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IGF-1 on Titanium Alloy Implants Enhances Their Osseointegration in the Rat Femur: A SEM study

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Biological fixation of uncemented endosseous implants requires the apposition of bone onto implant's surface in a process named osseointegration [1]. Osseointegration progresses slowly, and requires long periods of unloading. We have previously reported that growth hormone (GH) enhances Ti alloy implant osseointegration in adult rats [2]. GH is known to exert both direct effects on bone, as well as indirect effects, by stimulating hepatic and local production of IGF-1 [3]. IGF-1 is expensive and unsafe for systemic administration. The aim of the present research was to study the direct effects of IGF-1 on titanium alloy implants fixation, by implanting implants preloaded with IGF-1.

Ti-6Al-4V pins were were presoaked for 24 hrs in 0.1 mg/ml of human recombinant IGF-1 solution and then implanted in the distal femurs of 6-month-old Wistar female rats. IGF-1 adsorption to the implants was verified by ELISA. Animals were euthanized after 10 days. To evaluate mineralization, animals received 30 mg/kg body weight of oxytetracycline, 72 hrs before sacrifice. Undecalcified sections of the femurs with implants were examined by scanning electron microscope (SEM). Morphometric analyses were performed with an aid of ImagePro software, as described previously [4]. SEM revealed that the implants underwent fixation in bone within the distal epiphyses; in the diaphyses only bone marrow was found around the control implantsin the medullary cavity, while the JGF-1 loaded pins were surrounded by trabecular bone (Fig. 1A-D). Two parameters of osseointegration: bone volume (BV) and bone-implant contact (BIC) were measured on SEM images of cross-sections from femoral epiphyses and diaphyses. Bone volume was measured within a distance of 0.3 mm from implants' surface. The morphometric results indicate that both the BV and BIC were significantly increased in increased around the IGF-1 pins in comparison to the controls (Table 1). Also, tetracycline fluorescence revealed an increase in mineralization around JGF-1 loaded pins in comparison to control pins.

In conclusion, our findings revealed that adsorption of IGF-1 directly onto the implant's surface improves implant fixation without unnecessary systemic effects of IGF-1.

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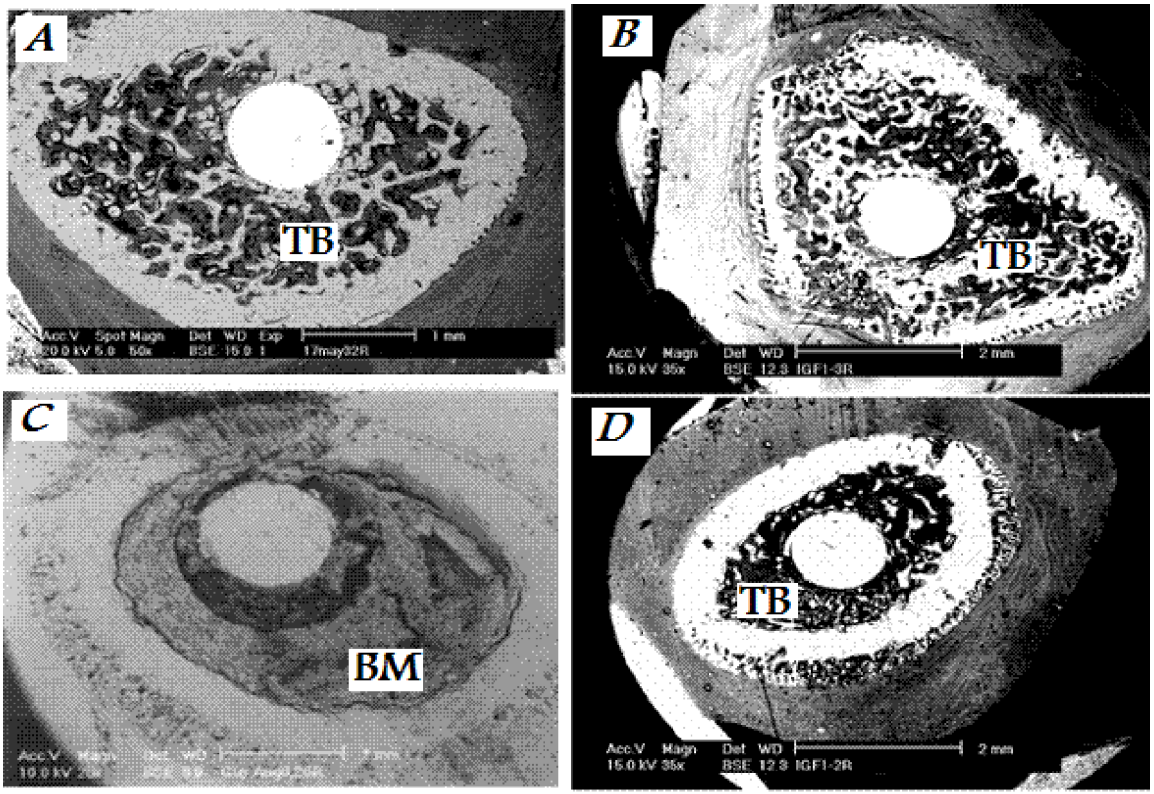

Fig. 1. SEM images of transverse sections of rat femurs, 10 days after implantation. A,epiphysis-control implant; B, epiphysis - IGF-1 implant; C, diaphysis-control implant; D, diaphysis - IGF-1 implant. BM, bone marrow; TB, trabecular bone. Note that no TB is seen in the medullary cavity of the femur with control implant (C).

Table 1. Effect of GH bone volume and bone-implant contact in the rat femur.

Site	Implant	Bone volume (%)	p<	Bone-implant contact (%)	p<
Epiphysis	Control	47.4 ± 4.3	-	72.5 ±7.9	-
	IGF-1	48.8 ±8.6	NS	65.8 ±7.2	NS
Diaphysis	Control	0	-	4.3 ±1.1	-
	IGF-1	24.8 ±7.6	0.01	37.1 ±14	0.01

BV and BIC were measured on SEM images with ImagePro. p-significance in comparison to control by ANOVA; NS-nonsignificant.

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