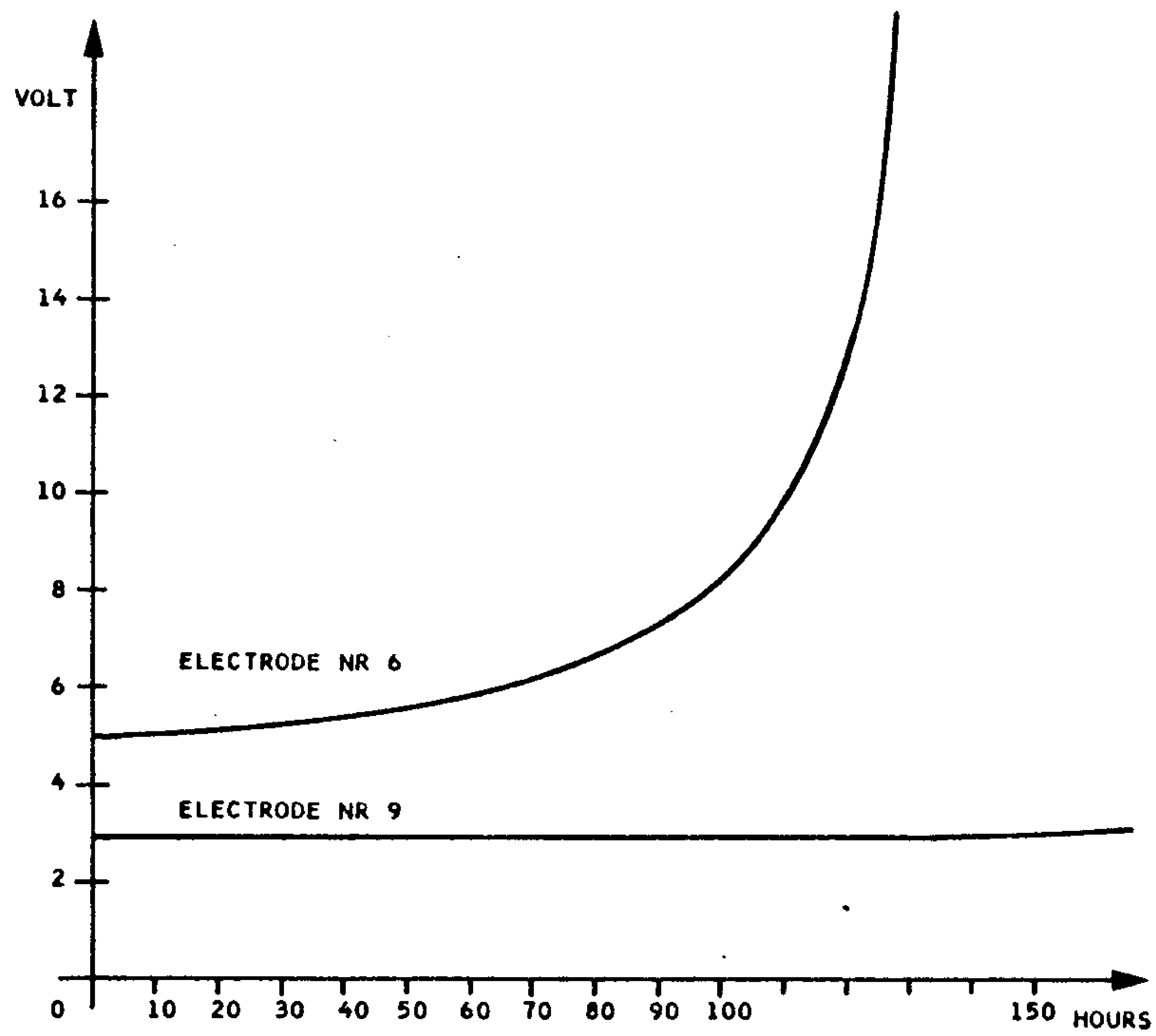


Fig. 13: Electrode's voltage during in vitro test

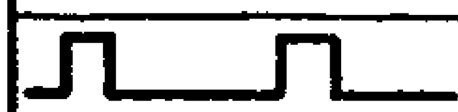
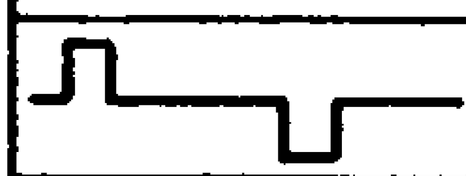
ELECTRODE NR.	1	2	3	4	5	6	7	8	9	10
CURRANT mA	8	8	8	8	8	8	8	4	4	2
FREQUENCY Hz	80	80	80	40	40	10	10	80	80	80
PULSE DURATION ms	1	1	1	2	2	2	2	1	1	1
 1										x
 2	x			x		x		x		
 3		x								
 4			x		x		x		x	
VISUAL STATEMENT: WELL								x	x	
VISUAL STATEMENT: MEDIUM		x	x							x
VISUAL STATEMENT: WORST	x			x	x	x	x			
RESISTANCE INCREASE (%) PAST 100 HOURS	35	7	30	24	35	67	45	4	4	20

Fig. 14: Preliminary results of an in vitro study concerned with the optimization of impulsedesign

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