Experimental and Computational Investigations of In-Vivo Behavior of Bone-Implant Osseointegration

1 Project Overview

1.1 Goals

The ultimate goal of this project will be the development of analysis and simulation techniques for long term *in-vivo* behavior of bio-mechanical implants and supporting bone structures. Together with limited animal testing this should provide insights into the design features of implants that affect long term survivability. In particular, we will study dental implants. We will develop *realistic* computer simulations of their in-vivo behavior accounting for the real geometry, heterogenous material properties and the time dependent remodeling and resorption that is often observed in clinical practice.

Success in this goal will provide an increased understanding of fundamental behavior of bone-implant systems and powerful tools to develop new implant designs. We will also develop "real-time" variants of this simulators for use in surgical planning. While the immediate focus of these tools will be dental implants and associated bone structures, the techniques developed will be of much wider applicability. Such realistic simulations will require the use the most efficient simulation techniques on the best available hardware, namely optimized adaptive versions of the finite element method on modern high performance multi-processor computers. Limited animal testing will be used to tune and validate the numerical simulations. This combination of optimum use of computing strategies and experimentally validated tools will lead to the high quality low cost simulations.

Over the last two years we have developed some simulations and identified important issues needed for development of realistic simulations of the in-vivo behavior described above. The aim of this project is to conduct animal testing and then using new analysis techniques and suitable high performance computational resources (for example at the newly established Center for Computational Resources, University at Buffalo) produce validated simulations.

1.2 Proposal Outline

In the next section we emphasize the broad impact and multi-disciplinary nature of the project. Subsequent sections are used to describe fundamental concepts, the advancements in analysis required, preliminary work and a program of limited animal testing.

2 Impact and Multi-disciplinary Nature of Research

A pro-forma addressing only the primary U.S. market based on implant sales from 19 implant companies projects implant sales growth from about $ 310 million in 1996 to about $ 757 million in 2000 based on an average implant cost of about $ 200. The market is currently dominated by European manufacturers benefiting from early Swedish and German research. We anticipate significant cost reduction and longer term survivability by the use of alternate designs. The key to the development of these systems will be the use of simulations of life-cycle behavior made possible by the research outlined here.

Development of long term in-vivo behavior simulation tools will allow us to explore multiple design alternatives – new thread designs, different biocompatible coatings and more optimal load bearing sizes and shapes at minimal product development cost. Thus the iterative design optimization methodologies that have dramaticaly improved most other mechanical systems can be made available to implant designs supplanting the one-shot design and proof methodologies currently practiced.Similar efforts by Brunski and Prabhu et. al. [5, 6, 16] have also generated early promising results.

The research work proposed will require significant advances in the engineering analysis domain and will also generate new insights into the fundamental behavior of implant systems. Investigators from the school of engineering and school of dental medicine have already started working closely in developing the preliminary analysis work. An effort that has already generated one publication by Patra, Meenaghan et al. [27].

3 Fundamental Concepts

In this section we will briefly review fundamental concepts of dental implants, bone mechanics and finite elements.

3.1 Implant Basics – Osseointegration

Endosseous dental implants have gained recognition as a reliable treatment modality during the last three decades [2]. A variety of endosseous dental-implant systems have become available to clinicians with different designs, materials and surface topography. They include metals such as commercially pure titanium (CP-Ti), the alloy of Titanium ($Ti6Al4V$), tantalum, cobalt-chromium and ceramic materials(predominantly hydroxyapatite). Some of these systems make claims for osseointegration while others promote fibroosteal integration, biointegration or bony ankylosis.

The most important post-implantation tissue response considered crucial for success of dental implants has been described as osseointegration or the amount of bone in contact with the implant surface at the light microscopic level [8]. This percentage of bone contact ranges, in the literature, from 40-90 % , depending upon its location in the maxilla or mandible. Due to its physico-chemical properties, commercialy pure titanium was believed to achieve osseointegration [3]. More specifically, the biocompatibility of CP Ti is thought to reside in the oxide layer and any alteration of its properties would affect the osseointegration process.

In spite of a large volume of data or information at the light microscopic level, there is still little precise knowledge or information available regarding the factors which influence host response at the implant-tissue interface in order to achieve maximum osseointegration and improve long term integrity or survival of threaded implant systems [31]. Load distribution, surface preparation, bone quality – all are known to have a significant role in the process. Other variables that affect implant survivability include implant designs, surgical techniques, bone condition/quality, stress shielding etc. For instance it has been postulated that stability is directly related to the contact area. Unstable implants are known to lead to micromotion causing wear and eventual failure.

3.2 Bone Mechanics

There are a several comprehensive texts on the mechanical properties of bone notably the ones edited by Hastings and Ducheyne [17] and by Cowin [9]. The recent review of Fung [13] also has a complete updated presentation. Bones have a complex microstructures designed to optimize their performance in their mechanical functions of carrying the load of the body and protecting vital organs from injury. The porous liquid filled structure of trabecular bone is very efficient at absorbing energy and transmitting compressive stresses while the fibrous laminate type structure of cortical bones is well suited for their primary function as load carrying constituents. Further, as observed by many since Wolff in 1892, bone continualy adapts its structure and properties to its function. There has been a tremendous volume of work to characterize the mechanical properties of bone. The anisotropy, viscoelaticity, and complex fatigue and fracture behavior have all been documented. The monographs cited above are fairly comprehensive in describing most of these properites. However, these sophisticated mechanical models have rarely been used in the computer simulation of these systems. Most current simulations have used oversimplified models like homogeneous linearly elastic static models. The primary reason for doing so has been the unavailability of computing capabilities capable of handling the complexity and volume of computations necessary to relax these assumptions.

3.3 Finite Element Methods – Basics

In the last two decades, finite element methods have revolutionized the design and analysis of mechanical systems. Simply stated, the method enables one to simulate on the computer any physical system, by constructing approximate numerical solutions to the partial differential equations that charaterize a physical system. At the heart of the method are the 'finite elements' into which it breaks up complex geometries. Approximations to the behavior of the system are then constructed over each of these finite elements. The local approximations are then assembled to provide global system behavior. The quality of the approximation clearly depends on the number of these elements and the quality of the approximation over each of these elements. Appropriate combinations along with the use of supercomputing can lead to approximations of unprecedented quality(see for e.g. Patra [24, 25]).

4 Engineering Innovations to Improve Analysis Tools

4.1 Simplifications Prevalent in Most Current Analysis

Recently Rieger et al. [30] have conducted a systematic study of dental implants from several leading vendors. Their analysis while somewhat inconclusive because of the major simplifications used, indicated uneven stress distributions with unacceptable levels of local stresses in parts of the bone. Analysis conducted by Meijer et al. [20] also indicates that the simplifications introduced in the loading has a major effect on the computed stress in the bone and suggested redesign of implant systems to optimize the loading patterns.

All analyses carried out up to the present time have used several simplifications in the loading conditions, material characterization and the geometry representation used. These simplifications were necessiated by the limits on the capabilities of the computers and finite element technology used. The major simplifications made in most implant analysis to date have been: *two dimensional* representation of geometry, *use of only static axial loads* to simulate implant performance, assumption of *homogeneous, linear elastic behavior* of bone characterized by single elastic moduli, assumption of *perfect bonding* between bone and implant. Further there appears to be insufficient study of *time/load dependent material behavior* of bone.

4.2 New Analysis Directions

We propose now to relax most of the simplifying assumptions on the analysis and thus obtain fresh insights into the behavior of different types of dental implants. We now outline some of the major new thrusts in the analysis.

4.2.1 Realistic 3D geometry and boundary conditions

We propose to use full *three dimensional representation* of the geometry. This will enable more correct modeling of the geometry and loading especially for cases where the geometry and loading do not posses axial symmetry or a constant cross section.

4.2.2 Complex Dynamic Loading

The implants are subjected to a complex loading regime during use. The actual loading includes *axial and lateral loads that are applied repeatedly in a cyclic manner.* Most previous analysis has relied on simplifying it to a static axial load. Thus predictions based on this analysis may be in error. We propose to study the performance of the implants subjected to a variety of loading situations. In particular we will examine the effect of complex multiaxial dynamic loads like those generated by a prosthesis in use. Instead of estimating the loading on the implants we will attempt to model the actual prosthetics and thereby obtain more realistic loading scenarios. We will also attempt to study the effect of *repeated loading cycles* and resulting phenomena such as bone resorption and atrophy, that are very important to implant performance but difficult to model. The pioneering work of Hart et al. [15] will provide a nice starting point for our efforts in this direction.

4.2.3 Advanced Material Models

Current analysis has characterized the bone as being uniform linearly elastic and isotropic. True properties of bone are quite different. We propose in this analysis to make use of more accurate characterizations. We will attempt to account for the anisotropy and inhomogeneous nature of bone. Modern theories of homogenization developed to model composite materials like bone need to be employed in conjunction with appropriate mechanical laws. We will try to account for the time and load dependent response of bone using a material model that incorporates these effects. An example of such a characterization is Cowins' recent model of trabecular bone response to loads [13] :

$$\begin{aligned} T &= \beta_1\ I + \beta_2\ E + \beta_3\ K + \beta_4\ K^2 + \beta_5(\ KE + EK) + \beta_6(\ K^2E + EK^2) \\ K_{,t} &= \alpha_1\ I + \alpha_2\ K + \alpha_3\ K^2 + \alpha_4\ E + \alpha_5(\ KE + EK) + \alpha_6(K^2E +\ EK^2) \\ tr\ K_{,t} &= 0 \qquad\qquad \text{where}\ \ K_{,t} = 0 \text{ when }\ E = E_0 \\ v_{,t} - {v^0}_{,t} &= \text{ function of } (trE, trK^2, trK^3, trEK, v - v_0) \end{aligned}$$

In these equations T is the stress tensor, K is the deviatoric part of the fabric tensor which describes the geometric pattern of the trabecular bone, E is the strain tensor, E_0 is a specific reference strain, v is the solid volume fraction of trabecular bone and the various αs and βs are functions of the invariants of E and K. We shall thus try to account for the load dependent remodeling response over time.

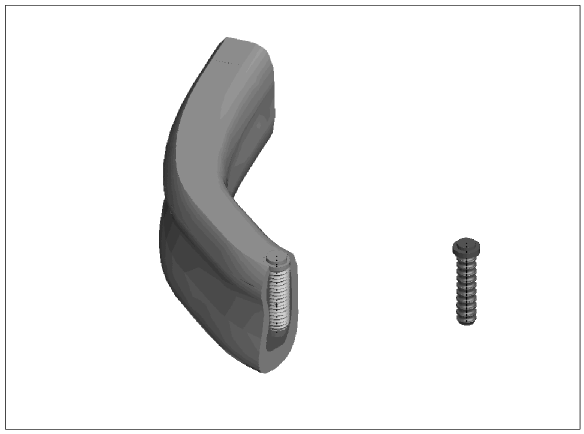

Figure 1: Simplified 3D represenatation of jaw bone and implant

4.2.4 Homogenization Techniques

Modeling bone structures requires the use of some homogenization technique to characterize of the properties of the inhomogeneous material based on properties of each of the constituents. Simplistic formulae based on volume fractions and other similar ideas have been shown to be ineffective. Oden and Zohdi [32] and more recently Patra and Max [28] have suggested the use of a modeling error based adaptive homogenization technique for such randomly heterogeneous systems. In this scheme the material property representation is adjusted locally until a very good representation is finally obtained.

4.2.5 Modeling of contact and partial osseointegration

The contact between the bone and implant is critical to the effective transmission of load. Thus far it has been assumed that the contact has been perfect i.e. 100 % osseointegration. However, clinical studies seem to indicate that this may not indeed be the case. In fact anterior and posterior maxilla have cortical bone osseointegration at 50 and 25 % respectively. Motivated by frictional contact fomulations popular in mechanical systems we will introduce rigorous contact formulations to model partial osseointegration. The lower osseointegration can also be modeled (somewhat crudely) by a variety of other techniques like introducing random gaps and softening bone locally.

4.3 Consequences of new Analysis Directions

The immediate consequence of implementing the new analysis directions is a *tremendous increase in the computational complexity* of the simulation. The relaxation of the analysis assumptions will increase the computational costs tremendously. For instance just relaxing the 2D assumption in a 3 D jaw bone model shown in Fig. 1 required 65,000 tetrahedral finite elements to model just the geometry accurately! A FEM mesh good enough to obtain a satisfactory simulation would require at least 5 to 6 times that many elements. If we have to use this along with simulation of the time dependent loading(at least a 100,000 cycles) and inhomogeneous material models(material property evaluations at a minimum of 64 points per element) the calculations are soon beyond the capability of most computers. The answer is to optimize the computational process and use the latest multi-processing supercomputers capable of the computations necessary. This would make possible the realistic simulations we desire. The target is to make every FLOP count and use as many of them as possible. This combination of optimum use of computing strategies and the use of the latest multi-processor hardware will lead to the high quality simulations we need as part of our design optimization loop.

The second major consequence is the need for appropriate in-vivo data against which these complex simulations may be validated. While, some data is indeed available it is largely in-vitro data and/or insufficient final state (failure or success) type of observations. We will have to create a suitable data set with continuous observations of animal subjects. This data set can then be used to a) tune parameters in the material models b) validate the simulations.

5 New Computational Techniques

The challenge posed above can be met by customizing recent developments in the techniques used in finite element modeling and the latest generation of high performance computers.

5.1 New finite element algorithms

New finite element algorithms using solution adaptivity, better quality element representations and more efficient solution methods can produce tremendously more accurate simulations at lower cost. Solution adaptivity entails local modification of the finite element mesh by changing either the sizes of the element and/or the local polynomial order of approximation based on on some measure of the local quality of the approximate solution. Thus we produce a grid customized for the problem at hand and a very high quality solution at minimal cost. Such techniques have been shown to save orders of magnitude in computational cost over conventional meshes(see for instance Oden and Patra [26]). For example a suitable solution adaptive mesh would reduce the 65,000 element calculation described before to one using at most 10,000 to 15,000 elements.

5.2 Use of supercomputers for Implant-bone simulation

The use of the current generation of high performance multi-processor supercomputers simulation (for instance those acquired by the SUNY Center for Computational Research) has revolutionized the nature and quality of most simulations for physical systems. These multi-processor computers provide computing capabilities orders of magnitude larger than earlier generation machines. Significant physical problems long considered "unsolvable" are now routinely being done on these systems. In conjunction with the above improvements in meshing and solution methods, the use of these computers should enable us to carry out all the analysis directions identified earlier, leading to new insights and better designed implants. The computational strategy we propose here will combine adaptive finite element meshes which optimize computations required to obtain a given simulation quality, and multi-processor computing which maximizes availability of computing power. Similar strategies can be seen in the work of Shephard, Flaherty and co-workers [12, 7]. With funding from the National Science Foundation, Patra, the PI on this effort has been engaged in developing computer software that enables the computational strategies described above. This software will be made available for this study.

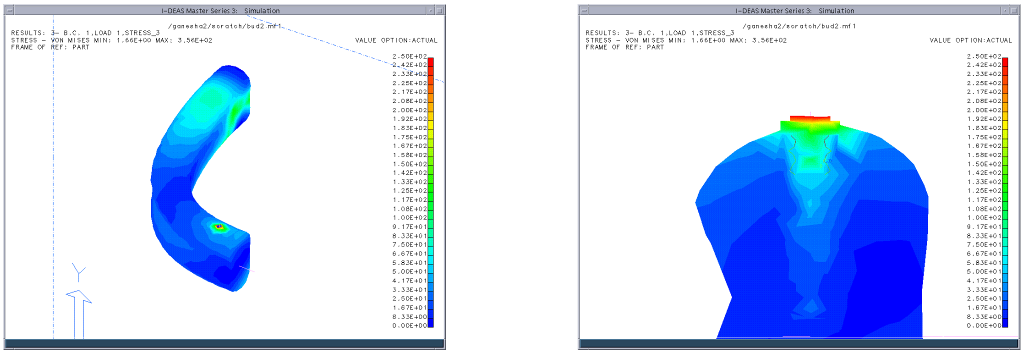

Figure 2: Von Mises Stress contours on 3D geometry and details on a section

6 Preliminary Analysis

We have started preliminary work on the various new analysis directions identified earlier. The preliminary results are very promising and indicate that many new insights may be obtained by fully exploring all the new analysis directions. However, all the results obtained to date have been purely computer based studies. Without, experimental correlation none of the results/insights can be given full credence. The principal goal of this pilot study will be to perform limited animal studies and then use the data generated, to tune and validate the simulations described below.

6.1 3D geometry effects

The first analysis direction we explored was to relax the simplification of 2D geometry and the concomitant artificial boundary conditions used in a lot of prior analysis. For the purpose of this preliminary analysis we used a general purpose finite element program IDEAS and an Ultra Sparc 2 computer from SUN Microsystems. This model and subsequent analysis using a very coarse finite element model and assumptions of homogeneous linear elastic material models for bone and static multiaxial loading showed that the stress distribution in the existing BUD medical devices implant was highly concentrated around the flange area with litlle or no stress in the lower regions of the implant. 2 This result was very different from several 2D analyses published in the literature that indicated that the primary stress concentration would be at the tip of the implant. The flawed conclusion having been derived from the use of an artificial boundary condition used in simplifying the geometry to 2D. However, even this preliminary analysis with only one implant and very simplified geometry seriously taxed the computer we used. Adding on any further complications would not be feasible without the use of the advanced algorithms and supercomputers we have proposed.

6.2 Adaptive Homogenization

Assume that we can obtain material distribution data like that shown in Fig. 3 from experimental observation (for instance by using the radiography proposed in the next section). We begin the anlaysis by introducing a coarse mesh. The analysis is first made on this coarse mesh using material properties averaged at the element level. Solutions obtained on this coarse mesh and the material distribution data are post-processed as in Zohdi et al. [32] and then the mesh is adapted wherever the modeling error is high. After several cycles of this we get meshes like those in 3b. This mesh

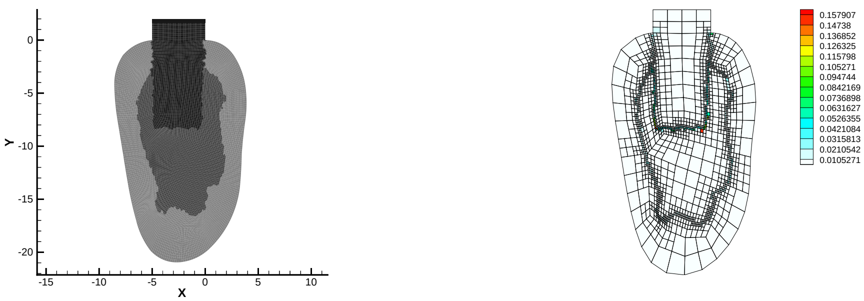

Figure 3: Typical 2 D cross section of bone/implant and corresponding adaptive mesh and modeling error

minimizes the modeling error.

6.3 Time/ Load dependent Models for Trabecular bone

We have also started an effort to construct models for long term behavior of bone implant systems using finite elements and appropriate constitutive laws for modeling bone behavior. A simple time and load dependent beam based model of trabecular bone structure developed by Guo et al. [14] has been implemented as a first step. This model attempts to simulate fatigue and creep in human trabecular bone. The analysis is being done currently with 2-D frames but this technique can form the basis of a more general 3-D study. Also being simultaneously developed is the software for the analysis which could be used for similar studies on different bones in various loading situations. The trabecular bone specimen is modeled as a 2-D honeycomb structure made up of an array of hexagonal cells. Fig. 4a. shows an example of such a geometry. Each trabecula is considered a linear elastic frame element i.e. a combination of a rod and a beam. Initial microcracks are assumed to exist in the trabeculae and grow according to the Paris law with each loading cycle. The crack distribution is governed by a random beta distribution function. Once the crack reaches a prefined threshold size, the trabecula is removed from the structure, thus weakening it. When the stiffness shows a 10 % drop, the structure is assumed to fail. Fig. 4b. indicates the response of a simple 2-D frame assembly for such problems. We observe the dependence of loading on time to failure. We are currently developing analogous models that use 2D elements instead of the beam structure. The cost of the computation which is quite manageable in this setting will be much larger for the 3D setting and render the simulation undoable without some of the developments that will be the subject of this study. The crack growth laws used need to be tuned with experimental data on bone loss to be effective. Regrowth of bone may also be modeled by adding trabeculae at some predetermined rate.

.

7 Test Set-up for In-Vivo Loading of Dental Implant

In the next three sections we describe a study for animal testing to complement the analysis. The results obtained from this analysis will enable us to tune and validate the analysis. First we describe the test set-up for in-vivo loading. We follow up with the description of the surgical procedures to be used and then the radiography and other imaging processes for data collection. The animal model

Figure 4: Model of trabecular bone and effect of load levels on the number of cycles to failure

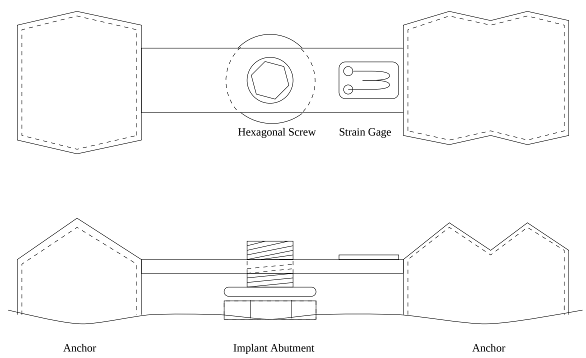

Figure 5: Preliminary Design of Intra-oral Loading Device

will give use a set of informations that will make possible the relation between the in-vitro data obtained from the FEM study portion of this project with the histological and radiological findings, that is where bone loss will occur according to the FEM analysis, will be compared with the true histological findings obtained after loading the implant with a know, calibrated force. Also, the same findings will be compared to the radiographic analysis. The bone loss, visible radiographically, should confirm the area of highest stress resulting from the FEM study.

7.1 Fabrication of the intra-oral loading device

Alginate impressions will be used to capture the dental anatomy and create study models of the teeth and tissues. Custom trays made of acrylic will be fabricated on the study models and subsequently used to take a stable and accurate poly-vinyl-siloxane (PVS) impression. These final PVS impressions will be poured in gypsum dental stone which will be used for articulation and design of the device. Re-pouring the PVS impression with phosphate bound refractory investment will yield the working models used to fabricate the device. Wax and plastic patterns will be used to create the geometry of the 'bridge' and subsequently invested using standard dental investment techniques. Burn out of the wax and plastic will yield a mold which will be used to cast the device in a suitable alloy.

The next steps are to retrieve the metal casting and subsequently finish and polish to an acceptable surface finish not to harbor any bacteria. A hole will be tapped over the location of the implant and a hex screw will be fitted. A strain gage will be affixed to the surface of the bridge to allow indirect measurement of the applied force to the implant. The appliance is now ready for static testing and calibration with subsequent cementation into the beagle's mouth.

7.2 Procedure for calibrating the loading device

Using elementary beam mechanics, equations have been derived to predict the strain at the location of placement of the gage and this will correspond to an applied load. The final device will be rigidly attached to a test stand in an ambient environment of 37^0C which can measure the applied load and the corresponding strain. Any deviation from the theory will be used to calculate a correction factor. We are calibrating for temperature of the test environment, the resistance due to test wires, and any geometry deviation.

7.3 Procedure for loading the device and recording the data

The cemented device, with great accuracy, will allow measurement and transfer of load to the implant. A predetermined load of 0.784 N (80.0 grams force) will be applied periodically to the implant. A constant load will be place for 10 minutes each daily for 3 months. Procedure; First clip in the measuring wires to the strain gage and connect to the measurement equipment. One person will monitor the output of the strain gage and the second person will tighten the hex screw until the predetermined strain is achieved. The clips are removed and timing of the load interval will begin. After 10 minutes the load will be removed by loosening the hex screw. Each loading event will be documented to include the time of the day, strain measured, and duration of the applied load.

8 Animal Study

Rationale. The animal study will give us the possibility to test in vivo what it has been postulated in vitro. Furthermore, the in vivo loading study with the strain gauge and the experimental bridge, the histological apsects and the sequence of radiographs, will enable us to correlate all the aspects of the study.

8.1 Surgical Procedures

Four young male Beagle dogs (approx 1 year old) will be used in this study. Study will be done after approval of the protocol from the University of New York at Buffalo Institutional Animal Care & Use Committee. Animals will be checked for physical examination and full dentition, and kept in quarantine for one week prior to the entry in the study. On day O, the dogs will be premedicated with Acepromazine (0.2 mg/kg body weight) and Athropine (0.02mg/Kg body weight). After 30 minutes, general aneshesia will be induced with Telazol (0.1cc/10lbs body weight, I.V.) and intubation with Isofluothane gas (1-3At this time, local infiltration with Xylocaine and 1:50.000 Epinephrine will be injected in the buccal fold of the mandible, in the premolar and molar region. An impression will be taken with Poly-Vinyl-Syloxane Impression Material of both arches. These impressions will be subsequently poured and a cast model prepared. The model will be then used to prepared a custom made tray. After the impression is checked for precision, all mandibular premolars, including the Ist, IInd, IIIrd and IVth premolar will be extracted. Teeth will be first hemisectioned in the mid-portion of the crown in a corono-apical direction and after complete separation of the mesial root from the distal root, one root at the time, with a rotation movement will be extracted with dental forceps. During the extraction, attention will be paid not to damage the alveolar crest as well the interradicular bone septum. Per each socket, alveolar bone width and height measurements will be taken with a sterile periodontal probe and a sterile caliper. Reference points will be the Cementum-Enamel Junction (CEJ) of the Canine and First Molar, respectively adjacent to the extraction sockets. This measurements will be used as a guide for the proper length of the implants to be placed later in the study. After the extraction will be completed, one side at the time, two vertical releasing incisions will be done buccally, and the flaps coronally repositioned and sutured with a simple loop suture with Black Monofilament Nylon 4-0 suture material (ACE Surgical Supply Co., MA) so as to be able to cover the extraction sockets with soft tissue, to expedite healing. Dogs will observed until full recovering from the anesthesia will occur. The animals will be put on a soft food diet, not to dislodge the flaps. They will receive systemic antibiotics and antiinflammatories to control for post-operative infection and pain, as surgical standard procedures indicate, in relation to their body weight. The animals will be monitored for vital and behavioral signs, to indicate any discomfort. One week later, the dogs will be sedated, the sutures removed and a new impression using the custom-made trays previously prepared will be taken. Depending upon the healing stage, the dogs will be fed with normal hard dog food. Paramenters such as body weight and behavioral modification will be monitored routinely.

8.2 Implant Placements.

Using the model obtained, a custom made radiographic film holder will be fabricated, for each mandibular side for each dog. These labeled film holders will be used later in the study to take standardized radiographs to be used for the subtraction radiography technique as described by Hurzeler et al [17]. Three months after extractions, animals will be sedated and anesthetized as previously described. Intraoral radiographs using the custom made film holder and regular intraoral periapical radiographic films (Size 4, Kodak, Rochester, NY) will be taken and immediately processed and developed and analized for bone quality, variations and indicative dimensions. Then, full thickness flaps will be raised both buccally and lingually in the edentulous areas. Surgical application of two Sustain(r) Screw Type Root Form Dental Implants (Lifecore Biomedical, Chaska, MN) will be inserted according to manufacturer indications. The sites will be prepared according to standard surgical procedures. After exposure of the mandibular edentulous bone, the sites will be prepared using standardized burs mounted on slow speed hand piece activated by a surgical motor, under copious sterile saline irrigation. The interactive bridge previously described (section 7.3) will be used as surgical guide for placement of the test implant. A sequence of a pilot drill bur followed by burs of increasing diameter will be followed, until to reach the chosen site depth dictated by the bone height, showing on the radiograph previously taken. For all implants, a standard diameter of 3.3 mm will be chosen. A manually activated torque limiting ratchet of 20 N will be used to finalize the final position of each implant. The second implant will be placed respecting the required minimal distance of 7 mm between the centers of each implant, measured form the first implant. Also, the screws will be inserted in the alveolar bone with the coronal part or neck of the implants extruding of about 2 mm from the bone ridge. At this time the cover screw of each implant will be screwed on the head of the implant. Clinical measurements, that is the distance of the edge of the cover screw to the bone crest, as well as the width of the mandible at the implant site will be taken, beside the same measurements taken immediately after extractions. The flaps will be repositioned and sutured as above described, to fully cover the implants. At this time the appliance fabricated in the dental laboratory will be definetively cemented to the two abutments, respectively, the canine mesially and the first molar distally. Radiographs will be taken at this time. The dogs will receive post-operative care, including observation of vital signs, systemic antibiotics and anti-inflammatories.

8.3 Soft and Hard Tissues Healing .

The dogs will be monitored daily, to control for any distress and behavioral modification. Gently, daily the wound sites will be brushed with a Toothette Sage 6000 (Sage Products Inc., IL) soaked in Chlorhexidine 0.12The diet, during the soft tissue healing time will consist of soft food. After suture removal, hard food will be given. Four weeks after implant placement, a set of radiographs will be taken. At this time the areas containing the implants will be analyzed. All the implants heads will be surgically exposed, if needed. The loading screw will be applied and the force applied will match the one established by the FEM studies. To notice that only one implant per site with be subjected to loading, while to non-loaded one will serve as control. The loading screw will remain in the "loading" position for 10 minutes as described in the section 7.3. The animals will receive a full mouth toothbrushing 5 times a week with a Medium Hardness Tooth Brush (Butler 401). The screw will be activated regularly every week for a period of 3 months. At each month, a new set of radiographs will be taken following the methods and the materials previously described.

8.4 Block Sections Harvesting and Histological Technique.

At the end of the three months of loading period, the animals will be sacrificed with an overdose of sodium penthobarbital. The mandibular section containing the implants and the bridge will be dissected and freed from muscular attachments. By means of a Stryker Orthopedic Oscillating Saw, a block section containing the implants will be harvested and immersed into a fixative solution containing 10the loaded and the non-loaded, will be prepared. Subsequently each block section will be cut into two halves following a mesio-distal direction along the corono-apical long axes of the inplant, so to have exactly two halves of both implant and surrounding bone. One half will be processed for decalcified histological analysis and the other half for non-decalcified histological analysis [29].

8.5 Histological and Radiographical Data Analysis.

After processing for both decalcified and non decalcified methods, the halves will be prepared to be observed for light microscopy (decalcified sections) and SEM/Back Scattered imaging Analysis. Morphometric Measurements will be taken, from the most coronal part of the cover screw, the the most coronal level of mineralized bone. This measurements will be compared with the clinical measurements, to observe any bone height changes, keeping the hard implant surface as reference point. Data from both microscopic morphometric measurement will be compared to identify any areas of bone loss or absorption. Contemporarily the radiographs will be examined by Subtraction Radiography Analysis. This technique allows for determination of bone mass loss or gain. Briefly, each radiograph image is taken by a video camera and memorized by a computer provided with software developed for this analysis. Each image of the same site will be taken, and ideally overlapped by the computer program. The software will allow to identify , by overlapping the images, areas of bone resorption and apposition along the implant perimeter. The data so obtained will compared to the histological data, and ultimately related to the FEM data.

References

[1] M. Ainsworth , J. T. Oden,"*A Posteriori Error* Estimators, *Computational Mechanics Advances, Computer Methods in Appl. Mech. and Engg.* , 1997.

[2] T. Albrektsson and H. A. Hanson, " An ultrasound characterization of the interface between bone and sputtered titanium or stainless steel surfaces", *BIOMATERIALS* 1986; 7; 201-205.

[3] T. Albrektsson and M. Jacobsson, "Bone-metal interface in osseointegration", *The J. of Prosthetic Dentistry* May, 1987; 57;597-607.

[4] R. Adell, V. Leckholm, B. Rockeler, and P. I. Branemark, “A 15 year study of osseointegrated implants in the treatment of the edentulous jaw”,*Int. J. Oral and Maxillofacial Surg.* 1981;10;387-416

[5] J.B. Brunski, “Avoiding pitfalls of overloading and micromotion of intraosseous implants.” Dental Implantology Update 1993;4:77-81.

[6] J. Brunski and A. Prabhu, Research Projects and Publications Web Page http://www.rpi.edu/ prabhu/publication.html

[7] C.L. Bottasso, M.S. Shephard, “A Parallel Adaptive Finite Element Euler Flow Solver for Rotary Wing Aerodynamics” SCOREC, Report 1995-10, Rensslaeer Polytechnique Institute.

[8] P. I. Branemark, B. O. Hanson, R. Adell, U. Breien and J. Lindstroom, “ Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10 year period”, *Scand. J. Plast. Reconstr. Surg.* 1977;11;Suppl 16.

[9] S. C. Cowin, ”The Mechanical Properties of Cancellous Bone” in Bone Mechanics, ed. S. C. Cowin, CRC Press, 1989.

[10] S. C. Cowin, A. M. Sadegh and G. M. Luo “An evolutionary Wolff’s Law for trabecular architecture”, *J. Biomech. Engg.*, vol 114, pp. 129-136.

[11] C. R. Culliton, M. A. Meenaghan, S. E. Sorenson, G. W. Greene and J. D. Eick, “A Critical Evaluation of the acute system toxicity test for dental alloys using histopathological criteria”, *J. of Biomed Materials Research*, 15:565-575, 1981.

[12] K. D. Devine and J. E. Flaherty, “A Parallel Adaptive hp-Refinement Finite Element Methods with Dynamic Load Balanci for the Solution of Hyperbolic Conservation Laws”, SCOREC, Report 1995-14, Rensslaeer Polytechnique Institute.

[13] Y. C. Fung, “Biomechanics”, Springer Verlag, New York, 1993.

[14] Xiang-Dong Guo,Thomas A McMahon,Tony M Keaveny,Wilson C Hayes and Lorna J Gibson, “Finite element modeling of damage accumulation in trabecular bone under cyclic loading”, , J.Biomechanics vol. 27, No.2,pp 145-155,1994

[15] R. T. Hart, ”Computational Techniques For Bone Remodelling”, in Bone Mechanics, ed. S. C. Cowin, CRC Press, 1989.

[16] S.J. Hoshaw, J. B. Brunski, and GVB. Cochran “ Mechanical loading of Branemark implants affects interfacial bone modeling and remodeling.” Int J Oral Maxillofac Implants 1994: 9:343-360.

[17] ”Natural and Living Biomaterials”, ed. G. W. Hastings and P. Ducheyne, CRC Press, 1984.

[18] L. C. Hartman, M. A. Meenaghan, N. G. Schaaf, and B. Hawker, “Effects of Pretreatment Sterilization and Cleaning Methods on Materials Properties and Osseoinductivity of a threaded implant”, *Int. Journal of Oral and Maxillofacial, implants*, 4(1):11-18, 1989.

[19] M. B. Hurzeler, CR Quinones, P Schupbach, JM Vlassis, JR Strub, RG Caffesse, “Influece of the supra-structure on the peri-implant tissues in beagle dogs, Clin. Oral Implants Res 1995; 6(3):139-148

[20] H. J. A. Meijer, F. J. M. Starmaans, W. H. A. Steen and F. Bosman, "A Three Dimensional Finite Element Analysis of Bone Around Dental implants in an Edentulous Human Mandible", *Archs. Oral Biol.* vol. 38 no. 6, 491-496.

[21] M. A. Meenaghan , J. R. Natiella and J. R. Armitage, and G. W. Greene Jr. , "Evaluation of Endosseous Metal Implant sites in Rhesus monkeys: with special reference to fluoroscence microscopy to study the in vivo distribution of newly forming bone. *J. of Biomat. Med. Dev. Art. Org.* 1(3):481-498, 1973

[22] M. A. Meenaghan, T. W. Budd, K. Nagahara and K. L. Bielat and N. G. Schaaf, "Funtional Response between Intra-osseous implant and Bone: changes at the implant bone interface under occlusal force", Proceedings of Symposium of Japanese Society of Oral Implantology, 5(2):103-112, 1992.

[23] K. Nagahara, K. Mouri, H. Kanematsu and M. A. Meenaghan, "An in vivo evaluation of an osteoinductive implantable material produced by psteoblastic cells in vitro" *Int. J. of Oral and Maxillofacial implants*, 9(1):41-48, 1994.

[24] A. Patra, J. T. Oden, "Computational Techniques for Adaptive *hp* Finite Elements", to appear in *Finite Elements Applications in Design*

[25] A. Patra, "Parallel Adaptive *hp* Finite Elements For Viscous Incompressible Flows", *PhD Thesis*, University of Texas-Austin, June, 1995.

[26] J. T. Oden and Abani Patra, "A Parallel Adaptive Strategy for *hp* finite element computations", *Comput. Methods. Appl. Mech. and Engg.*, vol. 121, 1995.

[27] A. Patra, J. dePaolo, K.S. D'Souza, D. de Tolla, and M. Meenaghan, "Analysis and Redesign of Dental Implants", Implant Dentistry, vol .7, no.4, 1998.

[28] A. Patra and K. Max, "Adaptive Homogenization and Mesh Refinement For the Control Of Numerical and Modeling Errors" submitted to *Comput. Methods Appl. Mech. Engrg.*

[29] G. Pecora, S. Andreana, J.E. Margarone, D de Leonardis, A. K. Garg, U. Lattanzi, P. Bush, "In vivo study of bone-implant contact on smooth versus rough surfaces", American Academy of Osteointegration, Annual Meeting, San Francisco, March 1997.

[30] M.R. Rieger, M. Mayberry and M. O. Brose, "Finite Element Analysis of six endosseous implants", *Journal of Prosthetic Dentistry*, 1990, vol 63, pp 671-6.

[31] A. A. Rizzo, "1988-Proceedings of the consensus development conference on dental implants", *J. Dent. Educ.* 1988;52:692-695.

[32] T. I. Zohdi, J. T. Oden and G. J. Rodin, "Hierarchical modelin g of heterogeneous bodies", *Comput. Methods Appl. Mech. Engrg.* 138 (1996) 273–298.