Carlos Nelson Elias

Historically, and by definition, Dentistry is a profession belonging to the health sciences, which takes care of human health, studies and treats the stomatognathic system, comprising the face, neck and oral cavity, including bones, masticatory muscles, joints, teeth, tissues, vessels and nerves.

Engineering is a profession that is part of the exact sciences, to acquire and apply mathematical, scientific and technical knowledge in the creation, development and implementation of utilities, such as materials, structures, machines, devices, systems or processes that perform a particular function or purpose. In creation processes, development and implementation, Engineering combines many expertise in order to enable the utilities, taking into account society, technology, economy and environment.

As in Dentistry, Engineering is also a very comprehensive science, comprising a range of more specialized branches, each one with a more specific emphasis on certain fields of application and certain types of technology.

In Brazil, over the past 20 years of osseointegration, it has been observed a marked and growing association between these two distinct areas, making Dentistry and Engineering to exchange information and use cross-terminologies to name, define and better understand some classic phenomena widely studied in literature.

Dental Press Implantology brings to this interview one of the greatest scholars, competent professional and responsible for this healthy interaction: The Metallurgical Engineer, MSc and PhD in Materials Science from the Military Institute of Engineering (IME), a scientist and researcher, Prof. Dr. Carlos Nelson Elias. He discusses various issues related to the Brazilian Dentistry and contemporary Implantology, where he has played an important role and still participates decisively in the development of materials, designs and surfaces of implants used in the national market. An enlightening exhibition revealing the great history of osseointegration in Brazil.

He is, currently, an Associate Professor of IME, twice selected as "Scientist of the state of Rio de Janeiro" (2004 and 2008), a researcher at the Research Foundation of the State of Rio de Janeiro (FAPERJ) and fellow researcher level 1C of the National Council for Scientific and Technological Development (CNPq). Dr. Carlos Nelson Elias is also collaborator of the courses of Orthodontics – UFRJ, Endodontics – UERJ, Metallurgy – UFF and Endodontics – Estácio de Sá. He has experience in Metallurgy and Materials Engineering, with an emphasis in Physical Metallurgy, working on coronary stents, dental materials, development of dental implants, surface modification of dental implants, endodontic instruments, orthodontic appliances, coloring of titanium and simulation.

Our interviewee has 185 articles published in scientific journals, one book, 17 book chapters, 230 papers presented at national and international conferences, 40 from MSc and 14 from PhD. Consultant of the journal Acta Biomaterialia, American Journal of Orthodontics, Clinical Implant Dental Research, Implant News, Indian Journal of Dental Research, Journal of Biomedical Materials Research Part B, Journal of Mechanical Behaviour of Biomedical Materials, Journal of Nanomedicine, Materials Research, Materials Science and Engineering: C, Revista Brasileira de Engenharia Biomédica, Revista Gaúcha de Odontologia, Surface and Coating Technology. Besides having a patent application in the Brazilian PTO, related to the surface treatment of implants.

With this vast experience, it is common to hear in the background of the Brazilian Implantology that the recognized researcher and professor Dr. Tomas Albrektsson (University of Gothenburg) is to Sweden and to the world as respected as the researcher and professor Dr. Carlos Nelson Elias (Military Institute of Engineering – IME) is to Brazil and to the world. Science and research are thankful to them!

Luiz Rogério Duarte

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Your basic graduation is in Engineering. What is the sub-area and how did you began working with Dentistry?

My graduation is in Metallurgical Engineering with MSc and PhD in Materials Science.

After the doctorate (1990) I was invited to be a teacher in the Militar Institute of Engineering (IME) and minister the discipline "Failure analysis of materials". At the end of this course, students presented an experimental work. When defining the work for the students, an endodontist came to the IME (Dr Hélio Pereira Lopes) with a fractured endodontic instrument. Dr Hélio wanted to know the cause of the fracture. I forwarded the mission to the best student in the class. My surprise was that the explanations and mechanisms involved in the failure of the Gates bur were similar to an axis of a tank, with a diameter of 2 inches. This intrigued me and I did the work myself to check. The conclusion was that the failure mechanisms of materials are similar and independent of the size of the piece. This happened 22 years ago and even today Dr Hélio conducts researches in the IME every Wednesday.

We got used to hearing comments that you are almost a dentist. How do you, Sir, see this statement and how did you got used to so many different terms from the fields of Orthodontics, Implantology and Dental Prosthesis?

Being almost dentist is a joke from my friends. Dentistry is much more complex than engineering. For example, students, when they get in our laboratory to do some mechanical testing, they bring 30 samples. It's hard to convince them, as well as their supervisors, that in the materials area the "N" is 5. The behavior of materials is predictable, while the predictability of the performance of the organism involves variables which have no control. Here is the beauty of Materials Science, to develop biomaterials that have predictable interactions with the organism. We are no longer making adjustments to the materials used in other areas. The titanium alloy itself was developed to another area and is widely used as a biomaterial.

As for the different terms, I and Dr Hélio talked over 2 years without understanding each other. Yet it is still difficult to accept some terms like "shear bond strength", "brittle", "wire gauge" and others.

When did your involvement begin in the production of implants in Brazil? What is your participation in this governmental policy of industrial technical development?

The beginning of my activities in implant was not planned. Dr José Henrique Cavalcanti introduced me to Dr Rodolfo C. Alba 18 years ago (Conexão Sistemas de Prótese). On the occasion, Dr Rodolfo produced prosthetic components, wanted to produce implants and had many problems with the production process.

The first job was to develop an Au-Pd alloy for screws. Using the phase diagrams was possible to select the color and chemical composition of the alloy. This alloy is still used to make the connection gold screws for prostheses. The second work that I received from Conexão seemed to me very simple: "Washing implants and removing manufacturing oils". When I started studying dental implants I found that the problem was complex and the surface could not have any contaminants influencing the success of treatment. To solve the immediate problem and save some time, we used carbon tetrachloride. This material requires a lot of care when using it and its use was ceased soon after we develop another method, which is used nowadays.

The first works occurred in an era when the imported implants prevailed in the national market. Some practitioners had a craft production with low quality. We cannot deny that the company Conexão was a major responsible for the development of the national market. Since the first congresses, there has always been the participation and interaction of teachers and users of all systems. The goal has always been to "develop the national market with quality."

Considering that Conexão was one of the first companies to manufacture implants in Brazil on an industrial scale and I participated in this challenge, I admit that I had a small part in the development of the market. After my participation in the industrial production, they started sending me invitations to seminars, conferences and participation in ABNT to create the technical standards. These activities allowed the transmission of new concepts, so far ignored by professionals.

Militar Institute of Engineering – Rio de Janeiro, Brazil.

In how many graduation courses do you work as a collaborator today? What is your work routine at the IME?

I do not know the number of post-graduation courses that I cooperate. Many students come to me and I do not know their origin. Students showing interest in researching, developing scientific knowledge and not just doing a job for a diploma will always be welcome.

I work at the IME as a teacher in Biomaterials but I have to make many trips to attend courses, seminars, conferences and demand of resources for research. In 2011 there were 34 trips, working about 50 hours / week to monitor the work of our dentists students from MSc and PhD in Materials Science.

Talking specifically about implants, how do you see the quality of evaluation of these products by the companies? What methods of control does the dentist have on these products in terms of market and government?

Firms have great difficulty in the analysis of their products. This is due to the lack of qualified laboratories and costs of analyzes. Only the best companies make the product evaluation for validation and registration at ANVISA. Some companies refuse to provide products for studies or they do not request proof test, fearing there will be information transfer to other companies. Among researchers there is an ethic in which the results of the work belong to the company concerned and cannot be disclosed without permission. Still, when we analyze the implants from major national companies we have observed that some present similar quality to the imported implants.

Professionals find it difficult to assess the quality of implants since there is the need for electron microscopy.

Indirectly, the quality can be evaluated by the product presentation, visual finish, with adaptations components, surgical instruments resistance and ease to handle. Also, making records and monitoring of patients.

The implant surfaces development is much studied by companies in terms of marketing. How to assess whether the product really works the way it is said?

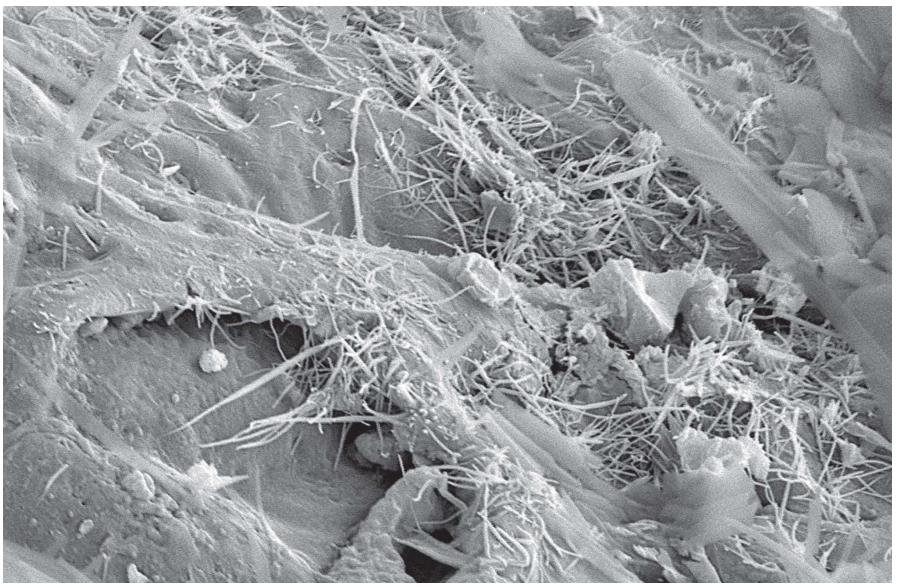
The surface treatment is one of the parameters used as company marketing since it is essential in the selection of surgical technique, site of installation and for osseointegration. The quality evaluation can be done by controlling the rate of success and analysis of causes of errors, except the spurious losses due to the product. The company itself has an interest in these data.

We know that you have developed a surface that has shown excellent results. How was the experience and how long did it take to be on the market?

The development of surface treatments involves *in vitro* and *in vivo* trials. We begin by selecting the treatment methodology (acid-etching, abrasive blasting, anodizing, particle deposition or combination). After obtaining the samples of different treatments it is made the surface analysis in a scanning electron microscope (SEM) for selecting the treatment conditions that showed the best roughness, homogeneity, cavities size and other parameters. Based on the experience gained over the years, through the SEM image it is possible to know whether a particular surface have or not properties suitable for osseointegration. Following, we cultured cells (osteoblasts, fibronectin, etc.). The last step requires the cooperation of surgeons to animal testing. We repeated the tests with guinea pigs at least 3 times to guarantee the results. The development takes about 5 years. The last phase is the clinical proof which is controlled by the company. At the end of all this process, comes the frustration knowing that another company made the commercial launch already.

You are a senior researcher of CNPq. What is the importance of this fact in your research? Do you, Sir, have had support in this regard?

I am a level I researcher at CNPq. To be held in this position there is a curriculum evaluation by the partners. Less than 10% of researchers have this classification. Being level I does not have big advantages since we have to take more students, publications, projects, the responsibility to evaluate about 25 projects per year, reviewing the work of dozens of different



Interaction of osteoblasts with titanium surface.

scientific journals and worse, CNPq refuses to help the participation in international congresses.

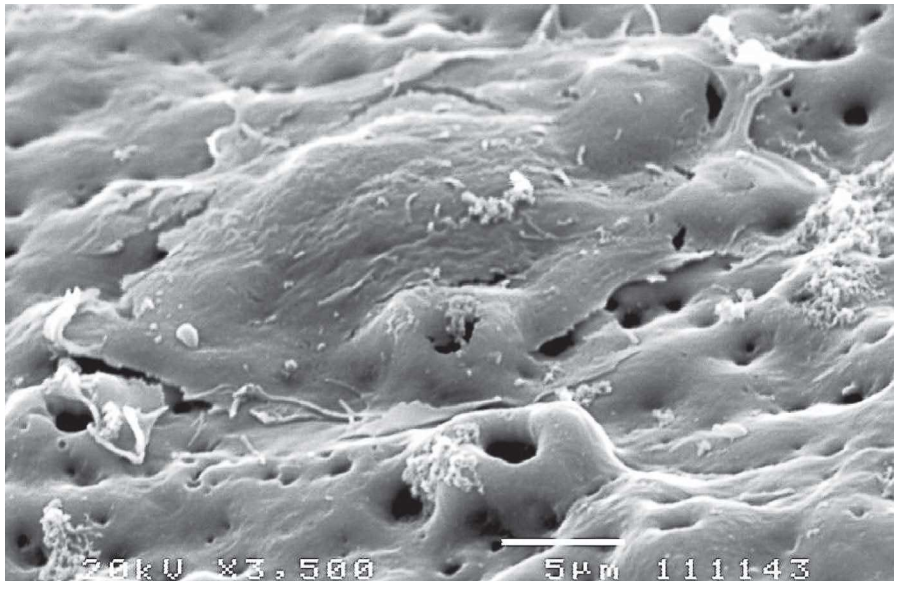
The advantage is that government agencies promoting research (CNPq, CAPES, FINEP, FAPERJ) consider the curriculum as an assessment item of the project to obtain resources.

What lines of research currently occupy your department? Is there a new trend that could influence the market?

In the EMI we have MSc and PhD in Materials Science. The course is free and most students have scholarship. Several dentists students who had attended our courses are in prominent position in universities. Nowadays, we have dentists working in Endodontics, Orthodontics, Prosthodontics, Periodontics and with implants. The works involve the characterization of materials and products, as well as development of biomaterials. All teachers in the Program of Materials Science at IME do research with dual application. Today we have researches on metals (implants and Ti, Cr, Co and Inox prostheses), polymers (biodegradable and bioabsorbable), ceramic (bioglasses, synthetic hydroxyapatite, scaffold) and composites (adhesives with nanoparticles).

Currently, our chief concern is to set the proper torque for implant placement. This work is developed with the guidance of Prof. Paulo Perri de Carvalho, which is consistent with the idea that the implant installation does not require high torques. The installation torque should be enough to get primary stability. High torques can increase the primary stability but the result is not worth the injuries to the bone and the implant. Excessive torque compresses the bone, reduce the local blood vascularization, creating cracks in the bone and require more time for osseointegration.

We are used to hear that all imported product are better than the national ones. Regarding dental implants, do you agree with this statement?



Osteoblast during cell spread contacting the surface of the implant.

No. There are Brazilian companies that offer excellent products. I've done consulting for an European company, which to reduce costs changed the manufacturing process, did not analyze the influences on product quality and had significant increasing in implant loss. So there are good products in the national and international market, as well as low quality products. Professionals should be aware of the company's infrastructure, monitoring quality control of products, whether there are investments in research, qualification of assessors, publications with

reputable scientific evidence and developments. Companies encourage visits to their facilities and provide the information permitted to evaluate.

How many theses have you oriented? What areas does your research cover today?

I have oriented 40 master students and 18 doctoral students. For being an army officer I worked with shields and explosives until 1994. From this date on, only in the biomaterials area. This work resulted in 240 publications in journals and 280 conference presentations. Biomaterials researches involve applications in dentistry, cardiology and orthopedics. I try to do basic research that can be harnessed for the development of products. In most cases there is participation of companies.

What is your experience about nanotechnology? Do you believe that this level of greatness can improve cell behavior regarding to osseointegration?

It is defined nanometric dimensions as those having size less than 100 nanometers. When making the implant surface analysis it shows that all have some characteristics with nanometric size. The difference is in the fact that this feature arose due to treatment with the goal of obtaining morphology with micrometer dimension or is derived from a specific treatment to create nanoscale features. Even the machined implant surfaces and with no treatments have nanoscale microcavities. There are implants which are processed to form nano surface roughness and others with deposition of nanoparticles in the surface (hydroxyapatite and other phosphates). These implants present some evidences that the surface improves the healing process and differentiation of mesenchymal cells. The explanation is not yet known, it was only found, because there are several researches on this topic.

What countries dominate the titanium processing technology as raw material? What is Brazil's position in this area?

The development of titanium occurred for applications in the military area (fighter aircraft and military weapons). Therefore, only warlike countries (United States, Germany, France, Britain, China and Russia) and Japan dominate the production of titanium metal.

In spite of Brazil having several deposits of titanium ore to produce titanium oxide in particulate form, it does not produce metallic titanium. The main Brazilian titanium ore mine in exploitation is located on the northeastern coast, right on the coast of Paraíba, immediately south of the border of the Rio Grande do Norte state, in a place called Guaju, in the county of Mataraca, approximately 125 km from João Pessoa. Around 95% of global exploitation of deposits of titanium ore is consumed by the pigment industry. The titanium pigment has high whiteness power, covering, brightness and opacity, being superior to other white pigments, such as lead carbonate, sulfates of barium and zinc, and zinc oxide. The pigments in particulate titanium oxide are used in the plastics, rubbers, textiles, inks, leather, paper and cosmetic.

Is titanium difficult to machine? What influence does this item have on the final quality of the product?

Titanium has a hexagonal crystal structure and this makes it difficult to be deformed and cut. During cutting, tools pluck pieces of titanium without cutting it. Plus, titanium has exothermic reaction when in contact with oxygen and during machining of implants there is the need of much cooling with special oils to prevent fire from lathes. All these factors make it difficult to machining, the surface finishing and manufacturing of implants.

We have young talent in research, as Prof. Luiz Meirelles (University of Rochester - USA) who ended up living and working abroad. Do you think that Brazil loses important manpower by not opening space for these people?

Our manpower market is big, with lack of qualified people to work. Only in 2011, CREA allowed up to 20,000 engineers to work in Brazil. On the other hand, there are some people like Prof. Meirelles, who are extremely skilled in one area and find it difficult to be placed. Brazil has a high investment in training doctors abroad and we don't take this people back. The cost to train a doctor abroad is approximately U$50,000.00. Universities take the largest number of doctors. Only big companies hire doctors to research activities, since other industries are unaware of the potential of doctorate professionals and employ them in other functions.

Zirconia became a headache in the esthetic cases in Implantology. What level of knowledge do we have to believe in the durability and strength of this material?

For 15 years zirconia was used in orthopedic prostheses and it presented some problems. Many researches were made and it was found that the purity, particle size and process influence the degradation of zirconia. Based on these results all the processing and the raw material were changed.

For the use of zirconia in dental prostheses there are certain limitations, mainly the thickness of the prosthesis, the size of the connectors, cantilever arm of multiple prosthesis, and the more critical one: hardness of the material. Moreover, it is observed the occurrence of chipping of the ceramic coating. We still have some problems that hinder its use in esthetic areas.

To work with zirconia is needed specific expertise from professionals. The preparation of zirconia and behavior is very different from alumina that is dominated by the prosthetic and prosthetists.

You were also recognized for your mathematical explanations about the biomechanics affecting dental implants. What is the most important on this premise: The theory or practice?

The performance of implants can be predicted by applying the concepts of biomechanics. All our implants developments are started by finite element simulations. In the simulations we employ the same equations that control the phenomena of metallic structures known for decades. Through these mathematical equations it is possible to determine the maximum resistance of implants and components, changing geometries and propose new ways. After the simulations, prototypes are produced for testing and validation of mechanical simulations.

Despite all this effort and conditions assumptions with critical loads, there are still cases of fracture implants. We found that the shapes of implants undergo changes, and surgical techniques, as well as prosthesis planning remain unchanged. For each new implant, training is necessary for the correct use.

In this context, the theory must be supported by the clinic. The theory provides the appropriate data that sometimes are not feasible in clinical application.

Returning to the surfaces of implants, how is the industrial processing of them? Do companies acquire this knowledge or outsource this service? Is there some sort of ANVISA control over them?

Most companies acquires the methods of surface treatment of implants. Few outsource or develop these treatments. When the company control this process it defines in detail the steps to be followed and validates the methodology. With the generated documents it requests the registering. ANVISA controls the company's infrastructure, analyzes the description of the treatment methodology and the existence of process and employees validation but does not analyze the quality of the final product.

Most Brazilian companies use surface treatments already recognized internationally by other companies. Does the type of surface treatment, alone, ensures the roughness pattern obtained?

If there is process validation and complete observance of treatment methodology, all implants of the same company have a high probability of being similar. This is not enough, though. The process may be standardized at the company, but the characteristics of morphologies may be not the most appropriate. Just because the company uses a particular treatment process, for example, acid-etching, it does not mean that the surfaces of the implants are similar. Companies use different acid, concentrations, time and temperature. Again, it is important to conduct research and clinical evidence.

Prof. Tomas Albrektsson and Prof. Carlos Nelson Elias during XIV CIOBA in Salvador – Brazil, (2006).

Studies have shown that the surface roughness with a S_a between 0.85 and 1 µm would be ideal for bone repair and this finding is not well spread by companies, in general. How to know if we are making use of an implant with this roughness?

In the past machined implants were marketed and coated with plasma spray. The firsts had a roughness around 0.75 µm, anisotropic surface and machining marks. The latter had higher roughness, around 2.5 µm, which does not influence the behavior of cells and were also removed from the market. The two surfaces had major limitations for employment for not having adequate roughness; were not suitable for low density bone or immediate loading. Research has shown that treatments with acid-etching or abrasive blasting create roughness around 1.0 µm. The difficulty is to get the same homogeneity and roughness over the surface. The best implants have surface roughness in the range mentioned, from 0.85 to 1.0 µm.

To find out the efficiency of the surface, the professional must be based on scientific publications of products, more than in marketing documents.

What is the real influence of a suitable surface treatment in non-standard cases, such as: Short implants and grafting area?

The surface treatment influences the primary, secondary and tertiary stability. After osseointegration, implants with treated surfaces are capable of oral load

distribution more efficiently. This is very important as in critical situations for short implants, regenerated bone sites and in patients considered critical.

What is already proven on the effect of nanostructures in accelerating and improving the repair process?

There are only proofs that it improves performance, but it is still lacking explanations of the mechanisms involved in the process of osseointegration.

How about the incorporation of ions on the surface or even its polarization?

This is proven. The incorporation of phosphate nanoparticles, atoms of Ca, P, Mg and F improve the biocompatibility of titanium. Treatment of polarization, also known as anodization, electrochemical and oxidation, allows the incorporation of any type of particle on the surface of the implant to increase its efficiency.

As an expert in biomaterial, how would you classify titanium? Biocompatible, inert or bioactive?

There are two classifications of biomaterials regarding the biological behavior. The first one classifies them as biotolerant, bioinert and bioactive. The second classifies biomaterials in bioinert, bioactive and bioreactive.

The apparent discrepancy in the terms used in the classification of biomaterials does not exist. The two classifications are equivalent. A biomaterial considered biotolerant (stainless steel alloys and Co-Cr) is considered as bioinert in the other criteria. Titanium is considered bioinert in a classification and bioactive in the other one. The most important thing is the criteria used to classify biomaterials.

Biotolerant or bioinert: The implants are separated from the adjacent bone by a layer of soft and fibrous tissue. It is not observed contact in osteogenesis. Almost all synthetic polymers and the vast majority of metals and ceramics observe this category. Examples: gold, Co-Cr alloys, stainless steel, zirconia, alumina, polyethylene, polyamide, polymethacrylate, polytetrafluoroethylene and polyurethane.

Bioinert or bioactive: The implants are in direct contact with bone cells, with participation in osteogenesis. Despite not observing a chemical reaction between the implant and bone tissue, occurs the connection with the biomaterial and bone cells, characterizing osseointegration. Among these biomaterials, it is highlighted the commercially pure titanium, tantalum and niobium.

Bioactive or bioreactive: In this case there is interaction between the implant and the bone tissue with influence in the mechanisms involved in osteogenesis. There is ions exchange with the tissues; there are chemical bonds between the biomaterial and the tissues, promoting osteoconduction. Among this biomaterials class are the tricalcium phosphate, tetracalcium phosphate, bioglasses and hydroxyapatite.

Currently, several companies have used titanium alloys in the manufacturing of implants. Would there be some loss in bone response?

Currently, there are only three metals that present osseointegration: Commercially pure titanium, niobium and tantalum. It is understood as osseointegration the definition of ISO 16443, according to which "osseointegration is the contact of the bone cells with the biomaterial surface." The Ti-6Al-4V alloy has no osseointegration and the example is the mini-implants used for orthodontic anchorage. However, when

the implants of Ti-6Al-4V are subjected to surface treatment to have a predominance of titanium oxide, there is osseointegration. For those ceramic and other metal alloys a treatment promoting osseointegration is still not known.

The most part of the effort has focused on the relationship of the implant surface with the bone, with remarkable progress. However, very little has been developed to improve their relationship with the soft tissues. Would this not be the time for focusing in this area? What is the current status of research regarding this?

In the past, treatment with dental implants aimed at the restoration of masticatory ability and the success of the treatment was assessed by osseointegration. Today, the patient wants immediate restoration, followed by esthetics. In this case, the biological sealing is important. Few studies examine the interaction soft tissue with prosthesis material, being that we constantly observe in patients a gingival retraction showing the metal parts, damaging esthetics. There is a dichotomy between the esthetic and the sealing. Not always the biomaterial that has the best esthetics (ceramic), presents the best biological sealing and mechanical strength.

For the manufacture of ceramic prosthesis we use materials that were developed for other applications (alumina and zirconia).

We need to research materials for specific application with mechanical strength, biocompatibility and ability to allow the adhesion of fibroblasts. This area still has a gap.

At last, we would like to know about future trends. Which are the new ways of osseointegration in terms of biomaterials?

Researches are focused on the development of implants where it is possible to incorporate patient's own cells to accelerate osseointegration. We have already conducted researches with fibronectin which presented good results in *in vitro* assays. The adhesion of RGD also gives good results. There is difficulty in incorporating BMP.

All these procedures are performed in very small scale and with control. To transform these researches in products we need to run through many obstacles, including the incorporation of cells and keep them active for long times, even after sterilization. Incorporate controlled amount of different products. The risk is to incorporate something that will be removed by osteoclastic activity.

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