TURUN AMMATTIKORKEAKOULU
ÅBO YRKESHÖGSKOLA

Bachelor's Thesis

Up-Scaling Plan for TiO_2 Coating Process

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TURUN AMMATTIKORKEAKOULU

TIIVISTELMÄ

Bio- ja elintarviketekniikan koulutusohjelma

Tekijä: Ari Peltola

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Työ liittyy kastopinnoitusprosessin käyttöön implanttien pinnoittamisessa ohuella TiO_2-kerroksella, joka parantaa implanttien tarttumista elävään pehmytkudokseen. Työn tarkoituksena oli selvittää, miten kastopinnoitusprosessi saadaan tehokkaammaksi nykyisellä laitteistolla ja minkälaisia laitemuutoksia tarvitaan ja miten ne vaikuttavat, kun halutaan kasvattaa tuotantokapasiteettia asteittain. Toisena näkökulmana selvitettiin tuotannon noston mahdollisuutta suunnittelemalla uusi näyteteline pinnoituslaitteistoon. Lisäksi selvitettiin prosessissa käytettävän TiO_2-soolin ikääntymisen ja ilmavirran vaikutuksia pinnoitukseen ja pinnan muodostukseen.

Kastopinnoitusprosessin tehostamissuunnitelma perustui laskuihin yksikköprosesseista ja eri laitevaihtoehdoista. Uusi näyteteline suunniteltiin tietokoneella Solidworks-ohjelmaa käyttäen. Näyteteline testattiin tuotanto-olosuhteissa. Soolin ikääntyminen ja ilmavirran vaikutukset pinnoitukseen ja pinnan muodostukseen testattiin tuotanto-olosuhteissa.

Nykyinen laitteisto mahdollistaa työskentelyn kolmessa vuorossa. Merkittävimmät pullonkaulat tuotannossa ovat kastovaihe ja lämpökäsittely. Uusi näyteteline kasvattaa tuotantomäärää merkittävästi. Soolin ikääntyminen ja ilmavirran vaikutukset kaikilla mahdollisilla vaihtoehdoilla antoivat hyväksyttävät tulokset.

Hakusanat: sooli-geeli, kastopinnoitus, TiO_2

Säilytyspaikka: Turun ammattikorkeakoulun kirjasto

TURKU UNIVERSITY OF APPLIED SCIENCES ABSTRACT

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This thesis concerns using the dip coating method for coating implants with a thin TiO_2 layer to improve attachment to soft tissue. The goal of this thesis was to study how to make the sol-gel dip coating process more efficient and to scale up the production volume by optimizing the dip coating process with the current equipment and to determine how various device configurations and process parameters affect the production. A second goal was to increase the production volume by designing a new stand for the current dipping equipment with specific model substrates. The aging of the sol and the xerogel (film) formation in different air flows were studied. The purpose was to determine how long a TiO_2 sol can be used for dip coating and how the air flows affect the coating structure.

The optimization was performed by making calculations on different options in the unit processes and device configurations. The new dipping stand was designed by using the Solidworks software and tested in production conditions. The aging of sol and the effects of air flow were tested in production conditions.

It is possible with the current equipment to work in 3 shifts, which triples the production volume. The significant bottlenecks of the unit processes were the dipping and heat treatment. It was shown that the new stand increases the production volume remarkably. The aging of sol gave acceptable results. All the possible air flows with the current equipment can be used to obtain acceptable results.

Keywords: Up-scale, TiO_2, dip coating,

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1 Introduction

Biomaterials are materials which are used in the human body for implants or a medical device to repair, replace, and regenerate tissue in the human body. One of the main goals has been to obtain a direct and firm contact between the living tissue and the biomaterial. A good soft tissue attachment with a biomaterial is one of the major challenges. One solution for the good attachment is to coat an implant or a substrate with a bioactive and biocompatible thin film, which can be done by a sol-gel dip coating method. Sol-gel is a process where a colloidal solution alternates from sol state to gel state.

This study is related to Vivoxid's MetAlive™ technology. MetAlive™ is based on the sol-gel dip coating method that represents a treatment option for any medical device that will be implanted in the body. MetAlive™ provides safe attachment to the soft tissue. Surface modification is performed by coating the substrates with a thin film, which increases bioactivity and biocompatibility.

The goal of this thesis was to study how to make the sol-gel dip coating process more efficient and to scale up the production volume by optimizing the dip coating process with the current equipment and to determine how various device configurations and process parameters affect the production. Another approach to increasing the production volume was to design a new stand for the current dipping equipment with specific model substrates. In addition, the aging of the sol and the xerogel (film) formation in different air flows were studied. The purpose was to determine how long a TiO_2 sol batch can be used for the dip coating and whether the aging and air flows affect the coating reactivity.

2 Background

Using biomaterials in medical applications to repair, replace, and regenerate tissue is common these days. Common applications are the implants. One of the most important properties of an implant is to stay in place in the tissue. The implant needs to have a specific surface which helps it to stay in place. This could be done by coating the implant with a biocombatible and bioactive material, such as TiO_2. Bone implants with bioactive and biocompatible coatings are quite common, but the newer invention is to adapt the implant to the soft tissue. These synthetic coatings are often bioceramics. The bioceramic coatings are commonly prepared by combining the so called sol-gel method with the different coating methods. One of the most common coating methods is dip coating. The sol-gel method is based on the formation of nanoscale, colloidal particles that can be used to form porous structures or films with various surface dimensions. This gives the possibility to control the surface structure, which is very important with respect to the tissue attachment process.

2.1 Biomaterials

A biomaterial is defined as a material which has an interface with a biological system or “A natural or synthetic material (such as a metal or polymer) that is suitable for introduction into living tissue especially as part of a medical device (such as an artificial joint)” [1]. Biomaterials can be very diverse. Biomaterials are very often synthetic, like plastics (PE, PLA, PLGA), ceramics (SiO_2, TiO_2, Al_2O_3, Calcium phosphates like HA), metals (Ti), composites (PE-HA). There are also natural materials like collagen and cellulose.

Bioactivity and biocompatibility are two essential properties of biomaterials. Biocompatibility is defined as "the ability of a material to perform with an appropriate host response in a specific application"[2], Bioactivity is defined as “one that elicits a specific biological response at the interface of the material which results in the formation of a bond between the tissues and the material.”. [3]

2.1.1 Bioceramics

As described in Figure 1, ceramic biomaterials, i.e., bioceramics are commonly used clinically. They are classified into several subgroups of which the bioactive ceramics is of major interest. Bioactive ceramics such as TiO_2 can be classified into two major groups. For example, the first group includes bioactive glasses and ceramics which can form biological hydroxyapatite on their surfaces after implantation. The second group covers calcium phosphate ceramics which are usually developed from chemical precursors. Materials from both groups could be used as powders, as solid objects, as composites, and as coatings. Powders and solids are used when mechanical requirements are low and composites and coatings are used when mechanical requirements are high. [2]

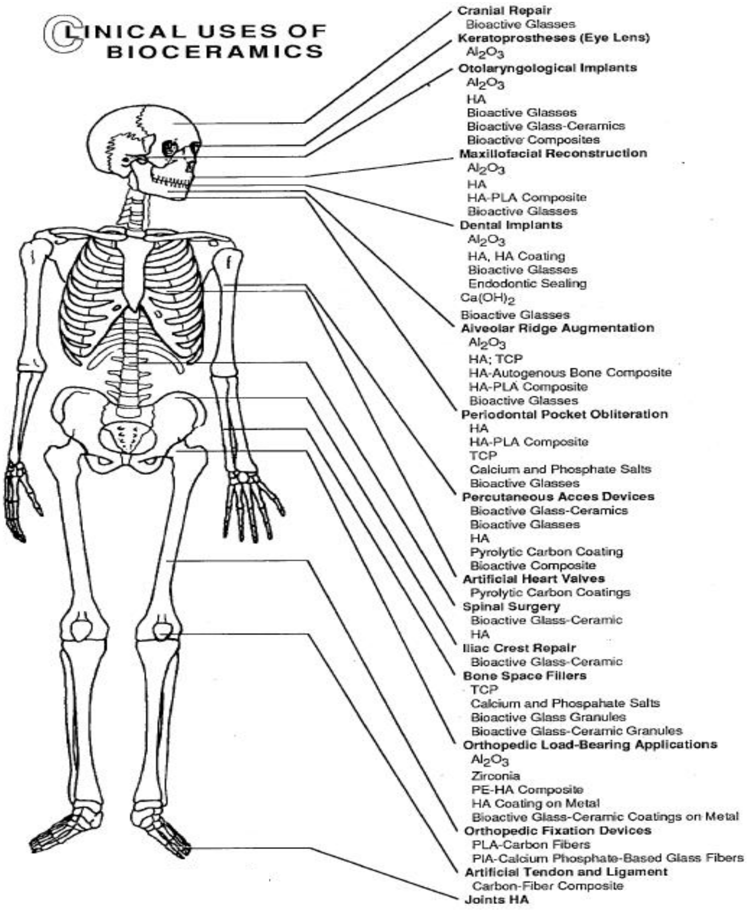

Figure 1. Clinical uses of bioceramics [3].

Ceramics and glasses have been used in many different applications for a long time. Lasers, diagnostic instruments, chemical ware, thermometers, tissue culture flasks, fiber optics are common areas of application. Ceramics are widely used in dentistry like gold porcelain crowns, glass-filled ionomer cements, endodontic treatments, dentures, etc. Using ceramics in implants inside the body is relatively new. In Table 1 the forms, phases and the functions of bioceramic are presented. [3]

Table 1. Form, phase and function of bioceramics [3].

Form	**Phase**	**Function**
Powder	Polycrystalline	Space-filling, therapeutic treatment, regeneration of tissue
	Glass	
Coating	Polycrystalline	Tissue bonding, thromboresistance, corrosion protection
	Glass	
	Glass-Ceramic	
Bulk	Composite	Replacement and augmentation of tissue, replace function parts
	Polycrystalline	
	Glass-Ceramic	
	Glass	
	Single Crystal	

2.1.2 Attachment interfaces

All material evokes a response from the host tissue, so no material which is implanted in the living tissue is inert. The response on the interface depends upon many factors, some of which are listed in Table 2. Ceramics are interesting materials for implants because they are non-toxic. [3]

Table 2. Factors that influence implant tissue interface response [3].

Tissue side	**Implant side**
Type of tissue	Composition of implant
Health of tissue	Phases in implant
Age of tissue	Phase boundaries
Blood circulation in tissue	Surface morphology
Blood circulation at interface	Surface porosity
Motion at interface	Chemical reactions
Closeness of fit	Closeness of fit
Mechanical load	Mechanical load

Table 3. Consequences of implant-tissue interactions [3].

Implant-tissue reaction	**Consequence**
Toxic	Tissue dies
Biologically nearly inert	Tissue forms a non-adherent fibrous capsule around the implant
Bioactive	Tissue forms an interfacial bond with the implant
Dissolution of implant	Tissue replaces implant

In Table 3, four general types of response are summarized [3]. Usually it is desirable for implant material to avoid a toxic response that would kill the cells in the surrounding tissues or release chemicals that are spread in the body fluids and cause damage to the object. In some applications this might be very critical. A very common response is the formation of a fibrous capsule. The capsule is formed from fibrous tissue and it is meant to isolate the implant from the surroundings. Nearly inert ceramics are biologically inactive but the tissue builds a fibrous capsule at their interface. The bioactive interface is the third type of the interfacial response. It forms a bond between the interfaces and holds the sides of the interface and the bond still and imitates the type of the natural tissue [3]. Bioactive interfaces of this kind change with time and reproduce like the natural tissue. This is a very important feature and should be accommodated [3]. Type 4 in Table 3 is the dissolution of the implant. Material is replaced by surrounding tissues. The dissoluble material must be degraded chemically by body fluids or digested easily by macrophages [3].

2.1.3 Attachments and response

Table 4 summarizes with examples four types of bioceramics with the different types of tissue attachment. The attachment of the tissue and the implant is proportional to the response of the interface. Factors influencing this response are listed in Table 2 and the effect type and the stability of the attachment are listed in Table 4. [3]

Table 4. Types of tissue attachment of bioceramic [3].

Type of implant	**Type of attachment**	**Example**
(1) Nearly inert	Mechanical interlock (morphological fixation)	Al_2O_3, Zirconium
(2) Porous	In growth of tissue into pores (biological fixation)	Hydroxyapatite (HA), HA coated porous metals
(3) Bioactive	Interfacial bonding with tissues (bioactive fixation)	Bioactive glasses, bioactive glass-ceramics, HA
(4) Resorbable	Replacement with tissue	Tricalcium phosphate, bioactive glasses

The Type 1 implant forms a fibrous capsule. The implant is not fastened very tightly so it will loosen quickly and might lead to clinical failure. Porous ceramics and HA coated implants are designed to attach implant in place. This is often called biological fixation [3]. The attachment type can handle more complex stress states than a nearly inert implant. Resorbable implants are designed to degrade gradually along with the time and be replaced with natural tissues. The bioactive implant surface reacts and leads to the bonding of the tissue and the implant. Every organ in the body consists of a combination of the four tissue types, epithelium, muscle, nervous tissue, and connective tissue. The significance of change in the tissue is a transient change or a continuing one. Change of the tissue will vary with the material. [3]

2.1.4 Soft tissue attachment to implants

The bond between the implant surface and the surrounding soft tissue is also important for the performance of many medical devices (e.g. canyls, stents and dental applications). To improve the surface bioactivity, hydroxyapatite (HA) coatings have been applied on a bioinert (e.g. titanium) implant surface [4]. The bioactivity of the implant can be enhanced also with porous sol-gel-derived titanium (TiO2) coatings, because of its capability to induce the calcium phosphate (CaP). [4]

2.1.5 Processing and microstructure

The objective of the bioceramic processing is to make a specific form of the material which will perform a specific function in the host which is described in Table 1. This means that making a solid object, a coating or powders is necessary. Bioceramics can be classified into eight categories based upon the processing method and the microstructure produced. The difference is in the microstructure derived from different starting materials and thermal processing steps making the materials. In Table 5, the examples of the material and its formation phase are provided. [3]

Table 5. Types of ceramic processing [3].

Type of ceramic processing	**Example**
1. Glass	45S5 Bioglass
2. Cast or rapidly solidified polycrystalline ceramic	HA coating
3. Polycrystalline glass-ceramic	Ceravital
4. Liquid-phase sintered (vitrified) ceramic	Glass-HA
5. Solid-state sintered ceramic	Alumina, zirconia
6. Hot pressed ceramic or glass-ceramic	A/W glass-ceramic
7. Sol-gel glass or ceramic	52S Bioactive gel-glass
8. Multi-phase composite	PE-HA

2.2 Sol-gel processing

Sol-gel processing is typically a low-temperature material manufacturing technique which starts from a sol phase and continues to a gel phase. The sol is a colloidal suspension which contains particles <1µm in a liquid. The gel is a colloidal suspension which contains a solid skeleton mixed with a liquid phase. The colloidal suspension contains two different phases where one is continuous. In the sol it is the liquid and in the gel it is the skeleton. In Figure 2 different possibilities to use the sol-gel and the sol to gel formation are generally shown. The skeleton is formed in different ways. The gel is formed by an entanglement of chains, polymeric is covalently linked, and particulate gels are formed by Van Der Waals forces. The continuity of the solid structure gives elasticity to the gel [5]. Gel dried by evaporation under normal conditions is called a xerogel. The surface area of dried xerogel is very large, 200-800 m^2/g and pore sizes can be larger than 1.0 nm. Controlled hydrolysis and condensation are needed to produce the narrow pore size. This reduces the drying stress gradients. An aerogel is prepared by drying a wet gel under supercritical conditions. Most gels are amorphous after drying. Supercritical drying is performed by replacing the liquid e.g. with acetone and after that washing the acetone away with high-pressure liquid carbon dioxide and then the liquid carbon dioxide is heated until its pressure exceeds the over critical point. Then pressure can be gradually released which allows gas to escape and dries the product. By heat treatment or sintering the gels can be processed further to obtain a porous ceramic. The surface area is commonly very large (100-1000 m^2/g). A pore-free ceramic is made by heating the gel to a temperature which causes the sintering. [5]

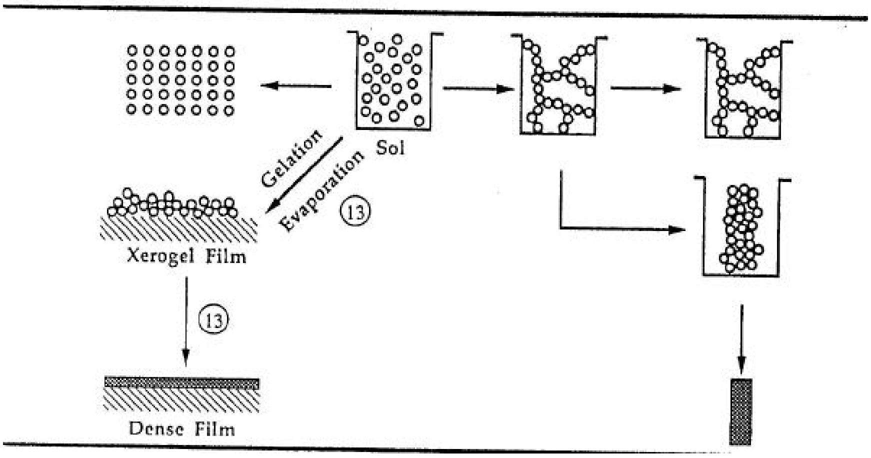

Figure 2. Sol-gel formation and the ways of usage [6].

2.2.1 Alkoxide method

Alkoxides, acetyl acetonates and inorganic salts are common precursors in sol-gel processing. Alcohols (e.g. ethanol) are commonly used as solvents and water as a hydrolysis agent. Alkoxides are popular precursors because they react easily with water. [7]

$$M(OR)_X + H_2O \rightarrow HO\text{-}M(OR)_{X-1} + ROH \qquad (1)$$

$$Ti(OR)_4 + 4\ H_20 \rightarrow Ti(OH)_4 + 4\ ROH \qquad (2)$$

$$(OR)_3Ti\text{-}OH + HO\text{-}Ti(OR)_3 \rightarrow (OR)_3Ti\text{-}O\text{-}Ti(OR)_3 + H_2O \qquad (3)$$

$$(OR)_3Ti\text{-}OR + HO\text{-}Ti(OR)_3 \rightarrow (OR)_3Ti\text{-}O\text{-}Ti(OR)_3 + ROH \qquad (4)$$

Precursors typically go through two main chemical reactions, hydrolysis and polymerization by condensation. In Equations 1 and 2, the hydrolysis is shown where the alkoxide group is replaced by water. $M(OR)_X$ represents alkoxides where M is a metal or a non-metal and R is an alkyl or a corresponding organic group . Equation 2 is valid when there is enough water in the sol. All OR-groups are replaced by OH-groups. Equations 3 and 4 show the polymerization by condensation. Equation 3 is water condensation and Equation 4 is alcohol condensation. [8]. Two partially hydrolyzed molecules can join together by condensation releasing small molecules (e.g. water or alcohol). This type of reaction can continue to build larger and larger molecules by the polymerization to 3D structures. The reaction speed of alkoxides can be controlled with pH. [7]

2.2.2 Salt method

With the salt method, the gel is formed by dissolving metallic salts with water when the water molecule attaches to a metallic ion. This is shown Equation 5. [8]

$$M^{Z+} + :OH_2 \rightarrow [M \leftarrow OH_2]^{Z+} \qquad (5)$$

$$[M(OH_2)]^{Z+} \leftrightarrow [M\text{-}OH]^{[Z-1]+} + H \leftrightarrow [M{=}O]^{[Z-2]+} + 2H^+ \qquad (6)$$

Equation 6 describes how acidity affects the hydrolysis. The sol-gel can be made by condensation or dispersion. In condensation particles grow slowly and in a controlled way. In dispersion particles are flocculated quickly. [8]

2.2.3 Aging and drying

Aging occurs in both the sol and the gel. Aging happens when reactions proceed. In the sol the more particles are formed and then particles are aggregated. The gel formation belongs to the sol aging process. It is the process when a solution suddenly loses its fluidity and change to an elastic solid. The gel point is the moment when the chain of bonds is formed and which forms the continuous skeleton. The aging affects on sol’s viscosity and the gels elasticity. The aging process will continue after the gel formation to the polymerization. The polymerization is described in the Section 2.2.1. The polymerization occurs primarily in the sol. The drying is a multiphase process. First the body shrinks by an amount of the liquid that evaporates. Next the gel or the film becomes too stiff to shrink and the fluid is withdrawn into the interior. The surface is now full of the air-filled pores. When the air invades pores, the liquid film continues to flow to the exterior and the evaporation continues to occur from the surface of the body. At last phase, the liquid is isolated into pockets and drying will continue by the evaporation and the diffusion. [6]

2.3 Dip coating

A dip coating is a method which is usually used to coat a solid material with some other material by dipping objects in suspension. The suspension that contains colloidal particles is often called the sol. For example, in this study case we use a TiO_2 sol to coat titanium parts with a thin film of TiO_2. Coatings and films are the earliest applications of the sol-gel technology. Thin films,<1 μm in thickness, formed by dipping use very little raw materials and may be processed quickly without cracking, which is a common disadvantage of the sol-gel processing. Large substrates, planar and axially symmetric substrates such as tubes, pipes, rods and fibers, which are not easily handled by a more conventional coating process, are good for the dip coating. Applications for the coating the different materials are very numerous. The different applications for films and coatings are optical coatings, electronic coatings, protective coatings, and porous coatings. Optical coatings alter the reflectance, the transmission, or the absortion of the substrate. Reflective or colored coatings have been used as antireflective surfaces in solar-related applications. Protective films prevent the corrosion or the abrasion, promote adhesion, increase strength or provide passivation or planarization. On porous films the pore volume, the pore size, the surface area, or the surface reactivity can be controlled. These properties can be varied by aging the sol and/or by controlling the relative evaporation and the condensation rates. The control of the pore size and the surface area leads to applications as sensor or catalytic surfaces. The surface reactivity may be modified by the appropriate choice of precursor metals. [6]

2.3.1 Film formation

The sol-gel processing is one of the most important technologies for preparing thin films by dipping, spinning or spraying. It requires less equipment than another thin film forming processes, such as CVD (Chemical Vapor Deposition), or sputtering, and it is less expensive. Huge advantage of making the thin films through the sol-gel process is the ability to control the microstructure of the deposited film e.g. the pore size and the surface area. [6]

2.3.2 Physics of dip coating and film formation

The dip coating process can be divided into five stages: immersion, start-up, deposition, drainage, and evaporation (Figure 2). Evaporation exists during the start-up, the deposition, and the drainage steps. [6]

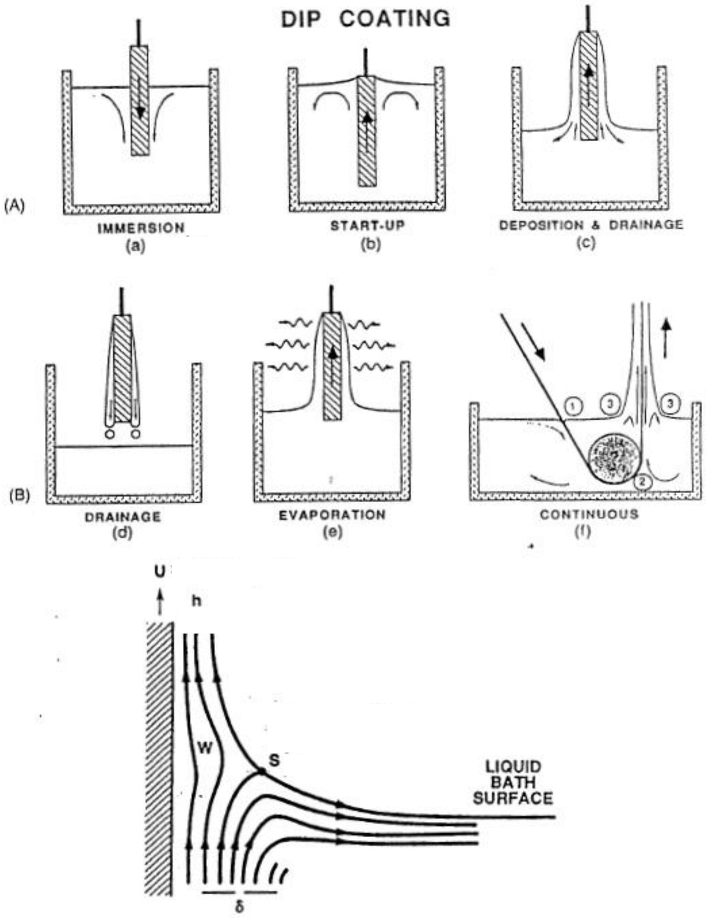

Figure 3. Stages of dip coating process [6].

The thickness of the film is the result of the dividing the upward- and the downward-moving layers shown in Figure 3. Six forces have effect on the film thickness. Forces that effect are the drag upward on the liquid by the moving substrate, the force of gravity, the resultant force of the surface, the inertial force of the boundary layer liquid arriving at the deposition region, the surface tension, the disjoining pressure (important for films less than 1 µm thick). The inner layer moves upward with the substrate and the outer layer is returned to the bath. [6]

The liquid viscosity (η) and the substrate speed (U) are the most important parameters when dipping and determine the deposited film thickness (h). In the deposition phase, the evaporation has an effect to solidify of the coating. The most significant factor in the evaporation effect is the amount of the diffusion of the vapor away from the film surface. The evaporation rate is independent of the liquid depth during dip coating. The movement of the substrate and the convection could make the evaporation irregular. [6]

The composition of the sol-gel in the bath may be unaffected by the evaporation and the convection but the thin film experiences the increase in the concentration. The thinner film needs the greater the overlap of the deposition and the drying stages and the slower substrate speed. The condensation continues to occur during the sol-gel film formation. The condensation and the evaporation will affect also on the deposition and the drainage stages. The evaporation rate can be controlled by the deposition ambient, the temperature and humidity. [6]

2.3.3 Deposition stage

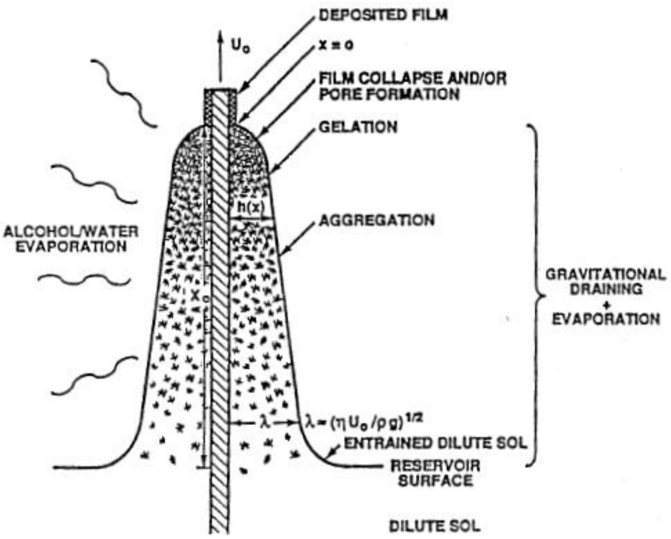

Figure 4. Schematic of the steady sol-gel dip coating process [3].

In Figure 4 is shown the deposition point of the dip coating process. The overlap of the deposition and the evaporation compact the structure and the condensation hardens the structure by increasing the resistance of the structure to compact at the same time. The aggregation and the drying happen in seconds to minutes during the dipping or the spinning. Duration of the deposition and the drying leads to the more compact and dried structures. The draining and the evaporation increase a shear stress with the attachment of the precursor type to the substrate during deposition. Continued shrinkage occurred from the drying and the further condensation reactions create a tensile stress to the film. [6]

3 Aim of the study

The objective of this study was to increase production volume of the TiO_2 sol-gel dip coating process with current equipment and create a variable matrix, which shows the bottlenecks of the production, and the configuration and device changes needed to increase production volume. This includes capacity calculations in shifts and with 1 or 2 person. Another approach to increase the production volume was to design a new stand for the current dipping equipment with specific model substrates. This was done by using the previously defined boundary values of evaporation and distance between the substrates to be coated. In addition, the aging of the sol and the xerogel (film) formation in different air flows were studied. The purpose was to determine how long a TiO_2 sol batch can be used for the dip coating and whether the aging and air flows affect the coating structure.

4 Materials and methods

4.1 Coating process

The coating process consists of several steps that are described in Figure 5. The first step is the preparation of a TiO_2 sol which is made by the hydrolysis and condensation reactions of a titanium alkoxide, Tetraisopropyl orthotitanate. The second step is to check the viscosity of the sol. These 2 steps are done only once for every batch. Prior to the actual coating process, a Ti substrate to be coated is first cleaned in an ultrasonic bath in acetone for 5 min, and then in ethanol for 5 min. After the cleaning, the substrates need to dry for 10 min. The next phase is the dipping of the substrate into the TiO_2 sol, i.e., the dip coating. There are several variables that may affect the process, but they are constant and must be controlled carefully. The dip coating includes the actual dipping and the xerogel formation. The xerogel formation takes 5 min. After the dipping and xerogel formation, the coated substrate goes to the heat treatment phase into a furnace at 500 °C for 10 min. Then the substrate is cooled down at room temperature for 10 min. The cleaning, dip coating, heat-treatment and cooling down is repeated several times depending on the desired number of layers, e.g., five times for the 5-layer coatings. After the fifth cycle the coated susbtrate continues to the final cleaning phase which is the same as described above. After the coating process, the substrates go to a quality test. The quality test is not included in the actual up-scaling study, but is used for the characterization of the coatings prepared with the varying device and process parameters (stand, aging of the sol and air flow).

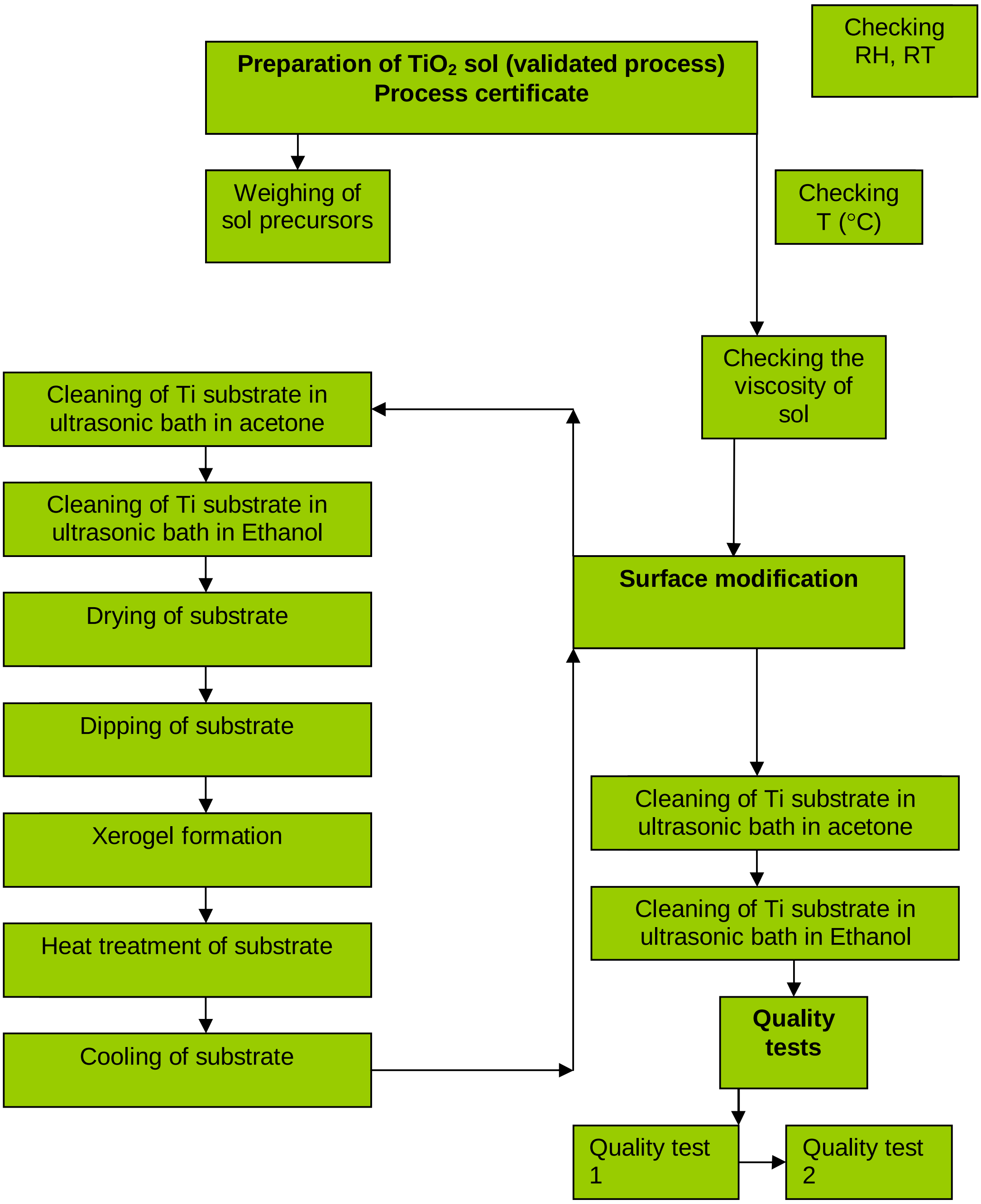

Figure 5. The coating process.

As described above, the coating process consists of several phases. Every phase has an individual set up of equipment, which have a characteristic function and purpose depending on the unit process in question.

4.1.1 Preparation of the sol

The controlled preparation of the sol is an important step in the coating process. If it fails, the process cannot be continued and sol must be prepared again. The sol is prepared in a batch process. The equipment and supplies needed to prepare the sol are quite simple, reagents, pipettes, a weighing balance, decanters, a magnetic stirrer, and a glycol bath.

4.1.2 Atmosphere control

The process conditions are exactly defined and only small variations are allowed. The most important variables are humidity and temperature. Humidity is important because the sol is highly reactive with water. The process is defined to be done at temperature of 20 ± 4 °C. The surrounding conditions are controlled by the central air conditioning. The cleanliness level of the room must be good enough to avoid small particles (µm scale particles) getting onto the surface of the substrate or into the sol. These particles may cause unwanted geometry or cracking on the coated surface. In addition, fume hoods or chambers are used to control and prevent inhaling of harmful gases and fumes.

4.1.3 Viscosity

Viscosity is one of the quality parameters of the sol, which is measured along with the visual observation. Viscosity is measured with a capillary viscometer. The capillary viscometer measures the time elapsed to the specified volume of a solution to flow through the tube, which is compared with the flow of a liquid of known viscosity like ethanol through the same capillary.

4.1.4 Cleaning

Cleaning is done in an ultrasonic bath containing suitable cleaning solutions. The ultrasonic bath produces ultrasound waves that enhance the effect of the cleaning solutions. In this case acetone and absolute ethanol (Aa) are used as cleaning solutions. The cleaning is done in a fume chamber.

4.1.5 Dipping

The dipping process is the most complicated unit process from the point of view of the equipment. It is very important that the dipping of the substrate occurs steadily and at a constant speed. After the dipping, the xerogel formation occurs in the condition where air does not flow because the flow of air may cause unwanted stripes to form on the surface. The dipping is done in a closed cabinet where the substrates are attached in a stand that is attached in a dipping device. The dipping device is controlled by the computer where one can adjust parameters like downward and upward speed. The closed cabinet also protects operators from inhaling the fumes and gases.

4.1.6 Heat treatment

Heat treatment is done in a furnace. When doing the heat treatment, it is important to follow up the minimum residence time for the substrate in the furnace. The treatment is done in a special furnace, which can produce a high enough, the temperature. The furnace contains six sensors, which indicate when the temperature is stable around the samples. Temperature is controlled by the computer.

4.2 Up-scaling methods

The purpose of the up-scaling in question is to study how to increase the production volume with the current equipment and to create a variable matrix, which shows the bottlenecks of the production with different device configurations and process parameters including possible device changes needed to increase the production volume. This includes capacity calculations in different numbers of working shifts with 1 or 2 operators. The bottlenecks become critical when there are several stands going through the process. The flow-through times in the coating process with different numbers of stands are shown in Table 6.

Table 6.Unit process times with 1, 2, and 3 stands.

	1 Stand	**2 Stands**	**3 Stands**
Pre-wash /min	15.7		
Dipping / min	20.4		
Heat treatment / min	18.5		
Cooling /min	10.0		
Wash / min	15.7		
5 Layer coating / min	338.3	358.6	379.0
5 Layer coating / h	5.6	6.0	6.3
1 Layer coating round / min	64.5		
values calculated without breaks			

To make the up-scaling calculations easier and more logical, the process is divided into 4 unit processes. The simplified process chart is shown in Figure 6. It is more practical in the optimization of the process. Every unit process is handled separately.

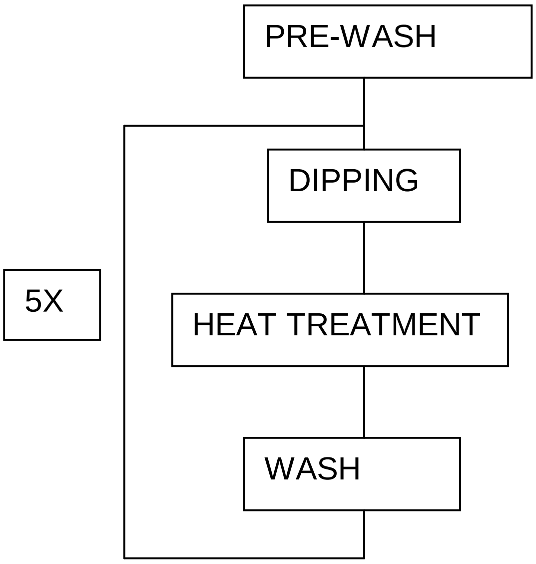

Figure 6. Simplified process flow chart for the up-scaling calculations.

4.2.1 Pre-wash and wash

As described earlier, the wash is made in an ultrasonic bath and the bath capacity is one stand at the time. In addition, the acetone and ethanol wash is performed in the same ultrasonic bath consecutively causing an extra waiting time. This unit process is not so critical for the whole process, because the wash takes only 5 min in each solution. However, the capacity can easily be raised by adding another ultrasonic bath for separate washes. Another possibility is to use a bigger bath with space for two stands at the same time. Different options for the pre-wash are described in Table 7. Different options are denoted with Type numbers. The corresponding Type numbers are also used in Results and Discussion. Different options affect the calculations on the flow-through times of the stands and the unit process times. The pre-wash is currently performed with Type 1 set up.

Table 7. Pre-wash options.

Type	Description
1	1 ultrasonic bath and 1 stand at the time. Acetone and ethanol wash made one after another
4	1 big ultrasonic bath for 2 stands at the same time. Acetone or ethanol baths can be done both at the same time
7	2 ultrasonic baths of Type 1. Acetone and ethanol have own baths.
10	2 big baths for 2 stands per bath.

4.2.2 Dipping

The dipping is currently performed with Type 2 set up. Table 8 is shows the different options for raising the capacity and removing the bottlenecks.

Table 8. Dipping options.

Type	Description
2	1 dipping vessel and 1 cabinet, 1 stand attached and removed from the device manually
5	2 dipping vessel and 1 closet, no automation, stand attached and removed manually. Same space for drying and evaporation
8	1 dipping vessel, Stand moving to dipping and away from dipping automated. Dipping automated
11	2 of Type 8 dipping system

4.2.3 Heat Treatment

Heat treatment is currently performed with Type 3 furnace set up. Table 9 is shows the different options for raising the capacity and removing the bottlenecks.

Table 9. Heat treatment variations.

Type	Description
3	1 furnace and 1 stand at the time. The stand fed and removed manually
6	2 furnaces and 1 stand at the time in one furnace. The stand fed and removed manually
9	1 flow-through furnace

4.2.4 Quality and packaging

After the coating process, the product continues to the quality tests and packing. Those phases are not included in the up-scaling calculations, but quality tests are used in the characterization and evaluation of the prepared films.

4.2.5 Stand

One of the devices that have a great influence on the dipping process is the stand where the substrates, e.g., implants are attached during the process cycle. Changing the number of fastened implants changes the production volume immediately. Drying and evaporation of the gel formed in the dipping are the most critical parameters with respect to the coating quality. Those have to be taken into account when designing a new stand. The structure of the stand was designed to fulfill physical and chemical parameters, such as distance and evaporation that are known to affect the coating quality. The minimum free space around substrate was thought to be 3.5 mm and minimum distance between two substrates 7 mm. The distances were given by the Vivoxid. The distances were the same as in the previously used stands, but the number of the attachment spots was different. There are 110 attachment spots for implants and the diameter of stand is 125 mm. The earlier version of the stand had 24 attachment spots. The prototype of the stand was designed using Solidworks software. Titanium rods with 4 mm in diameter and about 20 mm in length were used as test samples. All available attachment spots were used. 20 samples were used in the quality tests. The test sample positions in the stand for the quality tests are shown in Figure 7. The contact angle analysis and a specific reactivity test indicating the proper surface structure are used as the quality tests.

4.3 Testing

All the tests were done in the validated coating atmosphere and conditions. The contact angle analysis and reactivity tests were conducted according to the validated quality control procedure.

4.3.1 Aging of the sol

The effect of the aging of the sol was studied by dipping four 1 cm x 2 cm test plates into the TiO_2 sol after 0 h, 8 h and 24 h of aging. All set ups were done by using the same stand and at the same production conditions and all test plate spots were equal. Viscosity of the sol was measured at start and at 24 h. Different test set ups are shown in Table 10. This test gives information about how long one sol batch can be use. The contact angle analysis and reactivity test were conducted with all of the tests samples.

Table 10.Tests for aging of sols.

Test Set Up	Description
1	Sol was aged for 0 h. Viscosity was measured.
2	Sol was aged for 8 h. Viscosity was not measured
3	Sol was aged 24 h. Viscosity was measured

4.3.2 Air flow

Effect of the air flow on the surface formation was determined by dipping 1 cm x 2 cm plates in three test series with different air flows. 4 parallel samples were dried in each series. Different cases are shown in Table 11. Different air flows have an influence on the drying and evaporation. This test gives information about how the different air flows affect the xerogel surface structure and reactivity. The air flow was different in every test set up. Tests were done by using the upper and lower limits of the current device set up. The contact angle analysis and reactivity test were conducted with all of the tests samples.

Table 11. Air flow parameters.

Test set up	Description
1	No air flow
2	½ air flow
3	Full air flow

4.4 Coating characterization methods

The coating characterization methods, contact angle analysis and the reactivity test, were used to define the quality of the coatings in samples prepared with the new stand, after the aging of the sol and with different air flows.

4.4.1 Contact angle analysis

The contact angle analysis is a standard validated method to determine hydrophilicity and quality of TiO_2 coatings of Vivoxid. Contact angle is the angle at which a liquid interface meets the solid surface. The Concept is illustrated with a small liquid droplet resting on a flat horizontal solid. Then the contact angle is measured by a contact angle goniometer. [10] Hydrophobic surfaces give (high or even) >90° contact angle. Highly hydrophilic surfaces give 0° - 30° contact angle. [10]

4.4.2 Reactivity test

Kinetics of reactivity of a material is dependent on both crystallinity and specific surface area (derived from nanoporosity). The test is a validated method in of Vivoxid.

The reactivity test was performed as follows: TiO_2 modified Ti-sample substrates were placed at the bottom of 4 ml cuvettes and then 2 ml of operating solution on was pipetted the sample and the signal describing the surface-structure dependent was measures.

4.4.3 Coating capacity of the sol

½ liters of TiO_2 sol and its theoretical dry substance concentration is about 50 g.
Anatase of TiO_2 sol is about 3.9 g/cm^3 [11] and the porosity is about 20 % [12].
Volume of 50 g anatase is about 12.82 cm^3 and volume of porosity of 20 % is about $12.82 * 1,2 = 15.38$ cm^3
Thickness of coating is assumed to be 100 nm = 0.1 µm = 0.0001 mm = 0.00001 cm
From equation V (15.38 cm^3) = A (?) * h (0.00001 cm)
A = 1 538 000 cm^2
Surface area of sample rod and plate used in stand measurements is about A_1=0.8 cm^2.
From equation A/A_1= 1 922 500 units

5 Risk analysis

Risk analysis Failure Mode and Effects Analysis (FMEA) is used in this Study. The USA Food and Drug Administration (FDA) have recognized FMEA as a design verification method for Drugs and Medical Devices [9]. FMEA is used here for defining the risks of the coating process. Potential failure modes and potential causes are listed from the manufacturing point of view. This risk analysis will complete previous risk analysis made. The risk analysis and definitions are shown in Appendix 1.

6 Results and discussion

6.1 Coating process

The results for the different up-scaling options of the coating process are summarized in Tables 12, 13, and 14. Table 12 shows different options (size, number and type of operation or device) for the washing, dipping and heat treatment and they are more closely described in Sections 4.2.1 - 4.2.3. Table 13 shows the operation times for the single unit processes with the different options. Table 14 shows the number of stands flowing through the unit operations within an hour with the different options. The results are based on calculations where the current process times are used as starting values. The quality tests and packaging are not included in the calculations.

Table 12. Options for the coating process.

	Type	**Type**	**Type**	**Type**
Acetone wash	1*	4	7	10
Ethanol wash	1*	4	7	10
Dipping	2*	5	8	11
Heat treatment	3*	6	9	NA

* current set up

Table 13. Unit process times.

	min / Type	**min / Type**	**min / Type**	**min / Type**
Ethanol wash	10.6* / 1	5.3 / 4	5.3 / 7	5.3 / 10
Acetone wash	10.6* / 1	5.3 / 4	5.3 / 7	5.3 / 10
Dipping	20.4* / 2	15.3 / 5	6 / 8	20.4 / 11
Heat treatment	18.5* / 3	18.5 / 6	18.5 / 9	NA

* current set up

Table 14. Number of stands flowing through the different unit operations in an hour.

Stands flowing through / hour	**No. / Type**	**No. / Type**	**No. / Type**	**No. / Type**
Ethanol wash	5.7* / 1	11.3 / 4	11.3 / 7	22.6 / 10
Acetone wash	5.7* / 1	11.3 / 4	11.3 / 7	22.6 / 10
Dipping	2.9* / 2	3.9 / 5	10.0 / 8	5.9 / 11
Heat treatment	3.2* / 3	6.5 / 6	10.2 / 9	NA

* current set up

The results shown in Table 14 indicate that the smallest number will be the bottleneck of the production. The first column represents the current set ups of the unit processes. It shows that now the bottleneck is the dipping and the heat treatment is not far behind. To increase the production volume, bottlenecks must be removed by device changes.

To increase the production volume by increasing the number of employees is not reasonable with the current production equipment. Table 13 shows that an increase in the number of the production personnel from 1 to 2 is not logical, because only three stands can be handled per hour in the dipping and in the heat treatment phase. Practical experience has also shown that one person can handle the stands alone and more workers in the small production room could increase the risk of errors and mix-up with the stands.

Working in several shifts is sensible because the preparation of the coating with five layers with three stands takes less than 7 hours without breaks with the current production equipment (shown in Table 6). If needed, there is enough time to prepare a sol in every shift. The results in Table 15 show that working in shifts increases the production capacity. It shows also that the effect of the new stand (110 substrates attached to the stand) is huge. The production volume can be increased clearly only by investing in a new stand that can be installed on the current equipment.

Table 15. Production capacities.

Production volume / year	**5 layers**		
1 person			
Shifts / day	3	3	1
Substrates / Stand	110	24	24
N:o of stands in rotation	3	3	3
Dipping days / week	4	4	4
Weeks	52	52	52
Total	205920	44928	14976
Increase -%	1375 %	300 %	100 %

6.2 New stand

The results of the new stand show that it has the greatest influence on the production volume. In the currently used stand there are now 24 attachment spots for substrates (e.g., implants) and in the new stand there are 110 attachment spots The use of the new stand results in almost a five-fold increase of the production volume and the coating process takes the same time as with the old stand. It is very significant because it shows that the implants can be coated in larger groups. In addition, at least 3 samples with one stand and 4 samples with more stands will be destroyed in the quality testing, which is quite much with the current stand. The greater the number of the substrates in one stand is, the better the production capacity.

In order to show that the quality of the coatings is acceptable with the new stand, the coatings were analyzed by routine quality tests, such as a contact angle and a reactivity test. The contact angle analysis is a method to determine hydrophilicity. The reactivity test determines the kinetics of reactivity of a material. Table 16 shows the contact angle analysis results and Figure 7 shows the attachment spots from which the test implants were taken. The attachment spots were chosen to represent possible differences in coating structure due to, e.g., possible differences in evaporation and xerogel formation. The numbering goes from the outer circular to the center and in the clockwise direction.

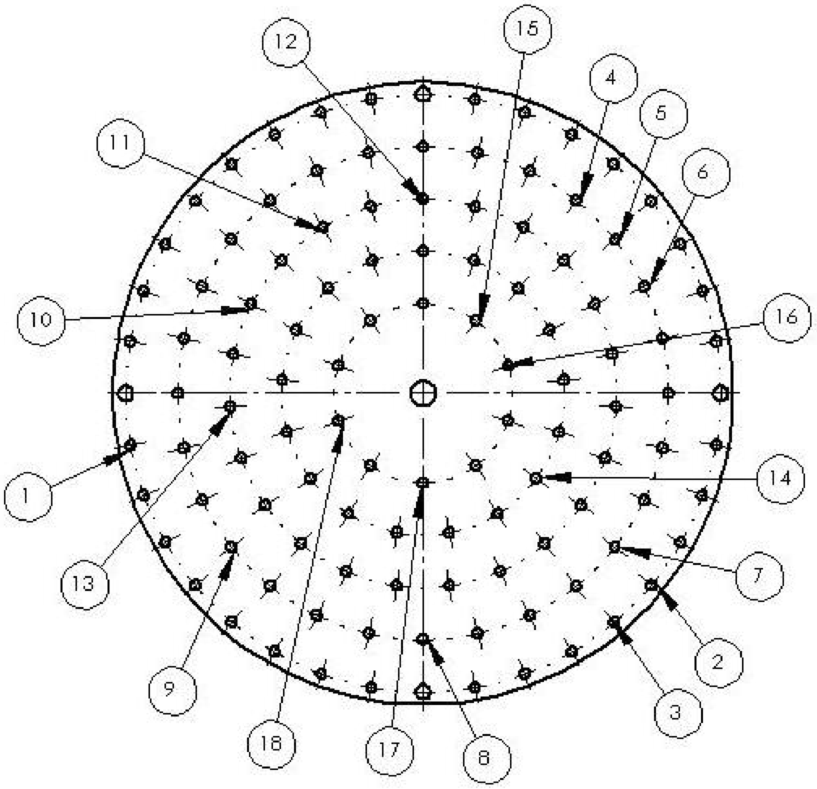

Figure 7. Attachment spots of the implants for the quality tests.

Table 16. Contact angle results on the coatings in the new stand.

	Drop1	**Drop2**	**Mean**	**St. Dev.**
Sample1	36.48	37.39	36.94	0.64
Sample2	38.74	38.54	38.64	0.14
Sample3	32.95	29.34	31.15	2.55
Sample4	36.12	33.45	34.79	1.89
Sample5	29.33	32.61	30.97	2.32
Sample6	34.54	34.13	34.34	0.29
Sample7	27.02	30.88	28.95	2.73
Sample8	38.84	33.16	36.00	4.02
Sample9	31.98	30.20	31.09	1.26
Sample10	28.89	26.40	27.65	1.76
Sample11	28.08	29.79	28.94	1.21
Sample12	29.94	32.82	31.38	2.04
Sample13	26.26	25.76	26.01	0.35
Sample14	31.67	27.96	29.82	2.62
Sample15	27.64	29.05	28.35	1.00
Sample16	29.31	34.78	32.05	3.87
Sample17	28.31	28.49	28.40	0.13
Sample18	37.26	36.65	36.96	0.43

The contact angle results were acceptable, i.e., within the specifications, but the results show that there was variation between the test samples. However, no trend was found. The variation might derive from the hand made stand that is not so accurate in positioning, e.g., it is possible that the samples were not exactly vertically aligned on the stand.

The reactivity test results in Table 17 were also acceptable, i.e., within the specifications, >18. Based on the quality tests, it is realistic to say that the new stand is feasible for the coating process with the current equipment.

Table 17. Reactivity test results for the coated implants in the new stand.

Sample	**Result**
1	22.25
2	20.48
3	25.30
4	24.52
5	21.46
6	24.50
7	20.14
8	24.45
9	22.45
10	35.13
11	28.76
12	34.71
13	31.25
14	26.52
15	28.47
16	29.46
17	27.55
18	21.86
Mean	26.07
St. Dev	4.55

The quality tests show that there is a possibility to increase the number of samples on the stand. According to the results it might be possible to attach more samples to the stand as far as the proper distance between the samples is kept in mind. The effects of the number of the substrates in the stand on the resulting nanostructure of the coatings cannot be concluded with certainty based on these two tests and more surface analyses might be needed.

6.3 Aging of the sol

The results in Table 18 show that there was a slight increase in the contact angles when using the sol that had aged for 8 hours, but after 24 hours of aging the contact angles were about the same as for the fresh sol. Also the standard deviation was greater for the coatings prepared with the sol aged for 8 hours. However, all the measured contact angles and reactivity test results (shown in Table 19) were acceptable, i.e., within the specifications. The viscosity of the sol was somewhat higher than the upper limit of the specifications after 24 hours of aging.

Table 18. Contact angle results for the coatings prepared as a function of sol aging

Aging of sol 0 h	**Drop1**	**Drop2**	**Drop3**	**Drop4**	**Mean**	**St. Dev.**
Sample 1	17.64	18.92	21.32	25.04	20.73	3.25
Sample 2	13.18	16.05	15.26	14.87	14.84	1.21
Sample 3	18.84	16.31	16.36	18.56	17.52	1.37
Sample 4	15.36	12.74	8.27	13.53	12.48	3.01
Aging of sol 8 h	**Drop1**	**Drop2**	**Drop3**	**Drop4**	**Mean**	**St. Dev.**
Sample5	13.08	25.34	23.04	27.32	22.20	6.32
Sample6	45.90	35.60	43.13	45.78	42.60	4.84
Sample7	19.59	19.33	34.77	34.45	27.04	8.75
Sample8	35.69	34.43	21.55	23.49	28.79	7.30
Aging of sol 24 h	**Drop1**	**Drop2**	**Drop3**	**Drop4**	**Mean**	**St. Dev.**
Sample9	16.04	19.45	21.57	19.68	19.19	2.30
Sample10	23.28	25.83	36.62	40.07	31.45	8.15
Sample11	23.30	17.89	18.91	19.04	19.79	2.40
Sample12	16.21	17.62	21.39	21.42	19.16	2.66

Table 19. Reactivity test results for the coatings prepared as a function of sol aging.

Code	**Sample**	**Scaled**	**Mean**	**St. Dev.**
Vivoxtio-09-09 samples 1-4 aging of sol 0 h	**1**	46.9	42.0	4.1
	2	42.3		
	3	36.8		
	4	41.8		
Vivoxtio-09-09 samples 5-8 aging of sol 8 h	**5**	45.9	42.2	3.2
	6	40.9		
	7	38.4		
	8	43.6		
Vivoxtio-09-09 samples 9-12 aging of sol 24 h	**9**	42.5	40.5	1.5
	10	39.1		
	11	39.8		
	12	40.6		

The objective of this test was to determine the behavior of the sol during the aging. The results indicate that the sol is usable at least for 24 hours, but viscosity increases slightly. There might be a possibility to raise the upper limit of the sol viscosity to use the sol for 24 hours, because the contact angle and reactivity test results indicate that somewhat higher viscosity (0,7 % over limit) does not affect the surface of the coating. This would decrease the number of sol batches and it helps the working in shifts by decreasing the amount of work and it also saves the precursors of the sol (one sol batch is sufficient for the coating of almost 2 million samples). Generally, the results indicate that the sol is usable at least for 24 hours but the effects of the aging of the sol on the nanostructure of the coating cannot be concluded with certainty based on these two tests and more surface analyses might be needed.

6.4 Air flow

The results in Table 20 show that there is a slight increase in the contact angles when the air flow increases. This indicates that the greater air flow might have some effect on the nanostructure and chemical reactivity of the coating. However, both the contact angles and the reactivity test results (shown in Table 21) were acceptable, i.e., within the specifications. This shows that the different air flows are usable in the coating process. Greater air flow creates unwanted stripes.

Table 20. Contact angle results as a function of different air flows.

Air Flow 1	Drop1	Drop2	Drop3	Drop4	Mean	St. Dev.
Sample1	14.37	16.00	17.59	12.21	15.04	2.30
Sample2	14.09	21.03	22.28	21.66	19.77	3.82
Sample3	14.84	15.93	21.20	16.53	17.13	2.81
Sample4	16.49	23.04	17.79	20.28	19.40	2.89
Air Flow 2	**Drop1**	**Drop2**	**Drop3**	**Drop4**	**Mean**	**St. Dev.**
Sample5	15.83	17.60	21.88	18.06	18.34	2.55
Sample6	22.00	17.32	14.33	15.87	17.38	3.31
Sample7	19.55	18.59	22.66	20.89	20.42	1.76
Sample8	18.32	21.13	22.12	18.03	19.90	2.04
Air Flow 3	**Drop1**	**Drop2**	**Drop3**	**Drop4**	**Mean**	**St. Dev.**
Sample9	25.62	25.32	24.62	22.39	24.49	1.46
Sample10	26.08	29.97	29.62	29.38	28.76	1.80
Sample11	20.83	31.30	27.25	23.44	25.71	4.57
Sample12	26.35	28.62	29.41	25.26	27.41	1.93

Table 21. Reactivity test results as a function of different air flows.

Code	Value	scaled	mean	stdev
Vivoxtio-10-09 Samples 1-4 5 min door closed+5 min door open and ventilation valve closed	1	36.6	28.9	7.5
	2	33.6		
	3	25.0		
	4	20.3		
Vivoxtio-10-09 Samples 5-8 5 min door closed+5 min door closed and ventilation valve 1/2 open	5	22.5	23.3	2.5
	6	23.3		
	7	20.8		
	8	26.8		
Vivoxtio-10-09 Samples 9-12 5 min door closed+5 min door closed and ventilation valve open	9	28.9	29.7	1.3
	10	28.4		
	11	30.2		
	12	31.2		

Preparation of sol was not included in the calculations of up-scaling process because sol is prepared 24 hours before it can be used. This derives to the situation where sol can be made, at the time when coating process is done, for the needs of the next day or shifts. Attaching of samples or substrates was not included in the calculations. Attaching is done at previous shift or before dipping shift starts.

7 Conclusions

It was shown that it is possible with the current equipment to work in three shifts, which triples the production volume. However, there is no need to increase the number of persons preparing the coatings, one is enough. The number of possible stands is three with the current equipment. The significant bottlenecks of the unit processes were the dipping and heat treatment.

It was shown that the coatings prepared with the new stand were within the specifications and the number of attachment spots could be increased to 110.

The sol aged for 24 hours gave acceptable results for the coating properties although viscosity was slightly beyond valid limits. 24 hours of aging would be beneficial by reducing working hours and the amount of precursors.

It was shown that all the possible air flows with current equipment can be used to obtain acceptable results in the quality tests, but the greater air flows resulted in unwanted stripes on the surface.

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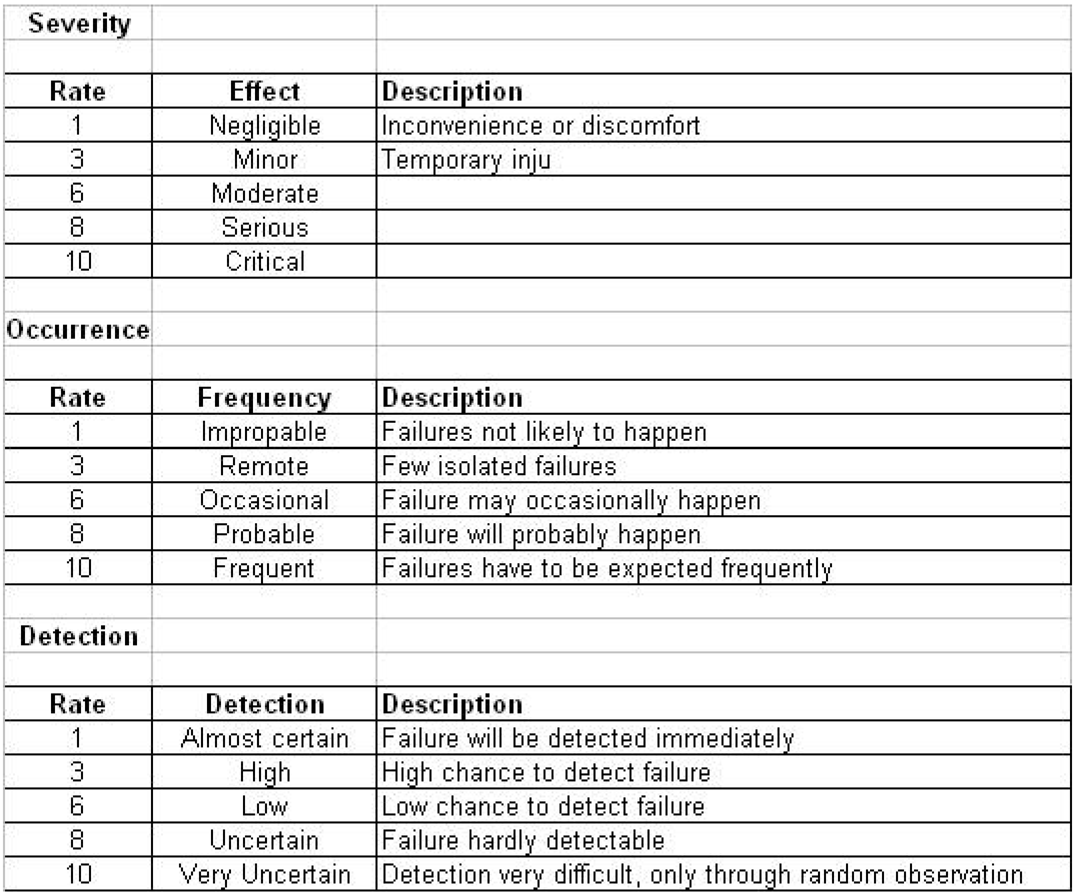
Function	Potential Failure Mode	Potential effects	S	Potential causes	P/O	Risk controls	D	Verification	RPN
Pre-wash	ultrasonic bath doesnt work	acetonic or Aa wash cannot be done	1	ultrasonic bath not plugged in	6	plug in	1		
			6	ultrasonic bath broken	6	another bath or quick repair	1		
			1	power failure	1	power guarantee	1		
	ouf of acetonic	acetonic wash cannot be done	8	out of acetonic	3	enough acetonic, order more soon enough	1		
	out of Aa	Aa wash cannot be done	8	out of Aa	3	enough Aa, order more soon enough	1		
Dipping	Dipper do not work	dipping cannot be done	10	glycol bath not working	6	make sure glycol bath is ok and on	1		
			10	dipper arm do not move	6	quick repair	1		
			3	camera do not work	3	change camera	1		
			3	decanter glass broken	1	another decanter available	6		

			3	wrong type of decanter	1	right type of decanter available	3		
			1	power failure	1	power guarantee	1		
			6	computer broken	1	another computer	1		
heat treatment	oven do not work	heat treatment cannot be done	10	oven broken	3	repair	1		
			1	power failure	1	power guarantee	1		
	sensor do not work	heat treatment cannot be done	6	sensor broken	3	another sensor	1		
			6	cable broken	3	new cable	1		
			3	cable not plugged in	3	plug cable	1		
Sol making	sol is dim	cannot be used	10	contains water	6	new sol	1		
	scale do not work	sol cannot be made	10	scale broken	1	repair	1		
			1	power failure	1	power guarantee	1		
			10	calibration did not succeed	3	repair or new calibration	1		
viscometer	viscometer do not work	sol cannot be used	10	viscometer broken	1	repair	1		
			6	not plugged in	1	plug in	1		
			1	power failure	1	power guarantee	1		
			10	calibration did not succeed	6	new calibration	1		



Severity

Rate	Effect	Description
1	Negligible	Inconvenience or discomfort
3	Minor	Temporary inju
6	Moderate	
8	Serious	
10	Critical	

Occurrence

Rate	Frequency	Description
1	Impropable	Failures not likely to happen
3	Remote	Few isolated failures
6	Occasional	Failure may occasionally happen
8	Probable	Failure will probably happen
10	Frequent	Failures have to be expected frequently

Detection

Rate	Detection	Description
1	Almost certain	Failure will be detected immediately
3	High	High chance to detect failure
6	Low	Low chance to detect failure
8	Uncertain	Failure hardly detectable
10	Very Uncertain	Detection very difficult, only through random observation