

EFFECT OF TANTALUM MARKERS ON LONGITUDINAL BONE GROWTH

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Small tantalum pins (0.50×1.5 mm and 0.32×1.2 mm), used as intraosseous radio-opaque markers, were investigated for their effect on growth in 62 young rabbits. The tetracycline growth method was used and a difference in daily growth rate between the marked right leg and the unmarked left leg indicated a slight growth stimulation. The growth rate was slightly stimulated (at most, $26 \mu\text{m}/\text{day}$) on days 1 and 2 after insertion, only if the larger markers were used. No growth effects were detectable on days 12 and 21.

Key words: growth; bone; rabbit; tetracycline; skeletal marker; tantalum

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Metallic markers for growth determination in long bones have been in use for a considerable period of time (Sarnat 1968, Desai & Sinkford 1974). The method has met with several obstacles. The marker has injured the bone, resulting in loosening and even rejection of the implant (Hedström 1969). The instability of the marker has sometimes invalidated its use as a fixed reference point (Ryöppy 1965). The implantation technique has at times been traumatic, involving operative interventions that have caused growth disturbances. In general, stimulating or retarding reactions have been seen in the marked bone and also secondary growth retarding reactions in the unmarked

bones (Tapp 1966, Hansson 1967, Hedström 1969).

Björk (1968) introduced a new type of intravital marker for use in roentgenography in clinical dentistry. Small pins about 1 mm long, made of vitallium or tantalum, were reported to have been successfully used since 1951 in mandibular marking for growth studies. A special instrument was constructed for implanting these pins into structures lying deeper than the mandibular to minimize the operative trauma of insertion and to facilitate correct placement (Aronson et al. 1974). The instrument inserts the pin percutaneously with a cannula introduced into the bone.

The present investigation used the tetracycline method (Hansson 1967) to study the growth effects of the implantation technique on the rabbit tibia.

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MATERIAL

Sixty-two rabbits aged 30 days were used; 1-2 litters for each series of investigations.

METHODS

Insertion technique for tantalum pins

The rabbits were under neuroleptanalgesia, Fluanizon and Phentanyl 6 and 0.12 mg/kg body weight (Hypnorm®, Janssen, Belgium). Under fluoroscopic monitoring the pins were inserted percutaneously with a special implantation instrument (Aronson et al. 1974). The tip of the instrument, a cannula, was introduced into the bone, and when in the required position the spring-loaded striking pin was released and the marker implanted in the bone. In a few instances the cannula had to be introduced several times into the bone before the desired position was obtained.

In the first series, pins 0.50×1.5 mm were used. The outer diameter of the cannula for these operations was 1.1 mm. In the remaining two series, tantalum pins 0.37×1.2 mm were inserted with cannulas of 0.7 mm outer diameter.

Localization of pins

In all series, one pin was placed in the proximal bony epiphysis of the right tibia. A second pin was inserted either in the proximal metaphysis or in the distal bony epiphysis of the same tibia. In one series, three pins were inserted: in the proximal and distal bony epiphysis and in the proximal metaphysis of the same tibia.

Tetracycline growth measurements

Intravital marking of the bone was done with intravenous tetracycline (oxytetracycline, 5 mg/kg body weight) according to the method of Hansson (1967). Tetracycline becomes deposited in the bone and cartilage as a fluorescent band in the calcification zone of the growth plate. As the bone grows, the growth plate moves in the epiphyseal direction leaving the fluorescent band in the metaphysis. A repeated injection of tetracycline will create a new fluorescent band. The distance between the two bands is the endochondral longitudinal growth occurring between the two injection occasions. Our measurement of the daily growth is accurate within 4-6 μ m, varying somewhat according to the investigated growth zone (Hansson 1967, Hansson et al. 1973).

Timetable for experiments

Short-term investigations (Series 1-3, 6, 7): Daily OTC injections were given on four consecutive days at intervals of 24 hours. After the first interval, the tantalum pins were introduced into the bony epiphysis of the right tibia. Longitudinal growth was thus obtained for a control day before and for two days after the pins were inserted. The rabbits were killed 30 minutes after the last OTC injection, and the right pin-marked tibia and the left unmarked control tibia were dissected free and prepared for growth measurements.

Long-term investigations: In one series (no. 4) growth on day 12 was investigated; in another series (no. 5) growth was investigated on day 21.

Processing of results

A. *Local growth effect:* The growth difference between the marked right leg and the unmarked left leg of each rabbit was computed separately as were the mean \pm S.E.M. for each series. A difference in growth was indicated by the marking procedure. Student's t-test indicated whether the growth was statistically significant.

B. *Generalized growth effect:* The lessening of growth rate during the two days after the marking procedure was computed as a percentage of the growth on the control day before marking. The mean value of all measurements made on each day was computed, as was the standard error.

RESULTS

A. Local growth effect

Table 1 summarizes the results according to pin size, localization of pins, and duration of experiment.

Control day: The difference in growth rate on the control day varied between — 7 and 5 μ m/day. Although statistically (almost) significant, this difference was biologically unimportant, as it coincided with the methodological error.

Large pins (0.50 \times 1.5 mm); short-term investigations

Pins in the proximal bony epiphyseal and metaphyseal region (Series 1): If the pins were inserted in the proximal epiphysis and metaphysis, there was no discernible effect on the daily growth

Table 1. Effects on longitudinal growth of implantation of tantalum markers in the rabbit. Difference in growth rate in $\mu\text{m}/\text{day}$ for implanted right tibia and left tibia (unimplanted) control for same rabbit.

Tantalum marker (mm)	Series	No. of rabbits	Region for markers			Growth plate	Daily growth ($\mu\text{m} \pm \text{S.E.M.}$)		
			Epiph. prox.	Metaph. prox.	Epiph. dist.		Difference implanted right	Difference implanted left	Control tibia
							1	2	21
0.50 × 1.5	1	16	×	×	Prox	0 ± 1	-1 ± 3	2 ± 2	12
						5 ± 2	26 ± 6*	20 ± 7	
	2	7	×	×	Prox	-2 ± 2	3 ± 3	0 ± 6	21
						4 ± 1 †	16 ± 5*	14 ± 5*	
	3	6	×	×	Prox	-7 ± 2*	-15 ± 6	-8 ± 4	12
1 ± 2						6 ± 6	3 ± 12		
4	9	×	×	Prox				12	
0.37 × 1.0	5	7	×	×	Prox				12
	6	10	×	×	Prox	-4 ± 3	-4 ± 3	-4 ± 4	12
						-1 ± 1	3 ± 4	2 ± 4	
	7	7	×	×	Prox	0 ± 2	-3 ± 2	-6 ± 1	12
0 ± 3						4 ± 2	4 ± 5		

* almost significant deviation from 0; $0.01 < P < 0.05$ (t-test).

† significant deviation from 0; $0.001 < P < 0.01$ (t-test).

expressed as a difference between the proximal epiphyseal growth in the marked right leg and that in the control left leg. In the distal growth zone, however, the marked leg showed a slight increase in growth, being 26 and 20 μ m longer than that of the unmarked leg. The difference was probably significant (Student's t-test) for day 1.

Pins in the proximal and distal epiphyses (Series 2): A slight increase in growth was found distally in the marked right leg; the increase was probably significant on the two days after pin insertion.

Pins in the epiphyses and in the metaphyseal region (Series 3): No significant difference was found in the daily growth between the marked right leg and the control left leg, in either the proximal or the distal growth zones.

Large pins; long-term investigations (Series 4 and 5): Neither type of marking, either in the two epiphyses only or with a third pin in the diaphysis, showed any significant difference in the daily growth on day 12 or 21.

Small pins (0.37 \times 1.2 mm); short-term investigations

Pins in the proximal epiphyseal and metaphyseal region (Series 6); pins in the proximal and distal epiphyseal regions (Series 7): No significant difference in growth rate was observed in either type of experiment.

B. Systematic growth changes

By day 1, the growth rate had fallen 11 ± 8 per cent (S.E.), and by day 2 17 ± 10 per cent compared with the control day - 1.

DISCUSSION

The present study investigated whether the trauma of tantalum pin insertion was serious enough to invalidate the use of

the pins for X-ray growth studies. Two factors could contribute to a local growth effect. Firstly, the operational trauma involving skin, periosteal and bone penetration by the cannula holding the pin. Secondly, the local irritation of the pins. A special histological study of the second factor showed that the tantalum indicators did not harm the bone; the indicators were found to be fixed (Aronson et al. to be published). These investigations lend no support to a tissue reaction of a magnitude that would disturb the growth by the presence of the tantalum indicators. Growth effects are therefore more likely due to the trauma of insertion.

Our findings show only a minor local growth effect when large pins are used. A slight stimulation of the growth on the operated side was noted in the distal tibial growth zone when pins were inserted proximally; it was also noted in the distal zone when pins were inserted in the two epiphyses. These growth disturbances were transient and had disappeared by day 12. The statistically (almost) significant differences in two of the growth zones of the control day can be ignored, as the differences coincided with the methodological error.

These findings agree with previous investigations into experimental traumatic growth disturbances (Hansson 1967). The trauma most comparable with our pin insertion is the experimental periosteal incision in the rabbit tibia. This trauma (compared with other major traumas such as medullary destruction and plugging of the marrow cavity) caused only a slight increase in the growth on the operated side compared with the unoperated side. The magnitude of the local growth effect after periosteal incision was about the same as we found after insertion of large pins. Compared with cortical and medullary traumas, the growth effects after pin insertion are minute, indicating that the trauma is slight.

Insertion of the small pins caused no detectable difference in growth between the operated and the unoperated leg. This trauma was thus less pronounced and so slight that growth disturbances were undetectable with the highly sensitive tetracycline method.

The smaller cannula size of the insertion instrument, combined with the increased technical skill in handling it that was acquired by the time the experiments with small pins began, contributed to the absence of demonstrable local growth effects from small pin insertion. Small pins were therefore placed in correct positions in the bone more rapidly and more easily, thus lessening the operational trauma.

The systemic decrease in growth rate found in this investigation is somewhat larger than that found in previous investigations (Hansson 1967). This is probably due to factors other than the insertion procedure itself. Inhomogeneity of the rabbit material (different races, different breeders) and seasonal variations might explain the large standard deviation and also the larger decrease in growth.

It is thus evident from this investigation that tantalum indicators are suitable for intravital marking in rabbit growth studies. As slight local growth effects can be detected on the first 2 days after insertion, but not after 12 days, it is recommended that growth studies should not be started until at least 2 weeks after insertion of markers.

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