

Characterization
AND
Performance
OF
Calcium
Phosphate
Coatings
FOR
Implants

HOROWITZ/PARR, EDITORS



STP 1196

STP 1196

Characterization and Performance of Calcium Phosphate Coatings for Implants

Emanuel Horowitz and Jack E. Parr, Editors

ASTM Publication Code Number (PCN):
04-011960-54



ASTM
1916 Race Street
Philadelphia, PA 19103
Printed in the U.S.A.

Library of Congress Cataloging-in-Publication Data

Characterization and performance of calcium phosphate coatings for implants / Emanuel Horowitz and Jack E. Parr, editors.

(STP : 1196)

Papers presented at a symposium sponsored by ASTM Committee F-4 on Medical and Surgical Materials and Devices in Miami, Fla. on Nov. 17, 1992.

"ASTM publication code number (PCN) 04-011960-54."

Includes bibliographical references and index.

ISBN 0-8031-1854-6

1. Hydroxyapatite coating--Testing--Congresses. 2. Orthopedic implants--Materials--Congresses. 3. Dental implants--Materials--Congresses. I. Horowitz, Emanuel. II. Parr, Jack E. III. ASTM Committee F-4 on Medical and Surgical Materials and Devices. IV. Series: ASTM special technical publication ; 1196.

[DNLM: 1. Calcium Phosphates--congresses. 2. Implants, Artificial--congresses. 3. Biocompatible Materials--congresses. QT 34 C469 1994]

RD755.65.C48 1994

617'.9178--dc20

DNLM/DLC

for Library of Congress

94-4736

CIP

Copyright © 1994 AMERICAN SOCIETY FOR TESTING AND MATERIALS, Philadelphia, PA. All rights reserved. This material may not be reproduced or copied, in whole or in part, in any printed, mechanical, electronic, film, or other distribution and storage media, without the written consent of the publisher.

Photocopy Rights

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by the AMERICAN SOCIETY FOR TESTING AND MATERIALS for users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of \$2.50 per copy, plus \$0.50 per page is paid directly to CCC, 222 Rosewood Dr., Danvers, MA 01923; Phone: (508) 750-8400; Fax: (508) 750-4744. For those organizations that have been granted a photocopy license by CCC, a separate system of payment has been arranged. The fee code for users of the Transactional Reporting Service is 0-8031-1854-6/94 \$2.50 + .50.

Peer Review Policy

Each paper published in this volume was evaluated by three peer reviewers. The authors addressed all of the reviewers' comments to the satisfaction of both the technical editor(s) and the ASTM Committee on Publications.

To make technical information available as quickly as possible, the peer-reviewed papers in this publication were printed "camera-ready" as submitted by the authors.

The quality of the papers in this publication reflects not only the obvious efforts of the authors and the technical editor(s), but also the work of these peer reviewers. The ASTM Committee on Publications acknowledges with appreciation their dedication and contribution to time and effort on behalf of ASTM.

Foreword

This publication, *Characterization and Performance of Calcium Phosphate Coatings for Implants*, contains papers presented at the symposium of the same name, held in Miami, FL on 17 Nov. 1992. The symposium was sponsored by ASTM Committee F-4 on Medical and Surgical Materials and Devices. Emanuel Horowitz of Johns Hopkins University in Silver Spring, MD and Jack E. Parr of Zimmer, Inc. in Warsaw, IN presided as symposium chairmen and are editors of the resulting publication.

Overview

The symposium on the Characterization and Performance of Calcium Phosphate Coatings for Implants was sponsored by the ASTM Committee F-4 on Medical and Surgical Materials and Devices in response to the elevated interest and activity dealing with calcium phosphate-type coatings for surgical and dental implants. This publication provides the reader with a useful perspective of the preparation, characterization, and application of calcium phosphate coatings for implants, as seen in the year 1992.

Like the proverbial alchemist in search of the philosopher's stone, modern day biomaterials scientists and engineers have been looking for the ideal material to coat their implants. Such a material would elicit no adverse physiological response and under optimum conditions would contribute to enhanced biocompatibility and long-term reliable performance in service. Calcium phosphate-type materials, including hydroxylapatite, attracted the attention of many people working in biomaterials research and development, industrial production of implants, as well as surgical and oral implantologists. This was because, for example, the chemical composition of hydroxylapatite was similar to that of the inorganic component of natural bone and teeth and the numerous reports of enhanced biocompatibility of medical and dental implants coated with this type of material. Within Committee F-4, there has been a surge of activity within the Ceramics Section leading to the establishment of new task forces that are working on the development and promulgation of standards for calcium phosphate-type ceramics. Some of the limitations of some of these materials are recognized (e.g., brittleness, solubility) but research is underway in many laboratories aimed at improving their mechanical and chemical performance characteristics.

In the opening paper of this publication, T. D. Driskell reviews the early history of calcium phosphate ceramics and reports that the first successful coating using this material occurred in 1972. He briefly describes his efforts and those of others on plasma flame sprayed hydroxylapatite coatings. A. J. Tofe et al. emphasize that the characteristics of the HA powder significantly influence the quality of the final coating. Thus, control of the properties of the starting material and the plasma spray conditions determine the degree of crystallinity and the HA coating implant bond strength. The synthesis, x-ray diffraction, infrared spectroscopy, scanning electron microscopy, particle size distribution, and the surface area analysis of the starting HA powder are discussed. Some important aspects of the quality control and characterization of HA raw materials and coatings are covered in the paper by K. W. Flohr. He points out that large variations in the chemical composition, impurities, and crystallinity of the "as received" HA powders were found. Such differences in HA powders, even in separate lots from the same supplier, give rise to final coatings that have different properties.

Using prepared standard samples of hydroxylapatite containing known amounts of crystalline and amorphous HA, J. S. Flach and co-workers describe a rapid and inexpensive x-ray diffraction method for measuring crystallinity in hydroxylapatite coatings. The x-ray diffraction analyses were conducted at $2 - \theta$ between 25 and 40°, and from the obtained diffractograms, the area of the crystalline peaks for the standard samples was determined. The ratio of the crystalline area of a given standard to the crystalline area of the 100% crystalline standard $\times 100$ was used to calculate the relative crystalline peak area. The actual crystallinity of the specimens was determined from a calibration curve plotting crystallinity (%) versus relative crystalline peak area (%). J. P. Legeros et al. report an x-ray diffraction method for calcium-phosphate coatings that does not require standard samples but depends on data from the files of the Joint Committee for Powder Diffraction Standards

(JCPDS). The authors claim that some other diffraction methods do not take into account the effects of line broadening and convolutions on the accuracy of the crystallinity measurement. The method described in the paper is said to be capable of yielding the percentage of each crystalline and non-crystalline phase in the coating. A second paper by the Legeros group authored by R. Z. Legeros et al. discusses the variations in the composition and crystallinity of hydroxylapatite materials. The analytical methods used in this study included x-ray diffraction, infrared spectroscopy, scanning electron microscopy, and chemical analyses. Commercial and non-commercial calcium phosphates and related biological materials were investigated with regard to chemical composition and crystallinity. The dissolution properties of ceramic and non-ceramic calcium phosphates were measured. This study, like the one reported earlier by Flohr, demonstrates that calcium phosphate-type powders and coatings exhibit variability in composition and crystallinity. The authors state that this variability may affect resorption in-vivo.

In their paper on nondestructive characterization of hydroxylapatite coated dental implants by the XRD method, L. Keller and P. Rey-Fessler explain that "perfect" crystalline and "imperfect" crystalline HA are found in the crystalline fraction of plasma-sprayed HA coatings. Thus, different degrees of crystallinity can be obtained depending on the method of analysis used in the determination. Furthermore, the destructive method of preparing specimens for x-ray diffraction analysis may affect the degree of crystallinity and sacrifice other important information. The authors describe the methodology and the modified x-ray diffractometer that was adapted for characterizing plasma-sprayed HA coatings on 3 to 4-mm diameter dental implants.

P. S. Prevey and R. J. Rothwell report a quantitative, nondestructive x-ray diffraction method using an external standard to characterize the crystallinity and weight fraction of the contaminant phases of plasma-sprayed HA coatings. A detailed explanation is given for the theoretical development of the external standard methodology after which the experimental measurement method is described. An assessment of the accuracy and reproducibility of the method is given. The characterization of composite hydroxylapatite coatings for both medical and dental implants is described by V. Sahay et al. A porous metallic coating is first plasma sprayed on to the implant substrate. Then an HA-type coating is plasma sprayed on top of the previously deposited layer to form a strongly interlocked and interdigitated composite structure. The chemical, physical, and mechanical properties of the implant coatings are reported. In-vivo evaluation of the composite porous coating, based on implantation of coated implants in the tibia of dogs is presented in terms of histological findings. The clinical evaluation of composite porous-coated total hip implants is also discussed. M. S. Tung and P. Sung remind us that the bioresponse of implant materials "depends critically upon the properties of the material." In their paper on calcium phosphate-type reference materials, they stress the need for an HA standard reference material to be used in the analysis, characterization, and standardization of hydroxylapatite implant materials. The methods of HA synthesis and preparation of HA are discussed. The results of chemical analysis, x-ray diffraction, infrared spectroscopy, thermal analysis, solubility measurements, and particle size distribution measurements are reported.

In a study of the plasma sprayed induced compositional and phase changes in calcium phosphate ceramic coatings, S. R. Radin and P. Ducheyne report on the in-vitro dissolution rates of these coatings in a calcium- and phosphate-free buffer solution at physiological pH. The authors investigated monophasic calcium-phosphate powders, biophasic powders, and multiphasic commercial plasma-sprayed coatings. Of the materials studied, they claim that hydroxylapatite is the only thermodynamically stable compound at physiological pH. Their data indicate that the material transformations that occur during the plasma spray process leads to increased coating dissolution. Data are provided on the dissolution rates of plasma-sprayed coatings, monophasic and biophasic powders. The paper by K. A. Gross and C. C. Berndt deals with the structural changes of plasma-

sprayed HA coatings subjected to in-vitro testing. HA powder was prepared and then plasma sprayed on to stainless steel substrates. Both as sprayed amorphous and heat-treated crystalline coatings were immersed in Ringer's solution for various period of time. The changes in the different HA coatings during immersion are discussed, and a model is proposed to explain the changes in the microstructure of the coatings. P. Ducheyne and S. R. Radin report the results of their investigation of different single-phase calcium-phosphate ceramics immersed in simulated physiological solution similar in electrolyte composition to human plasma. Hydroxylapatites with different crystallinity and chemical perfection, α -TCP, β -TCP, and TTCP were used in the study. Calcium and phosphate concentrations in the solutions were measured as a function of immersion time. The authors provide data on the chemical surface transformations that occur in vitro. In the paper on hydroxylapatite coatings, J. F. Kay states that such coatings enhance bone adaptation, eliminate fibrous tissue seams, promote stronger bone implant bonding, decrease healing time, and inhibit corrosion of the metallic substrate. For non-precision implants where ideal bone contact is not attained, the HA coating is claimed to overcome the lack of direct implant-bone contact and foster bony proliferation and osseointegration. Kay asserts that the variable performance of HA coatings in vivo can be traced to the non-uniform properties of different coatings resulting from differences in their methods of preparation. HA coated and uncoated canine orthopedic devices were implanted in dogs for up to 52 weeks and data are reported on the interfacial bone-implant strength. HA-coated metallic implants gave consistently higher values than the non-HA coated implants. Tofe et al. address the nature of dissolution and resorption of dense and microporous hydroxylapatite. Scanning electron microscopy, x-ray diffraction, and infrared spectroscopy were used to characterize commercially available HA. They found, using human fibroblasts, that microporous surfaces facilitate cell-mediated resorption. T. Hanawa et al. provide an interesting perspective of the precipitation of calcium phosphate on calcium-ion-implanted titanium in neutral electrolyte solution similar to that of extracellular fluid. The surface of the calcium-ion-implanted titanium and titanium specimens were characterized before and after immersion in the electrolyte. They found that the precipitation of calcium and phosphate is greatly accelerated on calcium-ion-implanted titanium. A mechanism for this reaction is proposed.

Of special interest to manufacturers of calcium phosphate-type coated implants, medical and oral implantologists, and biomaterials scientists and engineers is the position of the Food and Drug Administration on these types of devices. T. J. Callahan et al. discuss the FDA's guidelines on the characterization of calcium-phosphate coatings on dental and orthopedic implants. The paper provides useful information on FDA submissions on calcium-phosphate coatings for orthopedic and endosseous dental implants. A list of relevant standards, methods and publications (Appendix A), as well as data on some chemical, physical, and mechanical characteristics of the calcium-phosphate powder and coatings (Appendix B) is presented. The last paper of this publication deals with ASTM Standards for bioceramics and information on retrieval and analysis. J. E. Lemons supports the need for the development of standards to compare and evaluate bioactive particulates and coatings and to facilitate the correlation of clinical data. Lemons discusses the early history of calcium-phosphate materials and points out that some of these investigations led to the preparation and promulgation of ASTM F-4 Standards (e.g., Beta-Tricalcium Phosphate for Surgical Implantation, ASTM F 1088). Within ASTM F-4, eight relatively new task forces concerned with calcium-phosphate powders and coatings are actively engaged in developing new standards or revising and updating existing standards. A detailed discussion is provided on device retrieval analyses conducted in the author's laboratory.

One final comment is considered pertinent. It may be unlikely that we will ever discover the ideal calcium phosphate-type ceramic or other implant material. Yet, if the implant material on hand

improves the medical condition and quality of life of the patient, we may have to use it until something better is developed.

Emanuel Horowitz

Johns Hopkins University,
Silver Spring, MD; symposium
co-chairman and editor.

Jack E. Parr

Zimmer, Inc., Warsaw, IN; symposium
co-chairman and editor.

Contents

Overview—E. HOROWITZ AND J. E. PARR	vii
Early History of Calcium Phosphate Materials and Coatings—T. D. DRISKELL	1
Hydroxylapatite Powders for Implant Coatings—A. J. TOFE, G. A. BREWSTER, AND M. A. BOWERMAN	9
Techniques for the Characterization and Quality Control of Hydroxyapatite Raw Materials and Coatings—K. W. FLOHR	16
A Calibrated Method for Crystallinity Determination of Hydroxylapatite Coatings—J. S. FLACH, L. A. SHIMP, C. A. VAN BLITTERSWIJK, AND K. DE GROOT	25
X-Ray Diffraction Method for the Quantitative Characterization of Calcium Phosphate Coatings—J. P. LEGEROS, R. Z. LEGEROS, A. BURGESS, B. EDWARDS, AND J. ZITELLI	33
Variations in Composition and Crystallinity of Hydroxyapatite (HA) Preparations—R. Z. LEGEROS, R. ZHENG, R. KIKKOWSKA, D. FAN, AND J. P. LEGEROS	43
Nondestructive Characterization of Hydroxylapatite Coated Dental Implants by XRD Method—L. KELLER AND P. REY-FESSLER	54
X-Ray Diffraction Characterization of Percent Crystallinity and Contaminants in Plasma-Sprayed Hydroxylapatite Coatings—P. S. PREVEY AND R. J. ROTHWELL	63
Characterization of Composite Hydroxylapatite (HA) Coatings for Medical and Dental Devices—V. SAHAY, P. J. LARE, AND H. HAHN	80
Calcium Phosphate Type Standard Reference Material: Development, Preparation, and Characterization—M. S. TUNG AND P. SUNG	99
Changes in the Characteristics Arising from Processing and the Effect on In-Vitro Stability of Calcium Phosphate Ceramics—S. R. RADIN AND P. DUCHEYNE	111
Structural Changes of Plasma-Sprayed Hydroxyapatite Coatings During In-Vitro Testing—K. A. GROSS AND C. C. BERNDT	124
The Effect of Calcium Phosphate Ceramic Composition and Structure on In-Vivo Precipitation Reactions—P. DUCHEYNE AND S. R. RADIN	140
Hydroxylapatite-Coatings for Non-Precision Implant Placements—J. F. KAY	149

Dense Hydroxylapatite (HA) and Microporous HA Resorption—A. J. TOFE, B. A. WATSON, AND H. S. CHEUNG	163
Calcium Phosphate Precipitation on Calcium-Implanted Titanium in Electrolyte—T. HANAWA, K. MURAKAMI, AND S. KIHARA	170
Calcium Phosphate (Ca-P) Coating Draft Guidance for Preparation of Food and Drug Administration (FDA) Submissions for Orthopedic and Dental Endosseous Implants—T. J. CALLAHAN, J. B. GANTENBERG, AND B. E. SANDS	185
Development of ASTM Standards for Bioceramics—J. E. LEMONS	198
Author Index	209
Subject Index	211

Thomas D. Driskell¹

EARLY HISTORY OF CALCIUM PHOSPHATE MATERIALS AND COATINGS

REFERENCE: Driskell, T. D., "Early History of Calcium Phosphate Materials and Coatings," Characterization and Performance of Calcium Phosphate Coatings for Implants, ASTM STP 1196, Emanuel Horowitz and Jack E. Parr, Eds., American Society for Testing and Materials, Philadelphia, 1994.

ABSTRACT: Bioactive calcium phosphate materials were developed by Driskell and his co-workers at Battelle Memorial Institute's Columbus Laboratories and successfully implanted At the U. S. Army Institute of Dental Research at Walter Reed Army Medical Center. in 1971. Coatings of these materials were applied to dental implants in 1972. Disappointment with results of earlier research and development of "bioinert" ceramic implant materials and coatings stimulated this departure into bioactive materials development. Subsequent work by Hubbard Jarcho, Kay, and numerous other researchers resulted in the development of additional variations of calcium phosphate materials and coatings. The substance of this research is the foundation upon which the field of calcium phosphate materials technology and hydroxylapatite coatings has developed.

KEYWORDS: ceramic implants, bioactive materials, Calcium phosphates, Synthetic bone grafting materials, resorbable biomaterials, bioactive coatings, implant coatings, hydroxylapatite

In 1920, Albee and Morrison reported accelerated bone healing using slurry implants of "triple calcium phosphate" powder in surgically created bone gaps in rabbits [1]. However, they published nothing further. In contrast, Haldeman and Moore in 1934 and Ray and Ward in 1952 reported the use of calcium phosphate powders of undisclosed composition as bone growth stimulators. They concluded that accelerated healing did not occur [2,3]. These early efforts attempted to use calcium phosphate powders of various compositions more or less as topical drugs to induce osteogenesis.

Materials oriented research ultimately leading to the development of calcium phosphate "structural" and void filling bone implant materials was begun at Battelle Memorial Institute's Columbus Laboratories in 1968 [4,5]. Porous blocks of phosphate bonded alumina to be used as permanent bone replacements in avulsive wounds were developed. These blocks were implanted in the mandibles of rhesus monkeys.

¹Director of Research and Development, Stryker Dental Implants, Div., Stryker Corporation Kalamazoo, MI 49001

2 CALCIUM PHOSPHATE COATINGS FOR IMPLANTS

Some specimens incorporated into the bone very nicely. Others were exfoliated over a period of several months. The recurring rejection problem was thought possibly to be an immune response indirectly resulting from the deep through and through porosity of the blocks. It was theorized that body fluids percolated throughout the tortuous porosity of the implant but then sometimes, became denatured because the fluids became stagnate. This was thought to be due to the compromised development of adequate vascularity throughout the devious and sometimes very small interconnections within the implant porosity, thus eliciting a denatured protein rejection phenomenon.

Porous alumina coated metallic bone plates were developed in 1970 [4,6]. Some of these ceramic coatings were applied as a slurry and then fired; others were plasma flame sprayed. Substrates used were medical grade stainless steel, chrome-cobalt alloy, titanium alloy, and tantalum. Spalling and cracking were experienced with some coating and substrate combinations, and adverse tissue responses with others. Because of the disappointing results, research was not continued with alumina coatings except in another related study where high density 99.8% alumina tooth implants with porous alumina coatings were developed [7,8]. This approach too was discarded after about six months of equivocal in-vivo results in monkeys. Most of the implants were quickly lost due to infection. The infections were thought to be most likely elicited from percolation of oral fluids throughout the porosity. Later, in 1971, a new tooth implant design fabricated from high density 99.8% alumina with serrated (finned) bone interfacing surfaces was developed. These consistently developed and maintained a direct bone/ceramic interface (osseointegration) and infections were no longer a problem[8,9].

Thus, it was because of the disappointing results experienced with large non-resorbable alumina porous block implants as well as with porous coatings that subsequent thinking was focused toward the concept of a bioactive bone grafting material. This approach was intended to allow rapid invasion of bone forming cells, rapid development of a good blood supply and gradual conversion of the implant site to natural bone which could then remodel normally. The first conception of a synthetic bone grafting material was to attempt to develop a composite material. This was to consist of hydroxylapatite (HA) particles in a collagen matrix. The concept however, remained merely that... as in the meantime the possibilities of other calcium phosphate compounds with greater potential for in-vivo resorbability than the relatively non-resorbable HA became intriguing. It was decided to try to develop a ceramic material that would totally resorb as it was replaced by bone and that would not contain any substances of biologic origin which might possibly elicit an immune response [10].

In 1971, three high purity calcium phosphate compounds were selected for in-vivo evaluation in rats and rabbits. The three compounds were mono-calcium phosphate, dicalcium phosphate, and β -tricalcium phosphate (β -TCP). Through in-vivo studies conducted at the U.S. Army Institute of Dental Research at Walter Reed Army Medical Center, β -TCP was selected as the most promising compound [10]. It was found to demonstrate excellent biocompatibility, resorbed while being displaced by rapid bone ingrowth and as discovered later, could be sintered into a relatively strong structural form. The original concept, was to develop a

resorbable porous block grafting material for use as a gap filler in large bony defects and a resorbable porous particulate form for smaller contained defects.

These implant materials were made from high purity β -TCP powder prepared in the laboratory at Battelle. Porosity was created and controlled by combining sized particles of naphthalene with sized particles of β -TCP. The mixture was cold pressed in a mold under high pressure. The resultant green body was heated to accelerate sublimation of the naphthalene, calcined, and then fired at 1100C to create a macro porous ceramic block [11].

Blocks of this material were surgically placed as inlay grafts in the femurs of dogs [12]. The results of these early studies indicated that rapid bone ingrowth occurred and a high degree of biocompatibility was evident. It was also obvious histologically that the β -TCP blocks tested underwent resorption while being replaced by bone with little evidence of an inflammatory response. Scanning electron microscopy (SEM) photographs suggested that an intimate bond was occurring between the bone and the ceramic. Further, the SEM photographs suggested that a chemical bond might exist. In another study, Cameron reported on β -TCP blocks obtained from Battelle. These were placed as inlay grafts in dog femurs. The blocks, which extended from within the medullary canal to 10mm or more beyond the periosteum demonstrated bone forming within the entire ceramic porosity [13].

Because of the observed ability of bone to form not only within the inlay portion of the ceramic structure but beyond the normal boundaries of the bone in which it was placed, it was felt that the material was functioning as possibly more than just an osteoconductive medium. It was also realized that it was inappropriate to describe these materials as being either osteogenic or osteoinductive. Therefore, the term, "osteophyllic" was coined to describe this phenomenon.

In 1972, the first bioactive coatings were developed and applied to experimental endosteal root form dental implants fabricated from high density Alumina which were also developed at Battelle [10]. The coating consisted of a high purity β -TCP slurry applied by spraying or dipping and then sintered on an aluminum oxide substrate. Coated endosteal root form dental implants were compared in-vivo to uncoated implants. All implants had serrated (finned) bone interfacing surfaces that had been demonstrated in earlier studies to osseointegrate. The serrations on the coated implants were filled in with the coating. The study was conducted in monkeys. While the coated implants healed well and appeared to biointegrate, substantial clinical advantages were not observed when compared to the uncoated versions which also healed rapidly and predictably osseointegrated.

Further research by the author on implant coatings ended for a number of years at this point. A major factor affecting this decision was that other researchers and clinicians had not been inclined to accept the claims or even the histology suggesting the direct bone/implant interface obtained in the Battelle studies. In retrospect, it should be kept in mind that in 1972, the concept of direct apposition of bone to a functioning (dental) implant interface (osseointegration) was not an

4 CALCIUM PHOSPHATE COATINGS FOR IMPLANTS

accepted phenomenon. The generally accepted view at that time was still that fibrous incapsulation around implanted materials placed in bone or other sites was all that could be expected[8]. Thus, to have additionally purported to have developed coated implants that developed what appeared to be a tenacious chemical bond with bone (biointegration) would likely have classified the Battelle research findings as pure science fiction. Nonetheless, research continued with particulate and porous block β -TCP implant materials. The β -TCP material was used by a number of researchers for in-vivo bone regeneration studies [14,15,16, 17,18,19,20].

During the years 1973-1975, Small blocks of β -TCP were used as a substrate for bone morphogenetic protein (BMP) by Urist. He was able to bind a surface layer of BMP throughout the porous structure. Specimens were surgically placed in rabbit muscle tissue. Blocks of β -TCP with BMP surfaces consistently exhibited normal appearing bone formation around the block and throughout the porosity. Block specimens of β -TCP untreated with BMP did not[21].

In 1973, Hubbard and his co-workers reported the development and successful implantation of a sintered mixed phase material which was predominately HA and β -TCP in a porous block form [22]. It was prepared from reagent grade tribasic calcium phosphate powder and was used successfully in a number of studies. It was considered resorbable, although this occurred at a slower rate than sintered porous β -TCP. Hubbard's material in a sense might be considered as a transitional bridge between the concept of resorbable high purity β -TCP bone implant materials and the more or less "non-resorbable" high purity HA materials, the appearance of which shortly followed.

In 1974, Roy and Linnehan reported the development of a replamineformate prepared from coral skeletal carbonate which was used with success in a variety of bone implant applications [23]. The HA replication of the coral skeleton offered a highly organized "biologic" interconnected pore structure. The rationale for this approach was the concept that better bone ingrowth might likely occur in a biologically oriented pore structure as compared to bone forming within synthetically created, randomly porous structures [24]. Some formulations of replamineform HA are intended to be resorbable, while others are considered to be a permanent bone implant material. It is produced in porous block and porous particulate forms.

Jarcho and his co-workers engendered widespread and intense interest with their development and applications of "Durapatite" a high density sintered HA block material. They first prepared HA in dense polycrystalline form in 1974. Their work was first published in 1976 [25]. Much research has been conducted using this material. It has been used clinically for filling of periodontal bony defects, alveolar ridge augmentation, high density sub-gingival tooth root forms, and for filling in tooth extraction sites to preserve alveolar ridge contours [26].

Ducheyne and his co-worker's used hydroxylapatite impregnated metallic porous coated implant surfaces to augment skeletal fixation in the late 1970's. The coating was applied as a slurry and then baked. They noted

"an apparent stimulation of bone ingrowth into the porous surface of the implant [27]

Valen produced a plasma sprayed HA coated endosseous blade implant which he began to market in 1980. The coating consisted of a base layer of particulate titanium plasma sprayed coating on the C.P. titanium implant substrate with a plasma sprayed layer of HA then applied on top. The coating trade name was "Hydroxyflex" which was used because Valen's blade implant was described as being "bendable without causing the coating to chip off" [28].

Kay developed the first HA plasma sprayed coatings which were directly applied to C P. titanium, titanium alloy, and cobalt/chromium alloy substrates in 1981 [29]. Tests using transcortical implants in dogs demonstrated that HA plasma spray coated metal implants could create a faster and stronger implant adherence in bone compared with uncoated metal controls [30]. HA coated subperiosteal implants have been used in humans since 1984 [31]. Extensive research using these coatings for various implant applications established the high level of interest in HA coatings which continues to exist today.

After forming a small research and development company in 1973, the author's research with endosseous dental implants and β -TCP ceramics for bone grafting continued [32]. Jarcho's development and use of HA particles as a bone augmentation material and later, Kay's work in 1981 with plasma flame sprayed HA coatings were followed with interest. The author's subsequent research with HA particulate materials and with HA coatings began in 1982. Early plasma flame sprayed HA coated specimens on metal substrates were prepared for use in experimental orthopedic related studies [33, 34].

Then, after forming another new company in 1985, it was decided to produce an HA coated version of the company's newly designed titanium alloy endosseous dental implant. The implant design was exactly the same as the uncoated version as the implant had originally been designed with an HA coated option in mind. The coated version was introduced in 1987.

During the latter half of the eighties, numerous companies have introduced HA coated implant prostheses for both dental and orthopedic applications. Subperiosteal dental implants with prescription HA coatings on custom cast cobalt/chromium frames were the first widely used commercial application [31]. Unfortunately, some early commercially available plasma sprayed HA coatings exhibited considerable variation in interfacial bond strength, stoichiometry, and crystallinity. These variables profoundly affect the degree of coating resistance to dissolution and its adherence to the implant. Loss of HA coating integrity through dissolution or delamination from the implant substrate often may result in loss of the implant and can occur at any time during the life of the implant [35].

Most of the early HA coated dental implant design concepts were relatively smooth walled macroscopically and rely predominately on the "bio-integration" capability of their HA coating as the major load transmitting mechanism of the implant to the bone. More recently, implant

designs have tended to incorporate a combination of mechanically retentive bone/implant interfaces such as screws, deep grooves, or finned designs combined with the HA coating. The HA coating then becomes a synergistic component of a hybrid implant design that is both mechanically retentive and still offers the attributes of biointegration [35].

Over the past decade, in academia and in the medical/dental industry, calcium phosphate materials, coatings technology and applications have become a significant and intense area of ongoing research and commercial activity. There are however incidences occurring where some HA coated dental implants, for example, are being lost due to coating dissolution, delamination, and infections over the long term; that is the reality. It is therefore, perhaps wise to keep in mind and consider that the science base of calcium phosphate materials and coatings technology is still in its youth. Many questions as to long term applicability or suitability of these unique and relatively new materials for biomedical applications remain unanswered.

REFERENCES

- [1] Albee, F. H., and Morrison, H. F. "Studies in Bone Growth - Triple Calcium Phosphate as a Stimulus to Osteogenesis," Ann. Surg. Vol. 71, 1920, pp 32-39.
- [2] Haldeman, K. O. , and Moore, J. O., "Influence of a Local Excess of Calcium and Phosphorus on the Healing of Fractures," Arch. Surg. Vol. 29, 1934, p 385.
- [3] Ray, R. D., and Ward, A. A., "A Preliminary Report on Studies of Basic Tricalcium Phosphate in Bone Replacement," Surgical Forum, American College of Surgeons, Philadelphia, W. B. Saunders, 1952, p 429.
- [4] Driskell, T. D. O'Hara, M. J., Greene, G. W., "Management of Hard Tissue Avulsive Wounds and Management of Orofacial Fractures," Report #1, Contract # DADA17-69-C- 9118, Supported By U.S. Army Medical Research and Development Command.
- [5] Bhaskar, S. N., Cutright, D. E., Knapp, M. J., Beasley, J. D., Perez, B., Driskell, T. D., "Tissue Reaction to Intrabony Ceramic Implants," Oral Surg. Oral Med. Oral Path., Vol. 31, 1971, p 282.
- [6] Driskell, T. D., O'Hara, M. J., Sheets, H. D., Green G. W., Natiella, J. R., "Development of Ceramic and Ceramic Composite Devices for Maxillofacial Applications," in Hall, C. W., Hulbert, S. F., Levine, S. F., Young, F. A., (eds.), Bioceramics, Engineering in Medicine, New York, Wiley-Interscience, 1972, pp 345-361.
- [7] Driskell, T. D., O'Hara, M. J., Niesz, D. E., "Surgical Tooth Implants, Combat and Field," Report #2 Contract DADA17-69-C-9181, Supported by the U.S.Army Medical Research and Development Command.

- [8] Driskell, T. D., "History of Implants," Cal. Dent. Assn. J., Vol. 15 No. 10, 1987, pp 15-25.
- [9] Driskell, T. D., McCoy L. G. Tennerly, V. J., Niesz, D. E., "Surgical Tooth Implants, Combat and Field," Report #3 Contract # DADA17-69-C-9181, Supported by the U.S. Army Medical Research and Development Command.
- [10] Getter, L., Bhaskar, S. N., Cutright, D. E., Perez, B., Brady, J. M., Driskell, T. D., O'Hara, M. J. "Three Biodegradable Calcium Phosphate Slurry Implants in Bone," Oral Surg., Vol. 30, 1972, p 263.
- [11] Driskell, T. D., O'Hara, M. J., Niesz, D. E., and Grode, G. A., "Management of Hard Tissue Avulsive Wounds and Orofacial Fractures," Report #3 Contract # DADA17-69-C-9118, Supported by the U.S. Army Medical Research and Development Command.
- [12] Driskell, T. D., Hassler, C. R., and McCoy, L. R., "The Significance of Resorbable Bioceramics in The Repair of Bone Defects," "Proceedings of the 26th Annual Conference on Engineering in Biology and Medicine, Bioengineering, Vol. 15, 1973, p 199.
- [13] Cameron, H. U., McNabb, I., and Pilliar, R. M., "Evaluation of a Biodegradable Ceramic," J. Biomed. Mater. Res., Vol. 11(2), 1977, pp 179-185.
- [14] Heller, A. L., Koenigs, J. F., Brilliant, J. D., Melfi, R. C., Driskell, T. D., "Direct Pulp Capping of Permanent Teeth in Primates using a resorbable form of Tricalcium Phosphate Ceramic," J. of Endo., Vol. 1, No. 3, 1975, pp 95-101.
- [15] Koenigs, J. F., Heller, A.L., Brilliant, J. D., Melfi, R. C., Driskell, T. D., "Induced apical Closure of Permanent Teeth in Adult Primates Using a Resorbable Form of Tricalcium Phosphate Ceramic," J. of Endo., Vol. 1, No. 3, 1975, pp 102-106.
- [16] Levin, M. P., and others, "Biodegradable Ceramic in Periodontal Defects," Oral Surg., Vol. 38, No. 3, 1974, pp 344-351
- [17] Levin, M. P., and others, "A Comparison of Iliac Marrow and Biodegradable ceramic in Periodontal defects," J. of Biomed. Mater. Res., Vol. 9, No. 2, 1975, 183-195.
- [18] Levin, M. P., and others, "Healing of Periodontal Defects with Ceramic Implants," J. Clin. Perio., Vol. 1 No. 4, 1974, pp197-205.
- [19] Mors, W. A., and Kaminski, E. J., "Osteogenic Replacement of Tricalcium Phosphate Ceramic Implants in the Dog Palate," Arch. Oral. Biol., Vol. 20 No. 5,6, 1975, pp 365-367.
- [20] Ferraro, J. W., "Experimental Evaluation of Ceramic Calcium Phosphate as a Substitute for Bone Grafts," Plast. Reconstr. Surg. Vol. 63 No. 5, 1979, pp 634-640.