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Comparative Bio-entrepreneurial Study of Titanium Implants in Orthopaedics

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Abstract: *Biotechnology has led to the formation of products with advanced technologies and also has high bio-entrepreneurship potential. Biomaterials have been extensively used as implants in orthopaedics. Traditional implants have challenges like a bone deformity or loss after loosening of the implants or bone tumour resection. The idea of using metallic implants like Titanium (Ti) can be considered as a good bio-entrepreneurship potential because of its high tensile strength, biocompatibility, and osseointegration properties. The basic ideas behind a productive business include strategies for product innovation, inspecting the effect of the product on consumers, and working on the feedback for product improvement. Following the disadvantages of using Ti in orthopaedics, Ti-based alloys were developed which can form biofilms exhibiting better characteristics. Research and development of the manufacturing of Ti and Ti-based alloys are directed towards the improvement of production processes to obtain better biomedical properties. Therefore, more promising variants of Ti alloys are innovated and developed which have better formability, biocompatibility, and mechanical properties. The bio-entrepreneurial approach of Ti-based biomedical business has been demonstrated using the famous case studies of the two Ti-based firms. The aim of Ti-based biomedical business is based on the regeneration capability of the bone. So, the quality of life of patients may improve if more innovations regarding Ti implants arise that can lead to a good business opportunity.*

Key Words: *bio-entrepreneurship, implants, innovation, titanium, titanium-based alloys, orthopaedics.*

1. INTRODUCTION:

Bio-entrepreneurship can be defined as using any biological entity or innovative ideas to establish a business and earn a profit [1]. Biomaterials like ceramic, stainless steel, or cobalt-based alloys are compression-resistant and biocompatible implants that are used in orthopaedics. The limitation of ceramic implants is that they become weak and brittle under pressure and tension. The purposeful objective of using artificial bones since the 1980s has been shifted from restoration of bone defects to regeneration of bone functions and to achieve this goal, material structures were needed that can function as a support for effective bone regeneration process [2]. Metals can be considered as alternatives for hard tissue replacements like absolute hip and knee joints, injury healing aids, spinal fixation products, and dental implants. Most metallic alloys are being used as an actuator in devices like vascular stents and orthodontic archwires. Metallic biomaterials can be classified into the following categories –

- Cobalt-based alloys
- Stainless Steels
- Titanium-based alloys

Metals like Titanium (Ti), on the other hand, find a good place in bio-entrepreneurship which are used as implants in orthopaedic surgeries like fracture fixation, joint replacement surgery, or spine resurrection [3]. Elemental Ti was discovered in 1790 and its binding to the bone as well as its use as a metallic implant in a human volunteer was first discovered in 1965 by Brånemark. Ti is highly resistant to forces, has high tensile strength, inertness, low Young's Modulus, biocompatible, and promotes effective osseointegration making it a good alternative to other biomaterials and are used in a vast array of cases where the resistance of the material becomes crucial [4]. The first successful implantation of a Ti-based dental implant led to remarkable improvement in the market and the strategies used for dental replacement. Ti, therefore, is now widely accepted as the prime material of choice for prosthetics, internal fixation, inner body devices, and other biomedical applications.At present, widely used implants in the market are ceramic and titanium. Ceramic implants are durable. Patients who are concerned about metals can request ceramic implants especially for dental implants, but long-term use of ceramic biomaterial can make it weak and shattered and thus require replacement with a new implant. So, in this position, Ti implants can be a good choice due to their high resistive nature and have the natural capability to match the implantation requirements in the human body. Other metallic implants like Cobalt-based alloys (Cobalt-Chromium) were used before Ti in earlier days. These metallic

implants are permanent. Non-permanent metallic implants include stainless steel but they are expensive [5]. Ti or Ti-based alloy implants are routinely used as hard tissue replacements in artificial bones, joints, and dental implants like Prosthetic Hip, Knee Replacement, and Fracture-fixation Devices (plates, screws, intramedullary rods) [6]. Companies that manufacture Ti or Ti-alloy implants are Pivot Implants, BioHorizons, ADIN Dental Implant Systems Ltd., Precipart, Tecomet, Argon Dental Vertriebs GmbH & Co.KG, etc. Ti-based implants are manufactured to last about ten years or more, however, in very few cases, longevity is not achieved due to lack of integration into the bone leading to failure of the implant. One of the causes of this failure is accredited to allergic reactions (erythema, urticaria, eczema, swelling, pain, necrosis, and bone loss) associated with Ti metal (Ti-G1 and Ti-G4) [7]. Innovation was required to overcome such conditions, so Ti-based alloy implants were developed. Innovation is the key to a successful business. Product innovation, as per the business glossary is "the development and market introduction of a new, redesigned or substantially improved goods or services". Not only for the development but also to meet the customer's demands and expectations, research and development are required. Among all the Ti alloys, Ti-6Al-4V (G5) alloy is commercially used in the biomedical field [8].

From initial discovery to subsequent development of orthopaedic implants and devices, the huge impact on the biomedical industry mostly lies in research and innovative approaches for metallic implants because of their superior properties over ceramic or polymeric biomaterials. In this study, the bio-entrepreneurial approach of Ti and Ti-based alloys and the stature of their research and development (R&D) process as orthopaedic devices are reported. The study also includes methods to improve their tribological characteristics and osseointegration property, so that a more biocompatible Ti-based alloy can be innovated and developed for benefit of orthopaedic patients as well as increase profit for the companies. The bio-entrepreneurship approach of two distinct Ti-based biomedical device companies has also been discussed in this study.

2. TITANIUM AND TITANIUM-BASED ALLOYS IN ORTHOPAEDICS:

In the early 1930s, Ti was considered suitable for fabricating implants because of its well-tolerability compared to Stainless Steels, Cobalt-alloys, and other traditional implants. It is light and due to its good mechanical properties like high tensile strength, inertness, and low Young's Modulus, it was a perfect match to be used as implants for orthopaedic surgeries. Ti was discovered to be the only metal biomaterial capable of osseointegration [9]. There were also hypotheses about a potential bioactive behaviour due to the steady growth of hydrated TiO_2 on Ti-implant's surface, which contributes to calcium and phosphorous absorption.

The increasing use of Ti and Ti-based alloys as biomaterials is due to their exceptional biocompatibility and good corrosion resistance characteristics, which in turn is because of the thin oxide layer formed on the surface, and strong mechanical properties including elastic modulus and less density, that render the function of these metallic implants equivalent to those of bones. Among all Ti and Ti-based alloys, widely used Ti implants in the biomedical area are the pure Ti (*p*Ti of G2) and Ti-6Al-4V (G5) alloy. They're generally used to replace hard tissue in bones, joints, and dental implants. The low elastic moduli of Ti and Ti-based alloys are typically considered as a mechanical advantage over traditional implants since the smaller elastic modulus will result in far less stress shielding. Ti usually forms a thin and adherent TiO_2 layer via the passivation and re-passivation process that acts as a protectant to the rest of the metal. This oxide layer creates a solid, protective, and durable barrier when it interacts with the air thereby, avoiding oxygen from escaping to the atmosphere and thus, ensuring resistance to corrosion [10]. Therefore, this layer enhances the biocompatibility and corrosion-resistance properties of the metallic implant and allows direct mineral deposition on the bone-Ti interface, and promotes osseointegration. The spontaneously TiO_2 film that is formed on the metal's surface prevents diffusion of metallic ions across the layer [11]. The surface morphology of the TiO_2 film should be such that it should hinder the ions from migrating across the TiO_2–bone interface and must stay on the surface of Ti-based alloys even though subjected to mechanical stress or abrasion [12]. Pure Ti is an allotropic metal consisting of both hexagonal alpha-phase (HCP) and cubic beta-phase (BCC). The alpha-phase is maintained at a temperature below 882 ºC and gets transforming to beta-phase when the temperature is increased beyond 882 ºC. using pure Ti as orthopaedic implants pose some challenges like non-longevity due to which integration with bones is not effectively achieved. Therefore, modification of Ti became a necessity for improving the longevity as well as osseointegration efficacy. This led to the innovative development of Ti-based alloys involving the combination of various other inert metals like Aluminium (Al), Vanadium (V), Nickel (Ni), Chromium (Cr), etc. Ti-6Al-4V alloy is used as biomaterial-of-choice in hip implants, knee implants, bone screws, and plates [13] [14]. These metals do not cause any hypersensitivity reactions such as nickel hypersensitivity which is caused by Stainless Steel in the adjacent tissues. The combination of metals like Al and V improves the efficiency of the Ti-alloy (Ti-6Al-4V) implant. The addition of Al stabilizes the alpha-phase and V stabilizes the beta-phase, and the presence of both the elements reduces the temperature of the transformation from alpha-phase to beta-phase. Also, the Modulus of Elasticity is much lower than other traditional implants. However, the addition of specific elements Aluminium and Vanadium can cause serious health effects. The release of Al^{3+} ions accounts for long-term Alzheimer's disease and Vanadium causes

cytotoxicity and adverse hypersensitivity reactions [15]. Ti and Ti-based alloys to be used as orthopaedic implants should meet the following characteristic properties –

- The use of potentially toxic elements (Al, Cr, V, etc.) should be in very less and acceptable quantity. It is better to avoid the use of such elements.
- The alloy should be resistant to corrosion.
- The alloy should bear the following mechanical properties including low modulus, high strength, and notched fatigue strength.
- The alloy should be easy to work with and ductile.
- The alloy should promote effective osseointegration and enhance longevity.

Accordingly, recent Ti-based alloys employed for biomaterial implants composed of non-toxic and non-allergenic elements having better mechanical properties and workability. Because of the poor tribological properties and corrosion issues, Surface Treatment methodologies have been developed to enhance the tribological characteristics along with near-surface strength, hardness, abrasive wear resistance, lowering the coefficient of friction, and preventing or reducing ion migration from the surface of Ti to the surrounding tissues [16]. Surface Modification strategies can be grouped into the following categories [17] – (i) morphological modifications; (ii) biochemical (along with physiochemical) modifications. The morphological modifications include Particle Blasting, Grinding, Polishing, Plasma Spraying, Acid or Alkali Etching, Anodization, etc. Biochemical modifications include Osteoinductive Biomolecular Cues (using cell-adhesive proteins and BMP-2 growth factors), Organic nanoscale Self Assembled Monolayers, etc. Designing of the first generation orthopaedic Ti-based alloys try to replace the V and Al metals with other non-toxic metals like Nb, Fe, Mo and Ta, Hf, Zr respectively. Some of the Ti-alloys are listed in *Table 1* [8].

Table 1. *Titanium-based alloys used in orthopaedics*

i.	CP Ti	ii.	Ti-13Nb-13Zr
iii.	Ti-6Al-4V ELI	iv.	Ti-12Mo-6Zr-2Fe
v.	Ti-6Al-4V	vi.	Ti-15Mo
vii.	Ti-6Al-7Nb	viii.	Ti-16Nb-10Hf
ix.	Ti-5Al-2.5Fe	x.	Ti-15Mo-5Zr-3Al
xi.	Ti-5Al-3Mo-4Zr	xii.	Ti-15Mo-2.8Nb-0.2Si-0.26O
xiii.	Ti-15Sn-4Nb-2Ta-0.2Pd	xiv.	Ti-35Nb-7Zr-5Ta
xv.	Ti-15Zr-4Nb-2Ta-0.2Pd	xvi.	Ti-29Nb-13Ta-4.6Zr

The primary aim of surface modifications is to enhance the physicochemical characteristics, corrosion resistance, and osseointegration of the implant. Developing coatings that improve the wear and corrosion resistance by increasing the hardness of the Ti-based alloys that can be applied by different surface modification strategies like surface oxidation, ion implantation, plasma spray coatings, as well as thermochemical surface treatments [18]. The Physical Vapour Deposition (PVD) process facilitates the generation of Diamond-Like Carbon (DLC) coatings that may be integrated with Ti which improves the biocompatibility, corrosion, and wear resistance of the substrate while minimizing the friction coefficient [19] [20]. Many innovative strategies involving thickening, or stabilization of the TiO_2 surface films have been proposed to achieve better biocompatibility. The biological interactions to Ti is determined by the chemical constitution of the surface as well as the potential of TiO_2 to absorb molecules and integrate the components [21]. Surface morphology (shape, orientation, and adhesion properties) plays a vital role in the regulation of cellular responses. The Plasma Electrolytic Oxidation (PEO) methodology allows for the modification of the function and distribution of the TiO2 surface coating that helps for corrosion protection, friction optimization, and osseointegration improvement of Ti-based alloys [22]. At the bone-Ti interface, the coating becomes concentrated and this morphological property causes improved surface roughness. Other features of this treatment include economic efficiency, environment-friendly, high hardness, excellent wear, and corrosion resistance, and exceptional bonding strength with the surrounding tissues.

3. BIO-ENTREPRENEURIAL APPROACH OF TITANIUM IMPLANTS AS BIOMEDICAL DEVICE:

The ultimate aim for any biomedical device is to improve outcomes for patients, this need should be considered at beginning of the process and not towards the end. With rising aging population, there is an increasing global market demand for high-quality, safe, and durable orthopaedic devices. The preliminary steps in starting any

biomedical business, especially for the orthopaedic devices should focus on the "3 Is" condition, i.e., Identification, Invention, and Implementation (as shown in *Fig 1*) [23].

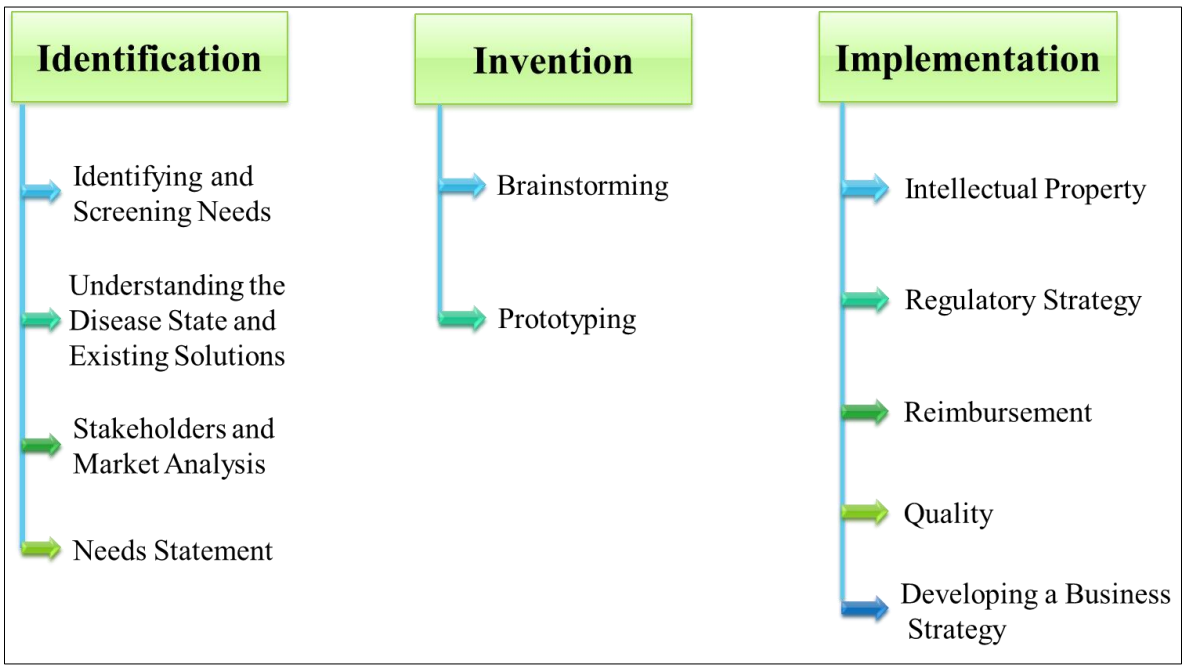

Figure 1: Conditions for starting a biomedical business

In the Identification phase, the Ti-based alloys are developed with an in-depth knowledge of the problem statement along with its specificity and precision analysis. The main problem statement hypothesize on developing a more effective, modified, and durable Ti-based alloy to be used as implants utilized in orthopaedic surgeries. So, for developing a new Ti-based alloy, the unmet clinical needs are usually identified. The first step of a bio-entrepreneurial approach for a Ti-based medical device company is to understand the necessity that entails learning everything to know about the problem including the clinical pathways, present and future prospects of the treatment strategy, current health economics, and the stakeholders who work together to produce or influence it. Therefore, it becomes important to develop a comprehensive understanding of the existing and prospective outcomes to a specific problem. Also, the identification of the stakeholders for the clinical process and then investigating the attractive attributes of the Ti-based alloys is a crucial step of bio-entrepreneurship that aids in the smoothness of the developmental process of the Ti-based alloy implants. Besides identifying the stakeholders, a typical analysis of the market is required for efficient screening of the current scenario.

The Invention phase consists of Brainstorming and prototyping for the entrepreneurial development of the Ti-based alloy orthopaedic implants. For searching potential solutions to the problem statement, a team of experienced innovators as well as fresh-minded intellects generate significant ideas for the development of the Ti-based alloys. With the help of Brainstorming sessions, maximum outcomes may be obtained in a short period by creating enthusiasm, achieving participant consistency, and incrementing the opinions throughout the group. After the selection of the final solution, prototype versions of the Ti-based alloys are created to technically meet the unmet criteria as quickly as possible. Individual levels of prototyping can be constructed in a stepwise manner, gradually decreasing the technical and potential challenges of the concept at each iteration. The final and the most significant phase is the Implementation phase, where the developed Ti-based alloy orthopaedic implants need to be protected by suitable Intellectual Property Rights (IPR). It is critical to carefully evaluate the regulatory framework for the newly developed Ti-based alloy implants. The procedure is tedious and labour-intensive, however, it enables commercialization of the product and also influences sales and marketing approaches as well as risk management procedures. The authorization is granted by FDA only after qualifying for the Quality Control or Assurance test (QA/QC) which in turn depends upon the biocompatibility and patient care of the Ti-based alloy implants. When implemented early, Quality standards might add substantial cost and value to the product. The medical device developed should draw reimbursements either from the payors or the patients, otherwise, hospital-based purchasing becomes essential. After successful consideration of all the above bio-entrepreneurial conditions, an effective business can be set up which moves onto the next level of capital investment. This is a crucial step for the effective commercialization of Ti-based alloy orthopaedic implants. The inventor gathers a team of marketing and commercialization professionals who can

successfully describe how the Ti-based alloy implants meet the previously unmet clinical conditions of using traditional implants and why the value proposition of the medical device supports the expenditure of the customer. Following are the two case studies of the healthcare companies on the introduction of two nearly identical inventions. The two companies, both in the Ti implant business, were chosen because their origins, technologies, and clients are similar. However, the spread took place in two different (institutional) environments: Sweden and the United States. The entire process is investigated, from invention to innovation and diffusion in the market. We'll look at how two separate competency blocs [24] influence two identical inventions, exploited in two distinct companies, one in Ohio and the other in Sweden. Both situations are highly comparable in every way (university origin, technological, market, etc.), but they were created in two contrasting institutional environments, Sweden and the United States. As a result, we may discuss the analysis experimental design. The entrepreneurial effort of choosing between different ideas and integrating inventions into new or different goods is resource-intensive in the innovation process. This is an economic, not a technological, process that is extremely costly and resource intensive [25].

3.1. Nobel Biocare:

Nobel Biocare is a Swedish medical device firm, founded in 1981, dominates the global market for dental implants. Nobel Biocare's products support a variety of healthcare markets with the goal of designing, manufacturing, and distributing the Brånemark System. The innovative aspects for successful development of the project had the following points – (i) Ti integrates with bone; (ii) The notion that bone requires special care; (iii) biocompatibility of Ti; (iv) design of Ti and its significance of production in a clean environment; (v) surgical methodologies. Customer resistance based on negative and mistrust of the osseointegration process by dentists was one of the major issues that the company was dealing with. But later with thorough investigations, the osseointegration was marked as one of the important innovations and therefore was approved. The Brånemark method's advantages were supported by the Canadian conference. Nobel Biocare is the only company with clinical documentation with a five-to-twenty-year follow-up period. Nobel Biocare also established a training center within the organization. Brånemark Osseointegration Center got established due to the sole focus of the company on dental implants. The Brånemark Osseointegration Center works closely with osseointegration researchers around the world on a variety of implant applications such as arms, legs, joints, etc. The FDA proposed that dental implants be classified as Class III devices, requiring full regulation, and approved the pioneering work of the company, this gave the company an advantage over its competitors.

In 1990, Brånemark and his team treated the first patient who received a leg prosthesis with Ti screws. Bofors (an ideal maker of screws) decided to create a subsidiary company to market and manufacture Ti screws and related equipment. Both the patient and the health care provider benefit from osseointegration. It has resulted in a significant reduction in treatment and healing time as well as overall costs allowing for the treatment of more patients. The osseointegration technique is now widely used in many fields, including dentistry and facial reconstruction. Alternative therapies, such as plastic surgery, are not always appropriate for rehabilitating patients therefore, osseointegration may play a significant role. Osseointegration is a new technology for attaching a prosthesis to the human body where the Ti connects the prosthesis to the skeleton directly. This reduces skin irritation and gave many patients a sense of stability and security. International collaboration with educational institutions and other groups around the world has been a key factor in the spread of osseointegration technology that aided in the confirmation of many of Brånemark's clinical findings. These centers were critical in demonstrating that by following the osseointegration techniques, consistent, reliable, and repeatable results could be obtained. Some patients were able to detect the type of ground they're walking on, whether it's grass or asphalt. Nobel Biocare bought Steri-Oss, an American firm, in 1998. Nobel Biocare's business in the United States was doubled as a result of the merger. Nobel Biocare has reached an agreement with the venture capital firms Novare Kapital and Swedestart to transfer operations in the CFRA business area to a new company to fund the development and marketing of bone-anchored hearing aids and facial prostheses, as well as new hearing rehabilitation products. In collaboration with Nobel Biocare, Brånemark developed a new method for dental implants known as Brånemark Novum that allows patients to get new teeth in a single day. With the new method, the dentist's treatment time is halved, and the cost of treatment is reduced. Nobel Biocare became the global leader of dental implants. Nobel Biocare's board of directors were convinced that adopting a new Swiss holding structure will provide significant benefits to the company. The holding structure will allow the company to reduce its corporate tax burden and bring it in line with that of other multinational corporations. The reasons for Nobel Biocare's new holding structure support the theory that institutional settings are important for firm growth. This is an illustration of how crucial they are.

3.2. AcroMed:

AcroMed is a biomedical device firm that holds a dominant position in the global spinal implant industry. AcroMed's creator Steffee had invented and developed the Variable Screw Placement (VSP) plates and screws.

Pedical Screw Fixation method was developed by Steffee where the bone plate is improved by replacing the holes with slots that better suited the spine. The bone plate is then fitted over the screws and secured with a nut once the screw has been inserted. The first devices were approved by the FDA in 1995 as pedicle screw devices. The company was started based on the suggestions of Ed Wagner to put forth the idea of pedicle screw devices into an entrepreneurship approach. AcroMed's devices were made entirely of stainless steel, but by 1988, Ti had been added to the mix. The Ti bar is more durable than steel. Some people may be allergic to stainless steel, thus, Ti is preferred instead. The doctor will select one of these based on the circumstances. As a result, it all depends on the type of injury or condition, as well as whether or not the implant should be removed. Customers seem to favour Ti, particularly the Japanese, who rely heavily on MRI or X-rays. They also have a different perspective on the body, such as Eastern medical philosophy, which emphasizes harmony, and hence chose Ti, which is more biocompatible. AcroMed has subsidiaries in the Netherlands and Japan. The corporation is committed to education and sponsors several workshops and physician training programmes. AcroMed brought considerable experience and knowledge in addition to finance.
Another intriguing notion employed by the firm is the so-called AcroLink, which is an interactive PC-based teleconferencing network that spans the globe. The surgeon can consult with another surgeon using this technology, as long as they both have the identical X-ray image in front of them and can converse over the phone. AcroMed also donates devices and implants to medical colleges around the world. Information and knowledge about the company and its products can be passed down from one doctor to the next, as well as through international gatherings and conferences. This makes interactive consulting easier because one of them can use a marker to make ideas or provide facts. In order to develop an artificial replacement for spinal discs, AcroMed collaborated with the Edison Polymer Innovation Corporation (EPIC) and the University of Akron. DePuy Inc. which already entered into the spinal implant industry bought AcroMed in March 1998. After being purchased by DePuy Inc. the company was able to manufacture wide range of orthopaedic implants. Spinal implants became the single largest product segment after the merger, accounting for around 20% of AcroMed-DePuy's revenue. DePuy, Inc., a Johnson & Johnson corporation, owns and operates AcroMed with its headquarters in Raynham, Massachusetts, it is one of the world's major designers, makers, and suppliers of orthopaedic devices and supplies.

3.3. Comparison Between the Two Firms:

In this section, following the above discussed case studies, the two Ti-based biomedical device companies are evaluated and compared (as shown in *Table 2*). The instances demonstrated that the business growth in the US case, AcroMed, was faster (in the early stages) than in the Swedish instance, Nobel Biocare [25].

Table 2. Bio-entrepreneurial Comparison between Nobel Biocare and AcroMed

Nobel Biocare	AcroMed
1. Nobel Biocare was founded with the goal of marketing and manufacturing dental implants. Dentistry was the first field in which the osseointegration technique was utilized. The osseointegration technique is now widely used in a variety of fields. For those who have experienced face injury due to an accident or disease, life-like facial characteristics based on identical Ti anchors used for teeth are now conceivable. The method is also employed in the field of hearing aids.	1. AcroMed's main products are various types of Ti and stainless-steel spinal implants. Steffee devised a screw that could be affixed to the spine during the healing process. Before the introduction of this product and approach to the market, neurologist surgeons were the primary players in the treatment and healing of back pain and scoliosis.
2. Nobel Biocare was founded on a completely new idea. It did not break even until 1988. It was established more than 15 years after the first patient was treated.	2. AcroMed was founded on gradual innovation. It was self-sufficient by 1986. It was founded barely two years after Steffee's discovery.
3. Nobel Biocare used new technology to an existing market.	3. AcroMed created or defined a new market utilizing a well-known methodology but in a completely new way. Steffee's innovation was revolutionary in this regard.

4. Brånemark's ability to comprehend the significance of the unexpected revelation that Ti combines with bone and is biocompatible led to the birth of a new industry. In addition, bone must be handled with the same care as soft tissue in the body.	4. Steffee came up with the innovation of screwing the vertebra together during a surgery session.
5. Brånemark's procedure was immediately accepted by physicians. Dental implants were approved by the National Board of Health and Welfare (NBHW) in 1976 and were included in the National Insurance System. It wasn't until 1982, when a Canadian physician presented a replication of the Brånemark approach at an international conference, that professionals began to fully comprehend the possibilities and benefits for the patient if treated in this manner	5. AcroMed, the innovative method introduced and created by Steffee was immediately adopted by the customer. Steffee received acceptance for his method at a conference, similar to Brånemark, emphasizing the significance of a well-functioning network with receiver competency for reaching the client.
6. Brånemark's approach was endorsed by NBHW but did little to promote it. The approval was granted on 1989 by the FDA.	6. The FDA initially rejected Steffee's approach for treating the spine in 1982. However, in 1984, AcroMed received approval for their product after submitting a new application form with the application region changed from the spine to the bone.
7. Although NUTEK had funded and supported Brånemark's osseointegration research for many years, the project was always in financial trouble. Brånemark was threatened with having to shut down his studies on several occasions because of the scarcity of competent venture capital.	7. AcroMed, on the other hand, had no trouble raising finance or transitioning from modest to large-scale production.
8. Nobel Biocare manufactures in-house. The capital requirements increased as a result, and output became less flexible. It was primarily funded by an existing large and well-known corporation.	8. AcroMed employs outside vendors for its production. It relied significantly on its funds. The venture was partially funded by the inventor and founders' savings.
9. Nobel Biocare profited from the surrounding hospital and university, and it might be said that it is based on a university-hospital model.	9. AcroMed, similar to Nobel Biocare, also profited from the surrounding hospital and university, and it might be said that it is based on a university-hospital model.
10. Nobel Biocare markets the products to professionally trained doctors in a surgical procedure developed by Brånemark, resulting in intimate customer relationships.	10. AcroMed markets the products to professionally trained doctors in a surgical procedure developed by Steffee, resulting in intimate customer relationships.

The two elements that may account for the disparity between the two firms can be concluded as – (i) in the case of Nobel Biocare, there was a lack of receiver competency that resulted in a negative attitude that had to be addressed. The failure of the invention and innovation process is due to a lack of expertise; (ii) access to competent venture funding, such as a straightforward way to commercialize industrially relevant research, is another crucial issue. It has also been demonstrated that own equity is critical for a firm's entry and growth. Thus, in the case of dental implants, a lack of qualified venture capital, as well as capital market regulation, has hampered commercialization. Furthermore, the incomplete competence bloc has restricted the innovation's exposure to the varied competence in the evaluation process, raising the danger of missing an apparent winner. This is the most important takeaway from the two incidents.

4. CONCLUSION:

Ti and Ti-based alloys are regarded as some of the most promising biomaterials due to better biocompatibility and osseointegration for biomedical applications. Interest in Ti-based alloys for biological and tribological components is rapidly developing in wide range of industries, especially in the biomedical field, due to their unique properties such as high strength-to-weight ratio, melting temperature, and corrosion resistance. Manufactured components of the Ti-based alloy implants are frequently in contact with the diverse environment including stationary or dynamic stress at varying temperatures. The thin TiO_2 surface film that passivates on the Ti surface can be damaged by these contact stresses, and the metal can be subjected to intense interactions with the surrounding environment that can cause high friction on Ti components, as well as corrosion resistance, resulting in the early failure of the implants. So, modification of Ti-based alloy implants becomes necessary to improve the success of bone implant fixation and the longevity of Ti-based implants. As a result, the development of various surface modification methodologies for Ti and Ti-based alloys are becoming increasingly important in order to minimize these effects and enhance the osseointegration and longevity of the Ti-based implant. This innovative strategy can be conceptualized into an effective entrepreneurial approach to develop biomedical device firms. The market for biomedical implants is enormous and evolving at a rapid pace. Innovation contributes in capital allocation and makes it competitive for firms to expand into new markets while serving the needs of patients and customers. Because these solutions are biological, they require development over time, and the R&D department is critical to have a stronghold on the business. To prevent commercial malpractices, the product must be secured by Intellectual Property Rights (IPR) once it has been implemented. With an increasing number of orthopaedic patients, it would be beneficial to design and improve Ti alloys with structural and biological capabilities to regulate bone healing limitations and abnormalities.

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