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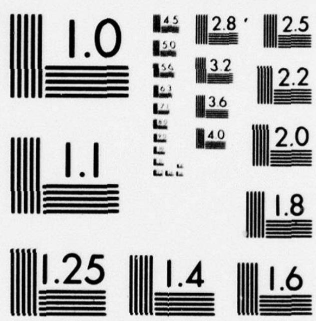

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Report Number 3 A041963

RESPONSE OF COMBINED ELECTRICAL STIMULATION AND BIODEGRADABLE CERAMICS

Third Annual Report

J. E. Lemons, Principal Investigator

March, 1978

Supported by
U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701

Contract Number DAMD17-75-C-5044

University of Alabama in Birmingham
Birmingham, Alabama 35294

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ABSTRACT

Investigations on the surgical correction of nonunion lesions in rabbit tibias with rod form porous tricalcium phosphate ceramics extended from one to nineteen months. Combinations of porous implant and iliac crest autogeneous bone grafts were included. Granular form tricalcium phosphate and autogeneous bone combinations were studied for segmental replacements in rabbit tibias while rod form segmental implants were placed in dog radii. Radiographic, general clinical, necropsy, histologic and metabolic methods were used to evaluate the experimental animals. Rod forms of porous tricalcium phosphate ceramic implanted at nonunion sites in rabbit tibias showed a low probability for correction in that only two of twenty obtained a bony union. A combination of rod forms and iliac crest autogeneous bone showed clinical union for ten out of twelve nonunions. Mixtures of granular tricalcium phosphate ceramic and autogeneous bone for segmental bone lesion correction in the rabbit tibia showed a dependence on the relative quantity of materials in the implant mixture. Segmental bone replacements at the mid shaft positions of dog radii showed that internal fixation could be utilized and the site provides opportunities for long-term studies. Gross and histological evaluations of implant sites and major organs in rabbits showed good biocompatibility for tricalcium phosphate ceramic implants. Investigations are continuing.

Report Number 3

RESPONSE OF COMBINED ELECTRICAL STIMULATION AND BIODEGRADABLE CERAMICS

Third Annual Report

J. E. Lemons, Principal Investigator

March, 1978

Supported by
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SUMMARY

This report summarizes the third year studies on one form of a porous tricalcium phosphate ceramic biomaterial. Methods include nonunion investigations utilizing the synthetic biomaterial alone and combinations of the synthetic biomaterial and autogeneous bone, segmental lesion replacements with granular tricalcium phosphate and autogeneous bone in rabbits, and rod forms for segmental replacements in dogs.

Nonunion connection with rod forms of tricalcium phosphate ceramic showed poor success while the combination with autogeneous bone showed good success. Segmental replacements in rabbit tibias with mixtures of granular tricalcium phosphate and autogeneous bone showed a strong dependence upon the relative quantities within the implant mass. Segmental replacements with rod form porous tricalcium phosphate ceramic shows this to be a good model for long term studies of this synthetic material. Investigations are continuing.

FOREWORD

In conducting the research described in this report, the investigator adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences - National Research Council.

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INTRODUCTION

Synthetic substances for the replacement of autogeneous bone graft in surgery have been proposed and investigated since the earliest bone surgical procedures. Certainly, treatment modalities for maxillofacial and orthopaedic surgery have significantly changed; however, no completely acceptable synthetic material has been developed. This is especially true with respect to the treatment of segmental defects and nonunions. In general, long-term rehabilitative courses are required for such defects. It is the objective of this research, to more fully investigate a quite promising candidate synthetic bone substitute material, porous tricalcium phosphate ceramic, in order to improve conditions for surgical corrections of lesions in bone. A result of this research could be a reduction in time of treatment for maxillofacial and orthopaedic procedures, a reduction in deformities, and a reduction in morbidity.

The technical objectives of this project are as follows:

1. To optimize the surgical methods to induce bone formation in association with porous tricalcium phosphate implants at nonunion sites in rabbits, and

2. To evaluate long-term tissue responses to porous tricalcium phosphate segmental replacements in dogs.

This report summarizes: (1) continuation studies on nonunion lesions in rabbits from the second year program[1]; (2) rabbit tibia nonunions developed and corrected during the third year; (3) initial investigations of tricalcium phosphate powders and autogeneous bone combinations in rabbits; and (4) initial investigations of tricalcium phosphate segmental replacements in dogs. A significant number of these studies are in-progress and will be reported at a later date.

Background

Research studies on the porous tricalcium phosphate ceramics similar to those under investigation and other porous bone substitute materials were summarized previously[1]. More recently, abstracts in the Journal of Dental Research and papers presented before the Orthopaedic Research Society and the Society for Biomaterials have confirmed the earlier studies. Studies are currently in-progress in a number of laboratories. The results of the two years of investigations in our laboratory are summarized below.

Biomaterial analyses of the porous tricalcium phosphate ceramics showed the following. Comparisons of structure by X-ray diffraction produced differences in relative peak intensities at selected 2θ angles but relatively consistant patterns sample to sample. The interconnected porosity had an average cross section exceeding 100 micrometers in diameter. The material could be fabricated to produce implant designs with no difficulties encountered in sterilizing or handling the material.

The New Zealand White rabbit animal model provides an adequate model for initial studies on porous tricalcium phosphate ceramic for evaluation of tissue ingrowth, the role of direct current electrical stimulation, biodegradation, tissue reaction, and nonunion replacements. The ability to remove the stabilization devices at 6 weeks for most of the rabbits is the earliest time experienced in this research. Most "inert" porous implants required 12-16 weeks. Immediate post operative care was uneventful; however, some transcutaneous pin track infections were encountered after 3-6 weeks. These problems were severe for some of the long-term nonunion animals. After removal of transcutaneous devices, the remainder of the animal care was routine.

This porous tricalcium phosphate ceramic, in this animal model, can serve as a scaffold with bone proliferation through the large interconnecting pores. Transverse sections showed relatively complete ingrowth of bone at 12 weeks. Radiographs and gross observation at necropsy showed considerable variability in the rate of tricalcium phosphate implant biodegradation. Some animals retained most of the implant after 64 weeks of implantation while others showed almost complete biodegradation. The implants showed hard and/or soft conditions by sharp probe examination. In general, the radiographic appearance of the rabbit tibias showed a steady progression toward normal anatomy after 6-12 weeks. The direct current electrical stimulation resulted in more periosteal callus, and did not appear to greatly influence the tissue ingrowth and biodegradation rates for the porous tricalcium phosphate ceramic implants.

Biomechanical strength comparisons from four point bending and determinations of the Work to Fracture of the lesion sites for implant and control conditions - at 3, 6, 12, and 64 weeks - showed similar ranges for the strength magnitudes at each time period. The average magnitudes of the Work to Fracture data increased with increasing time post surgery but showed a wide range within each group.

Gross observation of implant sites at necropsy showed minimal tissue reaction while histological evaluations showed similar tissue characteristics for experimental and control conditions. Comparisons of porous tricalcium phosphate implants and implants plus direct current electrical stimulation at nonunions showed quite variable conditions and a very low probability for reestablishment of bony union after porous tricalcium phosphate ceramic implantation.

METHODS

Materials

The porous tricalcium phosphate ceramic* biomaterials utilized for this phase of the program was the material remaining from the first and second year studies. Although additional materials were requested for the segmental replacement investigations, no materials were received. This supply limitation has slightly altered the project activities. To offset the materials limitation, other phases of the program were emphasized. The requested materials should be available in the near future.

Implant Fabrication

Where adequate material was available, segmental bone replacements approximately 1 cm long and 1 cm in diameter were cut to reproduce the anatomical cross section of the mid-shaft portion of the dog radius. A cross section view of the dog radius segment along with the rabbit nonunion replacement (longitudinal view) and size fractioned powder (-40 + 100 mesh) samples are shown in Figure 1. The samples are shown after dry heat sterilization in pyrex glass tubes. Each sample was weighed to the nearest milligram prior to implantation.

* Porous tricalcium phosphate from Battelle Memorial Institute, L. McCoy.

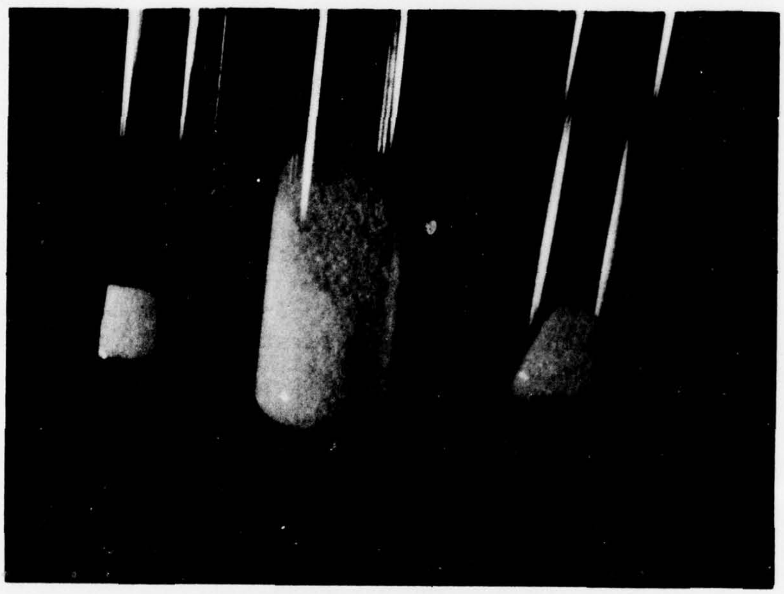


Figure 1. Porous tricalcium phosphate ceramic implant forms.
Left: Rabbit nonunion implant, longitudinal view
Center: Powder
Right: Dog segmental implant, cross section view

Animal Models and Surgery

The animal model for the nonunion phase of the investigation was the New Zealand White rabbit. The as-received animals were 4-6 months of age. The animals were anethesized using sodium pentobarbital via the ear veins and the animal prepared for sterile surgical technique. The surgical site was the tibio-fibular junction of the left rear limb. This site was centralized with four threaded Steinmann pins with the two central pins providing sites for electrical stimulation if required. The outermost pins were driven completely through the bone while the central pins were driven from one side only engaging both cortices. The central pins were insulated to the bone surface and the four pins were held together with acrylic splints placed externally to the animal. The surgical defect was just distal to the tibio-fibular junction, the defect was equal distances from each central pin, the defect was sized to 12 millimeters and the periosteum at the surgical site was removed by sharp dissection. Subcutaneous closure of the tissues for the nonunion group was accomplished using 4-0 Dexon. The segmental lesion in the rabbit tibia and the placement of the stabilization pins are shown schematically in Figure 2.

If the surgical site developed into a nonunion, a second surgical procedure was conducted to place a porous tricalcium phosphate into the nonunion site. The ends of the bone were resected to produce a correctly sized implant site. In some cases, where a nonunion was not formed and a bridge of bone connected the distal and proximal bone segments, chips or powders of the tricalcium phosphate were surgically implanted.

If the nonunion site with a tricalcium phosphate implant did not heal and the stabilization pins could not be removed, autogeneous bone transplants were conducted. The autogeneous bone graft was taken from the iliac crest of the pelvis following normal orthopaedic surgical procedures. In one series the tricalcium phosphate implant was retained with the autogeneous bone placed along the implant surface. In another series, the implant was replaced with a new tricalcium phosphate sample with autogeneous graft material. In the third series, a first nonunion correction with the implant and the autogeneous graft was conducted.

Initial surgeries were conducted to evaluate a combination of tricalcium phosphate powder and autogeneous bone. The 8 mm length segmental lesion in the rabbit tibia was selected, the periosteum was retained. The ratios of powder to autogeneous graft were 100% powder, 50% powder - 50% autogeneous bone and 100% autogeneous bone. The implant sample sizes were controlled by weight and the amount was selected for complete filling of the surgical lesion. These animals were evaluated radiographically, by gross observation and dissection, histologically, and by in-progress metabolic studies on the blood and urine. These initial studies were limited to six weeks duration.

Segmental implants were placed at the mid-shaft position of dog radii using a six hole stainless steel bone plate for bone fixation. The plate was positioned prior to surgical removal of the bone, to maintain proper anatomical alignment of the radius. The periosteum was not removed and the plate was removed after adequate healing. The dogs were evaluated radiographically and by general observation. A schematic drawing of the segmental bone replacement and the fixation plate position is shown in Figure 3.

Animal Follow-up

The surgical procedures and post operative recovery period was relatively uneventful. The anesthesia was sufficient to provide adequate surgical time and the animals

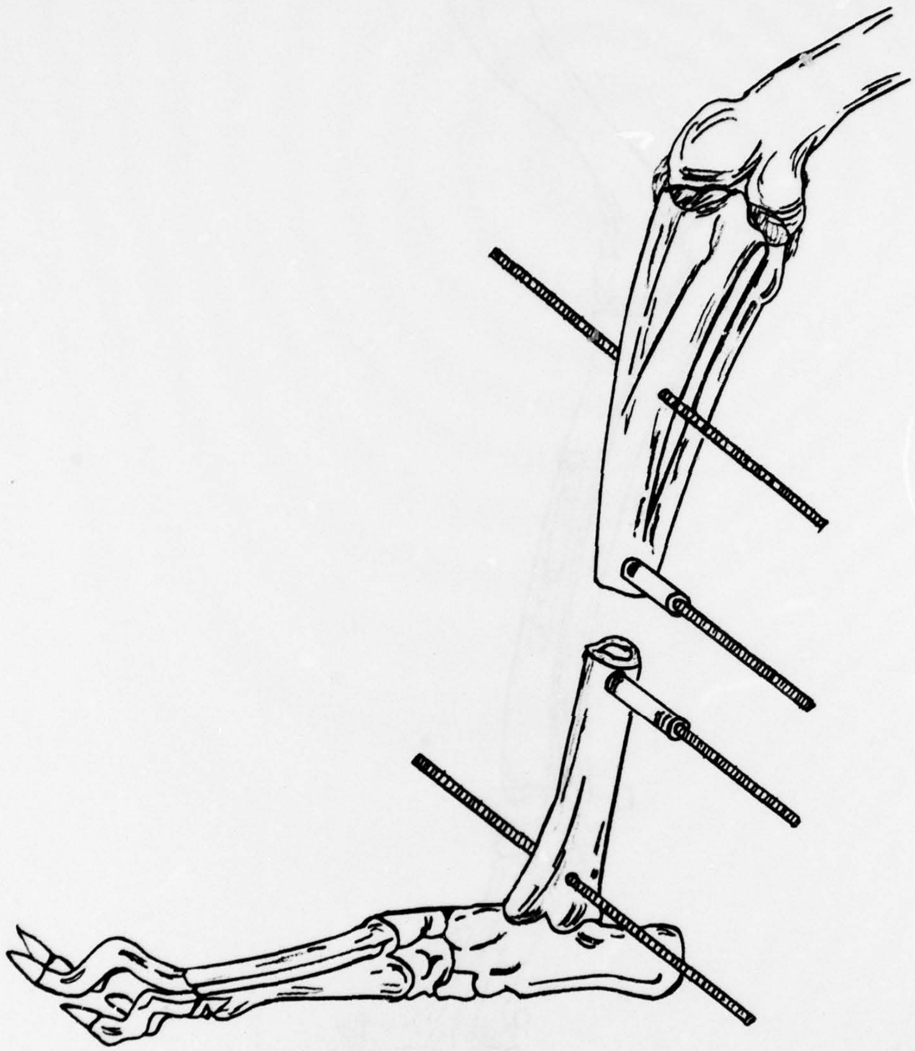


Figure 2. Schematic drawing of segmental lesion in a rabbit tibia showing the relative placement positions of the stabilization pins.

Figure 3. Schematic drawing of the segmental bone replacement and bone stabilization plate for the dog studies.

moved around within their cages shortly after completion of the surgery. The rabbits were followed on a daily basis by the Biomaterials Laboratory and the Department of Comparative Medicine personnel. All animal procedures were approved by and checked through the Department of Comparative Medicine with the staff veterinarians. Weekly radiographs were made on all animals for times up to 6 weeks post surgery. Some series were then discontinued for 3-4 weeks intervals, if the stabilization systems were removed or if the animals were in the nonunion study group. Anterior-posterior (AP) and oblique radiographs provided the best method for routine animal evaluation.

The rabbits receiving powder implants of tricalcium phosphate were evaluated by collecting blood and urine samples. Blood samples were taken through a 22 gage needle from an ear artery, collecting 2 milliliters of blood for each laboratory evaluation. Prior to blood collection, the animals were maintained in teflon treated metabolic cages for the 24 hour urine sample collection, During this period the animals were only allowed water.

Necropsy and Histology

The animals were euthanized by drug overdose after gross observation. The tibia and other tissues of interest were removed by sharp dissection and histological specimens taken. Examples of tibias and associated tissues were photographed using 35 mm color slide film. The contralateral tibia was removed if the specimen showed apparent bone like (rigid) biomechanical strength. Each removed tibia was photographed using a Polaroid MP-4 camera system and 55 P/N film for record purposes.

Specimens were fixed in 10% neutral buffered formalin with the bone samples submitted to decalcified preparation with Hematoxylin and Eosin staining or to non-decalcified thin sectioning for general and tetracycline fluorescence evaluations. The soft tissues were submitted for routine histological evaluation.

Three of the long term tricalcium phosphate implant rabbits were submitted to major organ evaluations conducted by our staff veterinarian - pathologist. The organs were removed, microscopically examined, fixed and gross sectioned at the time of necropsy. The specimens were then submitted to microscopic evaluation. The organs evaluated included the lungs, kidneys, spleen and liver.

RESULTS AND DISCUSSION

Materials

The porous tricalcium phosphate materials were fabricated and reduced to powder samples without difficulty. The powder samples were fractioned to a -40 +100 mesh size. Since the materials were previously studied for chemical reproducibility and microstructure, no additional material studies were conducted.

Surgery and Follow-up - Rabbit Nonunions

The third year nonunion correction studies using the New Zealand White rabbit emphasized the use of autogeneous bone graft in association with the porous tricalcium phosphate implants. Since a number of these studies were a continuation of the second year program, the rabbit surgery data are summarized in Table 1. A total of

TABLE 1. DATA SUMMARY ON TRICALCIUM PHOSPHATE RABBIT IMPLANTS

RABBIT #	INITIAL SURGERY DATE	DURATION OF EXPERIMENT	OTHER COMMENTS
205	01/16/76	04 months	05/20/76 - Sacrifice
206	01/16/76	02 months	03/05/76 - Sacrifice, displaced
207	01/21/76	01 month	02/05/76 - Sacrifice, displaced
208	01/23/76	19 months	07/30/76 - 0.726g implant
			03/24/77 - Pins removed
			07/06/77 - Died
209	01/23/76	19 months	07/30/76 - 0.878g implant
			04/22/77 - Added iliac bone
			07/05/77 - Pins removed
			09/19/77 - Sacrifice
211	02/13/76	10 months	04/16/76 - Removed callus
			07/09/76 - 0.308g implant
			12/14/76 - Sacrifice, fractured tibia
212	02/13/76	in progress	07/30/76 - 0.826g implant
			01/28/77 - Old implant removed, 0.360g plus iliac bone
			04/21/77 - Pins removed
213	02/27/76	03 months	04/16/76 - Procedure to clean infection
			05/14/76 - Sacrifice, infection
214	02/27/76	03 months	05/14/76 - Sacrifice, infection
215	03/03/76	16 months	07/30/76 - 0.738g implant
			02/14/77 - Old implant removed, 0.398g plus iliac bone
			04/21/77 - Pins removed
			07/20/77 - Sacrifice
216	03/05/76	09 months	04/16/76 - Procedure to remove callus
			07/30/76 - 0.743g implant
			10/27/76 - Pins removed
			12/20/76 - Sacrifice, severe infection
217	04/21/76	07 months	07/16/76 - 0.518g implant
			11/16/76 - Sacrifice, sick
218	04/21/76	09 months	01/12/77 - Sacrifice, infection
219	04/23/76	09 months	06/25/76 - 0.500g of 7 pieces
			01/05/77 - Sacrifice
220	04/23/76	07 months	06/25/76 - 0.500g of 4 pieces
			11/03/76 - Pins removed
			11/19/76 - Sacrifice
221	04/28/76	08 months	Bone broken during surgery
			09/09/76 - 2 pieces
			12/04/76 - Died, infection
222	04/28/76	01 month	Bone broken during surgery
			05/14/76 - Sacrifice, displaced
223	04/30/76	07 months	Bone broken during surgery
			06/25/76 - 0.500g of 2 pieces
			11/29/76 - Sacrifice, inner ear infection

TABLE 1. DATA SUMMARY ON TRICALCIUM PHOSPHATE RABBIT IMPLANTS continued

RABBIT #	INITIAL SURGERY DATE	DURATION OF EXPERIMENT	OTHER COMMENTS
224	04/30/76	08 months	Bone broken during surgery
			09/09/76 - 2 pieces
			01/05/77 - Sacrifice, infection
225	05/11/76	16 months	10/15/76 - 0.531g implant
			03/25/77 - Iliac bone added
			07/05/77 - Pins removed
			09/19/77 - Sacrifice
226	05/12/76	16 months	10/15/76 - 0.657g implant
			02/18/77 - Old implant removed, 0.389g plus iliac bone
			07/05/77 - Pins removed
			09/19/77 - Sacrifice
227	05/12/76	14 months	10/29/76 - 0.758g implant
			03/04/77 - Iliac bone added
			07/05/77 - Pins removed
			07/20/77 - Sacrifice, not biomechanically stable
228	05/26/76	16 months	08/27/76 - 0.429g implant
			01/14/77 - Old implant removed, 0.368g plus iliac bone
			04/21/77 - Pins removed
			09/19/77 - Sacrifice
229	05/26/76	03 months	08/04/76 - 2 pieces
			08/23/76 - Sacrifice, infection
230	05/28/76	07 months	10/22/77 - Several small pieces
			01/05/77 - Sacrifice
231	06/02/76	01 month	07/02/76 - Died
232	06/11/76	07 months	10/22/76 - Several small pieces
			01/05/77 - Sacrifice
233	06/17/76	15 months	08/27/76 - 0.475g implant
			01/07/77 - Old implant removed, 0.396 plus iliac bone
			03/17/77 - Pins removed
			09/19/77 - Sacrifice
234	06/18/76	05 months	11/03/76 - Sacrifice, infection
235	06/18/76	07 months	10/22/76 - 0.694g implant
			01/21/77 - Died, infection, displaced
236	06/18/76	07 months	10/22/76 - 0.599g implant
			01/05/77 - Sacrifice, infection, displaced
237	06/22/76	15 months	09/09/76 - 0.453g implant
			02/25/77 - Old implant removed, 0.378g plus iliac bone
			09/19/77 - Sacrifice
238	06/22/76	06 months	11/19/76 - 0.437g implant
			12/05/76 - Died

TABLE 1. DATA SUMMARY ON TRICALCIUM PHOSPHATE RABBIT IMPLANTS continued

RABBIT #	INITIAL SURGERY DATE	DURATION OF EXPERIMENT	OTHER COMMENTS
48B	06/03/77	1.5 months	7.5mm lesion, periosteum left, total iliac bone 07/20/77 - Sacrifice
38B	06/03/77	1.5 months	7.5mm lesion, periosteum left, total tricalcium phosphate 07/20/77 - Sacrifice
49B	06/20/77	1.5 months	7.5mm lesion, periosteum left, 50-50 mixture, powder - iliac bone
591	08/12/77	in progress	10/14/77 - Removed callus 12/09/77 - implant 03/11/78 - Pins removed
577	08/26/77	07 months	11/17/77 - 0.454g implant plus iliac bone 03/01/78 - Sacrifice
239	09/02/77	06 months	10/28/77 - 0.364 implant 03/01/78 - Sacrifice
240	09/09/77	05 months	12/02/77 - 0.412g implant plus iliac bone 02/08/78 - Sacrifice, animal sick
241	09/16/77	03 months	Bone broken during surgery 11/11/77 - Removed callus 11/17/77 - Sacrifice, infection
588	09/23/77	01 month	10/24/77 - Sacrifice, broken tibia

39 rabbits were included in the nonunion studies with the times extending from one to nineteen months. Two rabbits are currently in-progress in the long-term nonunion studies. Three rabbits included in the initial studies of powdered tricalcium phosphate and autogeneous bone mixtures are also included.

Examples of serial radiographs for two of the nonunion rabbits are shown in Figures 4 and 5. The upper radiograph in Figure 4 shows the rabbit tibia containing a tricalcium phosphate implant at five months after placement within a nonunion lesion. The tibia has bridged the gap along the posterior, but the bone is inadequate for stabilization pin removal. The proximal pin has fractured and the animal was not progressing toward additional callus formation associated with the lesion site. The second radiograph shows the surgical correction with new stabilization pins where required, a new implant and autogeneous bone. At 2.5 months after surgery, radiograph 3, the lesion has progressed and the stabilization pins were removed. The final radiograph shows the tibia at 8 months after placement of the new implant and the autogeneous bone. The animal was euthanized at this stage for further evaluation.

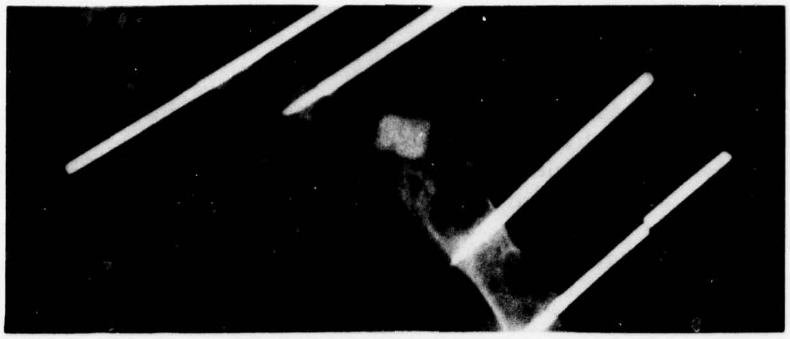
A similar series is shown in Figure 5. In general, many of the nonunion rabbits showed conditons quite similar to the situation shown in the upper radiograph. At 5 months after placement of the implant in a nonunion lesion, the site continued as a nonunion. Autogeneous bone additions greatly aided the process of new bone formation. The final radiograph in Figure 5 shows the animal at the time of necropsy, which is 7 months post autogeneous bone implantation. The animal experienced a breakdown of the skin along the foot and subsequent infection. This problem was often encountered with the caged rabbits.

In summary for the nonunion rabbit investigations where surgical corrections were attempted using rod form replacements of porous tricalcium phosphate, the following conditions were found. Two of the original twenty implants healed where the stabilization pins could be removed. Considering the remaining eighteen animals; six animals were lost prior to corrective surgery, eight out of ten treated with a new implant and autogeneous bone healed so that the stabilization pins could be removed; while one out of the two animals receiving autogeneous bone graft over the existing tricalcium phosphate implant showed healing to the point of removing the stabilization pins. Thus, with the addition of autogeneous bone in association with the porous tricalcium phosphate implants, resulted in surgical correction for a significant number of the nonunion rabbits.

Rabbit Granular Implant Studies

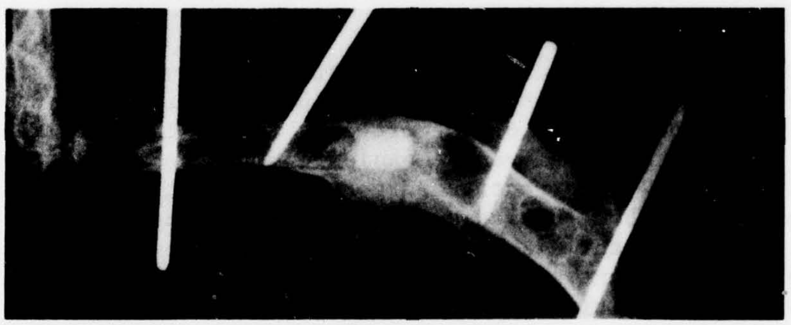
Initial investigations on powder or granular form tricalcium phosphate ceramic with and without autogeneous bone were initiated. Radiographs for the post surgery and six week conditions for the total autogeneous bone implant, 50% autogeneous and 50% granular and total granular implant are shown in Figures 6, 7 and 8 respectively. The fully autogeneous bone implant and the mixture showed clinical union at six weeks while the 100% tricalcium phosphate powder implant site shows incomplete healing at six weeks.

The autogeneous bone samples and granular tricalcium phosphate sample sizes were controlled by weight. An equal weight of each was used for the iliac crest bone and granular material for the 50 - 50 implant or a total combined weight for either of the pure materials. Since the tricalcium phosphate was dry and the bone



5 Months Post Implant

Correction: New Implant + Autogenous Bone

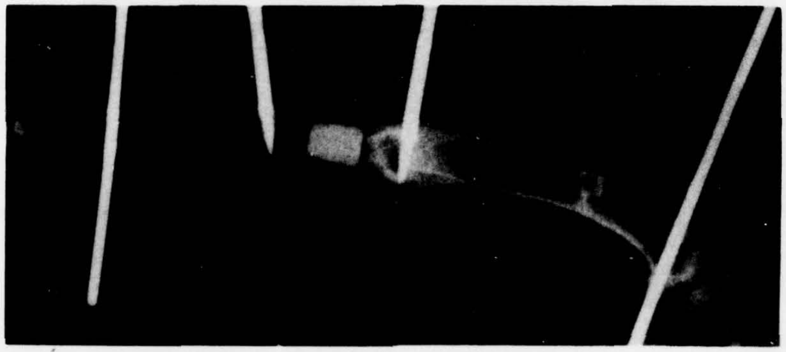


10 Weeks Post Implant

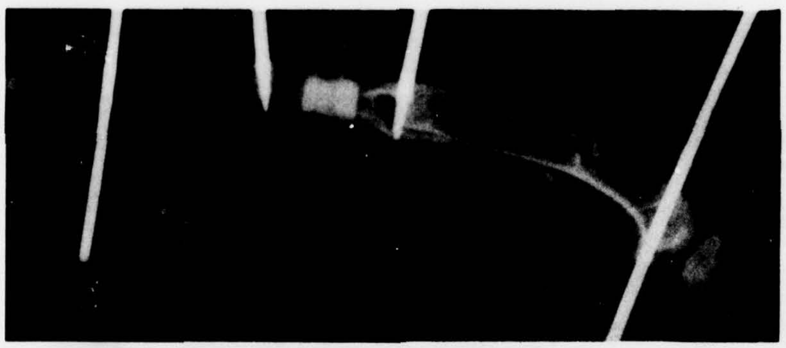
8 Months Post Implant

Figure 4. Serial radiographs on nonunion rabbit.

5 Months Post Implant



Correction: New Implant + Autogenous Bone



8 Weeks Post Implant

7 Months Post Implant

Figure 5. Serial radiographs on nonunion rabbit.

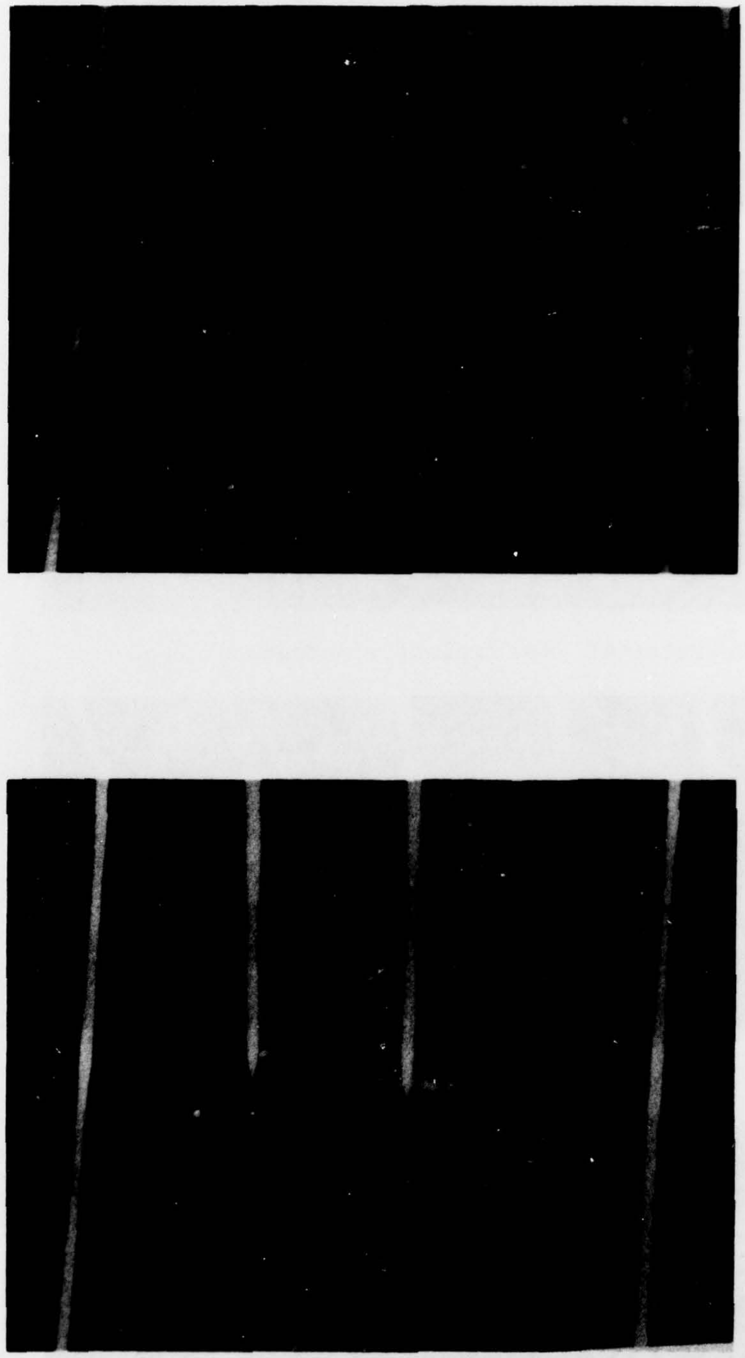


Figure 6. Radiographs for autogeneous bone graft in a rabbit tibia.

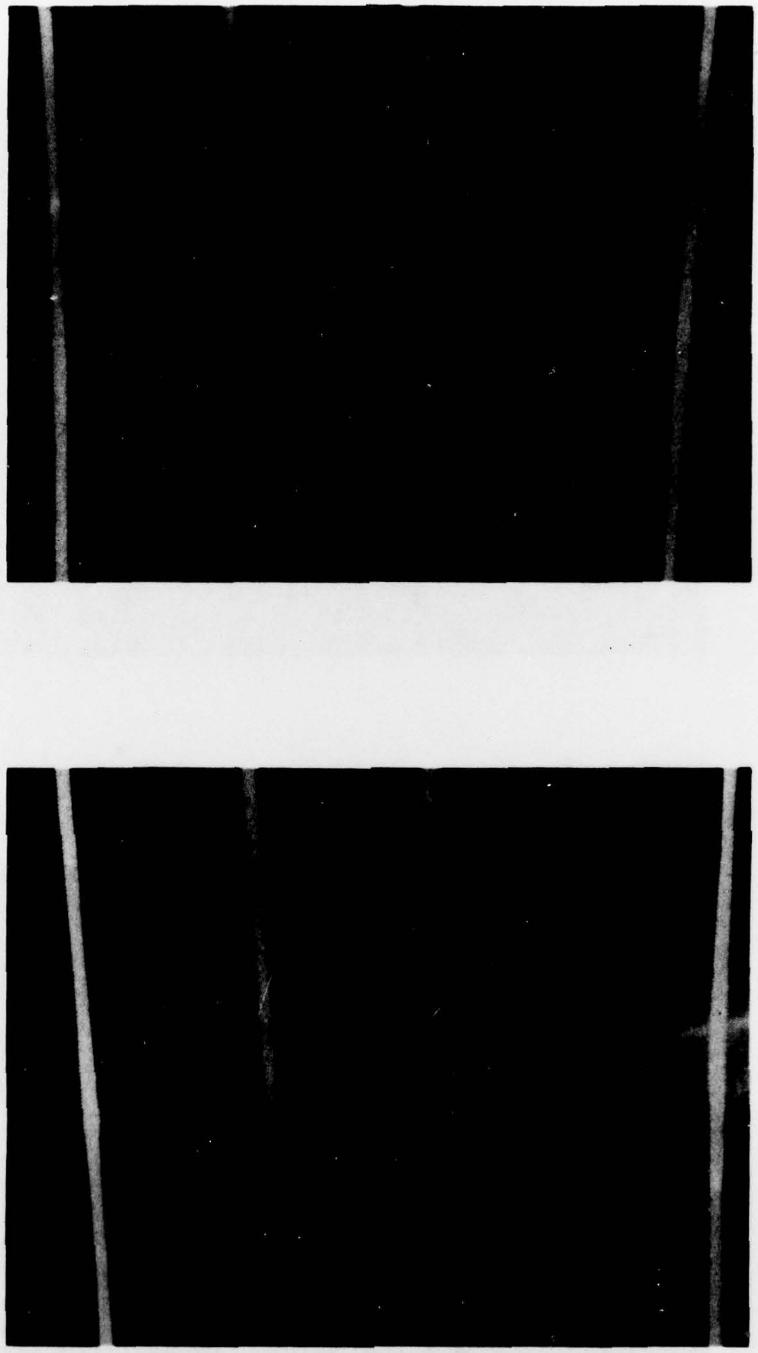


Figure 7. Radiographs for 50% autogeneous bone - 50% tricalcium phosphate powder implant in a rabbit tibia.

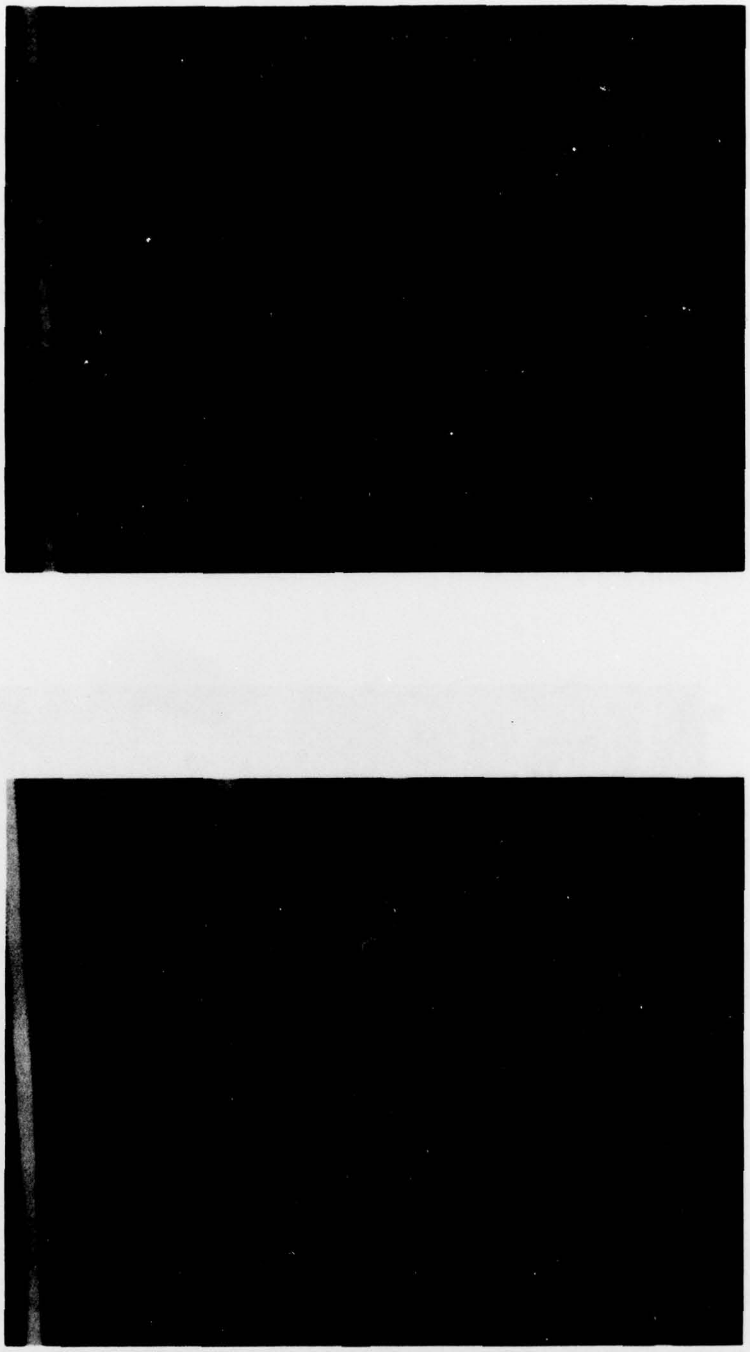


Figure 8. Radiographs for tricalcium phosphate ceramic powder implant in a rabbit tibia.

moist, laboratory experiments were conducted on samples of rabbit cancelleous bone and compact bone to determine ash (dry) weights. The cortical bone showed 68.2% inorganic while the spongy (iliac crest type) bone showed 32.6% inorganic substance.

These granular implant rabbits and a control were subjected to metabolic studies for calcium (Ca) and phosphorus (P) in the blood and urine. These data are summarized in Table 2 and shown graphically in Figures 9 through 12. A general evaluation of these data; discussions with individuals conducting this type of research and an overall assessment of our ability to develop statistically significant data, caused us to abandon the metabolic studies on rabbits.

Segmental Implants in Dogs

Methods were developed for placing segmental tricalcium phosphate implants at the mid-shaft positions along the radii of dogs. The internal fixation procedures utilizing a six hole on-lay plate provided adequate fixation. Examples of radiographs showing the post surgical condition, the bone callus prior to plate removal and post fixation plate removal are included in Figures 13 and 14. One dog healed uneventfully while the other required autogeneous bone graft to obtain a bony union of the radius.

The radius of the dog was selected for initial implantation because of the two bone anatomical site. This site appears acceptable for implantation and these studies are continuing.

Necropsy and Histology

The microscopic evaluation of the various tricalcium phosphate implant sites showed minimal reactions and no unusual features. This was true for the rod and powder form implant sites. Histological samples show conditions similar to controls and no significant adverse reactions. The organ studies and multiple microscopic sections showed no unusual features.

Histologically, the tricalcium phosphate implant sites show good biocompatibility characteristics for this synthetic material.

CONCLUSIONS

The conclusions from the third year studies on porous tricalcium phosphate bone implants in rabbits and dogs are as follows:

1. Rod forms of porous tricalcium phosphate ceramic implanted at nonunion sites along rabbit tibias showed a low probability for correction in that two of twenty obtained a bony union.

2. A combination of rod form porous tricalcium phosphate and autogeneous bone showed clinical union for ten out of twelve procedures for animals that could not be corrected by the tricalcium phosphate implant alone.

TABLE 2. BLOOD SERUM AND URINE CONCENTRATIONS FOR RABBIT METABOLIC EXPERIMENTS

		SERUM (mg/100 ml.)		URINE IN 24 HOURS (mg.)	
ANIMAL	WEEK	CALCIUM	PHOSPHOROUS	CALCIUM	PHOSPHOPOUS
Control	1	12.50	7.62	321.30	43.47
	2	13.80	6.50	473.00	129.80
	3	14.10	6.80	20.40	47.22
	4	14.90	4.89	295.00	26.10
	5	15.00	3.81	209.50	73.40
Autogeneous Bone	1	13.40	6.24	271.20	60.630
	2	13.80	5.80	328.15	85.905
	3	13.00	5.80	120.70	64.345
	4	-	-	-	-
	5	13.10	4.47	543.25	8.785
	6	13.10	4.87	265.00	95.000
50/50	1	13.20	5.39	173.40	59.790
	2	13.10	5.95	174.30	62.615
	3	-	-	-	-
	4	13.30	5.21	236.00	102.600
	5	13.70	5.02	169.10	89.490
	6	12.50	4.39	221.85	96.390
Tricalcium Phosphate	1	13.10	4.74	170.45	67.550
	2	12.70	4.51	339.84	88.464
	3	12.60	4.47	212.96	80.212
	4	-	-	-	-
	5	13.10	4.49	212.85	60.200
	6	12.40	4.22	111.50	28.500

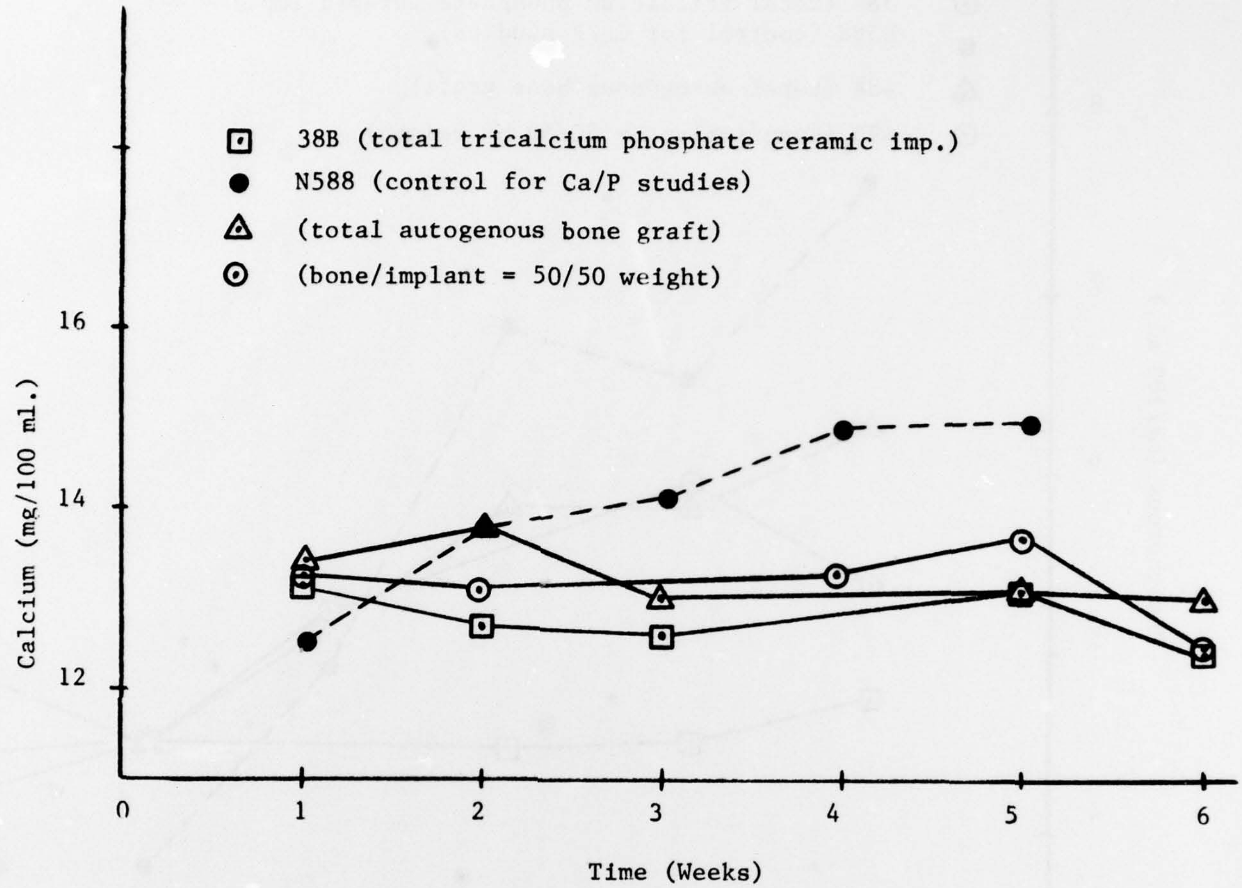


Figure 9. Calcium Level In Serum (mg/100 ml.) For Rabbit Tibia Implants.

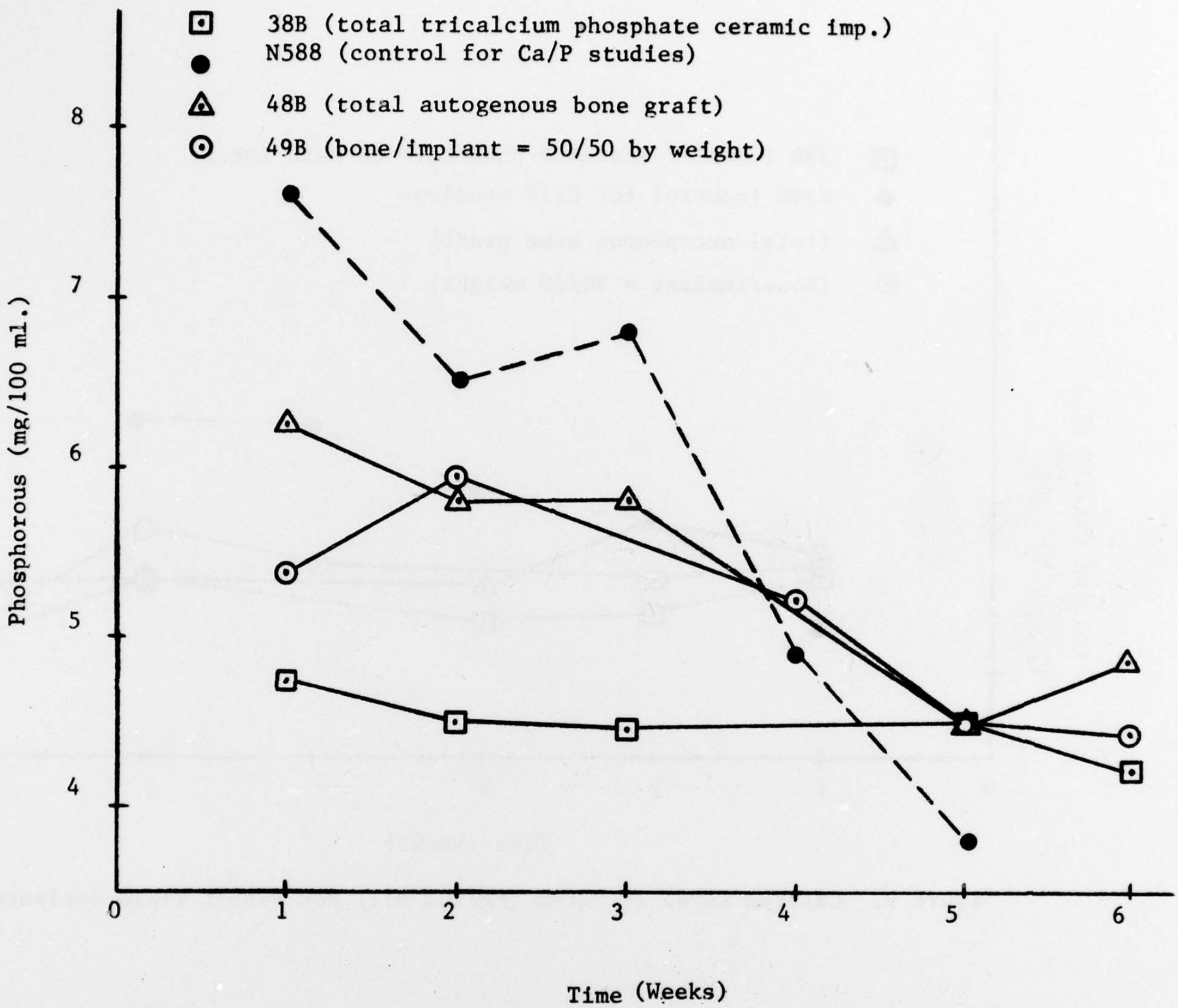


Figure 10. Phosphorous Level In Serum (mg/100 ml.) For Rabbit Tibia Implants.

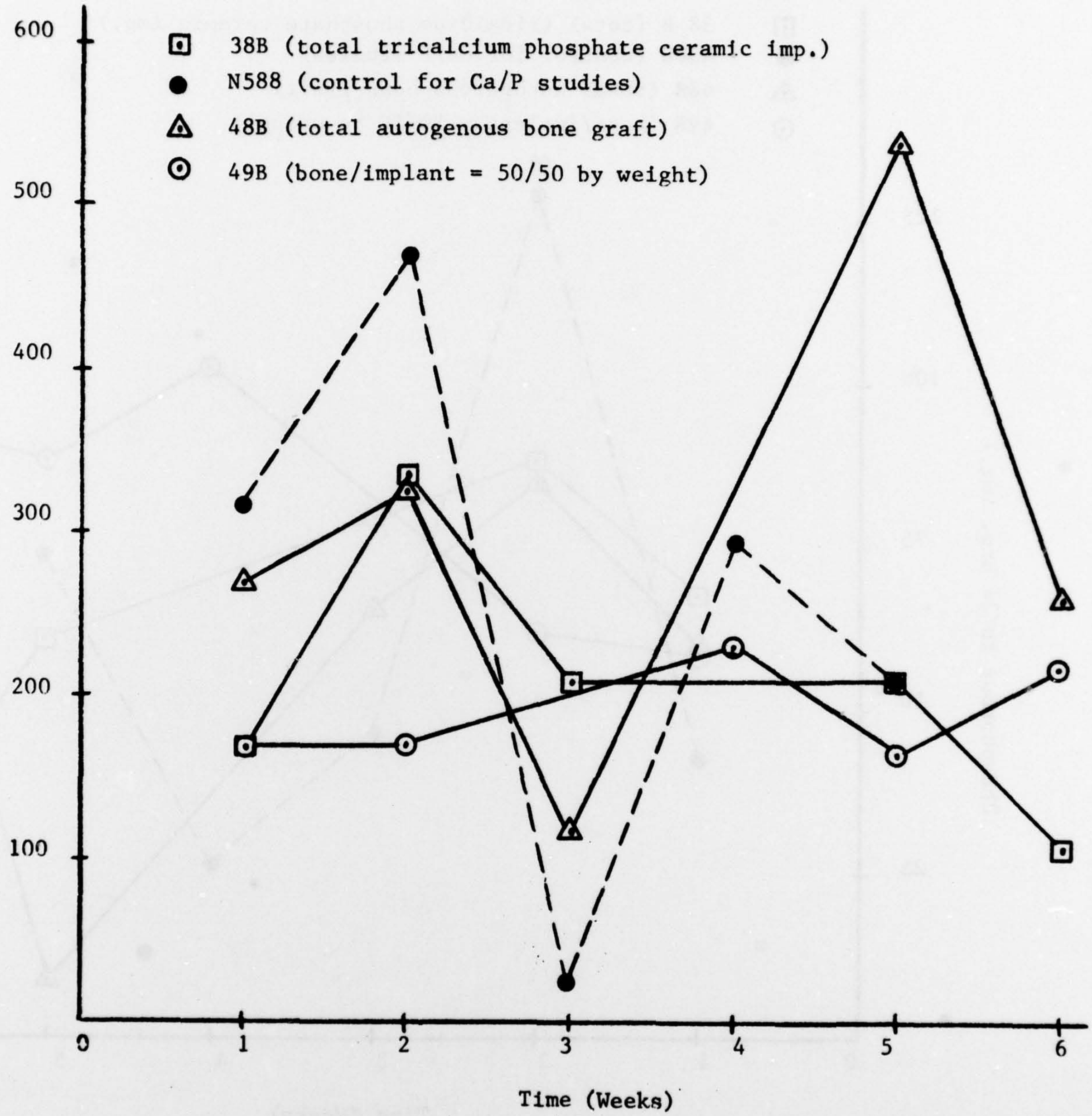


Figure 11. Total Calcium In Urine Output (24 hrs.) For Rabbit Tibia Implants.

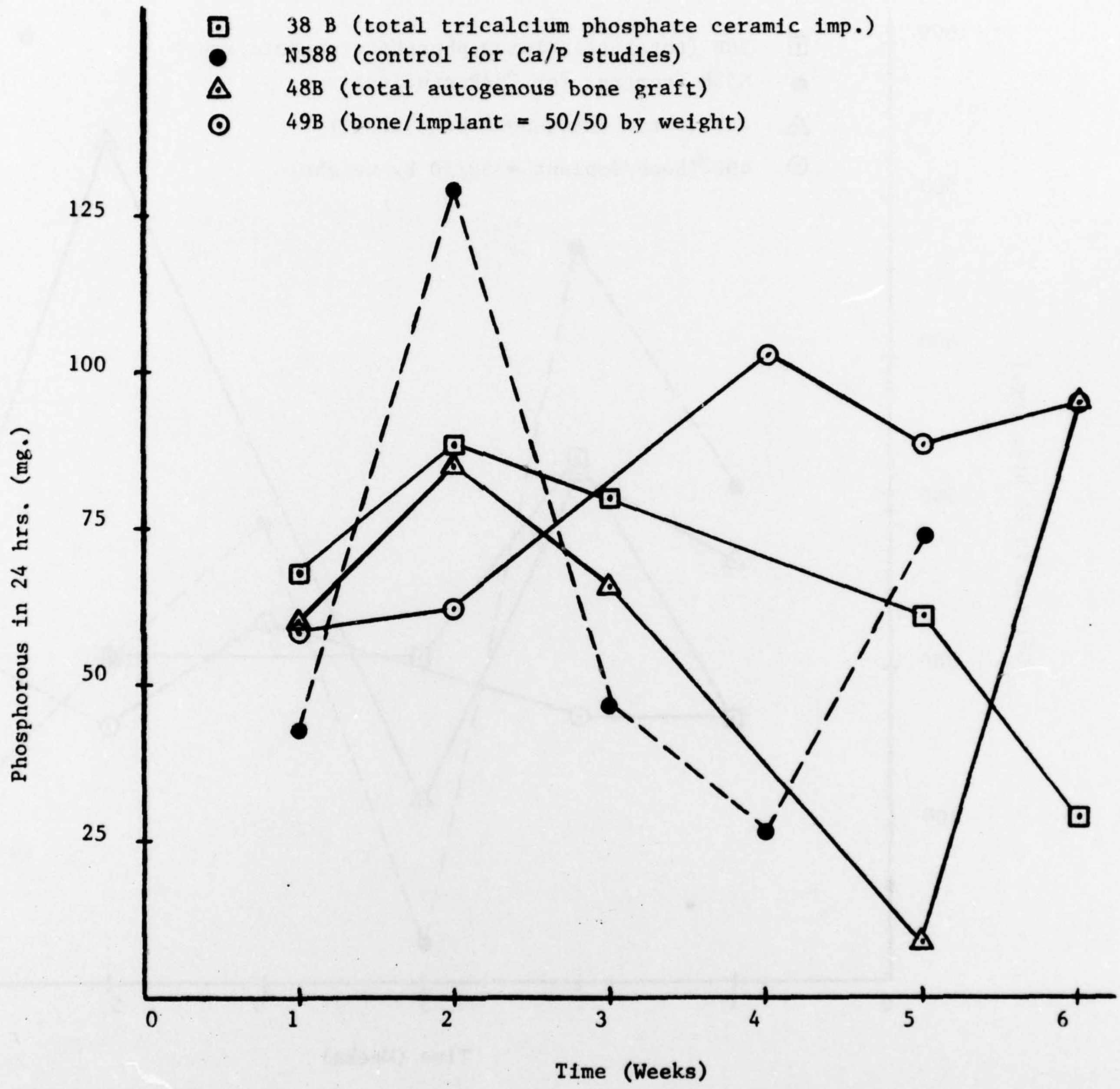


Figure 12. Total Phosphorous In Urine Output (24 hrs.) For Rabbit Tibia Implants.

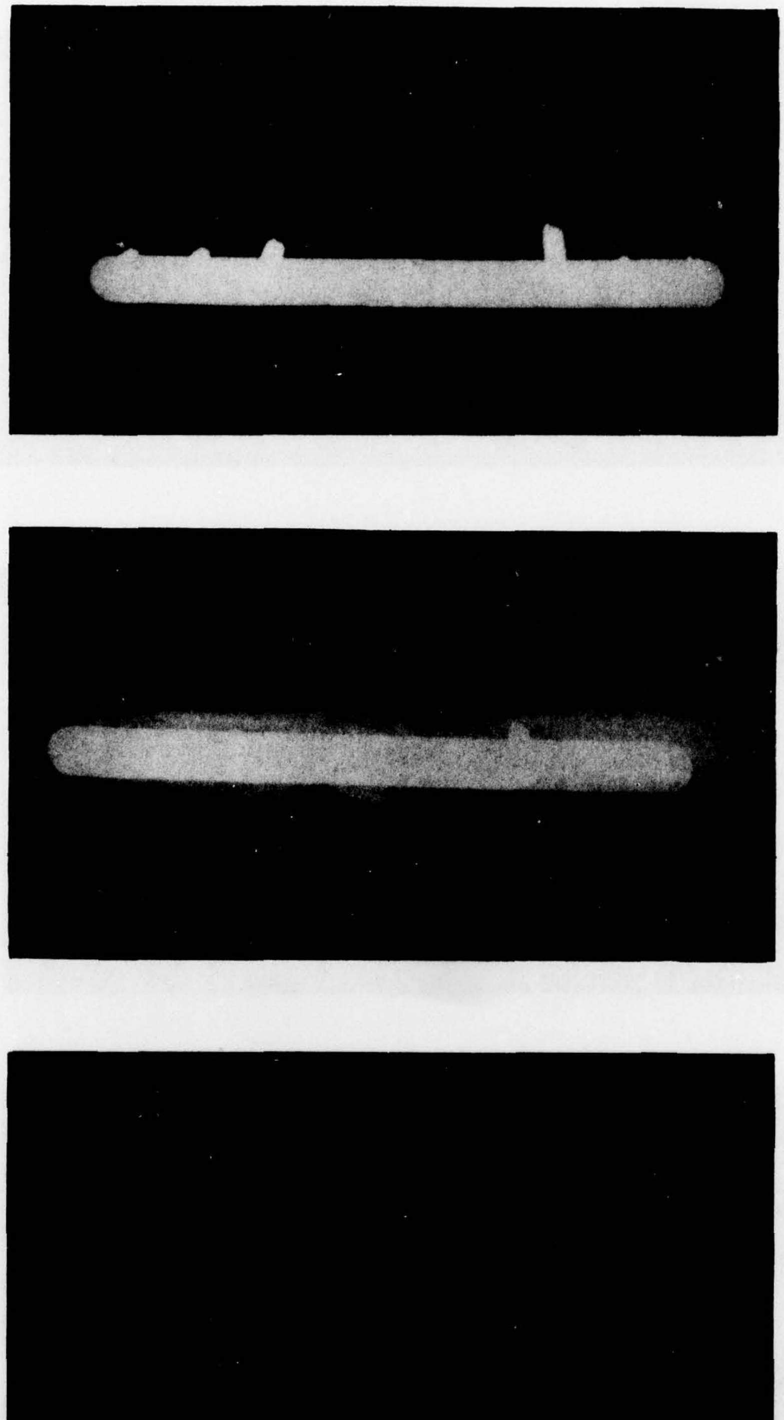


Figure 13. Radiographs showing a segmental replacement in a dog radius.

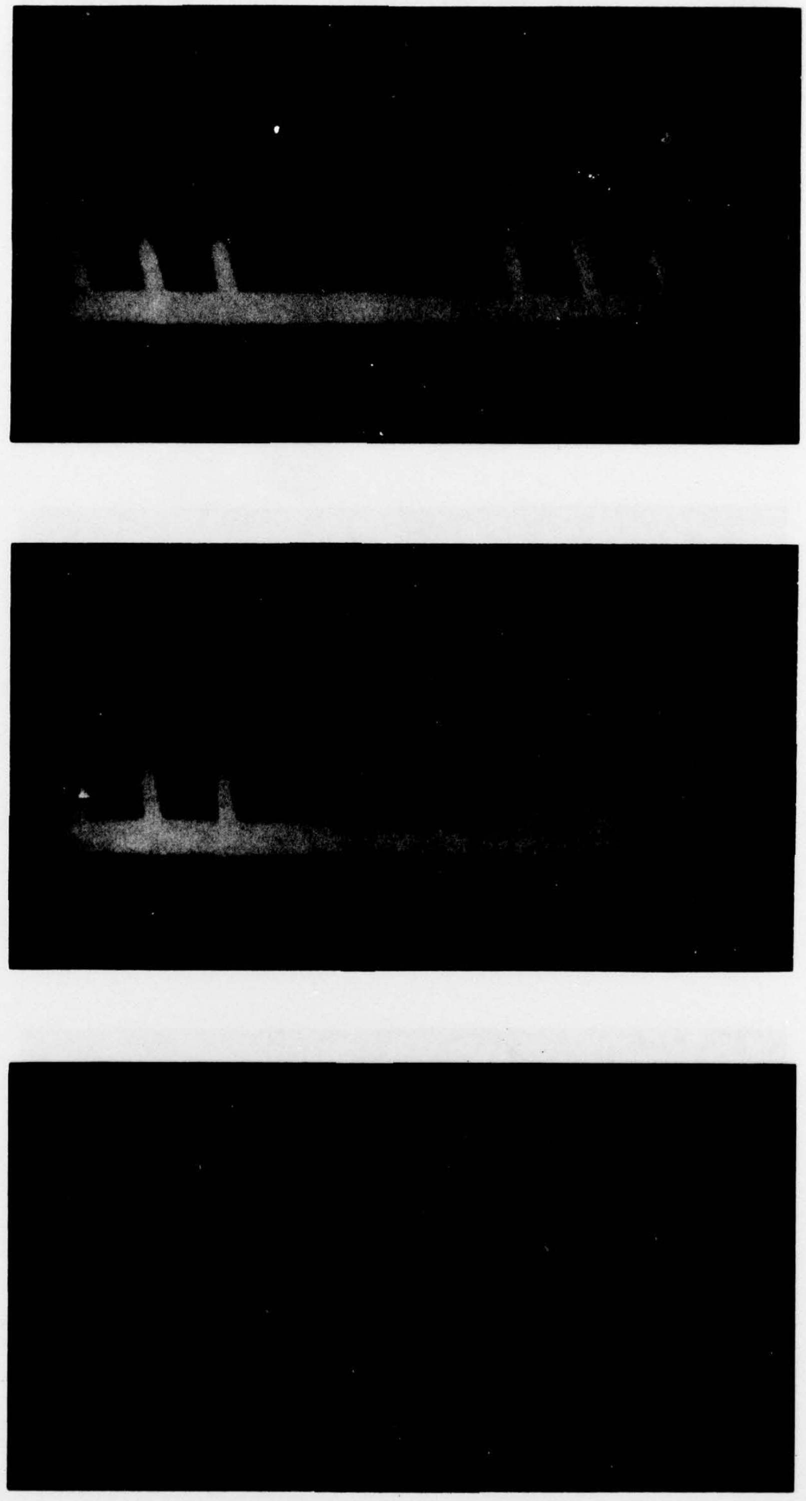


Figure 14. Radiographs showing a segmental replacement in a dog radius.

3. Mixtures of granular tricalcium phosphate ceramic and autogeneous bone for segmental bone lesion correction in the rabbit tibia showed a dependence on the relative quantities of materials in the implant mixture.

4. Segmental bone replacements at mid-shaft positions of dog radii showed that internal fixation could be utilized and the site provides opportunities for long-term studies.

5. Gross and histological evaluations of implant sites and major organs in rabbits showed good biocompatibility for tricalcium phosphate ceramic implants.

REFERENCES

1. "Response of Combined Electrical Stimulation and Biodegradable Ceramic", Second Annual Report, USAMRDC Contract DAMD17-75-C-5044, December, 1976.

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