Proc. of The Seventh International Symposium on External Control of Human Extremities. Dubrovnik : September 1981

QUANTITATIVE EVALUATION OF HUMAN MUSCLE ATROPHY FOLLOWING TOTAL DENERVATION*

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Abstract

The cross-section and X-Ray density of totally denervated muscle lodges was monitored for up to 14 months in five subjects by means of computerized tomography.
The results show that denervated muscles decrease their cross-section and density and their antagonists undergo similar changes expecially during the first few months.
Atrophy is not as irreversible as most textbooks report and the electrotherapeutic treatment is not as effective as it is believed to be in preventing muscle wasting.

Introduction

Neuromuscular diseases are in most cases associated to size changes or to degeneration and destruction of muscle fibers. Quite often, muscle tissue is replaced or infiltrated by fat or by connective tissue therefore making very inaccurate any attempt to estimate muscle size by external evaluations such as limb volume or circumference.

Evaluation of muscle size and of muscle tissue quality is very important for the assessment of therapies and for monitoring pathological states much as muscle denervation, muscle distrophy and many other diseases and disturbances.

Computerized tomography provides an excellent tool for this purpose and it has been applied to the investigation of the normal musculo-skeletal system (2,3,5,9)to the assessment of pseudohypertrophic muscular distrophy (11) and of musculo-skeletal tumors (1,4)as well as to cases of disuse atrophy following tenotomy (6).
Ultrasonic tomography has also been used (7,8,13) : since it has no radiation problem it can be applied often but the quality of the image is poorer than that obtained from a CAT scan.
The radiation dose of a CAT scan, on the other hand, is today lower than that of a standard X-Ray examination.

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*This work was made possible by an original suggestion of Prof. G.A. De Donato and by the cooperation provided by Prof. C. Mathis and Prof. E. Richetta of D.T.R. and of the Cellini Clinic in Torino, Italy.

In this research computerized tomography of the forearm and of the leg was applied with the purpose of quantifying the time course of muscle atrophy following total traumatic denervation of a muscle lodge.

A secondary objective of the work was to provide some data about the effectivness of electrotherapy in modifying the atrophy process.
The value of such therapy has never been positively shown in man and has recently been challenged by some researchers (10).

Materials and methods

Five patients with total traumatic denervation of either the wrist and finger extensors (radial nerve lesion) or of the foot dorsal flexors (peroneal nerve lesion) were identified during a one year period in the medical centers of Torino. Such pathology is indeed very uncommon since most lesions are partial and diffused (such as plexus lesions).
One subject had total denervation of both the dorsal and plantar flexors of the foot.
In no case the denervated muscles had received direct trauma or vascular damage except for modifications due to the denervation itself. The nerve lesion was never below the elbow or the knee.

CAT scans were made every 2-3 months at 1/3 and at 2/3 of the healthy and of the affected limb. The total lenght of the limb was measured from the olecranon to the stiloid process of the ulna or from the caput fibulae to the malleulus lateralis. The scans were made with a Siemens Somatom equipment with an X-Ray 7 mm thick and produced by o 125 KV acceleration potential.
The image was recorded on floppy disk.

The Siemens Evaluscope apparatus was then used to outline the muscle and bone area and the area and average density of the extensor and flexor lodges.

The X-Ray density information is provided in Houndsfield Units which are arbitrary units normalised with respect to the density of distilled water according to the equation:

$$H.U. = 1000 \cdot \frac{D_t - D_w}{D_w}$$

where : Dt = density of tissue under examination.
Dw = density of distilled water.

For a totally transparent material is Dt = 0 and H.U. = -1000, for water is H.U. = 0 and for a material with an X-Ray density twice that of water is H.U. = 1000.
The Evaluscope also provides the standard deviation of the density in the outlined region and the number of area elements (pixels) in it.

Fig. 1 shows C A T scans performed at 1/3 and 2/3 of the forearms of a 53 year old woman 45 days after total lesion of the right radial nerve. The muscle and bone area and the extensor and flexor lodges are outlined and the area and density values are shown numerically beside the picture.
Care was taken to perform sequentially taken scans at the same level and to outline the regions of interest in the same way.

The area error due to the repeatability of the manual outlining of a region of interest has been verified to be within ± 5% even in cases of small regions. The density errors are within±3% if care is taken to avoid including high density area elements (such as bone) in the region of interest.

Each evaluation consisted of the proximal and distal C A T scan, a clinical examination and an electrodiagnostic examination (EMG and strength - duration curves) and was carried out every 2 - 3 months. Early signs of reinnervation could however be clinically detected in between tests.

The parameters plotted as function of time from lesion are the ratio of the total (muscle and bone) area of the affected side to that of the normal side as well as the same ratio for each muscle lodge. The percentage of space occupied by each muscle lodge with respect to the total section is also computed and plotted as well as the density in H.U. units. The area ratios may be affected by a ±10 % error (worst case error) while the density values may be affected by a ± 3% error.

When electrotherapy was applied, exponential current pulses were used : the duration was either 250 msec or 500 msec, while the pause was 2 or 4 sec. Each daily session lasted about 10 minutes and involved two to four muscles.

RESULTS

Because of the limited number of cases no statistically valid data can be presented and discussion of the individual case histories is preferred.

Case 1 (Fig.2)

A 21 year old male was monitored for almost 14 months following a knife wound which cut the right peroneal nerve near the head of the fibula. This subject received regular daily electrotherapy (10 min/day) of the denervated muscles from the end of the first to the end of the eighth month.
Nerve grafting was performed following the trauma and minor voluntary contractions of the tibialis anterior and peroneous longus only began to appear eight months later.
The diagrams of Fig.2 show a substantial loss of right dorsal and plantar flexors section during the first six months.
At the distal level dorsal flexor atrophy continued until 55% of the muscle cross-section was lost after 14 months. Wasting of plantar flexors reversed and proximal dorsal flexor area stabilized after eight months. Density of both lodges on the affected side dropped within the first month to 85% of the contralateral side and slowly recovered mainly at the proximal level.

Case 2 (Fig.3)

An 18 year old male received a major trauma in the hip and thigh region with total denervation of both muscle lodges of the lower leg. Nerve grafting and transplant were performed providing reinnervation possibilities for plantar flexors only which (they only) were stimulated daily for a few minutes.The lowerleg showed no signs of reinnervation up to the 14th month. High atrophy of both lodges is evident with more dramatic wasting of the dorsal flexors at the distal level. Density is quite low on the affected side it shows an increasing trend and no significant difference between the two lodges.

Case 3 (Fig.4)

A 56 year old female had a total radial nerve damage following fracture of the humerus. Because of other problems in the cervical region and some practical difficulties she received no electrotherapy and only minor passive movement treatment of the wrist. The cross-section decrease of the wrist and finger extensors is very dramatic during 12 months and their density is also much lower than normal. It should be noted that a relevant decrease of density and cross-section affected the wrist and finger flexors as well.

Case 4 (Fig.5)

A 53 year old female received a radial nerve compression and damage following fracture of the humerus. Clinical and EMG signs of reinnervation appeared four months later. Marked atrophy was present already 45 days from lesion in both flexors and extensors (see also Fig.1), probably also due to a 30 day cast immobilization of the arm, and was more evident at the distal level.
Finger and wrist flexors recovered within 5-6 months while the extensors showed some recovery at the distal level and some loss at the proximal level stabilizing at 75% of the contralateral section. Density of the denervated muscles dropped quickly to 73% of the contralateral muscles (proximal level) but after six months was near the other muscles' values.

Case 5 (Fig.6)

A 36 year old male received radial nerve compression and damage following fracture of the humerus. A 40% loss of extensor cross-section was present three months later together with a 34% decrease of density (proximal section).
Both cross-section area and density increased and were much closer to normal values when normal movements resumed ten months after the lesion. The subject received electrotheraphy for three months a and half stopping it when the first signs of reinnervation appeared at the seventh month.

Discussion

Although the limited number of cases does not allow us to make any statistical observation, some interesting considerations may be proposed.

-In all five cases the denervated muscles have cross-section and X-Ray density lower than that of the contralateral muscles.

-In the four cases with single lodge denervation there is some transient decrease of cross-section and X-Ray density in the muscle lodge antagonist to the denervated one. This fact is probably due to disuse atrophy. Recovery of cross-section and density in the antagonist lodge is faster than in the denervated lodge.

-Even substantial atrophy of a single lodge (more than 50%) does not always produce a significant decrease of the total muscle and bone cross-section. If we consider that the subcutaneous fat layers are also included in the limb circumference or limb volume evaluations, it is obvious that such external measurements cannot be used to estimate muscle atrophy.

-Case 5 and, to a lesser extent, case 4 show that muscle wasting may be reversible. A 40% decrease of cross-section was almost entirely recovered in seven months by subject C.L. after reinnervation.

-Untreated or very little treated muscles undergo an atrophy process with loss of 8C -85 % cross-section in 12 - 14 months (case 2 and 3) corresponding to approximately 6-7 %/months.

-The general trend of X-Ray density seems to be a fast decrease during the first few weeks followed by a slow increase which may be either associated to muscle mass recovery or to further muscle wasting.

-It is hard to evaluate the effect of electrotherapy on such a few cases. In case 5 this treatment seems to have stopped and even reversed the wasting process, however in case 2 no significant difference is seen between stimulated and unstimulated muscles at the proximal level and only some cross-section difference may be observed at the distal level.
In case 1 a faster cross-section decrease takes place distally in the denervated dorsal flexors after interruption of stimulation. A larger number of cases is needed to reach some conclusions: four more cases are presently under examination and their results will be presented elsewhere.

-An interesting finding of this research is that total denervation of a muscle lodge is a very uncommon pathology: it does not seem to involve more than 1% of the patients affected by peripheral nerve lesions. In the other cases collateral reinnervation may take place before the main nerve trunks reach the muscles again. It is therefore important to assess the interaction between electrical stimulation and collateral sprouting.

Bulcke et al.(2,3) measured in 1979 the density of a number of muscles of the neck, of the shoulder and pelvic girdles and of the thigh and lower leg. In 64 subjects with age ranging from 10 to 60 years they found an average density of the triceps surae of 58.8 H.U. with a standard deviation of 15.2 H.U. and an average density of the tibialis anterior of 67.8 H.U. with a standard deviation of 19.3 H.U.. Other muscles had densities within this range of values.

Our density data match well with those found by Bulcke and show that, except for the wrist extensors of Case 3, the denervated muscle density does not decrease below 35 H.U. which could be considered the lower limit of the normal range. It should however be underlined that within the age range of 20 to 50 years, Bulcke found much smaller standard deviations averaging about 9 H.U. only: according to this value, for the given age range,the normal density values shoud be taken as 40 H.U. to 80 H.U..

Decrease of muscle cross-section because of disuse has been observed by other authors as well. Ingeman-Hansen (9) found a 26% decrease of quadricepts sections after five weeks of immobilization of the knee of two soccer players.
Haggmark (6) found a 23 % decrease of foot plantar flexors after six weeks of immobilization of seven athletes following Achille's tendon rupture.

Our case 1 shows a 28% decrease of foot plantar flexors section (distal level) after six months of denervation of the dorsal flexors. Our case 4 shows a 32% (distal) and a 19% (proximal) decrease of wrist and finger flexors following six weeks of denervation of the extensors. The other cases also show variable degree of hypotrophy of the antagonists of the denervated muscles.

Although the investigation of the atrophy mechanism was not the purpose of this work, some interesting observations about it may be obtained from the work of Haggmark (5,6) who found a good correlation between mean fiber size and muscle cross-section in 1978 and found a change of muscle fiber type composition of the immobilized soleus in 1979.

Conclusions

Computerized tomography appears to be an excellent research (and perhaps clinical) tool to monitor muscle atrophy and to assess the effectivness of therapy of denervated muscles.

Our preliminary results show that electrotherapy is not as effective as it is believed to be in preventing muscle atrophy. Perhaps its cost/benefit ratio should be reconsidered. Denervation atrophy is not as irreversible as most textbooks report.

Further research is however needed on a larger number of cases and other investigation techniques should be developed and applied to monitor changes in fiber size and fiber type of denervated and immobilised muscles.

Acknowledgements

This research has been carried out at the Centro Traumatologico Ortopedico di Torino and at the Cellini Clinic of Torino, Italy. Partial support was provided by the Special Program on Biomedical Engineering of the National Research Council of Italy under grant n.790123383 to C.T.O.
The authors are grateful to Prof. L. Fra for the neurological examinations,to Prof. C.A. De Donato for his suggestions and to Prof. C. Mathis and E. Richetta for making available the Siemens Somatom C.A.T. of the Cellini Clinic. The technical cooperation of Mr. Nino Roma and of Mr. Paolo Vallino is deeply appreciated.

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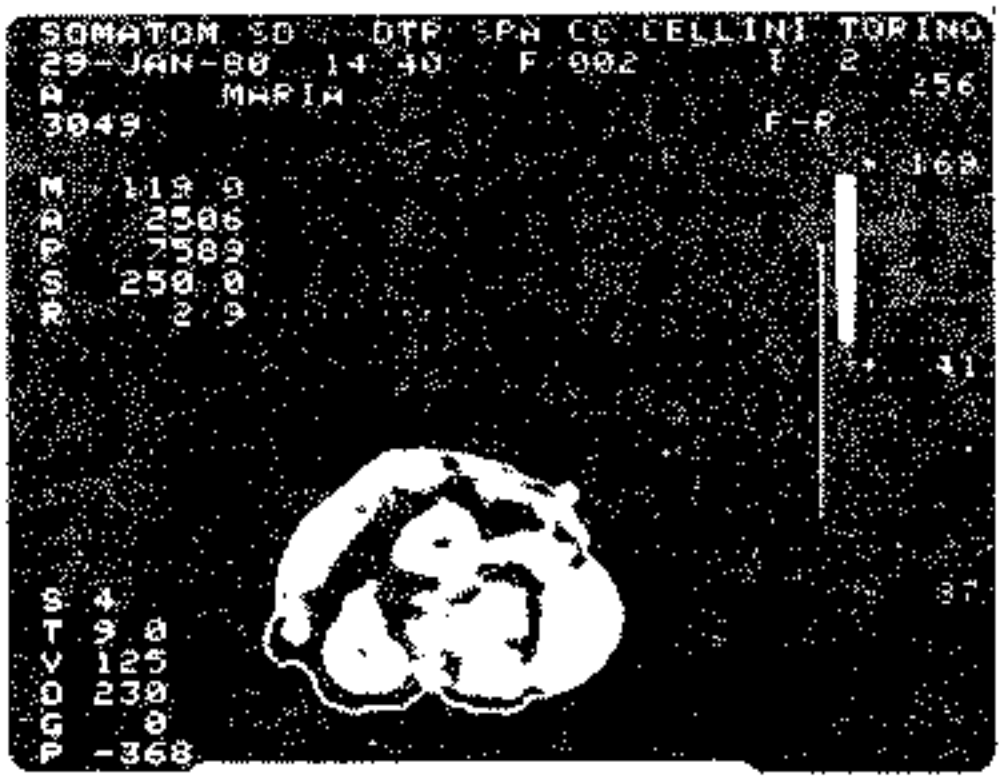
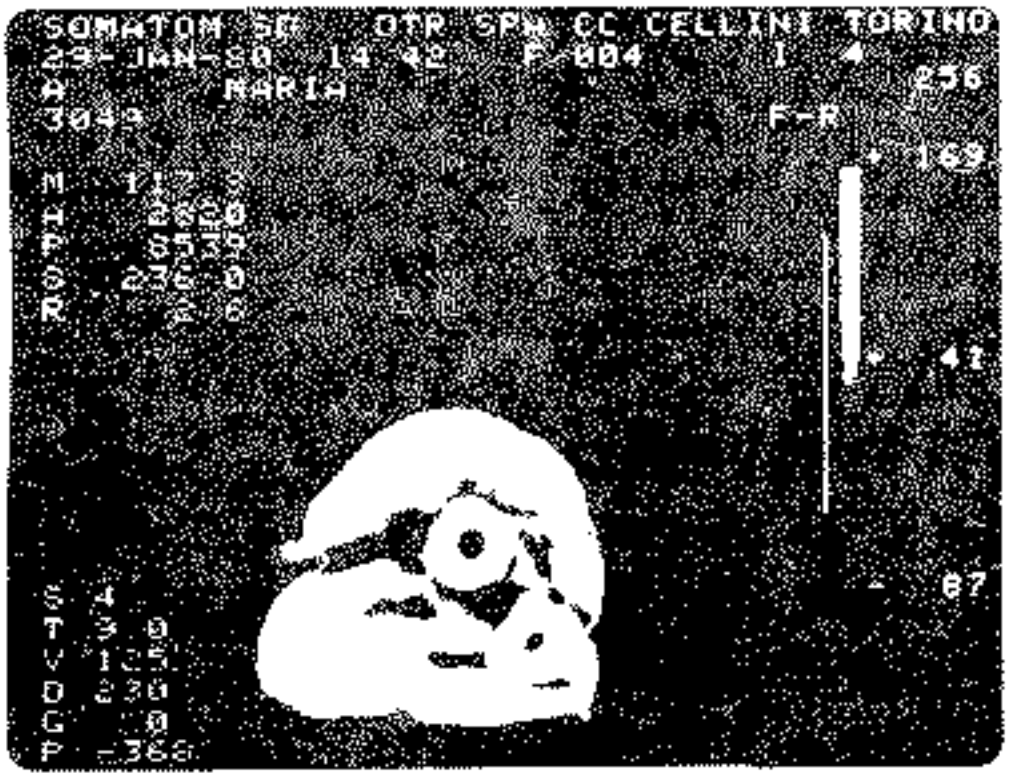


Total muscle and bone area .



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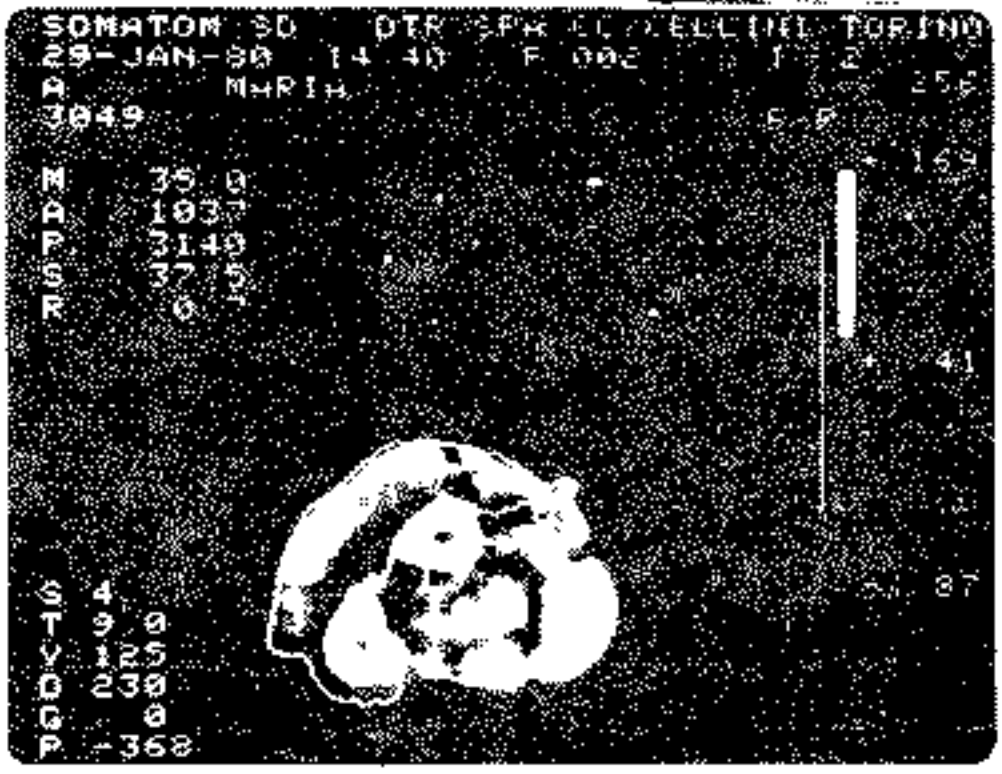
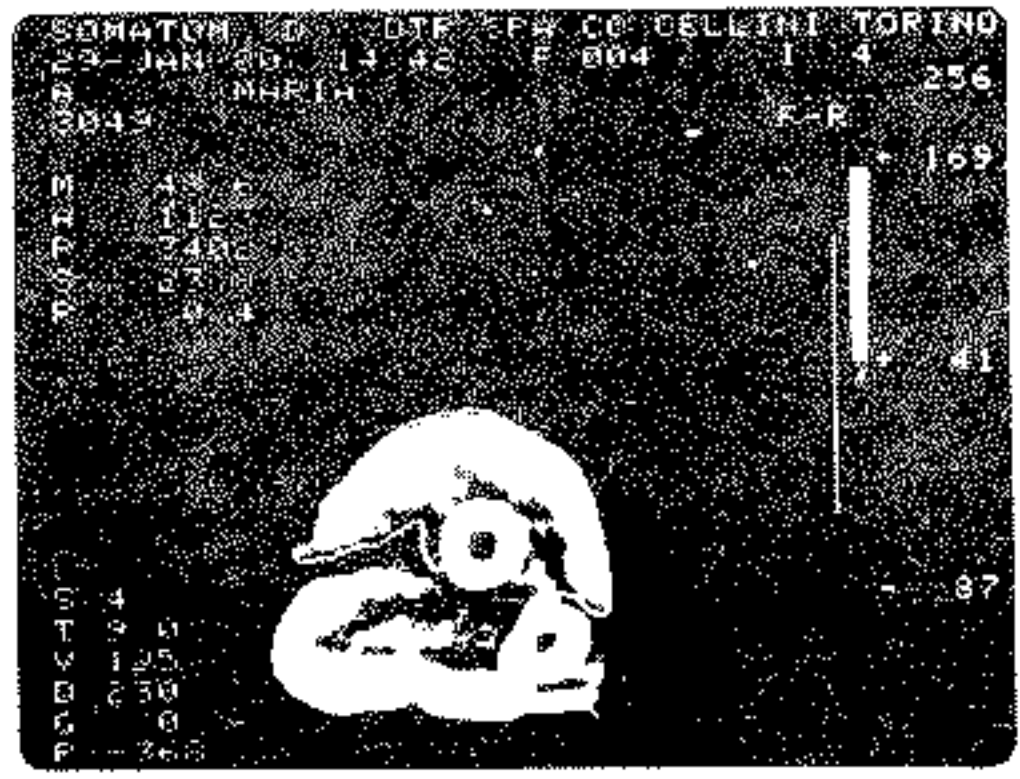
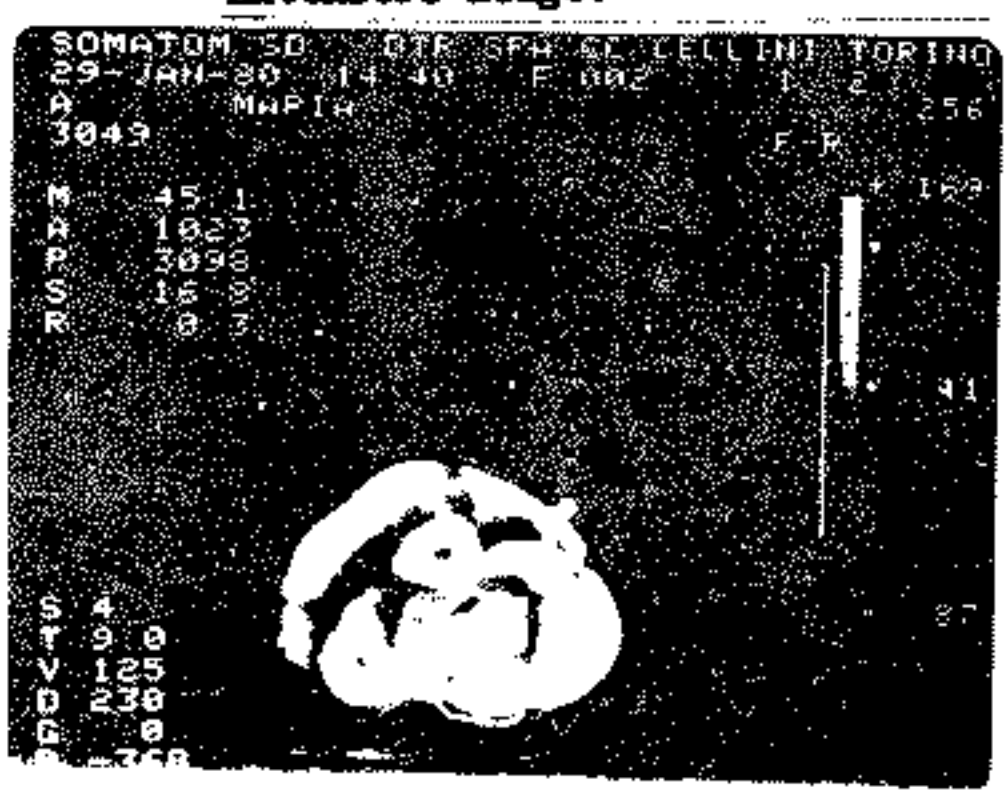


Extensors lodge.

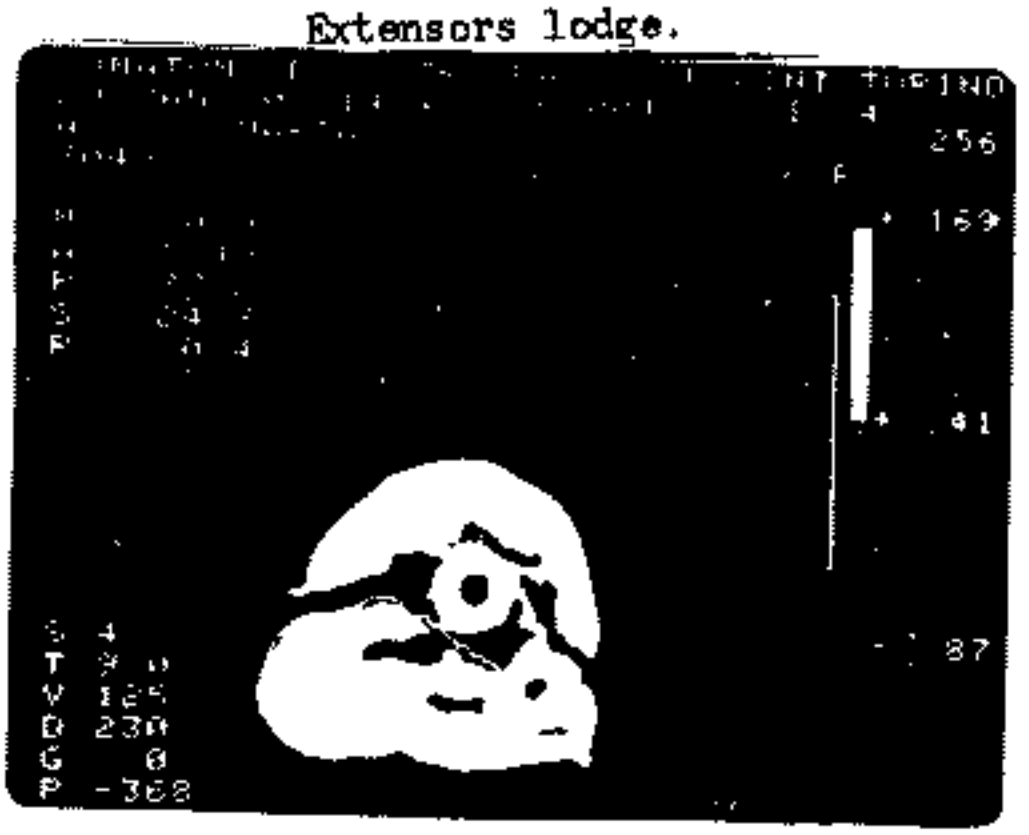


Extensors lodge.



Flexors lodge.

Right Side



Flexors lodge.

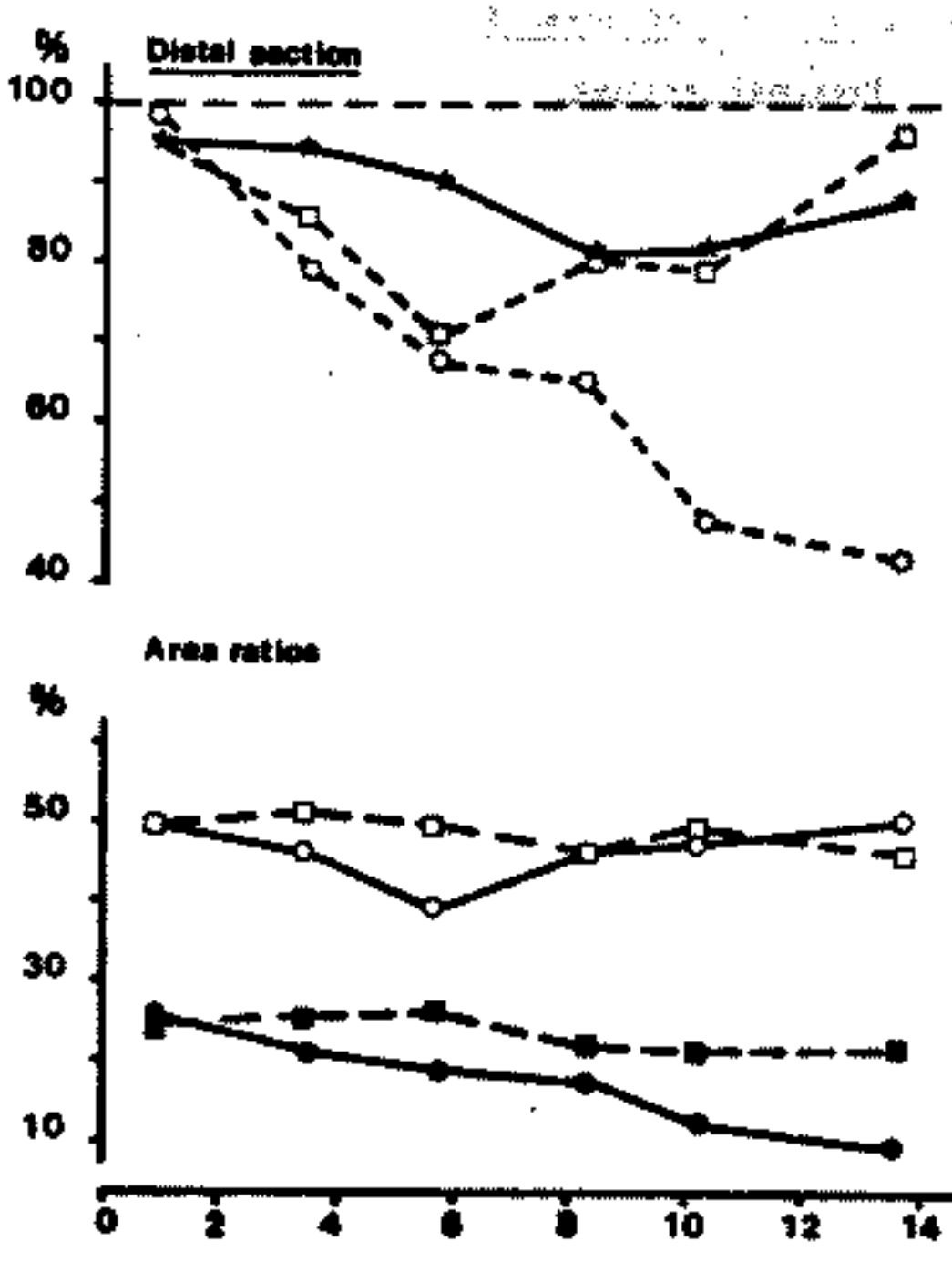
Left Side.

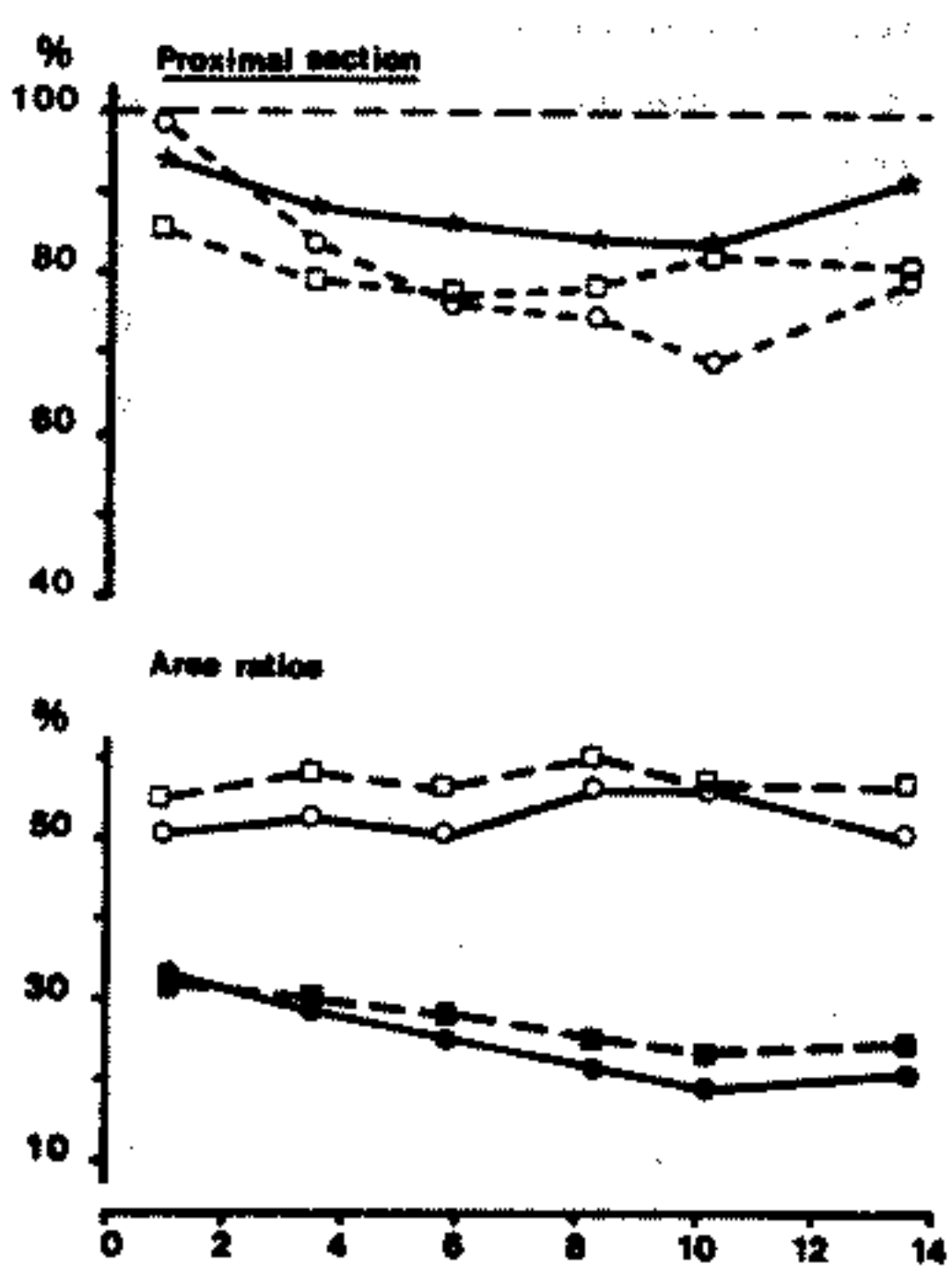
Fig. 1. Subject M.A. (Case 4). Proximal section forty-five days from total denervation of the right radial nerve territory.

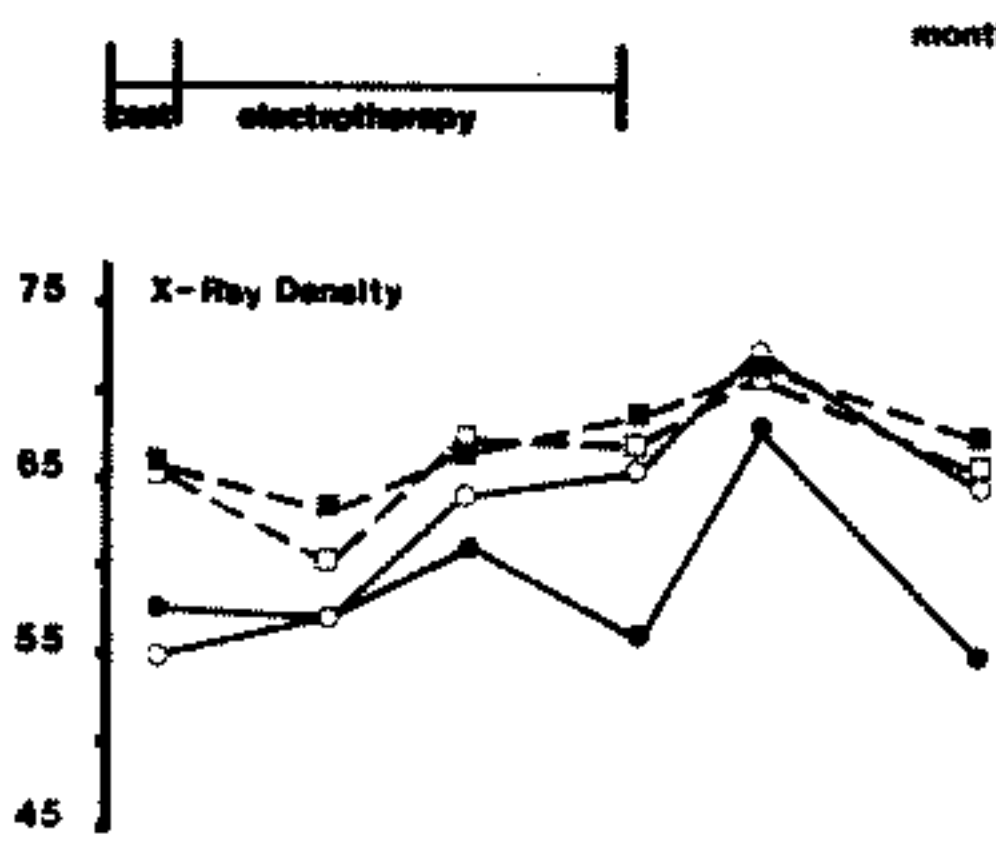
G.S. ♂, 21 years

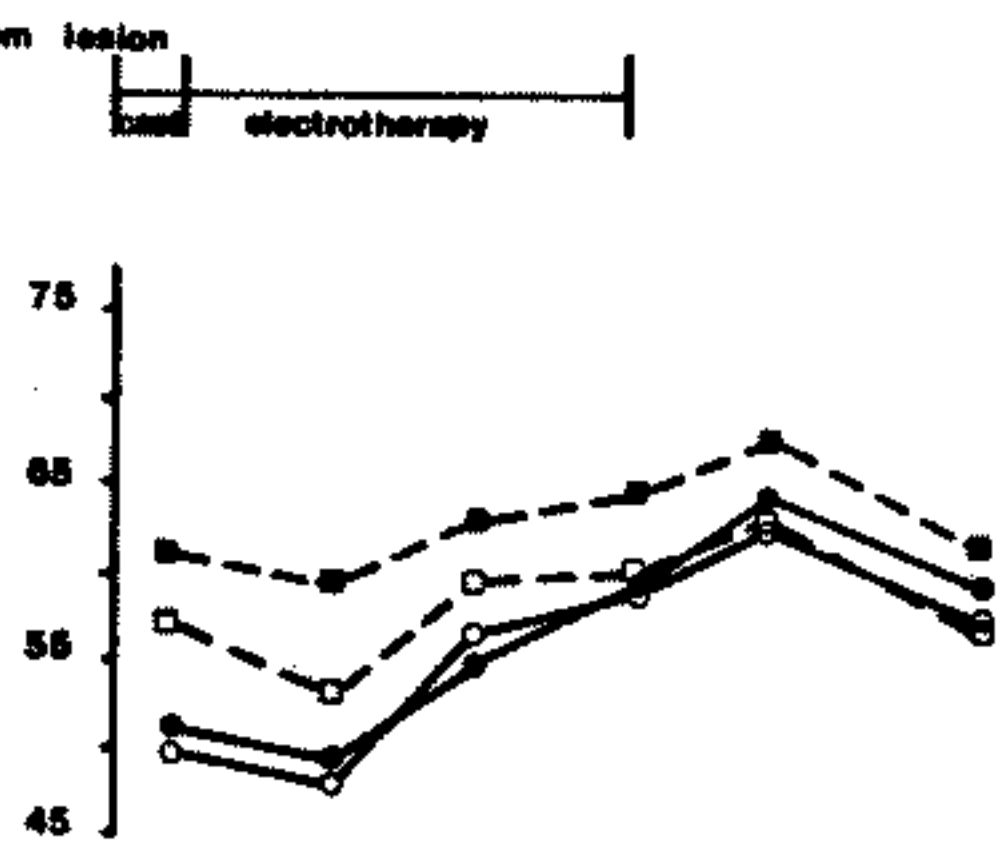
Peroneal nerve lesion on 1/1/1980

Total denervation of TA, PL, EA, EDC	Reinnervation of TA, PL









Area ratios

—●— Tot. A. / Tot. N. ; -○-○- Dors.Flex. A. / Dors.Flex. N. ; -□-□- Plan.Flex. A. / Plan.Flex. N.

—●— Dors.Flex. A. / Tot. A. ; —○— Plan.Flex. A. / Tot. A. ; -■-■- Dors.Flex. N. / Tot. N. ; -□-□- Plan.Flex. N. / Tot. N.

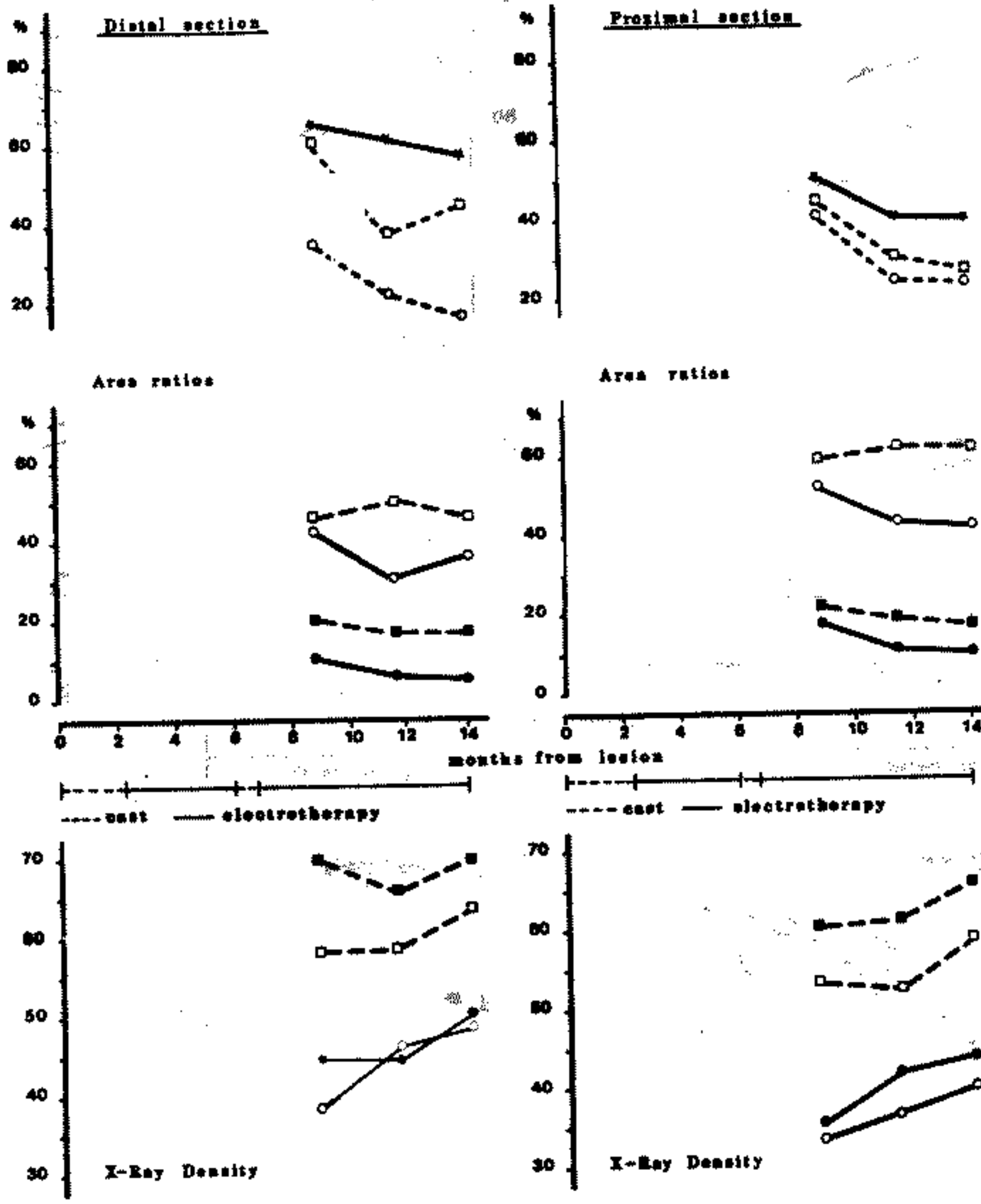
X - Ray Density

—●— Dors.Flex. A. ; —○— Plan.Flex. A. ; -■-■- Dors.Flex. N. ; -□-□- Plan.Flex. N.

Fig. 2 Case 1

M.D.N. ♂ 18 years. Left sciatic nerve lesion on Aug. 17 1970.

Total denervation of dorsal and plantar flexors. Electroth. of plan. flex. only



Area ratios

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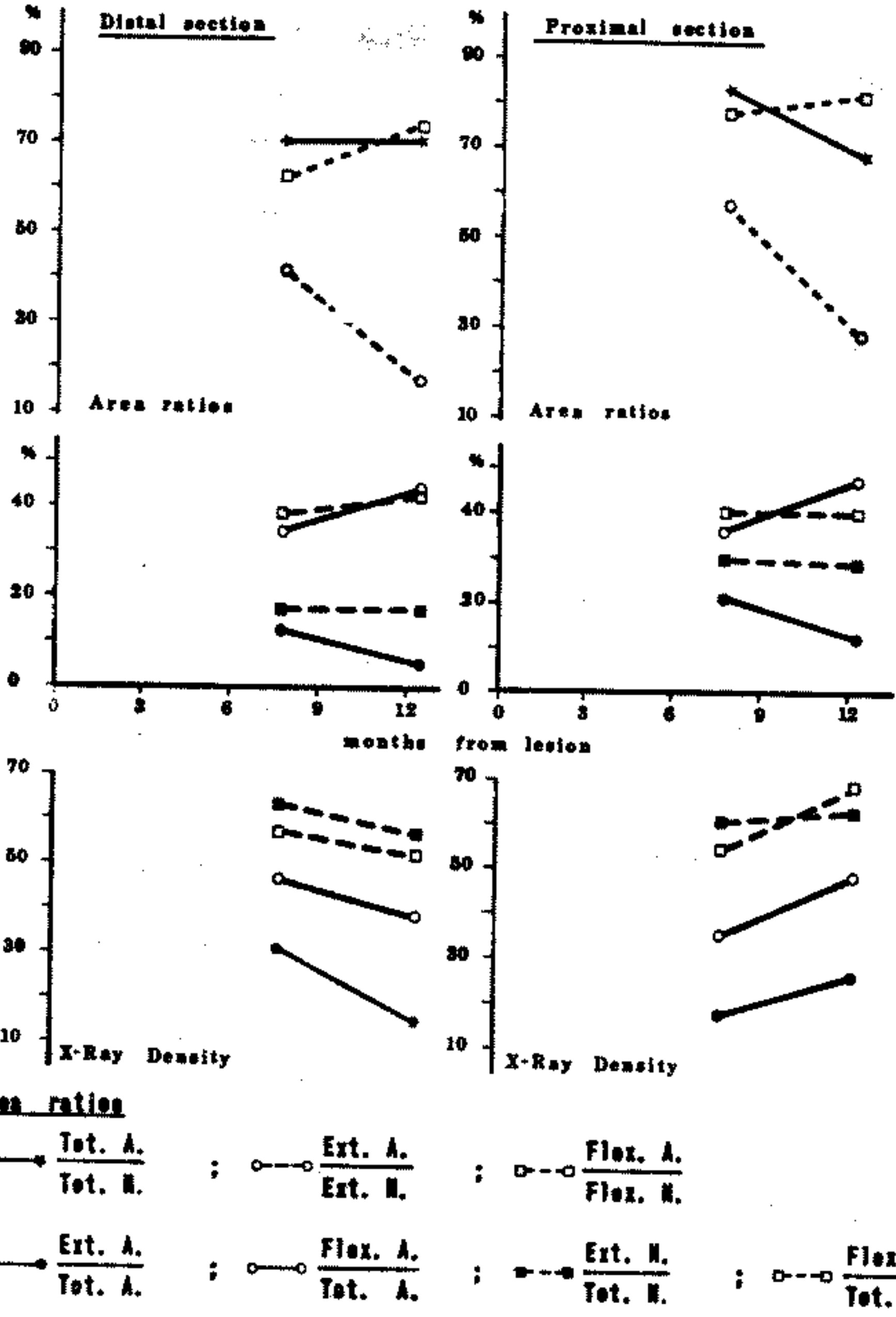
X - Ray Density

—●— Dors.Flex. A. ; ○—○ Plan.Flex. A. ; ■--■ Dors.Flex. N. ; □--□ Plan.Flex. N.

Fig. 3 Case 2

G. M. ♀ 56 years. Right radial nerve lesion on Aug. 17 1979.
Total denervation of radial nerve territory. No electrotherapy.



Area ratios

Tot. A. / Tot. N. ; Ext. A. / Ext. N. ; Flex. A. / Flex. N.

Ext. A. / Tot. A. ; Flex. A. / Tot. A. ; Ext. N. / Tot. N. ; Flex. N. / Tot. N.

X - Ray Density

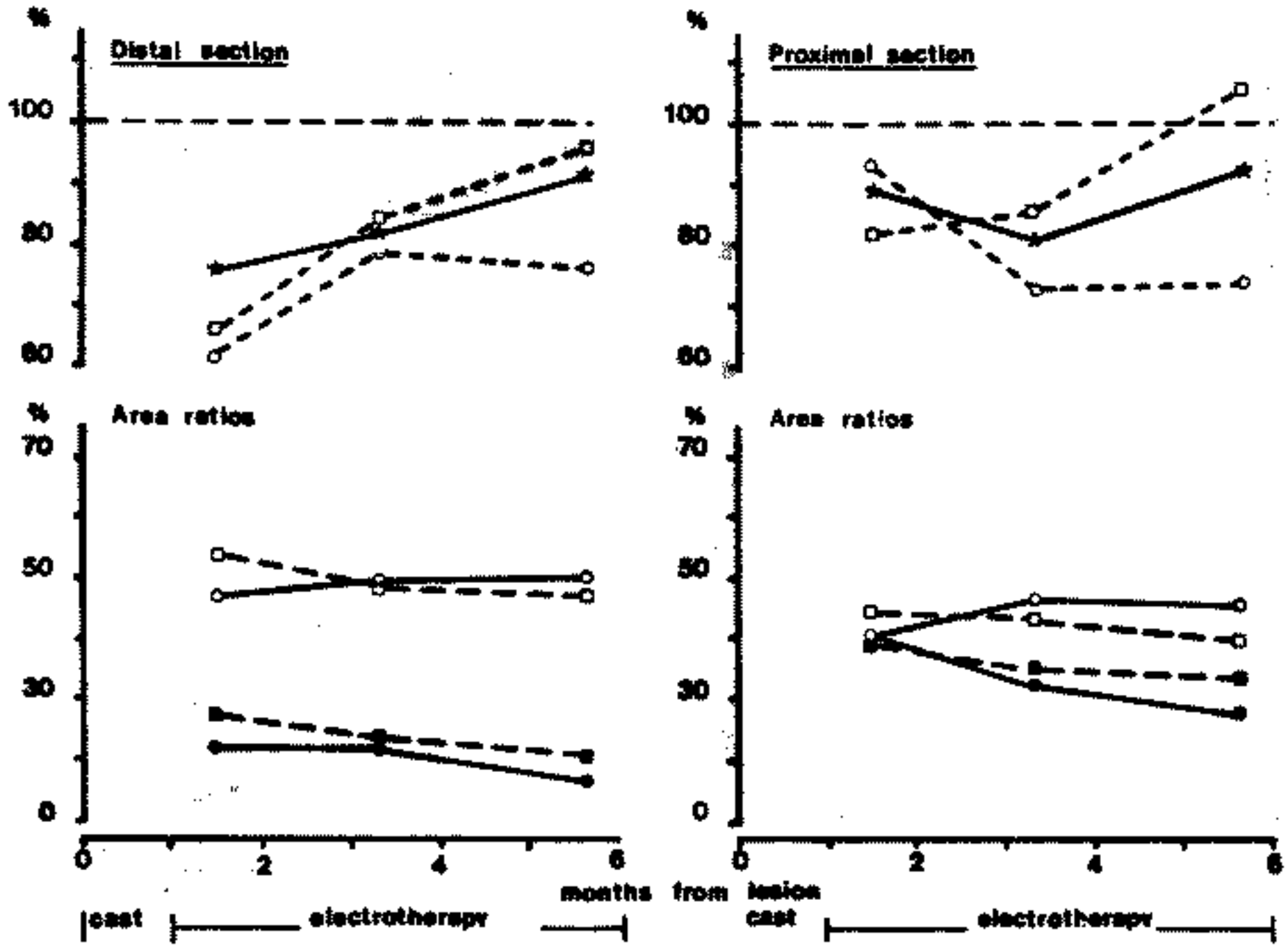
Ext. A. ; Flex. A. ; Ext. N. ; Flex. N.

Fig. 4 Case 3

M.A. ♀, 53 years
Right radial nerve lesion
on Dec.4 1979

Radial nerve territory totally denervated

Beginning of reinnervation



Area ratios

Tot. A. / Tot. N. ; Ext. A. / Ext. N. ; Flex. A. / Flex. N.

Ext. A. / Tot. A. ; Flex. A. / Tot. A. ; Ext. N. / Tot. N. ; Flex. N. / Tot. N.

X - Ray Density

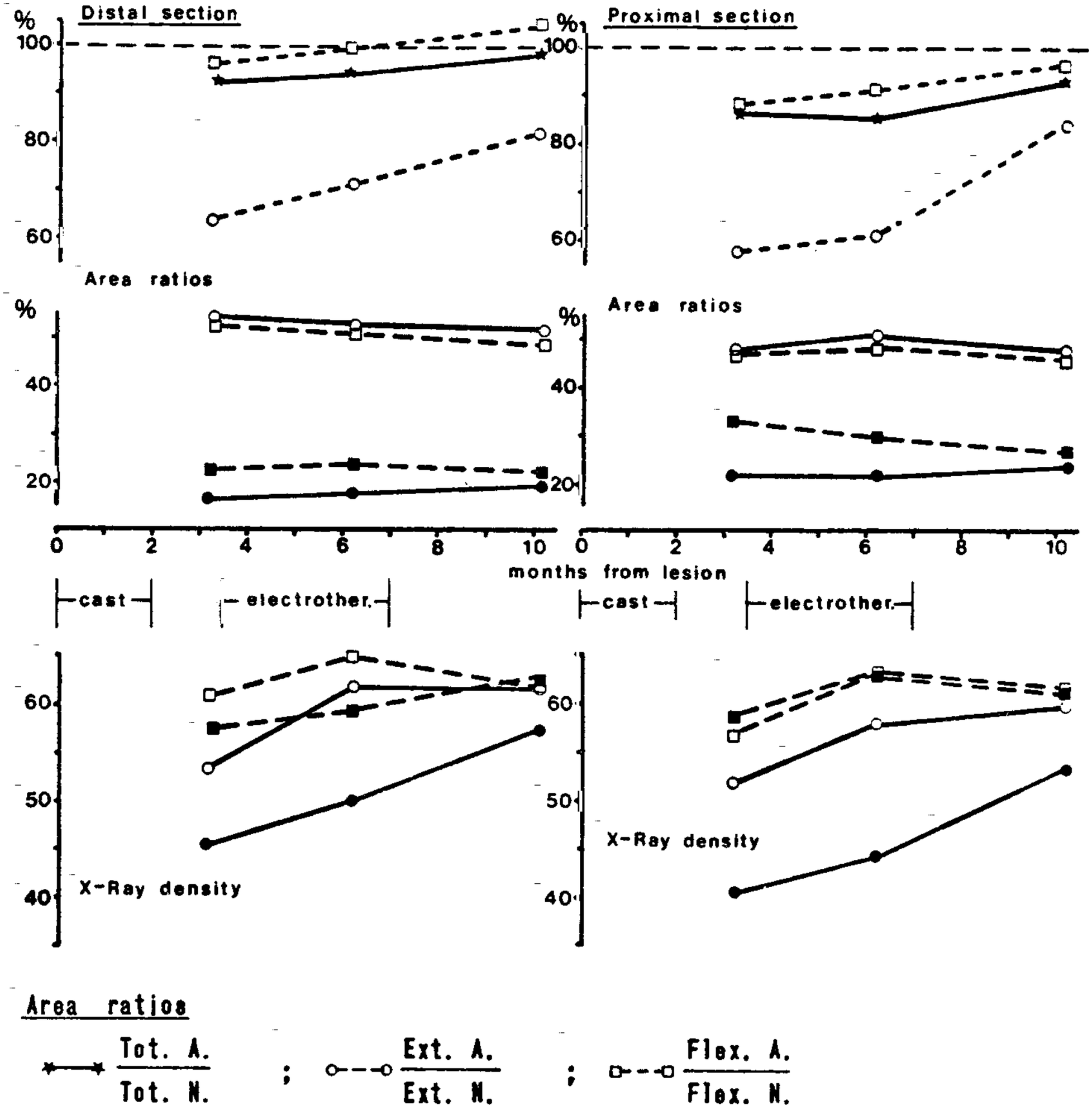
Ext. A. ; Flex. A. ; Ext. N. ; Flex. N.

Fig. 5 Case 4

C.L.♂, 36 years

Right radial nerve lesion on Nov 6 1979

No voluntary movements except EPL	reinnervation	normal movements



Area ratios

Tot. A. / Tot. N. ; Ext. A. / Ext. N. ; Flex. A. / Flex. N.

Ext. A. / Tot. A. ; Flex. A. / Tot. A. ; Ext. N. / Tot. N. ; Flex. N. / Tot. N.

X - Ray Density

Ext. A. ; Flex. A. ; Ext. N. ; Flex. N.

Fig. 6 Case 5