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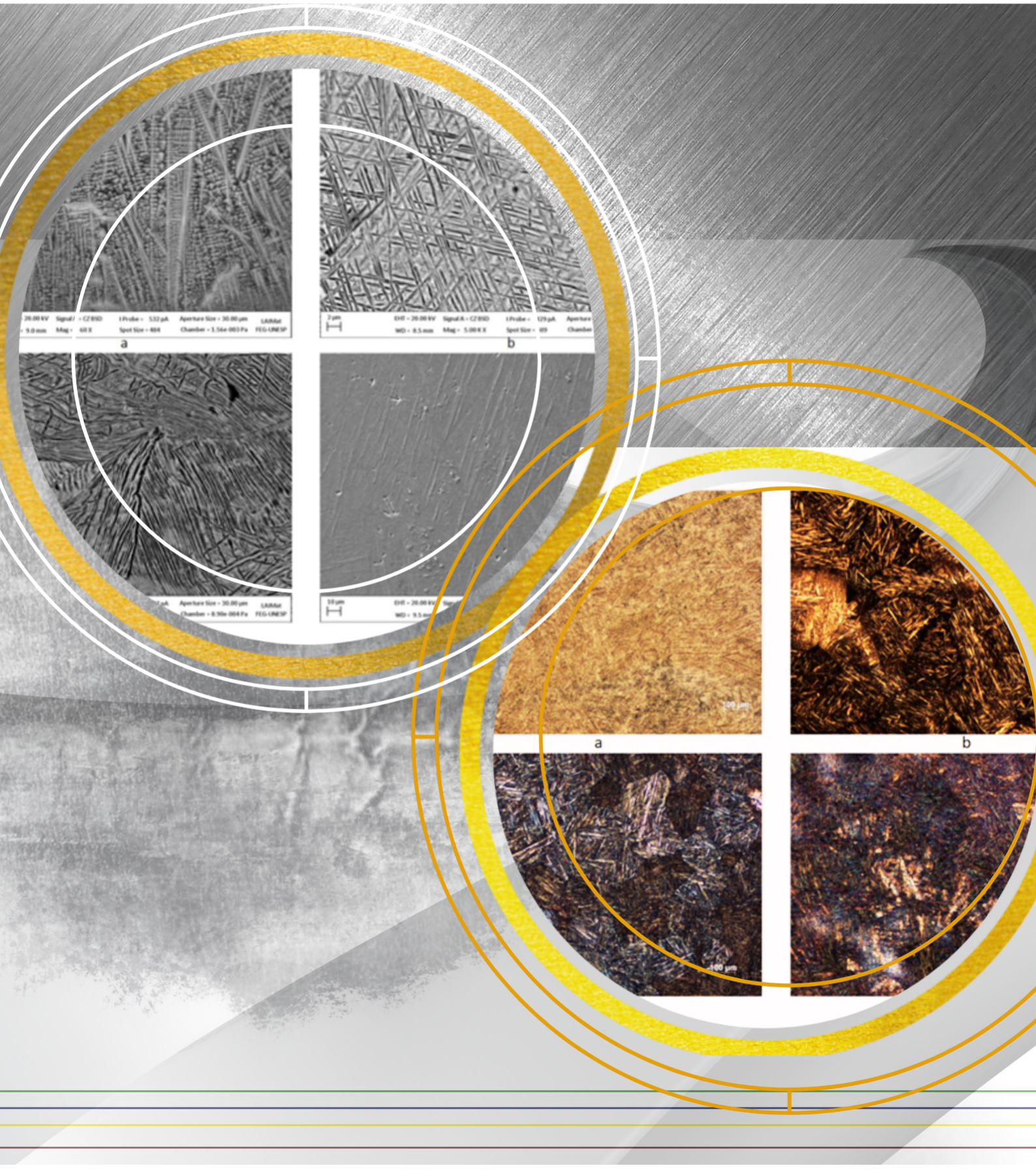

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Effect of heat treatment on microstructure and mechanical properties of Ti30Ta alloy for biomedical applications

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Abstract: As life expectancy increases, further research is needed to develop new materials for biomedical applications. Titanium and its alloys have great potential to be used for such a purpose due to their excellent bulk properties, such as mechanical strength. However, these properties are influenced by their microstructure which varies according to the processing method. Thus, this research aims to evaluate the influence of heat treatment on phase transformation and mechanical properties of Ti30Ta alloy which has been made in an arc melting furnace. The heat treatment has been carried out at 750°C, 800° C and 850°C for 12 hours, followed by water quenching. The β-*transus* temperature was determined by Differential Scanning Calorimetry and High Temperature X-ray diffraction. The phases and structure have been investigated through optical microscopy, scanning electron microscopy and X-ray diffraction. Microscopy images and X-ray diffraction analysis reveal the presence of martensitic phase α'' for the solution treated sample and both α'' and α' phases for recrystallized samples. Mechanical tests show an increase in mechanical strength for all samples after recrystallization and the highest value was observed for the sample treated at 750°C, although there was an undesirable increase of 30 GPa in Young Modulus.

Keywords: Titanium Alloys. Mechanical Properties. Biomaterials. Heat Treatment.

Introduction

In the latest years, new materials must be studied for biomedical implants, since life expectancy has been increasing. Over 500.000 hip replacement surgeries have been performed worldwide from the beginning of this century[1]. Nowadays, biomedical implants are made by using many materials, e.g. metals, ceramics, and polymers. The most common metallic materials used in prosthesis manufacture are stainless steel, cobalt-chromium (Co-Cr) alloys and titanium alloys [2]. However, when implanted into the body, elements like nickel, cobalt and chromium can be released into the patient's body due to corrosion and aggressive environment, thus bringing about toxic effects, as stated by Nicholson [2].

Despite to the toxicity of these materials, stainless steel (200 GPa) and Co-Cr (220 GPa) alloys have a much higher elastic modulus than the human bone (20-30 GPa). This difference of properties can result in an effect called stress-shielding which is an insufficient bone load that leads to bone resorption, implant failure and even another fracture. Thus, according to Kaur and Singh [3], titanium and titanium alloys are ideal replacements for hard tissues due to their lower modulus, higher biocompatibility and corrosion resistance.

In the 1960s, the most widely used titanium alloy in aeronautical applications was Ti-6Al-4V due to desirable properties such as mechanical strength and corrosion resistance. Afterwards, it started being used as material for biomedical applications. However, many studies confirm that its toxicity increases with time due to the fact that Al and V ions are released into the body, which may cause diseases, like Alzheimer's and local pain as stated by Kaur and Singh [3].

Thus, there are new lines of research for developing new titanium alloys without using aluminum (Al-free), such as Ti13Nb13Zr studied by Pérez *et al.*[4], Ti45Nb studied by Völker *et al.*[5], Ti15Mo studied by Chen *et al*. [6] and Ti70Ta [7].

Due to the broad difference between the elastic modulus of pure titanium and pure tantalum when compared to the elastic modulus of bone, these metals cannot be used in their pure form. Thus, an alternative is to use Ti-Ta binary alloys whose mechanical properties can be improved by adding the alloying element tantalum, thence not compromising biocompatibility as studied by Zhou *et al*.[7]. When tantalum was used as an alloying element, Zhou *et al.*[8] verified it acts as a β-stabilizer, which improves the stability field of the β phase and assists in the formation of the α'' martensitic phase, which has a lower elastic modulus and marginally lower mechanical strength than the other phases, thus allowing an improvement of these mechanical properties trough heat treatments and resulting in an alloy which possesses high strength-to-modulus ratio.

A potential replacement for biomedical applications is the Ti30Ta alloy which, according to Zhou *et al*.[8], has a low elastic modulus (69 GPa), high mechanical strength and a high strength-to-modulus ratio when compared to currently used alloys. According to Zhao *et al.* [9], its corrosion resistance is higher than that of Ti-6Al-4V alloy.

Thereby, purpose of this study is to evaluate the influence of heat treatment on phase transformation and

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mechanical properties of the Ti30Ta alloy using different processing routes. It has great potential for biomedical applications and the manufacturing process usually involves plastic deformation at a set temperature, which is generally higher than the β–*transus* temperature. Thus, it is interesting to evaluate its behavior so as to simulate these conditions.

Experimental procedure

Ti30Ta alloy processing

The binary Ti30Ta was processed using sheets of Ti (grade 2) and Ta (99.99%). All ingots were melted and remelted over ten times due to having different melting points. Then, they were homogenized under vacuum at 950°C for 24 hours in order to eliminate any residual chemical segregation and worked into bars of 10 mm in diameter by cold swaging. Bars were treated under vacuum at 900°C for 2 hours and then water quenched.

The subsequent treatments were carried out at 750°C (R750), 800°C (R800) and 850°C (R850) for 12 hours followed by water quenching.

A DSC analysis was carried out so as to determine the β–*transus* temperature. For such a purpose, it was used a small sheet made with the Ti30Ta alloy in a platinum crucible, and one crucible was used as reference (empty). Under vacuum, the system was heated from room temperature to 1000°C and then cooled and registered at 100°C. A plate of 0.2 mm in thickness was cut from the solution treated and heat treatment was performed at 750°C, 800°C and 850°C.

A high temperature X–Rays diffraction analysis was carried out with the purpose of determining the α to β phase transformation. It was performed using a Copper Kα irradiation at temperatures ranging between 15° and 100°, accelerating voltage of 40kV, current of 30mA at 0.2°/sec of scanning speed and a heating rate of 2°C/min using a PANalytical equipment, model X'Pert Pro.

The alloy's microstructure was analyzed using a Zeiss optical microscope, model Axio Imager.Z2m, and a Zeiss scanning electron microscope (SEM), model Evo LS–15, operated at 20kV. The samples were ground with sandpaper whose grit sizes ranged between 220 and 1500, polished with colloidal Silica and etched in a solution composed of 5 vol.% HF, 35 vol.% HNO_3 and 65 vol.% H_2O. Phase identification was performed by means of X–Ray diffraction analysis of bulk samples at room temperature using Copper Kα irradiation between 15° and 100°, accelerating voltage of 40kV and current of 30mA at a scanning speed of 0.2°/sec in a PANalytical equipment, model Empyrean.

Tensile specimens were machined by following the specifications laid down by the ASTM E 8M with 6mm in diameter and gauge length of 25mm. A strain gage was attached to the gage section of each specimen. A uniaxial tensile test was conducted at speed of 0.5mm/min and room temperature using a MTS 810 testing system and a MTS– 632.24C–50 extensometer.

Microhardness test of samples were the same as those which had been previously used for microstructural characterization. Vickers microhardness was measured with a Shimadzu model HMV 2T microdurometer and conducted with 1.961N of load for 15s.

Results and discussion

For the initial characterization of the alloy, samples were used in the following conditions: as cast, after homogenization treatment (24 hours at 950°C), after cold swaging and after solution treatment (2 hours at 900°C). During the melting process, the alloy surface in contact with the copper crucible underwent rapid cooling while the surface that was not in contact with the crucible which was slowly cooled. The resulting microstructure under such condition was a two–phase dendritic structure, due to the different cooling rates on the sample, which can be seen in Fig.1 (a). The homogenization treatment turned the microstructure into a secondary stable two–phase acicular α structure spread over a β matrix structure which had also been observed by Du *et al.* [10] and can be seen in Fig.1 (b). The cold swaging caused a severe plastic deformation in the alloy microstructure, but it has not altered the present phases, which is shown in Fig.1(c). The solution was then treated, thus resulting in a martensitic α'' phase and removing the structural deformation caused by cold working (Fig.1 (d)).

β phase formation temperature, also known as β–*transus*, has been studied using High Temperature X–Ray diffraction and DSC analysis. The high temperature X–Ray diffraction analysis showed a stable α" phase until reaching 600°C and a β phase was formed at 700°C and higher temperatures (Fig. 2). In the DSC analysis, endothermic reactions were defined as upright peaks and exothermic reactions were defined as downright peaks, whose results can be seen on Figure 3 which shows an exothermic reaction at 650°C followed by an endothermic reaction at 750°C. This means that there has been transformation from phase α to β, thus β–*transus* temperature is 700°C for this alloy. According to Mantani and Tajima[11], for CP Ti, the β phase is stable between 800 and 1000°C, which indicates that the addition of Ta has led to β phase stabilization at lower temperatures.

Optical microscopy images show the α'' phase decomposition into α› and β phases during heat treatment recrystallization, which can be seen in Fig. 4 (a) as one phase only and in (b), (c) and (d) as two phases. According to optical microscopy, the solution treated sample exhibits only one phase (α") while recrystallized samples show two phases (α" and α'). The same result was obtained by Zhou *et al*. [8] who submitted the alloy to heat treatment at a lower temperature.

Figure 1– SEM images of the Ti30Ta alloy in the following conditions: (a) as cast (100x) (b) homogenized (5000x) (c) after cold swaging (5000x) (d) after solution treatment (1000x).

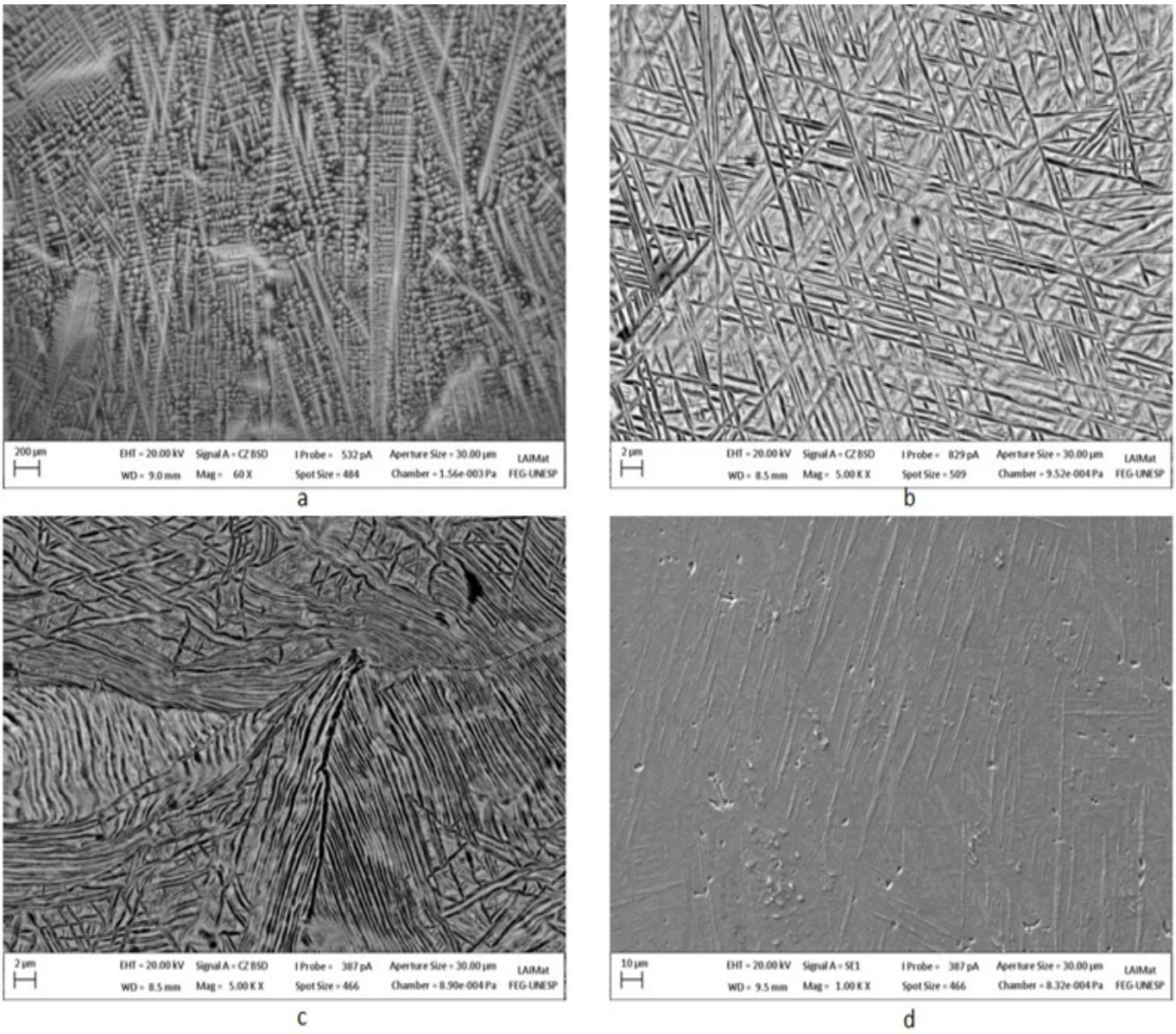


Figure 2 – High temperature X–Ray diffraction analysis of the Ti30Ta alloy after solution treatment at 900°C for 2 hours.

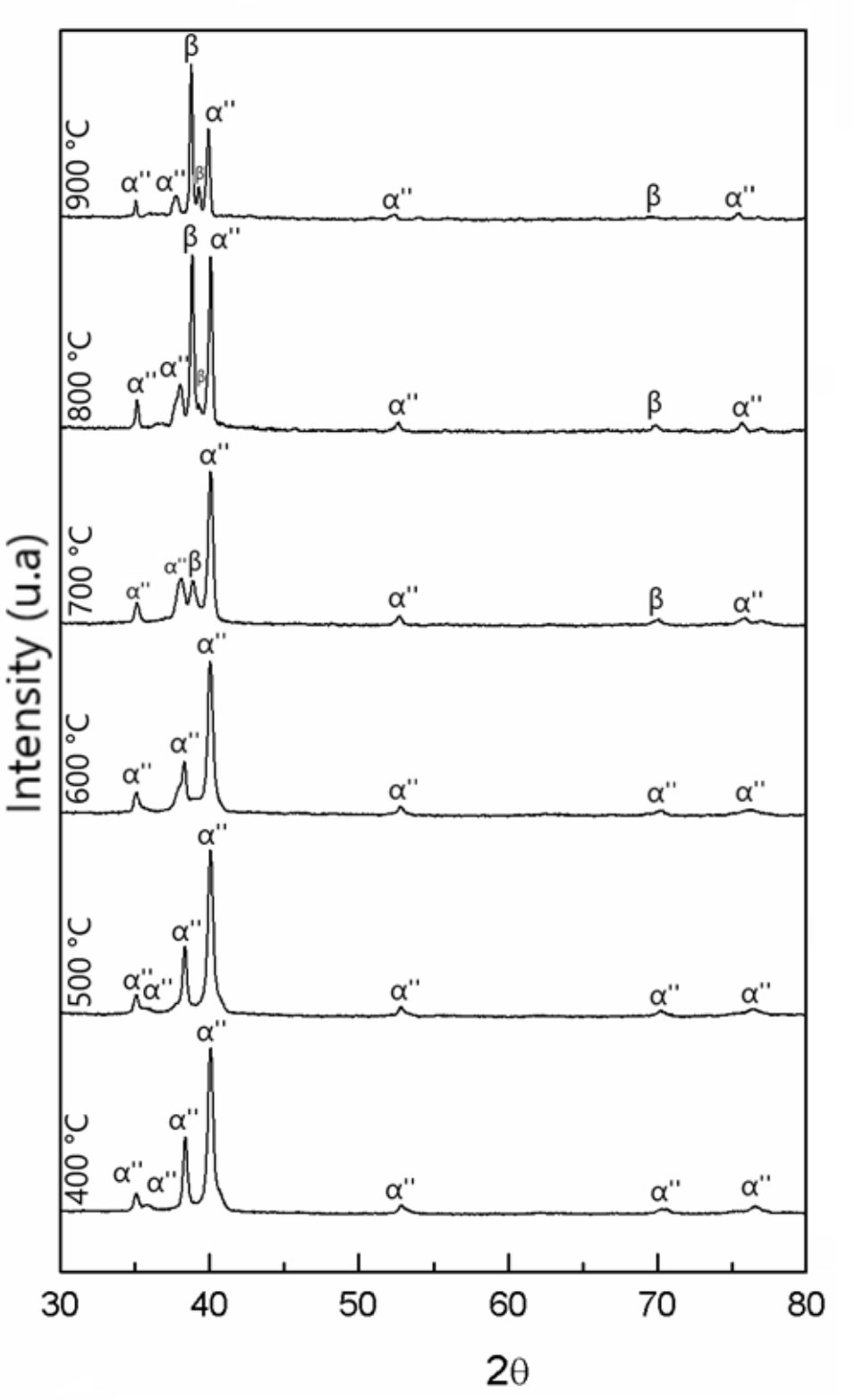


Figure 3 – DSC analysis of the Ti30Ta alloy after solution treatment at 900°C for 2 hours.

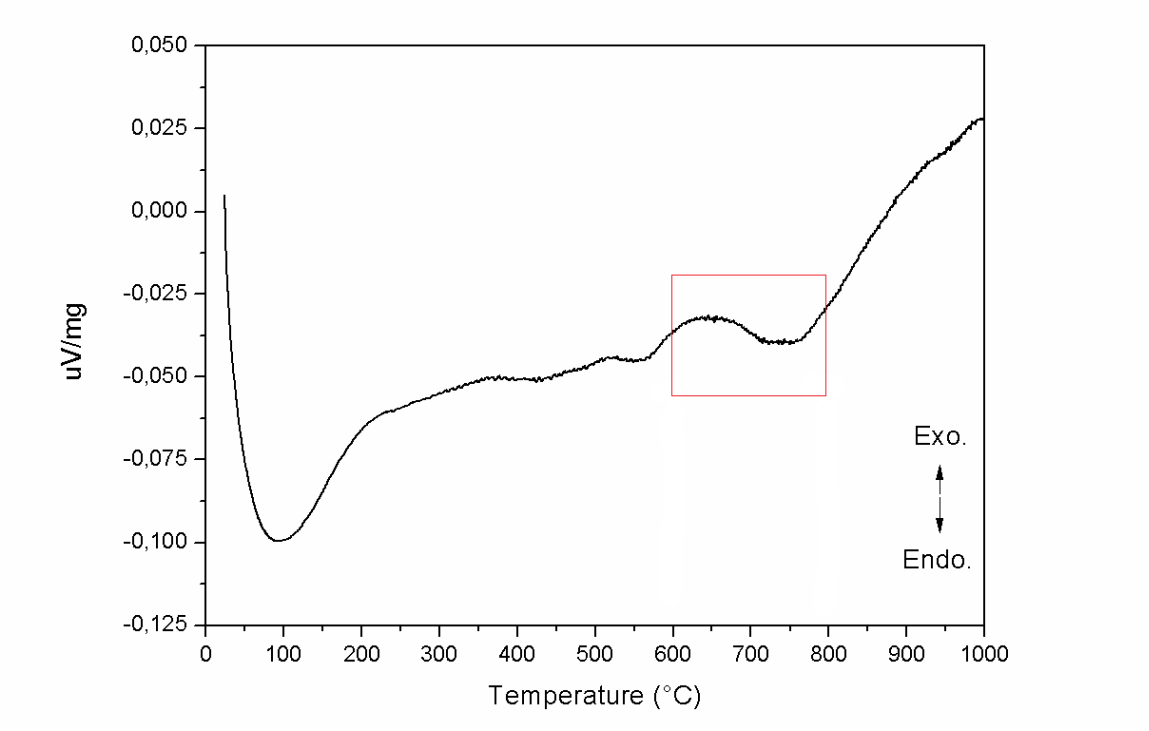
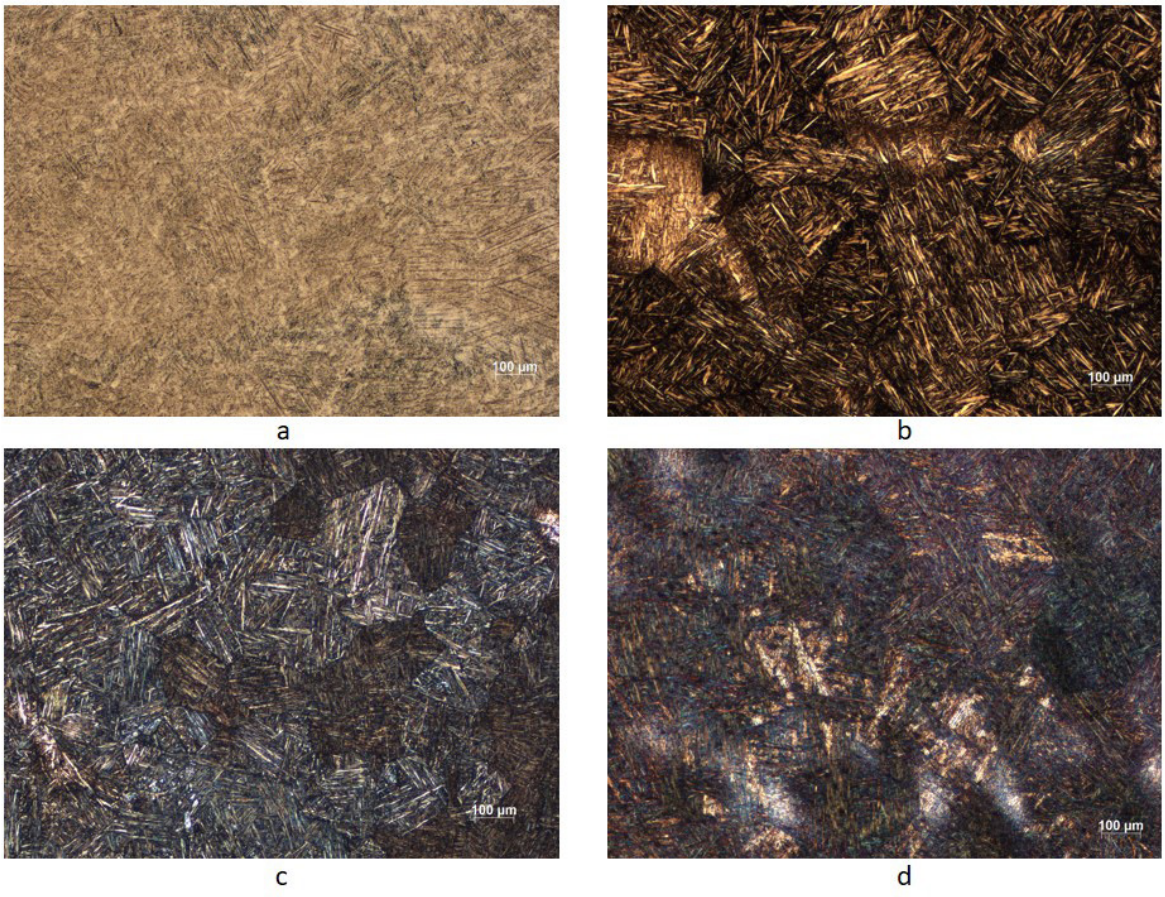
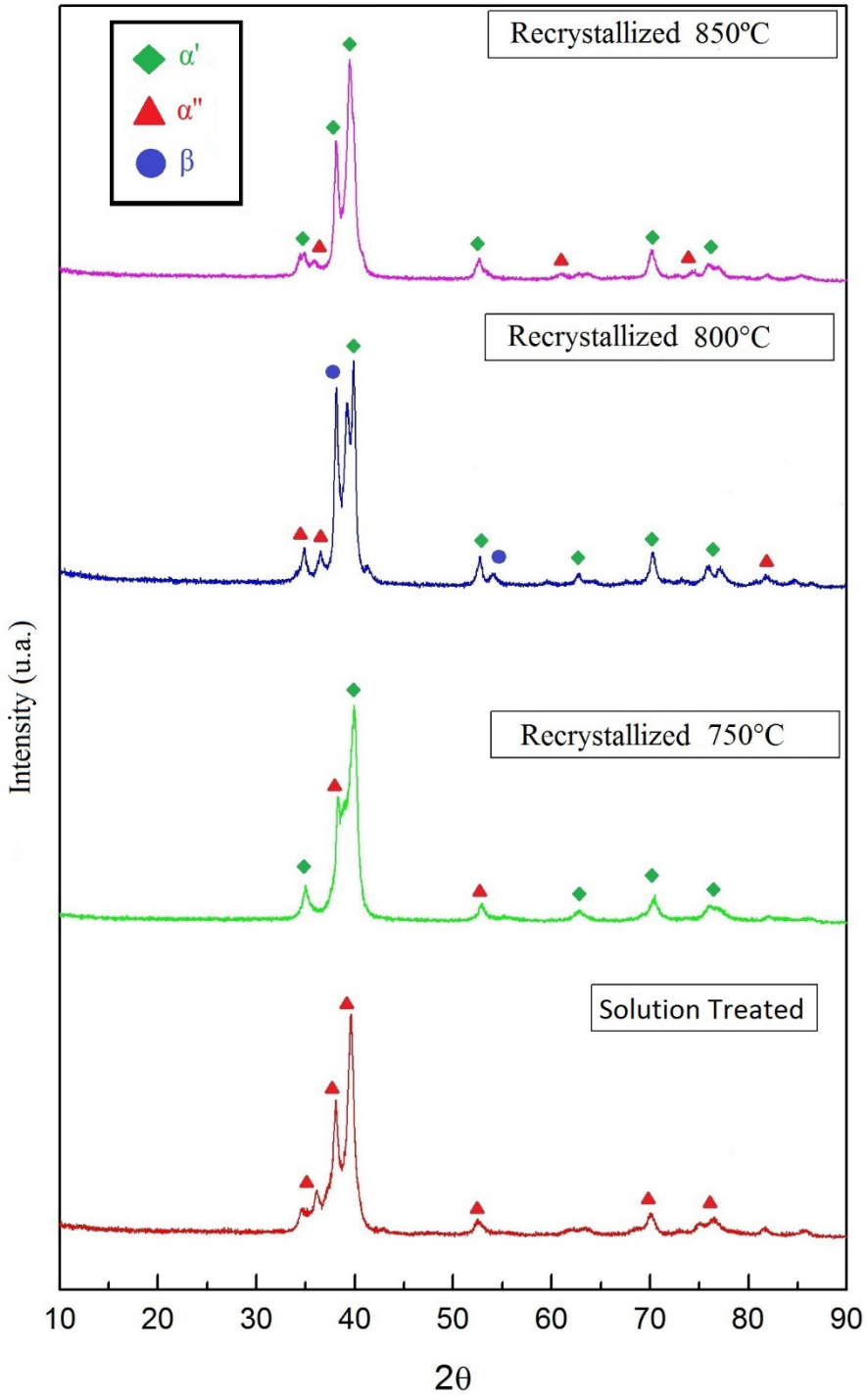


Figure 4 – Optical Microscopy images for Ti30Ta samples: (a) solution treated (b) recrystallized at 750°C for 12 hours (c) recrystallized at 800°C for 12 hours and (d) recrystallized at 850°C for 12 hours.



An X–Ray diffraction analysis was carried out in order to investigate the phases present in all samples, whose results are shown in Figure 5. Its results indicate that an α'' phase was formed for the solution treated sample due to rapid cooling, but there was no time for atomic diffusion and the entire structure transformed into a martensitic α'' phase. Furthermore, Zhou *et al*.[8] has obtained the same result while studying the α" phase decomposition on Ti–Ta binary system alloys. After recrystallization, the X–Ray diffraction analysis of samples have revealed the presence of both martensitic α'' and α' phases, which occurs due to heat treatment temperature and time. When structure β was quenched in water, there was little time for atomic diffusion, thus partially forming α' phase and α'' phase, which has also been observed by Zhou *et al.*[8] when this alloy underwent heat treatment at lower temperatures. According to Zhou *et al.*[12], α" phase decomposition is sensitive to both heat treatment temperature and tantalum content. Matsumoto *et al.*[13] studied a microstructure formed after performing heat treatment using the alloy Ti35Nb4Sn and observed that

Figure 5 – X–Ray diffraction patterns of Ti30Ta samples under the following conditions: solution treated, recrystallized at 750°C, recrystallized at 800°C and recrystallized at 850°C.



the transformation from α'' to β does not follow the same crystallographic path from β to α''. This is an explanation for the α' phase formation during its decomposition.

The results of tension tests are shown in Figure 6, through which it is possible to observe a different mechanical behavior by the alloy under the studied conditions.

According to Hao et al.[14]. the Young modulus of a multiphase material is sensitive to the individual modulus of each phase and their volume fractions, but it is not affected by precipitate or grain sizes. Thus, in a multiphase material, the Young modulus will be strongly influenced by the difference between each phase's modulus. According to Lee et al.[15], the α" phase has a lower Young modulus than the α' phase.

The values of mechanical properties of the alloy in the studied conditions are shown in Table 1, through which it is possible to observe a higher ultimate tensile strength (UTS) by the sample recrystallized at 750°C when compared to other samples on account of the presence of the α" phase and a higher fraction of α' phase. The solution treated sample presented lower UTS, lower Young modulus and higher deformation rate due to the presence of α" phase only. Samples recrystallized at 800 and 850°C have intermediate properties due to a balance between α" and α' phases. These properties make this condition suitable for biomedical applications due to the fact that they are closer to human bone features when compared to CP Ti or Ti–6Al–4V.

Table 2 shows the microhardness test results which are in agreement with the Tension tests results, thus exhibiting higher mechanical strength for the sample recrystallized at 750°C and lower mechanical strength for the solution treated sample.

Figure 6 – Tensile behavior of Ti30Ta samples in the following conditions: solution treated (ST), recrystallized at 750°C (R750), recrystallized at 800°C (R800) and recrystallized at 850°C (R850).

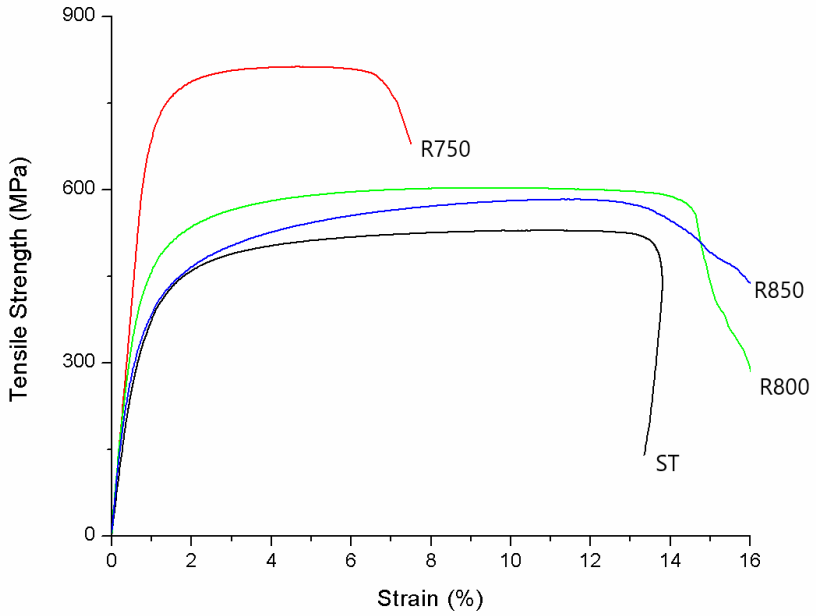


Table 1 – Mechanical properties of Ti30Ta samples in the following conditions: solution treated (ST), recrystallized at 750°C (R750), recrystallized at 800°C (R800) and recrystallized at 850°C (R850)

	Ti30Ta	**Ti30Ta Recrystallization**		
	Sol. Treated	750 °C	800 °C	850 °C
UTS (MPa)	528	812	602	582
σ_e (MPa)	357	711	423	360
E (GPa)	48	80	67	51
ε (%)	13,2	6,8	14	14,8

Table 2 – Microhardness values of Ti30Ta samples in the following conditions: solution treated (ST), recrystallized at 750°C (R750), recrystallized at 800°C (R800) and recrystallized at 850°C (R850).

Sample	Microhardness (HV)
Sol. Treated	194 ± 6,76
Recrystallized 750 °C	282 ± 15,65
Recrystallized 800 °C	227 ± 7,21
Recrystallized 850 °C	213 ± 10,76

Conclusion

The present study investigated how recrystallization heat treatment affects phase transformation, which has revealed the mechanical properties of the Ti30Ta alloy.

In conclusion, high temperature XRD and DSC analyses have determined *β–transus* temperature for the Ti30Ta alloy, i.e. 700°C.

The heat treatment of the solution has removed the structural deformation caused by rotary swaging and formed a new phase: the martensitic α'' phase. Subsequent recrystallization heat treatments have formed another phase, the α' phase, in addition to the α'' phase. Both phases have been identified by the XRD analysis, optical microscopy and scanning electron microscopy.

Mechanical tests showed a significant increase in the tensile strength for the sample recrystallized at 750°C when compared to the other samples, although there was also an unwanted increase in Young's modulus. Therefore, the solution treated sample showed the lowest Young's modulus and high tensile strength, thus being the most suitable for biomedical implants and a promising replacement for mechanical processing due to increasing tensile strength without compromising Young's modulus.

For this material, ideal conforming procedures should be carried out below the *β–transus* temperature, i.e. below 700°C, in order to avoid working the material at higher levels of strength and hardness.

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ORIGINAL ARTICLE

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The construction of a performance measurement system for self-evaluation of a graduate biotechnology program

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Abstract: The Literature on Performance Measurement Systems (PMS) is vast, however, little is found on the design stage of these for Higher Education. The purpose of this article is to present an SMD built for a Biotechnology Graduate Program (GP) to evaluate its performance. The Value Focused Thinking (VFT) approach was used to identify performance criteria. Mathematical modeling technique was used to identify the weights of these criteria through the Decision Support Method with Multiple Criteria: Analytic Network Process (ANP). Stakeholder decision compatibility was tested. Thirty-five performance indicators were built and grouped into eight fundamental objectives. The evaluation of the program identified that its strengths were Percentage of deadline fulfillment (by students) and Percentage of joint orientations between teachers and that managers should prioritize Percentage of patents or products students / teachers and Percentage teachers / students who participated as advisor / consultant.

Keywords: Graduate Programs. Performance evaluation. Performance Measurement Systems.

Introduction

Models of Performance Measurement Systems (PMSs) are addressed in the literature as an efficient way to obtain continuous improvement and enhance competitiveness of organisations in the market. However, designing a PMS is not an easy task, although there is no shortage of publications on performance measurement systems, there is a shortage of research elucidating how to build indicators and metrics (what and how to measure) that indicate precisely which activities contribute to performance using appropriate measurement theory [8].

The Coordination for the Improvement of Higher Education Personnel (CAPES – *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*) is the regulatory agency for Graduate Studies in Brazil and define criteria to assess Graduate Programs (GP) with the aim of continuously improving quality. However, the set of criteria adopted in the evaluation forms is not sufficient to capture the aspirations of all stakeholders for a GP. In addition, CAPES has recommended, from the 2017–2020 quadrennium onwards, that programs design and carry out their own Self-Assessment and Strategic Planning [3].

In the related literature, some authors, including Bressiani, Alt, and Massote (2001); Modell (2005); and Umashankar and Dutta (2007), argue that Higher Education Institutions are not accustomed to using PMSs to assist their management processes. In view of the importance of GP both for universities and for society at large, performance must be measured from various perspectives, to structure a management process that seeks continuous improvement. Hence, this paper hopes to address this gap.

The purpose of this article is to present a PMS built for a GP in Biotechnology to assess its performance, based on the perspectives of its stakeholders. The method for building the PMS includes: (1) Value Focused Thinking (VFT) – to identify the performance criteria with the stakeholders; (2) the Multicriteria Decision Method (MCDA): Analytic Network Process (ANP) – for mathematical modelling of criteria weights and for building scales; and (3), Compatibility ratios to check the proximity or distance of perspectives between decision makers.

In addition to the introduction, the work is divided into four other sections. The second section contains a literature review on the VFT approach and the ANP method in the construction of performance indicators and Biotechnology as a Graduate area. Section 3 explains the research method used to construct the PMS. Section 4 presents the PMS constructed and discusses the results found in the evaluation of the GP studied, and finally, section five provides the final conclusions and considerations.

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Theoretical reference

Performance Measurement Systems

This study adopts the concept of Neely, Adams, and Kennerley[32] that defines PMSs as a set of performance measures to quantify effectiveness and/or efficiency of past actions of an organization, aimed at management actions.

The literature reviews performed by Choong[5, 6,7 8] Yadav, Sushil, and Sagar[54]; and Valmorbida and Ensslin[51] about PMSs point to the need to customize performance measures according to organizational needs, contrasting frameworks such as the Balanced Scorecard or the Performance Prism. In general, although this aspect (PMS customization) is valued, companies still struggle with what they have to measure, the appropriate number of indicators, what to do with the measures found, and how to use them as a management tool and not just as measurements.

The methods for building PMSs presented in the literature seek to build SMP according to the needs of each company, but few present a step–by–step account of how the project took place, the planning and choice of indicators, and do not present details about the application, its difficulties and failures[35, 36]. According to Neely, Gregory, and Platts[33], the design phase of a PMS (selection of measurements and definition of metrics) is critical for success.

Value Focused Thinking and its support for construction of Performance Measurement Systems

According to Keeney[23], VFT is a method to assist the decision–making, which consists essentially of two activities: First identify what the decision maker wants and then figure out how to achieve it. VFT focuses on value and is recommended for problems involving complex applications with various alternatives, multiple objectives, and multiple stakeholders.

VFT has been used to build PMSs as shown in the Table 1; however, the works found do not focus on the Education sector. For more details on VFT, we recommend the readings of Keeney[16–19, 21, 23, 24] Keeney and Mcdaniels[16, 17]; Parnell et al.[37]; Keisler[22]; Keisler et al.[25]; Kenney, Bessette, and Arvai[15]; Marttunen, Lienert, and Belton [30] and Françozo; Belderrain[11].

Table 1– Value Focused Thinking (VFT) applications in Performance Measurement Systems (PMS) projects.

Author/ Year	Application
Barclay and Osei–Bryson (2010)	Performance criteria for Information Systems. VFT and Metric of objective question (Goal, Question Metric).
Chávez–Cortés and Maya (2010)	Sustainability indicators at local level and adequacy in the context of tourism development (Mexican community).
Kibira et al. (2018)	Environmental performance indicators for industrial processes.

Source: Authors.

The Analytic Network Process and its use in Performance Measurement Systems

ANP models a decision–making problem in network form, considering relations of dependence and/or feedback between: objectives, criteria, subcriteria, and alternatives[43]. In the construction of a PMS, major decisions require the employment of MCDA, either to assign weights to indicators (compare them) or to build scales (metrics) according to the subjective preferences of decision makers[38]. Table 2 shows a summary of MCDA AHP (Analytic Hierarchy Process) and ANP in PMS projects. No combination of VFT and ANP for PMS construction was found in the research literature.

Table 2 – Analytic Hierarchy Process (AHP) and Analytic Network Process (ANP) applications in Performance Measurement System (PMS) Projects (From 2013).

Author/ Year	Application
Ferretti and Pomarico (2013)	Employed the ANP and the Ordered Weighted Average (OWA) approach to compose a Multicriteria–Spatial Decision Support System; uses a value tree, does not detail VFT.
Song et al. (2013)	Use the AHP to assess client requirements in initial industrial product development.
Horenbeek and Pintelon (2014)	Employed PMS for maintenance
Van de Kaa et al. (2014)	Use AHP–fuzzy in standard battle technology decision making.
Guimarães and Salomon (2015)	Evaluated the priorities of the reverse logistics indicators in a small footwear industry in the State of Ceará, Brazil.
Liang (2015)	Measured the performance of interorganizational information systems in the supply chain of Thai IT industries (Balanced Scorecard + AHP fuzzy).
Yaraghi et al. (2015)	Compared the performance of the AHP with Monte Carlo at different levels of uncertainty.
Nisel and Özdemir (2016)	Used the AHP and ANP in sports–related decisions.
Kucukaltan, Irani and Aktas (2016)	Used the PMS for the logistics sector in Turkey, combining the Balanced Scorecard and the ANP.
Zong and Wang (2017)	Employed University Scientific Research Capacity Assessment (D–AHP)
Ho and Ma (2018)	Reviewed literature on approaches and applications: 2nd place Performance measurement – AHP.

Source: Authors.

The AHP is a special feature of ANP method. In AHP the hypothesis of interdependence and/or feedback among the decision-making elements is relaxed. Most of the works presented in Table 2 assume independence between performance criteria and, therefore, use the AHP. For more details on AHP/ANP, Saaty[39-46]; Salomon and Montevechi[47] are recommended.

Research method

The literature review that supported this study was performed in scientifically databases (Scielo, SpringerLink, Emerald insight, Science Direct, JSTOR, Web of Science, Scopus, and Google Scholar). The keywords used were performance measurement system, performance indicator, design, value focused thinking, analytic network process, and compatibility index.

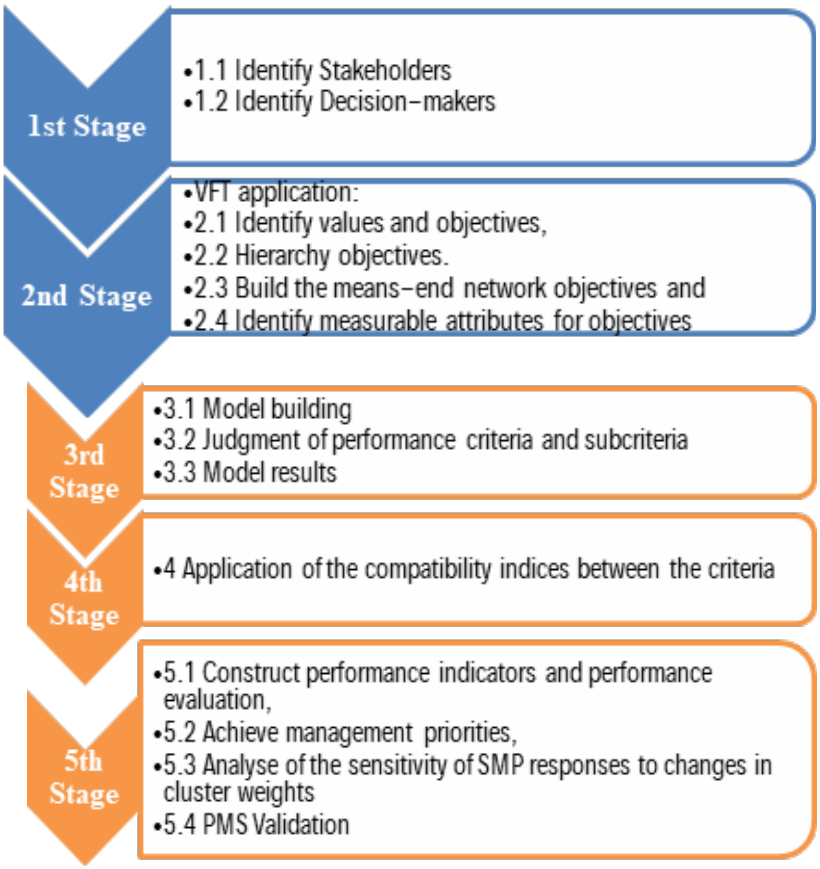
Figure 1 illustrates the research method used to construct and evaluate the analysed, which combines VFT (constructivist approach) with MCDA Analytic Network Process (rationalistic approach).

The subject of analysis was a Graduate Program in Biotechnology (GPB) of a Higher Education Institution (HEI) in the interior of the State of São Paulo, Brazil. In the constructivist phase, the first stage of the proposed method was subdivided into two sub-steps. The first entailed identification of stakeholders, and the second, identification of the decision makers involved with the construction of the PMS.

In the first stage, step 1.1, the stakeholders involved in the construction phase of the method were divided into groups: Organizations, that constitute the market needs of the programme; the HEI, represented by its members and with a major interest in improving the performance of the programme; the Community, symbolizing the return for the work conducted by GP; and CAPES, representing the government, in this case, through the Biotechnology area document and contained in the desires of the coordination and professors.

The representatives of the group 'Organizations', a professor with a professional background in a Biotechnology company and a businessman in the Biotechnology area with no relationship with the IES were interviewed. The 'IES' group for better comprehensiveness of the PMS was subdivided into coordination, faculty, student, and board representative. The 'Community' group, was represented by a person from the general society linked to the academic environment, working in a Graduation Program. For the construction of the PMS, the group composed of the coordinator, professors, and a student of the programme was defined as the main decision makers to involve in the decision-making processes and specific liaison with the programme – step 1.2 of the first stage. The criteria for selection and classification of stakeholders were based on the work of Ackermann and Eden (2011)[1].

Figure 1– Method for building Performance Measurement Systems for a Graduate Program.



Source: Authors.

The second stage of the proposed method was to apply the following four steps: 1) Identify objectives, 2) Hierarchize objectives, 3) Build means–end network objectives, and 4) Identify measurable attributes for the objectives. To this end, nine interviews were conducted with related stakeholders. These interviews lasted an average of 30 minutes and were validated by the interviewees after the recording was transcribed by the facilitator following the steps of VFT.

The guiding questions asked throughout the interviews were: What do you consider important to be measured/evaluated in a GP? What measures should a PMS cover for the GP? The questionnaire from Keeney[17] was also employed to stimulate identification of the objectives, for the construction of a PMS for the Graduate Program in Biotechnology.

The WITI (Why Is This Important?) test was applied, with the statements identified in step 1 (one by one). An individual hierarchy of objectives was structured for each interviewee. Following this hierarchization, the facilitator produced the hierarchy of objectives gathered from the nine interviews conducted to determine the fundamental objectives found. At this stage, the strategic objective of the group was identified.

Then, the network of objectives was elaborated, containing the strategic objective, the fundamental objectives, and their means. This was done by analysing the interviews and obtaining information from the decision makers, who also validated it. Depending on the structured network, the list of measurable attributes was also drawn up, by appealing to those involved according to the fundamental objectives established. These represent the performance criteria pointed out by the decision makers and CAPES (following the requirements of the area document) for this Biotechnology GP.

In the rationalist phase, Stage 3 – step 3.1, the multicriteria model was built with the aid of Super Decisions® software. Relationships of dependency and feedback between performance criteria were extracted from the objectives network and legitimized with decision makers participating in this phase.

Meetings were held with decision makers to verify judgements of relative importance between clusters, between PMS performance criteria and sub criteria, by peer review (step 3.2). The consistency of the trial matrices was also assessed.

In step 3.3 – model results, the establishment of the weights provided a strategic direction to the GP by enabling better prioritization of performance criteria. This step was made by group decision, carried out through the technique of Aggregation of Individual Priorities (AIP) geometric mean, according to Forman and Peniwati [10].

In the fourth stage, the compatibility rates S (Saaty), V (Valério), and G (Garuti) were applied to verify the proximity or distance between the opinions of the decision makers involved in the construction of the PMS. The compatibility indices were applied on the judgements in the clusters (set of fundamental objectives) and the performance criteria of the model. For details on the index calculations see Saaty[46]; Salomon[48]; and Garuti[12].

The fifth stage – step 5.1 – occurred in a preliminary meeting with one of the decision makers. It established levels for each performance criteria, accompanied by descriptors. Subsequently, another collective meeting was held with 3 of the 6 decision makers to sanction these levels and descriptors. The AHP method was then applied for relative comparison between the levels and to achieve the priority vector and consequently, the Function Value (FV).

The GP was evaluated for each performance indicator built, identifying the level of impact that best represented the Programme's performance. The GP global was obtained additively, multiplying the function value corresponding to each indicator by its weight (obtained in the third step). In step 5.2, the management priorities were defined, considering the potential that each indicator would contribute to increase the overall performance of the GP.

The sensitivity analysis was performed to check how sensitive the PMS is to a possible individual increase in weight of each cluster (step 5.3). Finally, in step 5.4, the validation of the PMS by the decision makers was based on the analysis of the representativeness of the results against the reality of the GP.

Results and discussion

The first and second stages of the constructivist phase produced the network of objectives presented in Figure 2. The network covers all the strategic and fundamental, objectives along with the mean of the GP, from the perspectives of its stakeholders.

The strategic objective of GP is 'To meet the needs of those involved in GP'. A fundamental objective and means to achieve it, from the perspective of the stakeholders, is exemplified in Figure 2: to offer the student quality training, the student must have knowledge, which can be assessed by means of the courses taken and in the offer of quality courses.

Table 3 shows the priorities (weights ordering) from each decision maker for the clusters (set of fundamental objectives) resulting from the steps of stage 3. Note that decision makers had different priorities in relation to clusters and that all had inconsistencies below 0.1 in their judgments (recommended for the AHP/ANP method). The decision makers on the program board were professors 1, 2, 3, 4, and 6 (which includes the coordinator) and 5 student representatives.

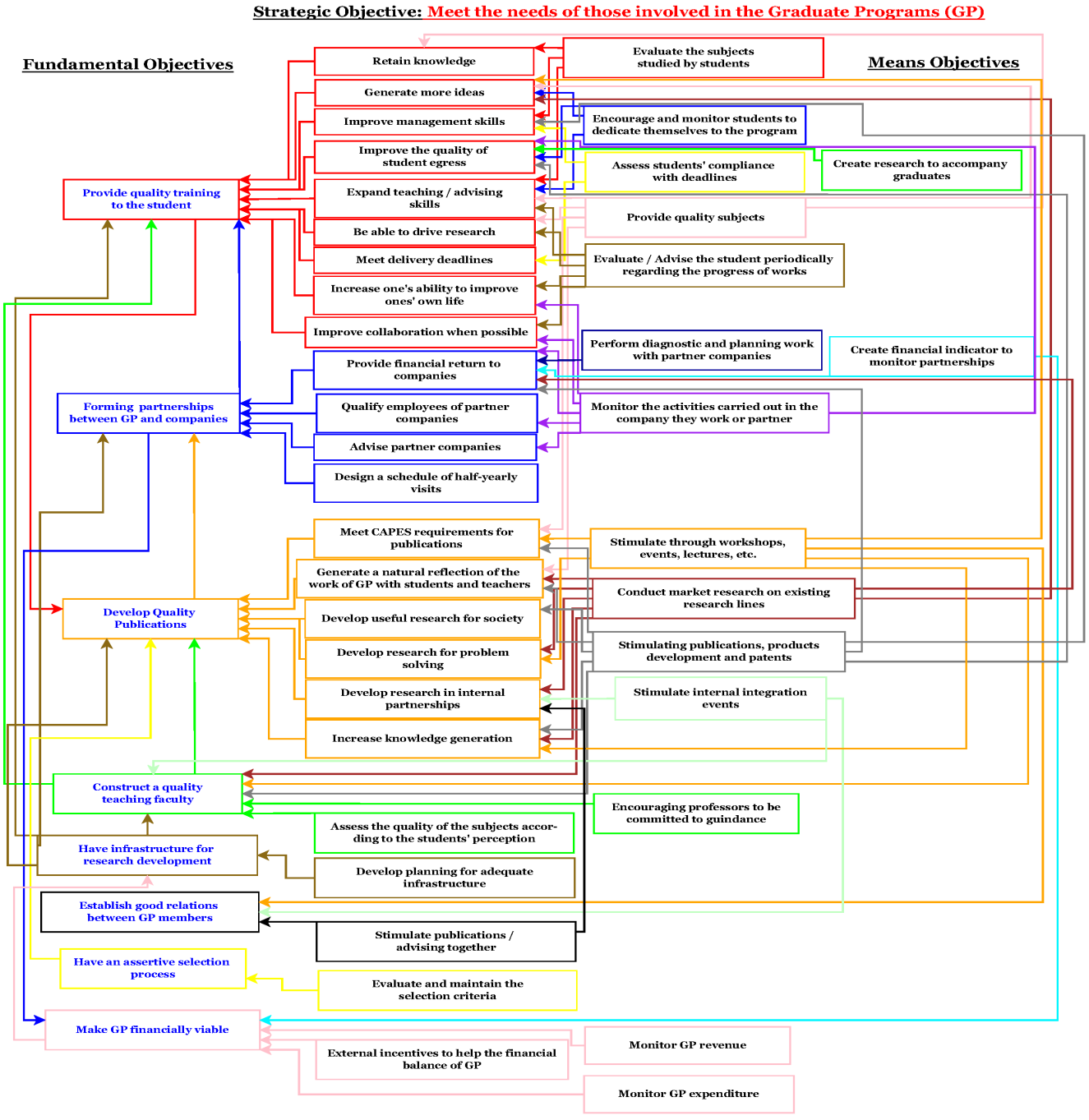
Considering the standardised geometric average, the three most important clusters were: 18.19%, to offer quality training to the student; 17.60%, to constitute a quality teaching staff; and 15.88%, to develop quality publications (totalling 51.68%). The professors naturally prioritize aspects related to the training of students and

faculty rather than the question of a good relationship between those involved, for example. Providing quality training to students is essential to the program according to the values presented in the interviews and proven numerically, such training needs a quality faculty that enables/supports this. Developing publications is inherent to the academic environment and carries with it the weight of CAPES as a regulating body.

The infrastructure cluster for the development of research was perceived with different weights among the professors themselves, which can be due to their specific needs for the lines of research developed. For some, the infrastructure was more important, and because it was a relatively new program. The formation of partnerships with companies was something valued by several of those involved and by the area of Biotechnology in general, highlighted in the area document by CAPES and necessary even as a support for the economic viability of the program. For decision–maker two, forming partnerships with companies was more significant than for the others. Economic viability is essential for the continuity of the program and had different weights among decision makers.

Table 4 presents the priorities of the performance criteria (top 10 in the ranking), considering the views of each of the decision makers interviewed. The first three

Figure 2 – Means–end network objectives.



Source: Authors.

positions, according to the normalized geometric average, were revenues/expenses with 9.10%, percentage of projects with external funding with 8.05%, and teaching publications in the quadrennium with 6.38%.

In Table 4, different rankings are noted for each decision maker. The revenue/expenditure rate indicator (AN) was the first in the ranking for decision–makers 1, 4, 5, and 6, highlighting the concern about the financial balance of the program. The second in the list, the percentage of projects with external subsidies (PA), which also denoted such concern, appeared in second place for decision–makers 2, 4, 5, and 6. Decision maker 4 marked the same order as the weighted geometric average for the first three indicators of the ranking, but not for the other indicators. The other decision makers alternated such initial positions or contemplate only one or two of the indicators among the first three.

Although, in the first positions, items were found in exchanged positions, the reasons that may lead to such different perspectives was complex, and such questioning to compare the answers obtained between them was not carried out, as this was not the objective of the work. However, the coordination, professors, and students had different and complementary perspectives and values within the GP, since each have different approaches to CAPES and IES. The application of the compatibility indices can contribute to this analysis.

In step 4, the following compatibility indices were applied: 'S' of Saaty [46], 'V' of Salomon[48], and 'G' of Garuti[12]. The indices were applied to check the distance from the weights assigned by decision makers to the performance criteria and those of the clusters in the model (set of objectives contained in the means–end network objectives). Both situations found incompatibility between decision makers, considering S and V, and little compatibility taking into account G. In other words, decision makers did not present a consensus on the relative importance of fundamental objectives and performance criteria.

The following is the construction of the performance indicators based on the performance criteria (step 5.1 of step 5). Table 3 exemplifies the construction of performance–indicator A, referring to the fulfilment of deadlines by students (qualification and defence), presenting the levels and their descriptors. For each level from 0 to 5 of indicator A, a value resulting from the decision makers' judgments on the levels, their respective value function, the target set for this indicator in the current quadrennium, and the result of the GP between the years 2017 and 2018 were associated.

The GP showed a 92% compliance rate for 2017 and 2018. Therefore, indicator A (Table 5) was classified in level 5. By multiplying the PV value for level 5 by the weight of indicator A (Table 6) – 100%*2.33%, the percentage of performance of indicator A (2.33%) in the GP performance was obtained. Carrying out the same procedure with the other criteria, in an additive way, the performance obtained for the PMS of the GP was 61.39%.

Table 3 – Priorities by clusters/decision makers.

Clusters/Decision makers	1	2	3	4	5	6	Geo. Mean	Geo. Mean Norm.
Offer quality training to the student	29.22%	15.48%	19.32%	10.33%	17.53%	14.02%	16.77%	18.19%
Establish a quality teaching staff	21.18%	22.44%	20.39%	8.38%	14.70%	15.26%	16.22%	17.60%
Develop Quality Publications	13.15%	10.93%	16.25%	21.08%	17.02%	11.71%	14.63%	15.88%
Possess infrastructure for research development	4.67%	11.20%	13.86%	14.42%	16.10%	16.14%	11.81%	12.82%
Form partnerships between GP and companies	7.83%	16.08%	10.63%	7.67%	13.24%	7.97%	10.13%	11.00%
Make GP economically viable	10.18%	6.97%	4.19%	15.22%	15.17%	6.80%	8.81%	9.56%
Have an assertive selection process	5.07%	13.88%	11.24%	9.35%	4.71%	6.05%	7.71%	8.37%
Establish a good relationship among those involved in GP	8.68%	3.01%	4.12%	13.55%	1.54%	22.06%	6.06%	6.58%
Total	100%	100%	100%	100%	100%	100%	92%	100%
Inconsistency	0.03	0.08	0.09	0.09	0.08	0.08	0.07	

Source: Authors.

Table 4 – Priorities by indicator.

Cod.	Indicator	1	2	3	4	5	6	Geo. Mean	Geo. Mean Norm.
AN	Rate of income/expenses (per year)	9.29%	5.66%	3.59%	14.42%	12.39%	8.86%	8.17%	9.10%
AF	Percentage of professors involved in external promotion (depending on the number of professors)	3.20%	7.96%	7.91%	8.23%	9.86%	8.78%	7.23%	8.05%
S	Percentage of publications (A1 – B4) professors (depending on the number of professors)	4.83%	3.95%	6.70%	7.16%	6.50%	5.96%	5.73%	6.38%
T	Percentage of patents/teaching products (depending on the number of professors)	3.32%	4.21%	6.19%	7.16%	7.16%	5.96%	5.46%	6.07%
L	Percentage of professors/students who participated in events with companies (according to the total number of professors and students)	2.57%	8.43%	4.47%	4.23%	3.90%	4.69%	4.42%	4.92%
K	Percentage of professors who made visits to Biotechnology companies (according to the total number of professors)	4.57%	4.63%	4.63%	2.38%	6.92%	1.31%	3.58%	3.99%
N	Average of projects with companies (per year)	2.78%	7.54%	4.04%	2.58%	4.22%	2.21%	3.56%	3.96%
AM	Percentage of starting/graduating students (depending on the number of students)	3.09%	5.63%	4.81%	4.08%	2.56%	2.08%	3.49%	3.89%
H	Percentage of graduates (in relation to those expected)	7.97%	2.60%	3.06%	1.11%	4.28%	4.17%	3.28%	3.65%
O	Percentage of publications (A1 – B4) students/professors (depending on the number of students)	2.73%	3.10%	3.48%	4.95%	3.01%	2.19%	3.14%	3.50%

Source: Authors.

Table 5 – Example of Levels. Vectors, FV, descriptors, results, and target for indicator A.

A Levels	Vector	FV (Vector Norm.)	Goal	Result	Descriptors
0	0	0%			Percentage of fulfilment of deadlines below 50% (total number of students)
1	0.11	33%			Percentage of compliance with deadlines lower than 51 – 60
2	0.14	44%			Percentage of compliance with deadlines is between 61 – 70 %.
3	0.19	57%			Percentage of compliance with deadlines is between 71 – 80
4	0.24	76%			Percentage of compliance with deadlines is between 81 – 90%.
5	0.32	100%	x	x	Percentage of compliance with deadlines is between 91 – 100 %.

Source: Authors.

Table 6 shows the percentage of performance for the indicators and their overall performance. The indicators with the highest percentage of performance (in view of the weight assigned) as a function of the levels recorded were Percentage of publications (A1 – B4) by professors (as a function of the number of professors), Percentage of professors involved in external promotion (as a function of the number of professors), and Income/expense rate (by year). The lowest performers are Percentage of student/professor books/chapters (as a function of the number of students), Percentage of awarded professors (as a function of the number of professors), and Average of integration projects with High School (per year)

Table 6 – Performance of indicators and general.

Ind.	Weight (Mean Geom. Norm.)	FV corresp. Level	% Performance Indicator	Indicator
S	6.38%	100%	6.38%	Percentage of publications (A1 – B4) by professors (depending on the number of professors)
AF	8.05%	57%	4.62%	Percentage of professors involved in external promotion (depending on the number of professors)
AN	9.10%	44%	3.96%	Rate of income/expenses (per year)
J	3.44%	100%	3.44%	Percentage of students who are advisors/co-advisors (according to the total number of students)
K	3.99%	76%	3.02%	Percentage of professors who made visits to Biotechnology companies (according to the total number of professors)
N	3.96%	76%	3.00%	Average of projects with companies (per year)
AM	3.89%	76%	2.95%	Percentage of starting/graduating students (depending on the number of students)
L	4.92%	57%	2.83%	Percentage starting/graduating students (depending on the number of students)
H	3.65%	76%	2.77%	Percentage of professors/students who participated in events with companies (according to the total number of professors and students)
T	6.07%	44%	2.64%	Percentage of graduates (in relation to those expected)
A	2.33%	100%	2.33%	Percentage of patents/teaching products (depending on the number of professors)
O	3.50%	57%	2.01%	Percentage of fulfilment of deadlines (according to the total number of students)
AL	2.75%	57%	1.58%	Percentage of publications (A1 – B4) students/professors (depending on the number of students)
G	2.71%	57%	1.56%	Average startings student per year
E	1.37%	100%	1.37%	Percentage of students who participated in external events (depending on the total number of students)
V	1.28%	100%	1.28%	Percentage of mentions (A and B) (according to the total number of students)
AK	1.68%	76%	1.28%	Percentage of professors integrated with the graduation (depending on the number of professors)
AE	2.67%	44%	1.16%	Percentage of satisfaction among GP professors (depending on the number of professors)
Y	2.00%	57%	1.15%	Number of scientific bases with access by the programme
P	3.43%	33%	1.13%	Percentage of professors with research fellowships (depending on the number of professors)
AI	1.13%	100%	1.13%	Percentage of patents/ student/professor products (depending on the number of students)
X	1.69%	65%	1.09%	Percentage of joint guidelines between faculty (projects with internal co-orientation per year)
U	1.76%	57%	1.01%	Average number of students per advisor (depending on the number of professors)
M	3.00%	33%	0.99%	Percentage of teaching books/chapters (depending on the number of professors)
AC	2.09%	44%	0.91%	Percentage of professors/students who participated as advisor/consultant (depending on the total number of professors and students)
Z	1.31%	65%	0.84%	Percentage of professors/students involved in internationalization projects (depending on the number of students and professors)
I	1.85%	44%	0.81%	Average numbers of subjects taught per professor (depending on the number of professors in the quadrennium)
AH	1.04%	76%	0.79%	Percentage of students awarded (as a function of total number of students)
AB	2.12%	33%	0.70%	Percentage of joint publications (A1 – B4) among professors (depending on the number of professors)
AG	0.91%	76%	0.69%	Percentage of professors/ students involved in extension/social insertion projects (depending on the number of students and professors)
AJ	0.62%	100%	0.62%	Percentage of professors/ students who participated in internal events (depending on the number of students and professors)
W	0.98%	57%	0.56%	Average of those who participate on committees (faculty/per year)
AD	0.88%	57%	0.51%	Average of integration projects with High School (per year)
Q	0.85%	33%	0.28%	Percentage of professors awarded (depending on the number of professors)
AA	2.60%	Not implemented		Percentage of student/professor books/chapters (depending on the number of students)
Total			61.39%	Percentage of teaching evaluation per student (depending on the number of students)

Source: Authors.

The top 10 positions of the GP management priorities are presented in Table 7 (step 5.2). Given the institutional characteristics, the concern with economic viability was significant and highlighted with the need to seek external incentives for research development. Partnerships with companies were also valued to assist in the financial health of the program, while taking cutting–edge research and knowledge into the companies. The evolution of GP in this direction could also allow the expansion of the infrastructure, which was valued and necessary.

The importance of publications and patents, already emphasized by the regulatory agency (CAPES), was also reflected in the management priorities (to make applied research efficient and capable of helping in the return of something more palpable to society), along with the need to bring the program closer to companies with visits and events that could facilitate partnerships and projects. The other indicators, although with lower priorities, should be monitored to ensure their collaboration in the composition of the PMS.

The PMS sensitivity analysis was performed, extrapolating the weights of each cluster individually, to check for any variation in the PMS performance (step 5.3). Changes in overall performance through cluster disruption are not considered to have a major impact. PMS was validated by decision makers, who judged it capable of portraying the reality of the GP for an adequate management process from the perspective of stakeholders, including CAPES. In addition, they reiterated their concern not to create an excessive number of metrics, particularly in view of the recent initiation of the programme.

Table 7 – Management priorities.

Ind.	Weight (Mean Geom. Norm.)	Levels	Management priorities	Description of Indicator
AN	9.10%	44%	5.14%	Rate of income/expenses (per year)
T	6.07%	44%	3.43%	Percentage of patents/teaching products (depending on the number of professors)
AF	8.05%	57%	3.43%	Percentage of professors involved in external promotion (depending on the number of professors)
P	3.43%	33%	2.30%	Percentage of patents/ student/professor products (depending on the number of students)
L	4.92%	57%	2.10%	Percentage of professors/students who participated in events with companies (according to the total number of professors and students)
M	3.00%	33%	2.01%	Percentage of professors/students who participated as advisor/ consultant (depending on the total number of professors and students)
AE	2.67%	44%	1.51%	Number of scientific databases that the programme has access to
O	3.50%	57%	1.49%	Percentage of publications (A1 – B4) students/professors (depending on the number of students)
AB	2.12%	33%	1.42%	Percentage of professors/students involved in extension/social insertion projects (depending on the number of students and professors)
AC	2.09%	44%	1.18%	Percentage of professors/students involved in internationalization projects (depending on the number of students and professors)

Source: Authors.

Conclusions

Thus, the geWneral objective of presenting a PMS built for a Biotechnology Graduate Program for self–assessment, integrating VFT with ANP, was achieved. As this was a recent program, the concern and appreciation of the planning aspects for growing development began in 2017 with the start of the planning and management project, which was in line with the new CAPES proposal from 2018. This concern shows that the program already recognized the need to structure its actions and plan itself before it was even required to in the evaluation process and not only to fulfil a proforma.

The PMS built incorporated the CAPES evaluation criteria and other valued by stakeholders. A point that called the attention of the Program Coordinator for immediate actions was the need for greater alignment and consensus among decision makers, which as diagnosed by the compatibility rates. On the other hand, a certain degree of divergence between opinions is valuable for a GP that is composed of stakeholders with different points of view, captured by the group decision (geometric mean).

PMS enabled monitoring the performance of the program throughout the four–year period, tracing actions that reflected results within the evaluation period. The specific criteria pointed out in the PMS helped in the overall result of the program and could indirectly generate positive impact on the CAPES criteria. Nevertheless, the coordination of the programme must be attentive to the performance criteria of CAPES (evaluation form) and their respective weights, as these change frequently.

However, through this research, we hope to collaborate with other GP or organizations that aim to build their custom PMS. This study presents the limitation of approaching a specific GP with individual characteristics observed at the time. Therefore, future studies should use the same research method for longitudinal comparisons in the same GP or even in other programs with distinct characteristics, in any area of CAPES to verify its applicability and effectiveness.

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Use of high energy milling and porosity insertion in the development of the MgZn system targeting biomedical applications

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Abstract: During the last decades, the study of biomaterials, which has been occupying a wide area, has been applied and complemented, with the objective of adapting to the advances in the standard of living of the population. With that in mind, the development of orthopedic implants with good long-term biocompatibility is increasingly necessary, as current materials intended for this purpose have many complications related to their mechanical properties and biocompatibility, characteristics necessary for materials with this purpose. Therefore, a relevant solution is the development of biodegradable metallic biomaterials, as they have excellent profiles for orthopedic implants, avoiding many problems found in currently used metals, such as toxicity and stress protection. Within this class of materials, magnesium is the fourth most abundant element in the human body and is important for bone regeneration. In this work, a new route for processing porous alloys of the MgZn system with 1.2 and 3% by weight of Zinc will be evaluated, using high-energy grinding, via powder metallurgy, where, in this research, we present promising characteristics since it presents the powder with suitable morphological characteristics for sample production without the need for a controlling agent that provides the porosity of the sintered material. Therefore, the development of metal alloys with porosity controlled by powder metallurgy is suitable for obtaining biomaterials with control of mechanical strength and modulus of elasticity, in addition to the possibility of controlling open porosity, essential for osseointegration.

Keywords: Biomaterials. Biodegradable alloys. High energy grinding. Porous magnesium alloys.

Introduction

Lately, studies have been carried out with metallic alloys based on Magnesium (Mg), in the search for the best composition for the manufacture of biocompatible and bioabsorbable orthopedic surgical implants, in addition to being the key to a series of biological functions in the human body, in the However, in recent years, the increased incidence of musculoskeletal injuries and defects caused by trauma, inflammation, sports and age, brings the need for greater demands for orthopedic implants, thus stimulating the development of the subclass of metallic biomaterials. Which are currently mainly represented by stainless steels and titanium alloys, since metallic biomaterials have great potential in load bearing applications, due to their mechanical properties in relation to other materials. However, they are still limited by the protective effects against stress caused by their high Young's modulus compared to natural bone and by replacement or removal surgeries that increase the cost and risk for patients [9,12] . Such characteristics may lead to the elimination of the step of removing the material implanted in the patient after complete bone consolidation of the fractured region, avoiding a second surgical procedure, which would have been impossible until the end of the 20th century. At this time, advances in alloys, surface treatments and coating technologies made it possible to control corrosive behavior, which would reduce contamination risks and costs, reigniting the field of Mg-based biomaterials. Another important characteristic of Mg alloys is linked to their degradation, which generates products, mainly Mg ions, which do not present observable toxicity to human tissue, since Mg is the fourth predominant mineral in the human body, acting as an essential element in building bones and soft tissue. Likewise, when excess Mg ions do not cause complications, as they are transported by the circulatory system and excreted in the urine, without causing negative effects in the body [10] .

However, there are still limitations related to the use of Mg alloys, because in fluoridated solutions, including body fluids, such alloys have a high rate of degradation, which leads to rapid corrosion, causing not only the premature loss of their mechanical integrity , but also resulting in accumulation of hydrogen in vivo, generating subcutaneous edema and alkaline elevation at the site. Thus, new alloys with addition of elements that increase their resistance to corrosion are in high demand. From a biocompatibility point of view, the most promising alloying elements are mainly concentrated in human nutrients, including Zn, Ca, Sn, Si and Sr [8,10,12].

Bearing this in mind, because from the point of view of mechanical properties, Zn is known as a good solid solution and precipitation intensifying agent in Mg alloys, being one of the main alloying elements used in Mg [1].

The use of metallic biomaterials began in the 1860s, when the metallurgical industry began to grow during

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the industrial revolution. Metallic materials occupy a prominent place in the engineering of biomedical implants because of their uniform properties (e.g., high strength and durability), ease of fabrication, and reasonable biocompatibility, all of which are desirable to achieve implant longevity[3,6] .

The powder metallurgy technique is a form of processing that has been explored to obtain the appropriate composition, adding several methods adopted to control and evaluate both the corrosion and the biocompatibility of biomaterials in the intended metallic alloys. With this evolution, Mg and some of its alloys have stood out in research as a biodegradable metallic material suitable for biomedical filler applications with physical and mechanical properties similar to those of bones, making them excellent candidates for implant materials for the treatment of bones fractures. Mg alloys have shown encouraging results when used as tissue engineering scaffolds[11].

Powder metallurgy, being a flexible manufacturing process capable of providing a wide range of new materials, microstructures and properties, creates several unique niche applications for powder metallurgy, such as wear resistant composites. The choice of a powder production process among several possibilities depends on: the understanding of the process, if it is economically viable, the final characteristics of the powder resulting from the process and if these characteristics are in accordance with the expected properties for the intended application[5].

From there, several works and published scientific researches emerged involving the techniques that, lately, have been used for the production of metallic biomaterials. It was also verified that the mixture of different powders via milling can enable the induction of chemical reactions at temperatures much lower than those normally required, a process called mechanically activated synthesis[7].

The present scientific and technological research work suggests the use of high energy milling and specific procedures of shaping and sintering at 580°C/2h in an argon atmosphere, for samples of the MgZn system, specifically Mg and Zn (with 1, 2 and 3 wt %) with variable porosity and density, for biomedical applications. Powder metallurgy techniques will be directly applicable and useful in defining sample geometries for microstructural, surface and mechanical characterizations. Thus, the studies of the present work will be concentrated on the process by metallurgy and high energy powder milling, which allow to improve the homogenization of the distribution of the elements of the MgZn systems.

Materials and methods

To obtain the samples, elemental powders of Mg and Zn were used in percentage by mass of the elements, the Mg powder supplied by the company Rima Industrial with a purity of 99.21% and the Zn obtained in alpha Aesar by thermo Fisher Scientific with a purity of 98.64% of the elements normalized to100% by analysis performed by X–ray fluorescence, in Axios MAX equipment, PANalytical brand , with semiquantitative analysis without standardization; at the Department of Materials Engineering, School of Engineering of Lorena, São Paulo State University – DEMAR–EEL–USP.

High energy milling of commercially pure powders was defined as a process to produce Mg samples with different Zn proportions. In each milling step,3.5 g of powder were used to homogenize the mass elements used from the weight ratio of the mass of the balls to the mass of the powder of 5:1. Tungsten carbide (WC) balls and flasks were used for all grinding and a SPEX 8000D mill was used in the Department of Materials Engineering at Escola de Engenharia Lorena at Universidade Estadual Paulista – DEMAR–EEL–USP because this mill in its process delivers greater kinetic energy to the spheres and generates a grinding process that tends to be more severe, improving the homogenization of the powder mixture. The milling times used were 1, 2 and 4 hours, to verify the efficiency of the mixture through the appearance of phases/mixtures with the composition of interest, and thus the powders obtained in each milling time condition were named Mg2Zn–1h , Mg2Zn –2h and Mg2Zn–4h.

Characterizations are extremely important to quantify and qualify the microstructure and mechanical properties of powders and sintered materials obtained via powder metallurgy. The samples obtained by high–energy milling of the mixtures were characterized by X–ray fluorescence (XRF), X–ray diffraction (XRD) and scanning electron microscopy (SEM+EDS).

Results and discussion

After the high energy powder milling step, the results are presented for the Mg2Zn–1h, Mg2Zn–2h and Mg2Zn–4h samples . Table 1 presents the results of the X–ray fluorescence analysis of pure Magnesium and Zinc powders when mixed with the presence of impurities, used in the calculation of the concentrations of the elements detected in the starting material as shown in Table 2, where you can – to observe the presence of the elements Mg, Zn, Ca, Al, Na, P and Si, after grinding the presence of the element Sodium (Na) was verified. It was observed that the percentages of Zn decreased for times of 2h and 4h of milling. The presence of tungsten carbide was not detected in any of the samples. It can be seen that the concentrations of the elements in the powders are similar, and the composition of the powders is close to the Mg+1 wt% Zn composition. The concentrations of Mg and Zn were close to the composition of the Mg2Zn alloy. This is due to the presence of impurities, used in the calculation of the concentrations of the elements detected in the starting material, as shown in Table 1.

Analyzing the X–ray diffractograms, Figure 1, it is possible to verify that the most intense peaks present in the samples under analysis are those of the element Mg

with compact hexagonal crystalline structure (Mg–HCP), which appears for the three milling times of the system. In this analysis, the MgZn 2 and magnesium oxide (MgO) phases, along with the presence of tungsten carbide, were verified for the three grinding times. After identifying all the phases present in the samples with the help of Malvern's HighScore Panalytical, this multifunctional software package with the Plus option, it was possible to obtain a semi–quantitative analysis of the milled powders and after identifying the peaks with the reference database, from the Crystallography Open Database (COD) by agglomerative analysis, based on its likeness. This results in a much better overview, similar or nearly identical are found, diffractograms and phase positions. identified they were plotted with the support of the program OriginPro 8.5 [2,4].

Powder samples were subjected to SEM+EDS analysis to assess morphologies. In Figure 2, which shows micrographs taken at 1500X magnification, the flake–shaped particles highlighted in light gray were determined by EDS to be composed of zinc. These particles are larger at milling times of 1 and 2 hours (Figures 2A and 2B, respectively). In the grinding time of 4 hours (Figure 2C) small zinc and tungsten particles can be found , also in the form of flakes, distributed on the surface of the magnesium particles.

Table 1 – Analysis of pure Mg and Zn powders, obtained by X–ray fluorescence, expressed in percentage by mass of the elements, normalized to 100%.

Mg		Zn	
Element	**Concentration**	**Element**	**Concentration**
Mg	99,21 %	Zn	98,64 %
Ca	0,51 %	Mg	0,91 %
Al	0,24 %	Ca	0,41 %
P	0,03 %	P	0,02 %
Si	0,01 %	Al	0,02 %
		Si	0,01 %

Table 2 – Analysis of powder samples after grinding at 1, 2 and 4 hours of Mg2Zn, obtained by X–ray fluorescence, expressed in percentage by mass of the elements, normalized to 100%.

Mg2Zn-1h		Mg2Zn-2h		Mg2Zn-4h	
Element	**concentration**	**Element**	**concentration**	**Element**	**concentration**
Mg	97,77 %	Mg	98,26 %	Mg	97,92 %
Zn	1,46 %	Zn	0,81 %	Zn	0,86 %
Ca	0,37 %	Ca	0,54 %	Ca	0,78 %
Al	0,21 %	Al	0,32 %	Al	0,37 %
Na	0,16 %	Na	0,03 %	Na	0,04 %
p	0,02 %	p	0,03 %	p	0,02 %
Si	0,01 %	Si	0,01 %	Si	0,01 %

Figure 1 – X–ray diffractograms of powder samples: (A) Mg 2Zn 1h, (B) Mg 2Zn 2h and (C) Mg 2Zn –4h.

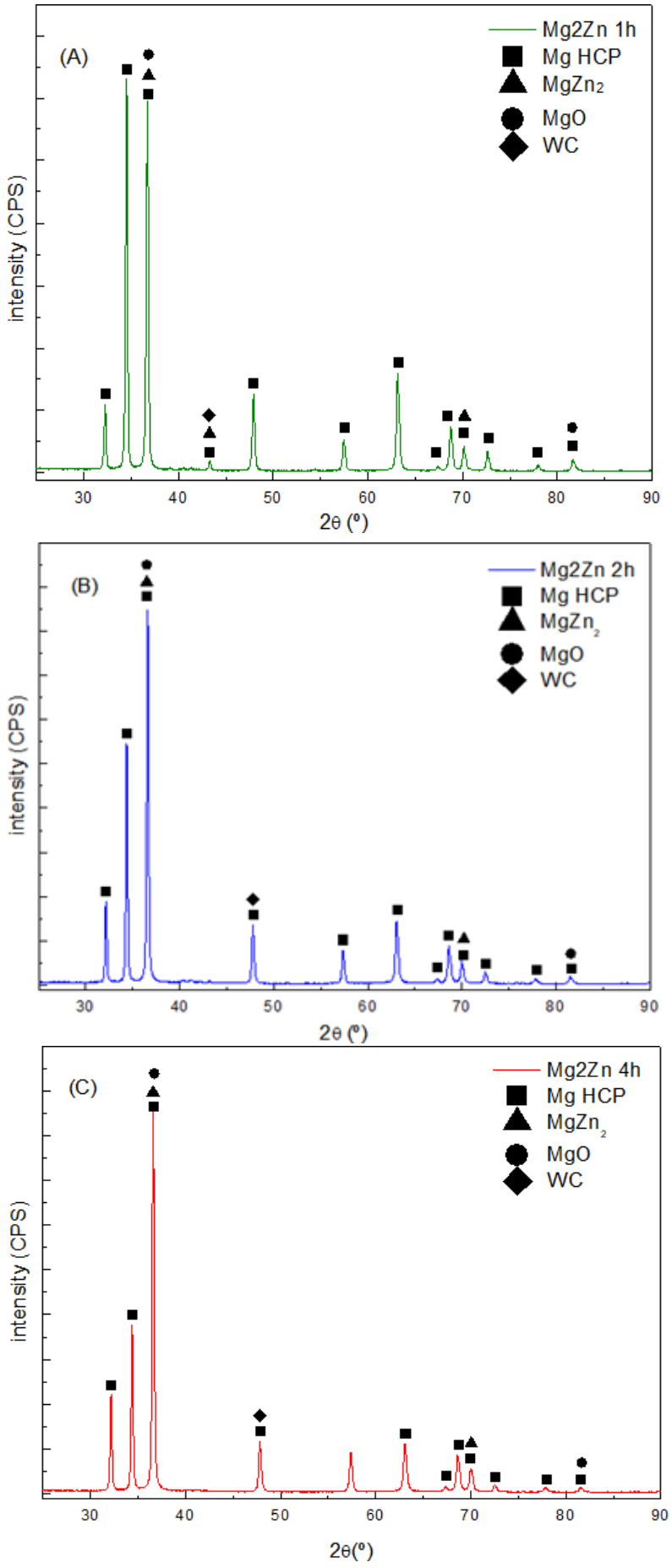
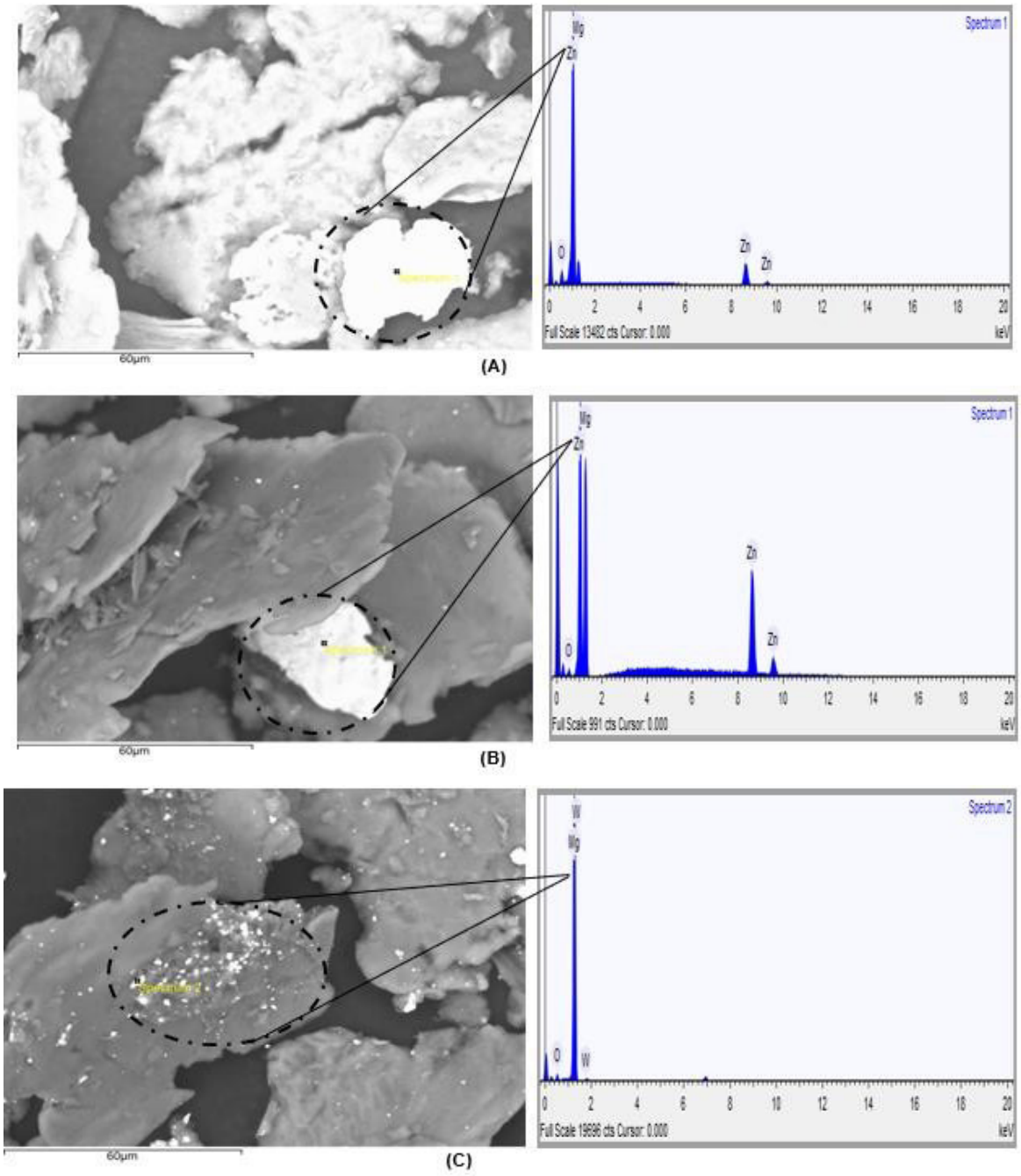


Figure 2 – Powder micrographs of Mg2Zn–1h (A), Mg2Zn–2h (B) and Mg2Zn–4h (C) samples, obtained by SEM+EDS with 1500X magnification.



Conclusion

With the XRF analysis of the elementary powders, it was possible to verify the loss of zinc mass with the increase of the milling time. High energy grinding allows introducing many defects in the powder particle structure. In addition to zinc being a light element, due to the high energy grinding being very severe, the friction between the particles generates irregularities on their surfaces, which leads to deformations and fractures in the particles of the elements used in this research, reducing their sizes, mainly to Zinc, due to its greater hardness. In addition, because they are in the form of flakes, the particles have greater roughness, lower packing density and greater angle of repose, which may allow the presence of pores for the sintered system.

Through the study of high energy grinding in a SPEX mill, it was possible to verify that the magnesium powder ground with 2% by weight of Zinc, for the grinding times of 1, 2 and 4 hours, presented particles of different sizes in the form of flakes. The presence of tungsten carbide was verified through SEM+EDS and XRD analysis, from the flask and grinding balls, which became a contamination in the powder obtained by the procedure.

It was possible to verify that the grinding times were not enough for the homogenization of the powders, since the analyzes show pure Mg with HCP structure, but it was possible to verify the presence of phases with $MgZn_2$ in the grinding of the elementary powders, which shows how much grinding heats the powder and predicts phase formation in the grinding process.

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RESEARCH PAPER

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Effect of synthesis temperature on crystallinity, morphology and cell viability of nanostructured hydroxyapatite via wet chemical precipitation method

Effect of temperature on hydroxyapatite properties

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Abstract: Hydroxyapatite (HA) is the main natural mineral constituent of bones and is a good alternative for biomedical applications because it is osteoconductive, non-allergenic, and non-carcinogenic, which ensures high biocompatibility. A commonly used method for obtaining hydroxyapatite is the wet route, which is simple and low-cost, produces only water as a final residue, and provides HA with a crystallinity comparable to that of bone tissue, which favors its biocompatibility. Therefore, the objective of this work is to synthesize hydroxyapatite via the wet chemical precipitation method at different temperatures (4°C, 30°C, 50°C, or 70°C) to observe the influence of temperature on crystallinity, morphology, and cytotoxicity. The results of X-ray diffraction show that all syntheses resulted in pure hydroxyapatite, while increasing the temperature led to higher crystallinity (10.6% to 56.2%) and the crystal size was slightly affected. The increase in temperature changed the particle shape from irregular to needle-like. Cell viability was tested by PicoGreen® in VERO cells for samples at concentrations of 30 and 300µg/mL, and the samples synthesized at 4°C, with lower crystallinity, caused less DNA damage to cells compared to the negative control.

Keywords: Calcium phosphate. Bioceramics. PicoGreen®. Scherrer's equation.

Introduction

Over the years, the need for replacement of damaged bone tissues has been increasing, and it is in this context that ceramic biomaterials arise, among which hydroxyapatite (HA) stands out [1]. The crystal structure and chemical composition presented by hydroxyapatite are similar to the composition of human bones and teeth. It is a bioactive ceramic material that presents biocompatibility and promotes the formation of bonds with bone tissue [2–4], as well as anticancer properties [5]. These factors have been crucial, justifying the numerous studies developed regarding its production and application in the biomedical field, particularly in the replacement of bone tissues [3,5].

One of the factors that has the greatest influence on the biocompatibility of hydroxyapatite as a substitute for bone tissue in the human body is its crystallinity. Hydroxyapatites with lower crystallinity have a higher rate of protein adsorption as well as an increase in the rate of release of bioactive calcium and phosphorus. These results in an increase in cell adhesion, proliferation, and differentiation compared to hydroxyapatites with high crystallinity. The promising effect of low crystallinity hydroxyapatite is due to the fact that in a crystal structure with this characteristic, solubility in body fluids is facilitated, which increases its bioactivity [5].

Among HA synthesis methods, the wet precipitation consists of preparing two solutions, one alkaline and one acidic, where the acidic solution is slowly dripped into the alkaline solution, resulting in the precipitation step of HA. After this step, the filtration, drying, and thermal treatment of HA follow [4]. Some of the advantages presented by this HA obtaining technique are low reaction temperatures, control of chemical composition, and control of microstructural properties[6]. The morphology[3,4] and stoichiometry of the obtained material can be altered according to parameters such as reaction time, reaction temperature, concentration[4], and "type/source" of reagents used[3], as well as drying and thermal treatment conditions[4].

Wet method synthesis temperature can alter some properties, such as crystallite size and degree of crystallinity, which may influence the biocompatibility of hydroxyapatite[2,6]. So HA will be synthesized at four different temperatures and the effect on the powder phases, morphology, crystallite size, crystallinity and biocompatibility will be analyzed.

Materials and Methods

In the present study, hydroxyapatite powder was synthesized using the wet precipitation method. Hydroxyapatite nanoparticles were prepared by using 0.5M calcium hydroxide ($Ca(OH)_2$) in an aqueous suspension that was temperature-controlled as required. Then, a 0.3M phosphoric acid solution was added at an addition rate of 2.5 mL/min to the calcium hydroxide suspension. The

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synthesis was carried out at four different temperatures, namely 4, 30, 50, and 70°C. The resulting solution was vigorously stirred for a period of 2 hours. The mixture was then filtered by vacuum filtration and dried at 100°C for 24 hours. Subsequently, the resulting white powder was macerated with a pestle and passed through a #200 mesh sieve before being separated for the following characterizations. In order to identify the present phases in the material synthesized at different temperatures, X-Ray diffractometer (D2 Phaser, Bruker) with a copper anode (CuKα radiation,λ=1.5406 Å) with voltage and current values of 30 kV e 10 mA, respectively and the scan rate was 0,05064 degree/s. The (020) plane was used to calculate the crystallite size by Scherrer's equation[7]

Hydroxyapatite crystallinity (Xc) was calculated using equation 1[8] :

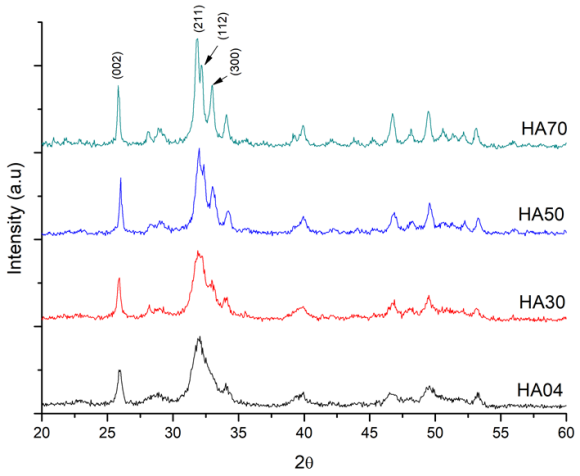
$$Xc = 1 - \left(V_{112/300} / I_{300}\right) \quad \text{(eq. 1)}$$

Where Xc is the crystallinity of the HA, $V_{112}/_{300}$ is the intensity of the valley between the diffraction peaks corresponding to the (112) and (300) planes, and I_{300} is the intensity of the peak corresponding to the (300) plane. The specific surface area was determined by nitrogen adsorption-desorption of Nitrogen (Quantachrome Instruments, NOVA 2200e) at 200 °C for 12 /h. To identify the functional groups present in the samples, Fourier transform infrared spectroscopy-attenuated total reflectance (FTIR-ATR) spectra were recorded (Perking Elmer, Spectrum Two). Powder morphology was verified by SEM (JOEL, JSM-6510LV). The thermal behavior of the materials was investigated using the technique of thermogravimetric analysis, using a Shimadzu TGA-51H equipment. A prospective in vitro study was conducted, in which a commercial cell line, adult monkey renal epithelial cells (VERO cell line), was used as an experimental model to investigate potential cytotoxic effects. After thawing, this cell line was maintained in polystyrene bottles (TPP) in culture medium containing 10% fetal bovine serum (Invitrogen), inactivated at 56°C for 1 hour, 100 μ/mL of penicillin (Invitrogen), and 100 μ/mL of streptomycin (Invitrogen), at 37°C in a humid atmosphere containing 5% CO_2. Weekly passages were performed in a laminar flow hood, so that each bottle received 5 mL of medium with a fixed number of cells at the time of passage (2.0 x 10^5 cells/mL). The volume, along with the above number of cells, was transferred to a new bottle with fresh medium. After obtaining satisfactory confluence for the experimental assays, the cells were seeded in 24-well plates. After the treatments, the plates were incubated in a CO_2 incubator at 37°C for 24 hours. The experiments were performed in triplicate. The evaluation of the cytotoxic effect of the structures was tested through the DNA PicoGreen® assay. To complement the determination of cell viability, a fluorimetric assay was conducted to quantify free DNA in the medium using the PicoGreen® reagent from Invitrogen (Life Technologies), which is a fluorescent dye that binds to double-stranded DNA. This procedure was performed in the culture medium where the cells are treated to determine the presence of double-stranded DNA in this medium due to possible cell rupture and cell death. The dye was added to the sample in a 96-well dark Elisa plate, with incubation for 5 minutes and fluorescence reading in the spectrofluorometer at 480 nm excitation and 520 nm emission[9].

Results and discussion

The X-ray diffraction (XRD) patterns of synthesized HA powders are displayed in Figure 1.

Figure 1- X-ray diffraction patterns of samples synthesized at different temperatures.



The X-ray diffraction peaks at 2θ = 25.8, 31.9, 32.2 and 32.9 correspond to the standard crystallographic file of pure hydroxyapatite (PDF – 009-00432). There were no undesirable phases such as β-TCP and CaO detected in any of the synthesized powders. The crystalline planes shown in the samples are (002), (211), (112) and (300) [5,8]. It can be observed that the increase of synthesis temperature, lead to an increase in peaks intensity. This growth occurred especially on the (002) peak, which indicates the growth of HA crystals along C-axis[7]. Table 1. shows crystallite size obtained by Scherer's equation, crystallinity degree calculated using equation 1 and specific surface area obtained by BET.

The crystallinity percentage of hydroxyapatite samples increased with synthesis temperature from 10.6 to 56.2, while the crystallite size increased from 27.4 to 42.2 nm. On the other hand, the specific surface area decreased from 90.9 to 50.1 m^2/g. György *et al*[10], relate the peak broadening effect of XRD patterns from

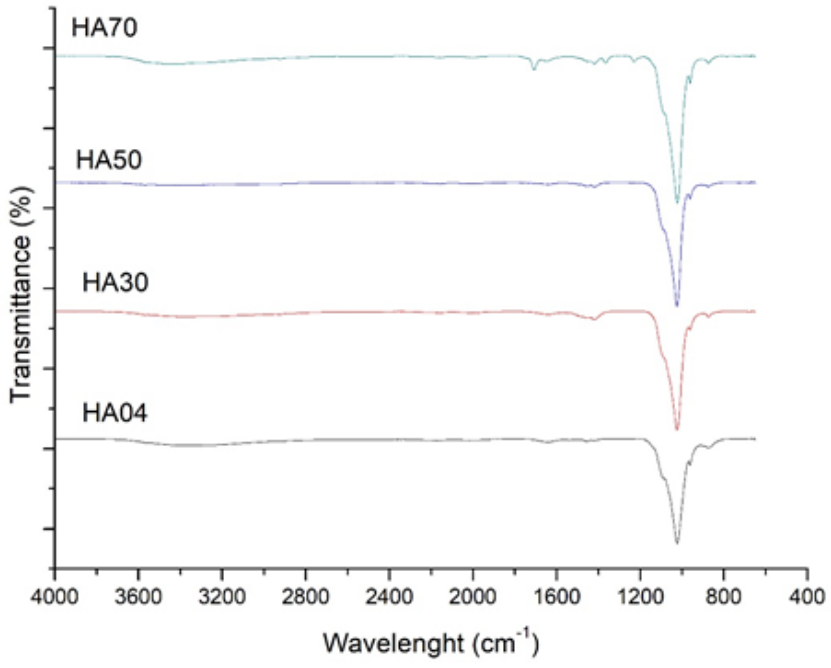
hydroxyapatite synthesized at low temperatures to either smaller crystallinity and crystallite size. The crystal size of hydroxyapatite (HA) changes with temperature during synthesis. During the early stages of particle formation, nucleation occurs, where small HA particles are formed. As the reaction progresses, these small particles begin to grow in size with the incorporation of additional calcium and phosphate ions from the solution[15,16]. Conversely, there was a decrease of the specific surface area measured by BET as a function of the increase in precipitation temperature, the same tendency was found by Lazic *et al.*[11] that synthesized HA in the temperature range of 22 – 95°C and obtained a specific surface area in the range of 58–23 m^2/g. The specific surface area of hydroxyapatite is an important factor since it can affect protein adsorption[12]. Figure 2 shows the FTIR spectra for the four synthesized samples.

It is possible to visualize hydroxyapatite characteristic band peaks for all samples. The broad band around 3400 cm^{-1}, can be attributed to hydroxyl group[13–15]. With the increase in synthesis temperature, there was an increment in the observed band at 1642 cm^{-1} which corresponds to the bending mode of H–O–H in water, indicating the presence of trace amounts of water in the synthesized powders[2]. The increase can also be observed in the peaks between 1400–1500 cm^{-1}, which correspond to the CO_3^{2-} vibrational peaks. These peaks replace some of the phosphate groups in the hydroxyapatite from natural[14,16]. According to Dey et al.[2], those CO_3^{2-} bands can appear in hydroxyapatites obtained by wet synthesis, due to the dissolution of atmospheric CO_2 in the reaction. Higher synthesis temperatures can facilitate CO_2 diffusion. A pronounced band at approximately 1024 cm^{-1} and a smaller peak at 965 cm^{-1} correspond to asymmetric (P–O) stretching vibration PO_4^{3-}, while the presence of HPO_4^{2-} in these powders is indicated by the 876 cm^{-1} transmission band[13]. Figure 3 shows the thermal analysis of HA investigated by thermal gravimetric analysis (TGA).

Table 1 – Crystallinity, crystallite size and specific surface area of hydroxyapatite synthesized at different temperatures.

Sample	% Crystallinity	Crystallite size (nm)	Specific Surface Area (m^2/g)
HA04	10.6	27.4	90.9
HA30	16.4	33.5	78.2
HA50	41.5	34.4	59.9
HA70	56.2	42.2	50.1

Figure 2 – FTIR spectrum of hydroxyapatite synthesized at different temperatures.



It is possible to notice a sharp drop from 30°C to around 200°C related to the elimination of adsorbed water[10,17]. The small mass decrease in the region between 200 and 650°C can be attributed to the removal of interstitial water[17]. For the hydroxyapatite synthesized at 4°C there was a small drop in the mass related to the conversion of the hydroxyapatite into β–tricalcium phosphate (β–TCP)[10]. Precipitation temperature has shown a significant effect on HA morphology, as can be seen in figure 4.

The effectiveness of nucleus growth and development plays a vital role in determining the crystalline structure of materials produced through the wet precipitation process, which functions via the nucleation–growth mechanism[4], this can be attributed to the size–dependent solubility of nanoparticles (NPs), where smaller particles exhibit higher solubility and surface energy, facilitating the dissolution and growth of larger particles [18].

Further research has indicated that the synthesis of hydroxyapatite at low temperatures results in crystals with irregular morphology, a lower specific surface area, and a greater tendency to agglomerate[4]. At a temperature of 4°C, the particles tend to aggregate, making it challenging to discern their morphology, indicating that there is insufficient driving force for crystal growth at low temperatures[10]. As the reaction temperature is raised, crystal growth is observed, consistent with the typical needle–like morphology of hydroxyapatite observed in X–ray Diffraction data[10,19]. To evaluate cell viability, a fluorometric test for quantifying free DNA was conducted. The DNA–PicoGreen® assay involves using a fluorescent dye that binds to double–stranded DNA in the medium, allowing for the detection of possible cell disruption and cell death[20]. To verify cell damage, two different concentrations of hydroxyapatite (30 and 300 µg/mL) for each synthesis temperature. Figure 5. shows the results obtained from the DNA–PicoGreen® assay.

The results showed no significant damage to the double strain DNA in HA04 sample for both concentrations. However, for other temperatures of synthesis the damage to the DNA was close to the positive control. According to Zhao[20], hydroxyapatite cytotoxicity depends on nanoparticle shape and that needle–like particles are more toxic than other shapes.

Figure 3 – TGA analysis of hydroxyapatite synthesized at different temperatures.

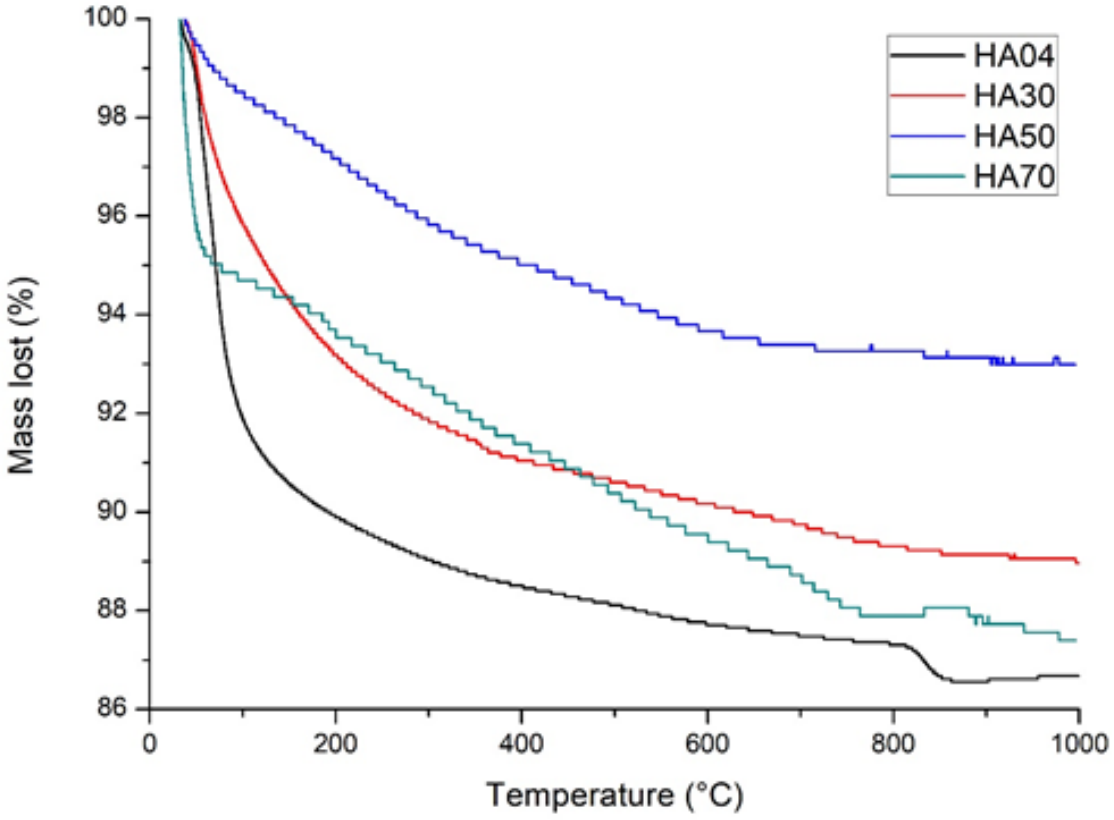


Figure 4 – SEM micrographs of hydroxyapatite

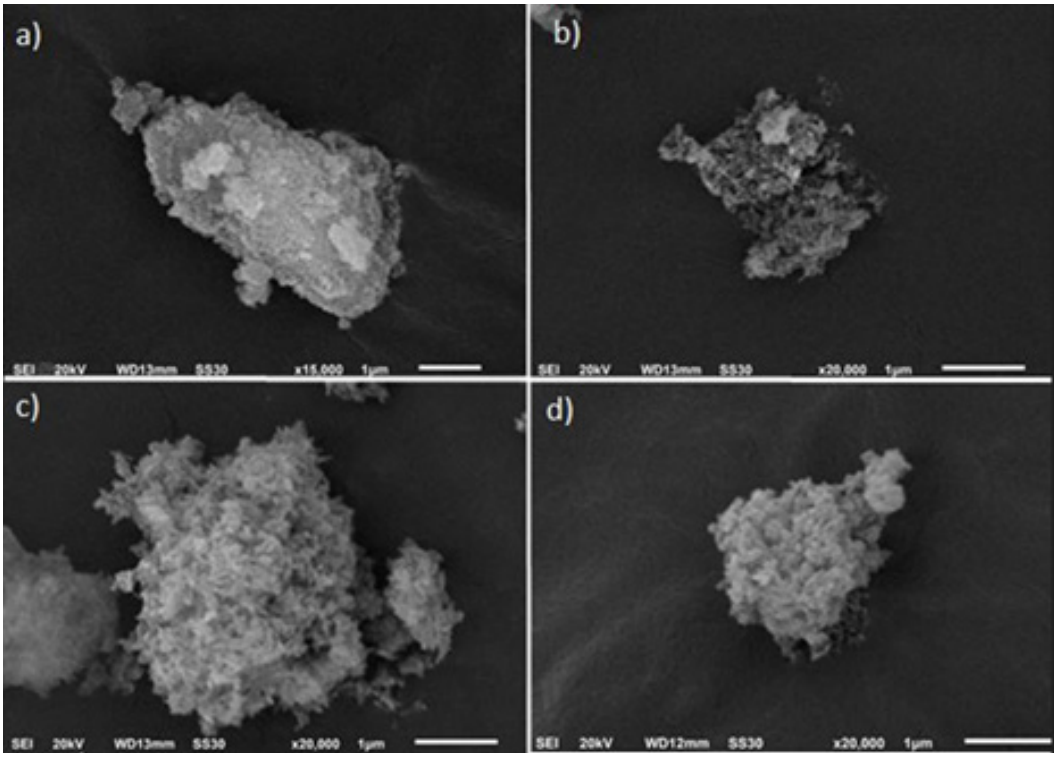
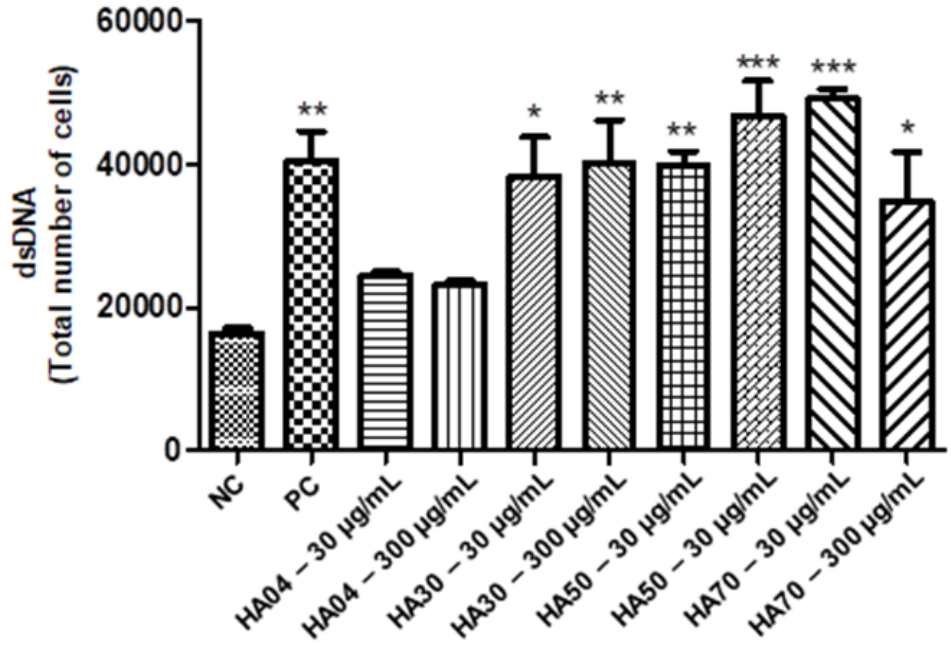


Figure 5 – Evaluation of the presence of double–stranded DNA using the PicoGreen® assay. NC (control negative); PC (control positive); HA04, HA30, HA50 and HA70 (30 and 300 µg/mL). Data are expressed as mean ± standard deviation (SD). Analyses were followed by one–way ANOVA, followed by Dunnett's post hoc test. Values with $p < 0.05$ were considered statistically significant, where * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.



Conclusions

The wet synthesis of hydroxyapatite was carried out at temperatures of 4, 30, 50, and 70°C. X–ray diffraction revealed that HA was the only phase present in the synthesized powders. There was an increase in crystallinity and crystallite size with increasing temperature, resulting in a hexagonal crystalline phase. Additionally, an increase in particle size and a decrease in surface area were observed by BET analysis. The irregular shape of nanoparticles synthesized at low temperatures was confirmed by SEM analysis also, there was a transition to needle–like structures with increasing temperature, which is characteristic of HA with elongation along the c–axis. The FTIR bands were characteristic of pure HA, and the mass losses observed by thermogravimetry were consistent with those of HA samples. In the cell viability test using PicoGreen®, lower toxicity was observed at 4°C compared to higher temperatures.

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RESEARCH PAPER

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Robotic arm inertial control for recreational child physiotherapy application

Robotic arm control to assist in the process of children's physiotherapy, making it fun and reducing the dropout rate of children/patients

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Abstract: According to expert reports, physiotherapy is not only a painful process but also uninteresting to children. The lack of dynamism and entertainment in the physiotherapeutic process makes it unappealing, hindering their development or even causing them to avoid it. In 2021, the "Robotic System for Pediatric Physiotherapy with Recreational Activities" project was developed, consisting of a robotic arm to assist in the physiotherapy process for children with Cerebral Palsy. According to the conclusions of the initial project, the developed control was effective in the proposed idea but not sufficient for implementing the project in rehabilitation environments. Therefore, this work presents a new control that is safer and allows for its application in assisting the rehabilitation of these children. This new control, applied with three MPU–6050 inertial sensors in conjunction with three Arduino Nano microcontrollers, enables the robotic arm to reproduce the movements of the human arm, allowing independent replication of forearm, arm, and hand movements. Through three NRF24l01 radio–frequency transmitters allocated to the circuits with inertial sensor and Arduino Nano, and adjusted to the user's arm, the movements are reproduced simultaneously and in real time. As a result, the prototype control functions reliably and robustly, successfully achieving its objective of providing a safer and more efficient physiotherapeutic process for the users.

Keywords: Robotic Arm. Inertial Control. Recreational Physiotherapy. Inertial Measurement Unit.

Introduction

Cerebral palsy is a neurological disorder of a non–progressive character that affects neuromuscular functions and occurs in the prenatal, perinatal and postnatal periods. This disorder can cause intellectual deficit and has as consequences motor and/or psychic alterations, epilepsy, paralysis, among others[1]. It has as one of its main causes hypoxias, a situation in which for some reason related to childbirth occurs the lack of oxygenation of the brain. In addition to this, they are also causes of it, traumas that occurred during childbirth, infections, diabetes, abnormalities of the placenta or umbilical cord, malnutrition, drug use, alcohol in pregnancy, hypoglycemia of the fetus, bleeding, genetic problems, and prematurity[2]. Treatment for this condition aims to improve existing skills and functions, develop new ones; and promote patient independence. In view of this and the diversity of signs and symptoms in patients, we have as some forms of treatment physiotherapy, occupational therapy and orthopedic surgery. As it has no cure, the forms of treatment aim to minimize symptoms to try to make life easier for patients; but with regard to physiotherapy as a treatment, its importance is the motor and cognitive development of the child, improving the patient's techniques and abilities; in the social sphere of the patient, it promotes the independence of the child, facilitating the performance of daily activities and communication[3]. Specific training, such as walking, sitting, picking up objects and exercises aimed at increasing muscle strength and/or better movement control are part of child rehabilitation, since physiotherapy prepares the child for a function so that it maintains or improves existing ones, always aiming at reducing muscle spasticity[4]. Rehabilitation is essential for children to perform adequately the daily activities, however, constantly treatment requires a long period of time and can become monotonous, tiring and demotivating. Knowing this, in 2015, the analysis on the influence of virtual reality (VR) with Nintendo Wii (NW), on the balance and gait of a child with cerebral palsy, showed that the use of this method provided improvement in static and dynamic balance, physical and cognitive performance of the child, also providing greater motivation and fun[5]. The conventional treatments employed by physiotherapists, which involve the use of simple equipment or subjective observations, have evident disadvantages due to their subjective nature and lack of certainty. Studies demonstrate that robot–assisted rehabilitation can contribute to the reorganization and recovery of the central nervous system, as well as the restoration of the patient's arm motor function. This is achieved through the application of precise, repetitive, and task–specific therapies. Additionally, rehabilitation robots can stimulate patient engagement through resources such as virtual reality and other methods[6].

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The application of ludic activities in the physiotherapeutic process makes the treatment more acceptable and pleasant for the children and consequently favors the child's development [7].

In recent decades, human beings have increasingly appropriated technology, which is constantly evolving, being a major milestone of this the digital revolution, which enabled an acceleration in the expansions and improvements of computers [8]. The knowledge to control such technological advances safely is essential for human–machine interaction. According to Isaac Asimov's first law of robotics, robots cannot harm humans or allow them to suffer any harm [9]. An example of non–compliance with Asimov's proposed law is the case of the artificial intelligence known as "ChatGPT" manipulating a person to perform a task, a situation exposed by the AI's owner in a report [10]. Therefore, it is important that the creation and maintenance of robots that have direct relationships with humans receive special attention to ensure their safety and minimize the dangerous risks for people. Devices designed to assist in limb rehabilitation must significantly improve the quality of life of their patients, otherwise it can cause dissatisfaction, leading to the discontinuation of treatment in a short period [11].

In view of the risks in the event of failures resulting from the lack of improvement of systems and circuits, whether electrical or mechanical, is important that projects that work in the Human's company need constant evolution. Then, it is idealized to improve specific parts of the project "BRAÇO ROBÓTICO TELEOPERADO APLICADO PARA A REABILITAÇÃO INFANTIL ATRAVÉS DO LÚDICO" presented by Silva et. al.[12], which was based on childhood cerebral palsy, which has physiotherapy as one of the forms of treatment. In this project, the robot's movements were controlled by a system of inertial sensors located in a glove on the patient's hand. It was possible to conclude the need for improvements, for example, increase the reduced number of replicated movements presented and the possibility of sudden movements.

Faced with these problems, is present the development of a system that makes the movement of the hand, arm and forearm independently through the application of inertial controls using Inertial Measurement Unit sensors. It was expected that with the application of a new inertial control system applied in different parts of the upper limb, the prototype could operate safely with a robustness control and more precision, therefore being applied in child rehabilitation environment, allowing the use combined with ludic activities.

Experimental procedures

The technology used as principle for the new control is based on Inertial Measurement Units (IMU) or inertial controls. The inertial controls have an inertial principle of operation, that according to Newton's first law, refers to the state of the matter of staying at rest or uniform rectilinear movement unless external forces are applied [13].

The inertial controls are aimed at monitoring acceleration, velocity, and position, in various directions and senses, of moving bodies, in addition to being portable and low cost. They are sensors that have associations of accelerometers and gyroscopes. The use of this technology enables several applications in controls and monitoring systems linked to human movement [14].

So, considering these functionalities, for the proper application of the technology, an inertial sensor was designed for each part of the patient's arm. Additionally, the methods used include the C++ programming language to develop the control logic and integration between the inertial sensors on the patient and the corresponding motors in the robotic arm. Literature review, mainly focused on cerebral palsy and therapies based on ludic methods to understand the needs and desires of the patients, specifically, children.

To achieve the independence of each control part in the child's arm, a transmitter circuit system was applied to the hand. Based on the development presented in the mentioned robotic arm system, it was replicated in identical circuits for the arm and forearm. The transmitter circuit system consists of 1 Arduino Nano®, 1 MPU6050 (orientation sensor), and 1 nRF24L01 (radio frequency module). This system can be observed in Figure 1.

The microcontroller Arduino Nano® is responsible for reading the values of the orientation sensor and make the communication between it and the radiofrequency sensor. The MPU6050 sensor is responsible to detect the position of the individual's upper limb links on three–dimensional coordinate system and send these positions values to the microcontroller. The radiofrequency module nRF24L01, in turn, sends the wireless signal transmitting the values of the axes to the robotic arm controller. Complete this circuit, two rechargeable 4V batteries connected in series as power supply, but it was represented on circuit software with two 9V batteries.

Only in the system embedded on the hand has a difference in comparison with the circuit represented in figure 1 (arm and forearm), this difference is an additional button to open and close the robotic gripper.

After completing the hardware of the transmitter circuits to the hand, arm and forearm, it was studied how to perform a wireless communication of these three transmitters respectively, for 2 receivers, that is, for actuating the robotic arm.

Each sensor applied here contain a library in the Arduino application. The library that enables the wireless communication between sensors is called RF24. But, in this application it was necessary to modify the library to be able to communicate the three transmitters with two receivers on the robot–ic arm system. This modification was necessary to avoid signal interferences.

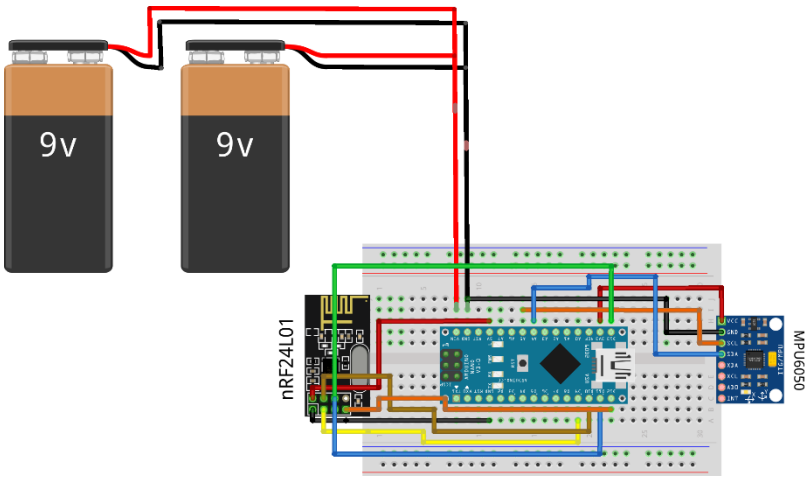
In the first tests each transmitter was given a different address that would later be identified by the receiver and the values of the axes are sent in a data package called "msg". However, it was necessary to designate a specific identification for each transmitter because the values of the 3 transmitters when arriving at the receivers would be mixed causing possible problems in the future. Therefore, the solution adopted was to send together with the axis values of each transmitter circuit, a number chosen arbitrary for identification of different ones, so the values 99, 100 and 101 were assigned to the corresponding hand, forearm, and arm circuits, respectively.

Both the three transmitters would perform the main same function, which is to send the X, Y and Z axis values, but the values sent by the MPU6050 are not of integer type and the servomotors used to work with integer values, so it was necessary to convert these MPU6050 values into integers using specific functions on microcontroller program to a proper communication between the system on the human arm and the robot arm. The scheme of communication can be observed in figure 2.

In the receiver circuit, the structure used to simulate the human arm was a acrylic arm in a black color. The robotic arm was chosen due to its sufficient 5 Degrees of Freedom (DoF), its good flexibility, and its great resistance due to its material, it is approximately 50 centimeters tall and has good stability in movements.

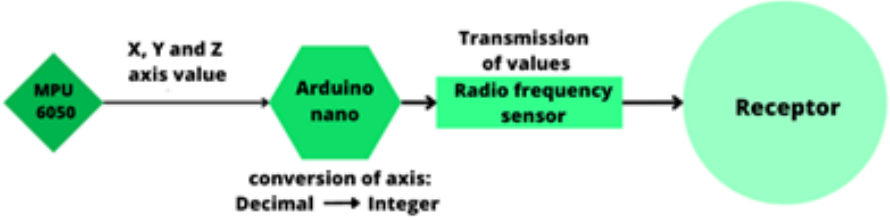
It is known that the human arm has seven Degrees of Freedom. The human arm has two spherical joints, each type of joints like this provides three DoFs to the arm, being the shoulder joint and the wrist joint, when combined with the simple revolute joint in the elbow in which there is one more DoF, is given the seven Degrees of Freedom. However, due the redundancy of this system in order to position the arm in the three–dimensional space is necessary just six DoFs. So, making some analyses was conclude that due to the most tasks in the rehabilitation environment being done in the plane reference, e.g., to move an object from one point to another on a table or to move an object from bottom to top, the five DoFs presents in the robotic arm are considered sufficient for the application of the project.

Figure 1 – System embedded in each link of the human arm.



Source: Own Authorship, 2023.

Figure 2 – Transmitter operation flowchart.



Source: Own Authorship, 2023.

The system of robotic arm consists of the following components: 1 protoboard, 2 Arduino UNO® microcontrollers, 5 MG996R servomotors, 2 9g micro servomotors, 1 nRF24L01 radio frequency module and a 400W ATX power supply. The acrylic robotic arm simulates a patient's arm in a ludic environment, where the servomotors perform the movement of the joints of a human arm. The robotic arm aforementioned and chosen for this application can be seen in figure 3.

Figure 3 – Robotic Arm.

Source: Own Authorship, 2023.

The Arduino UNO is fundamental for the development of the new control, since it is responsible for managing the entire logic of the new system. Initially, the use of one microcontroller was evaluated to perform the functions of the receiver circuit. However, after some tests performed, it was seen that only one unit of this microcontroller did not have sufficient processing capacity for the data flow. It was then noticed that the Arduino receiver was receiving 28,512 bytes and using another 11,132 bytes of its own programming, consuming 39,464 bytes and its limit is based on 32 Kb. It was necessary the use two microcontrollers to drive the robotic arm, but in the future, it will be changed by a new microcontroller model with better data processing capacity. In Table 1 is possible to understand the processing costs.

There are two nRF24L01 radio frequency modules present in each Arduino and are designed to receive the data from the transmitters and communicate to control the servomotors. The robotic arm has five servomotors, being one servomotor applied to the movement of the base rotation that corresponding to the shoulder rotation movement, two servomotors associated with the same base but applied to carry out the elevation, so called, flexion and extension movement of the link corresponding to the human arm in the robotic arm, another one for the flexion / extension movement to the link that corresponds to the forearm and a last one for the flexion / extension movement of the wrist. There are two additional micro servomotors, the first responsible to rotation movement of the wrist and another one to open and close, or, flexion / extension movement of the gripper. All these motors are powered by a 400W power supply aforementioned. This circuit is shown in figure 4.

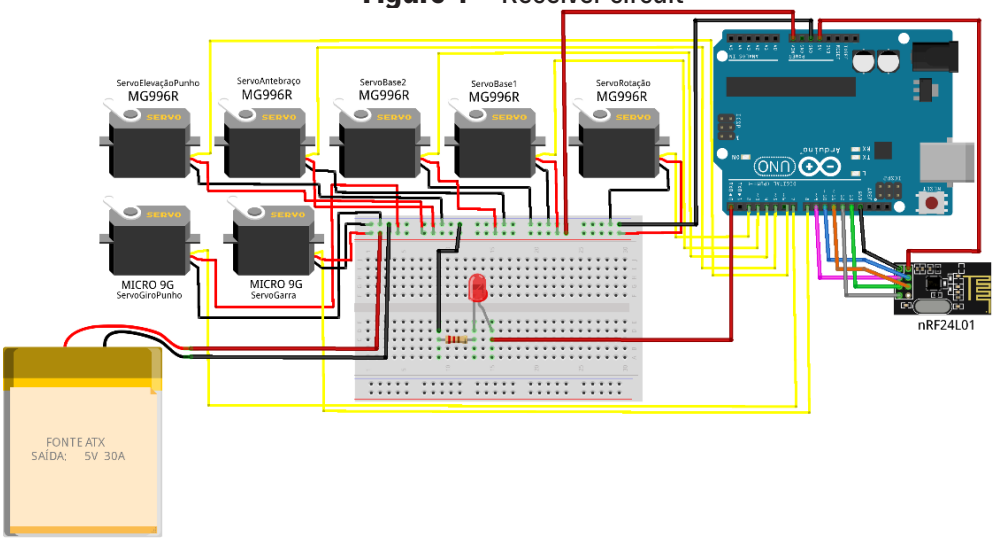
Completing to the logic operation idea of the new control, the radio frequency receiver modules were first indicated to which addresses it must communicate to receive the signals from the three transmitters. The transmitters were identified using an identification number corresponding with the motor that each one need control as already explained. After this, the data received, that is, the values of the cartesian coordinates, are converted into angles so that the motors can follow every small variation of motion values in real time. In figures 5 and 6 is shown the described system, it is possible to observe in detail how the communicators and microcontrollers are divided and what each one must control.

Table 1 – Consume of bytes.

Bytes spent on each part of the circuit	
Circuit	**Byte consumption**
Transmissor: Hand	11.270 Bytes
Transmissor: Forearm	10.710 Bytes
Transmissor: Arm	6.352 Bytes
Receptor:	11.132 Bytes
Total	39.464 Bytes

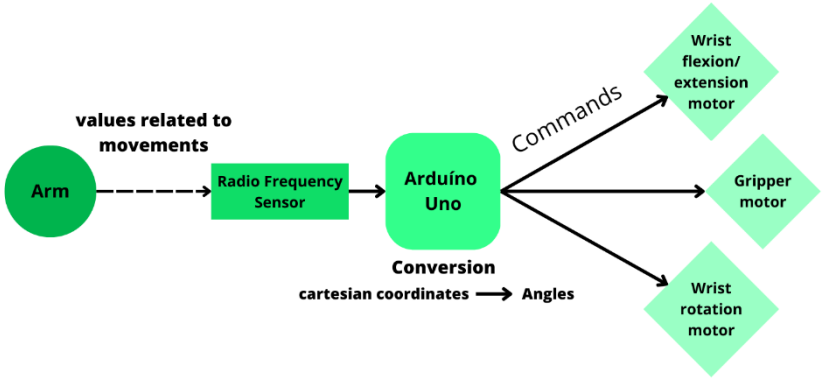
Source: Own Authorship, 2023.

Figure 4 – Receiver circuit



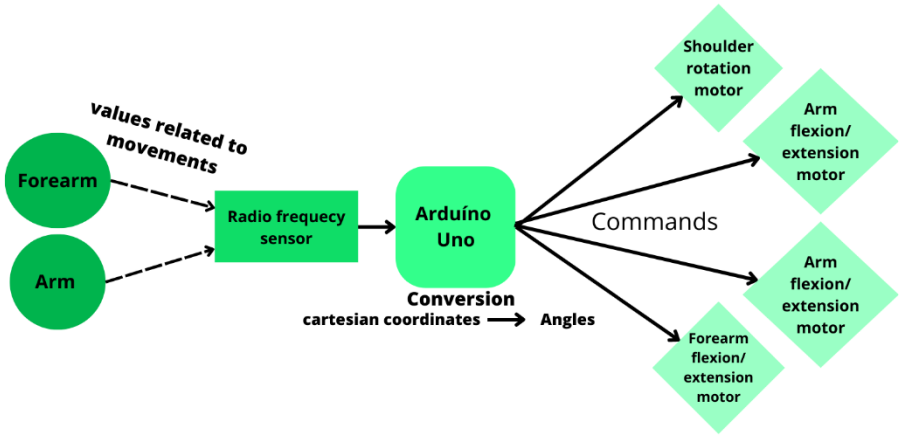
Source: Own Authorship, 2023.

Figure 5 – Receiver operation scheme.



Source: Own Authorship, 2023.

Figure 6 – Operation scheme of the second receiver.



Source: Own Authorship, 2023.

Results and discussion

After carrying out the communication tests between transmitters and receivers, applying independent control of each link of the robotic arm and finally integrating the whole system, that is, simultaneous operation of all sensors, motors, and systems an independent control of the links in real time can be observed.

It was verified that a stable communication was established at several points, but some interferences can be observed in specific situations. As with the nRF24L01 operation, as it operates at 2.4 GHz, when the system is close to some device that used to use the same frequency is possible occurs these not desirable noise signal making it difficult for the robotic arm to reproduce fluid movements in some situations. However, when communication did not suffer from these external interferences, it was observed that the prototype was able to fluidly replicate the movements made by the user, thus presenting the operation of the new control as expected in environments with a few numbers of equipment working at the frequency of 2,4 GHz, as in the case of physiotherapy environments.

Trying to adjust this communication problem, it is intended in the future to change the channels in which the module operates, defining channels that have as little external interference as possible. In addition, as previously described, due to the low processing capacity of the microcontroller used, it was decided to use two microcontrollers to reduce the processing data problem, but to reduce the volume occupied by the hardware, it is ideal to use only a microcontroller with a suitable processing data capacity, as the Arduino DUE microcontroller, for example.

Having fulfilled the proposed objectives for the safe operation of the robotic arm, we sought to improve the operator's experience with wearable sensors. With the use of adjustable Velcro, all members of the development team were able to use the transmitter circuits, unlike the previous project where such flexibility did not exist due to the size of the glove that housed the old transmission system. This alteration is also reflected in the final application of the project, as it enables its use by patients with different arm sizes.

Conclusion

Based on the arguments presented, it is concluded that the project has positive results, since the success in the operation of the new idealized control can be observed and this provided good stability in the movement in relation to the old control used. The improvements applied also provided a good fluidity during its movements and improved the precision of the movements operating in what is considered "real time", where as soon as the operator performs the movement, the robotic arm can reproduce it in a very short period of time.

This "real time" operation is defined by peer observation, that is, being observed by the human eye, no delay can be noticed. However, in a future improvement this could be measured with an electronic system to prove this concept.

For the definitive use of the robotic arm developed in child physiotherapy it is necessary, first of all, the evaluation by a professional in the rehabilitation area.

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Analysis of the bioprinting market in Brazil and its status in the global scenario

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Abstract: Additive manufacturing (AM) is a constantly growing manufacturing technique that can be used from the prototyping stage to the final product in several industries. 3D bioprinting is a variant of conventional AM that uses bioinks, i.e., inks with the presence of cells, to manufacture living biological structures. These structures can be used in applications in the medical field and with therapeutic potential, such as the fabrication of tissues and organ models, drug testing, among others. Considering its importance in the global scenario, this work aimed to evaluate the growth related to 3D bioprinting research in Brazil and in the world, and to analyze the Brazilian market compared to the global panorama. For this, qualitative research, literature search in research bases, and the search for patent records were used. The exponential increase of studies in the area was identified, through graphs with trend lines, exposing its enormous potential for development. It was possible to perceive the notable advance in the use of bioprinting worldwide, as well as in Brazil, a leader in research in the area in Latin America, although it is still lagging behind other countries, occupying the twentieth position worldwide in scientific contributions.

Keywords: 3D bioprinting. Biofabrication. Additive manufacturing. Biomaterials.

Introduction

The development of new technologies and solutions in the health area becomes increasingly necessary, since this area is evolving, in recent years, to a more customized approach[1]. Additive manufacturing (AM) represents a progress in this area, since this technique allows a customized production. A variation of this technique is 3D bioprinting, differentiated by the use of bioinks for 3D printing, which are materials composed of cells. Bioprinting can be used to manufacture three-dimensional living structures that mimic the human body [2,3].

Bioprinting may be used for several purposes, such as the manufacture of prostheses, assistive devices, organ models, among others. There is a recurrent shortage of tissues and organs in human tissue banks, which has a tendency to increase in the next years, highlighting the need for an alternative for the development of materials and equipment for this type of shortage. Thus, one of the main purposes regarding biomedical applications, in the long term, is the biofabrication of functional organs, which aim to be used in transplants[4,5].

Although research in the field of bioprinting advances exponentially each year, the development of structures with complex functionalities, shapes, and sizes is still a challenge[6] and therefore the evaluation of suitable techniques for biomanufacturing is essential. Currently, the main bioprinting deposition approaches include inkjet; extrusion; stereolithography; and laser-assisted. Each of these different techniques has specific properties and limitations, to be used depending on the desired characteristics of the final printed structure[4,5].

In addition to using the appropriate technique, the choice of materials is also of enormous importance. The ink used for bioprinting is called a bioink, and cellular material is an obligatory component. In addition to cells, the bioink may contain biomaterials, in order to amplify its printability properties[7]. Hydrogels are the most used type of biomaterial, because they are polymers that have a good interaction with water, providing cell viability, besides presenting a good crosslinking factor, essential for bioprinting[8].

Regarding the bioprinting scenario, it began in the mid-1980s, with the advent of 3D printing, but it was in 2004 that there was a major milestone in the area with the fabrication of the first three-dimensionally bioprinted bladder, made from autologous cells[9,10]. However, it was only around 2015 that Brazil experienced a boom in this market, with the opening of the first companies and startups in the area of bioprinting, which opened doors to the current context, in which the country is in constant development, both in relation to research and the number of companies present in the country[11]. Thus, this work proposes to assess the research advances in the area of 3D bioprinting, as well as analyze the insertion of the Brazilian market in the global context in relation to this area.

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Methods

Research Mapping

Initially, in order to analyze the general panorama of research on bioprinting, a comprehensive search on the subject was conducted. In order to obtain all the results referring to the growth of the area, the period of publication was not limited, and the term "bioprinting" was applied to all the fields of work in the databases. The searches were performed in Science Direct, Scopus, and Web of Science, through institutional access via the CAFe (*Comunidade Acadêmica Federada*) service of the CAPES Periodicals platform.

Intellectual Property Search

To identify the registration of patents in the field of bioprinting, a metric related to innovation, a search was conducted both in the national database of the Brazilian National Institute of Industrial Property (INPI), as well as in the international databases World Intellectual Property Organization (WIPO), a global entity composed of 187 member states, and European Patent Office (EPO), a European institute.

Table 1 shows the terms used for the search in these databases, and the same terms used in the international databases were used for the INPI search, only translated into Portuguese, except for the term "tissue engineering", which was removed because it returned many results outside the scope. To ensure that all data involving the area of bioprinting would be identified, the Boolean operator OR was used, returning records containing any of the search terms.

Table 1 – Approach used for patent search.

Database	Search Terms	Observations
INPI	*bioimpressão 3D*; *engenharia de tecidos*; *bioimpressão de tecido*; *bioimpressão*; *biofabricação*	Due to the limitations of the platform's search tool, each term had to be searched separately. Search applied to the record title.
EPO	3D bioprinting; tissue bioprinting; bioprinting; biofabrication	Search applied to all text fields, in English, French and German.
WIPO		Search applied to all text fields.

Source: Own elaboration.

Brazilian Market Mapping

In this phase, qualitative research was used to map Brazilian companies and startups in the bioprinting industry, through the companies' own websites. This was necessary, since this is a type of data that is not unified in any database. For this, search platforms and social networks were used, since these represent the main means of dissemination of these companies, being the websites: Google, LinkedIn and Instagram. For this purpose, searches were made using the terms "company/startup + bioprinting".

Also, as a model for the representation of this data, a 2019 study conducted by Dr. Mayasari Lim[12] was used as a basis, in which she sought to map all companies in the bioprinting industry. The classification of Brazilian companies and startups was performed in a similar manner to that done by Dr. Lim, by area of activity, but adding the category of "education/training".

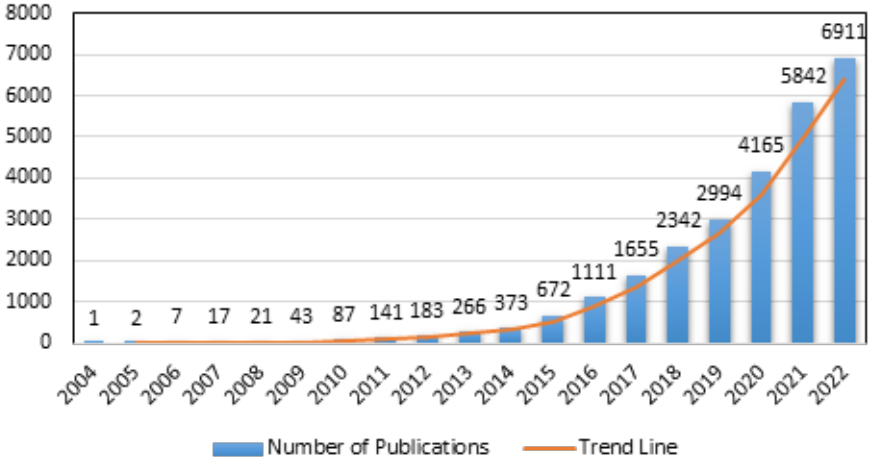
Results and Discussion

Bioprinting Publications

The Scopus database was chosen for this analysis because it returned a larger number of data, allowing for a more complete study. As it is possible to visualize through Figure 1, a total of 27,091 results were identified, with the first publication dating from the year 2004, referring to a journal article accepted for publication in 2003 and the first work to mention of the term "bioink"[7]. An exponential trend in the number of publications can also be observed, with the highest number for the current year 2022, with 6,911 publications and over 250 papers to be published in 2023. The documents that were analyzed at this stage include: full papers; review articles; book chapters; and papers published in event proceedings.

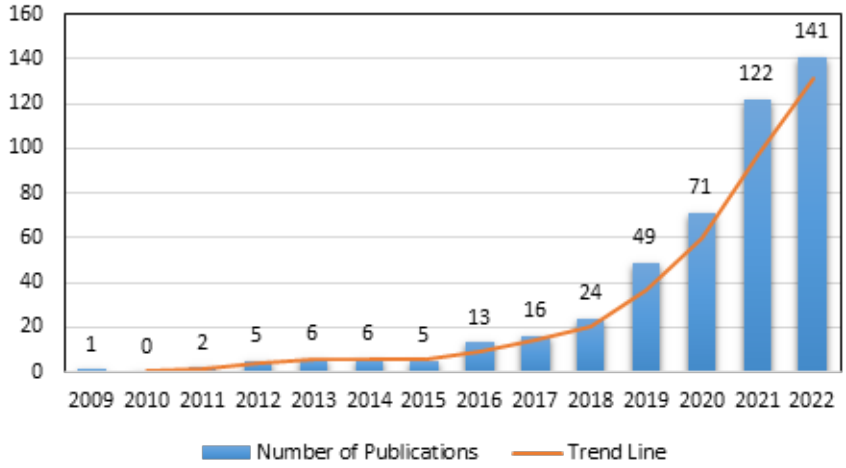
In addition, one can also analyze these documents distributed by the country or territory where the study was conducted, in order to understand the dissemination and encouragement in each region. Brazil is the twentieth country in the descending list of number of publications, and is also the first among Latin American member countries, with a total of 465 publications. The country with the greatest scientific contribution is the United States, with more than 7,000 publications, followed by China, with 6,776 publications. This may show how, still, countries that are considered more economically developed are ahead in the bioprinting research scenario. Leading the number of publications in Latin America, Brazil, when analyzed separately, also presents a behavior of exponential increase in the number of papers, as presented in Figure 2.

Figure 1 – Papers by year of publication in the area of bioprinting (2004 – current).



Source: Scopus.

Figure 2 – Papers by year of publication in Brazil in the area of bioprinting.



Source: Scopus.

Intellectual Property Registrations

Since the process of granting a patent is long and bureaucratic, the numbers regarding the requests for registrations were analyzed. When searching for patent applications related to the area of bioprinting in Brazil, the INPI platform returned 12 results, with the first requested in 2011 and granted in 2018.

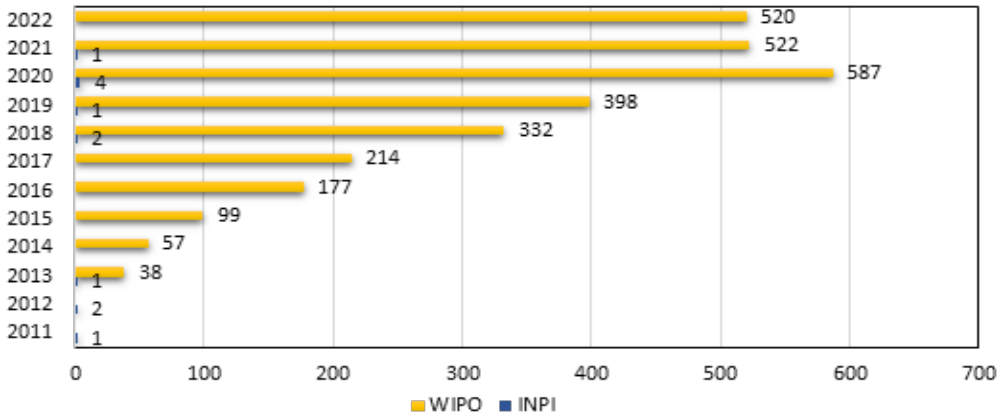
For the searches for international intellectual property records WIPO and EPO returned, respectively, 3,058 and 2,752 results, an expressive number when compared to Brazilian records. Since both platforms group records from several countries, many duplicate records of the same invention can be displayed. In both international bases, it could be observed the publication of dozens of registration requests in recent months, while, when comparing with the Brazilian base, the last patent filing at INPI dates from early 2021.

The WIPO platform also allows an analysis of various components of patent registrations, such as by country and applying institution. When analyzing the registrations by territory, the United States leads with 1,127 applications, while the United Kingdom is the territory with the lowest number of registrations on the platform, with 17 applications. When filtering these results by the applying institutions, one can see that the registrations are divided between companies and research institutions, with the company Organovo Inc. leading the ranking, with more than 100 applications.

It is important to note that when analyzing the records further, one realizes that some records relate to traditional 3D additive manufacturing, rather than 3D bioprinting, but it was not possible to eliminate these results without losing data relating to bioprinting. The same limitation is observed in the EPO platform.

Figure 3 shows a comparison in patent publication between Brazil and the rest of the world, using data from INPI and WIPO. Most patent filings in Brazil occurred in the last 5 years, representing 8 applications, 5 of which are related to the registration of bioprinting machines or bioprinting systems, and methods for bioprinting. Although the Brazilian intellectual property registration database does not contain many patent applications, it is possible to note a change and growth in the number of these, demonstrating the development and increased interest in the area of bioprinting in Brazil.

Figure 3 – Patent registrations published in the area of bioprinting in Brazil and worldwide.



Source: Adapted from INPI and WIPO.

Map of Bioprinting in Brazil

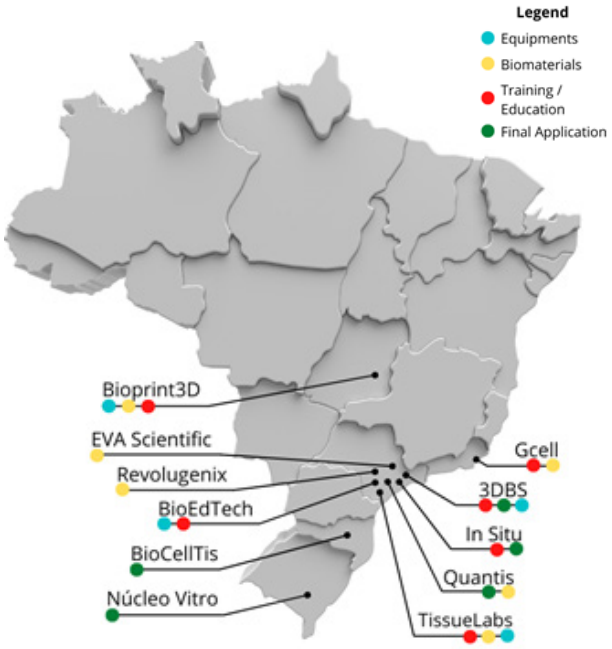
The bioprinting scenario in Brazil is constantly developing, with companies active in the commercialization of equipment and materials, in the development of bioprinted products, as well as training and consulting[11]. With this in mind, we sought to conduct a mapping of companies and startups active in this sector in the country using as a basis the study of Dr. Mayasari Lim, which proposed to map, in 2019, all companies in the field of bioprinting, subdivided by their performance, being them: supplier of tools or hardware; supplier of bioink or materials; and distributor focused on applications[12].

Later, in 2020, the same researcher published an update with new companies that emerged, or that she had left out in the first version. As far as Brazil is concerned, the first version of the map presented only one company, 3D Biotechnology Solutions. In the 2020 version, the scheme has the presence of 6 Brazilian companies[13]. However, as presented through the study by Massaguer and Millás in 2019[11], it is known that Brazil has a larger number of companies and startups active in the area of bioprinting. Therefore, the more in-depth mapping was elaborated for Brazil alone and Figure 4 presents the result of collecting this data. Similarly to Dr. Lim, it was possible to characterize the Brazilian companies in the following categories: suppliers of equipment, such as bioprinters; suppliers of materials, such as hydrogels; suppliers of training; and suppliers of products for final applications, such as biocuratives.

It was possible to identify, currently, 11 companies active in the bioprinting business in Brazil, an expressive number for a relatively new area, but one that points to a notorious room for growth. As illustrated separately through Figure 5, it is possible to observe that most companies work with the offer of training and education and with the supply of biomaterials. There is an overlap of activities, since a company may have more than one area of activity.

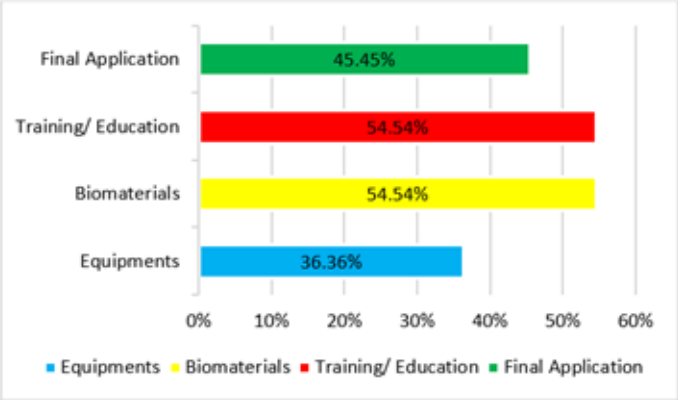
Furthermore, one can notice a tendency for these establishments to be distributed in the southeastern region of the country, a technological hub and a region of high investments in research, with almost 60% of all bioprinting-related companies. Among the 11 companies and startups mapped, only In Situ is not established in a capital, being located in the countryside of the state of São Paulo. It is worth noting that Revolugenix, despite having been created in 2011, has only recently started to operate in the field of bioprinting.

Figure 4 – Map showing the geographical distribution and areas of activity of bioprinting companies in Brazil.



Source: Own elaboration.

Figure 5 – Graphical representation of bioprinting companies' areas of activity in Brazil (%).



Source: Own elaboration.

Conclusion

With the advent of 3D bioprinting, a range of new possibilities have emerged in the area of biotechnology and regenerative medicine. Likewise, the number of researches on the subject has been growing exponentially, and the investments made in the area are increasing every day.

By analyzing the publications and intellectual property registrations, it is possible to notice the remarkable advance in the use of bioprinting worldwide, as well as in Brazil, the leader in research in the area in Latin America, being the twentieth country with the largest number of publications on the subject. The countries that lead this ranking of published works are, respectively, the United States and China, with more than 7 and 6 thousand articles, which can be justified since they are economic powers and invest massively in research.

Regarding patent applications, the international research platforms, WIPO and EPO, returned around 3 thousand results each, while the INPI platform, of Brazilian national search, returned only 12 results. This can be justified by the difficulty found in the international platforms to filter the records related to conventional 3D printing, besides showing several duplicate requests, because they were made in more than one country, while INPI allows a more individualized search, filtering the records more easily. Of this total of 12 requests, 8 were made in the last 5 years.

Through these comparisons, one can see how Brazil is behind the main countries contributing to research and development in 3D bioprinting nowadays. Despite this, the country is in an exponential growth of development, observed through its scientific contributions, which have jumped from 24 to 141 productions per year in the last 5 years.

Furthermore, with the elaboration of the bioprinting map in Brazil, it was possible to visualize the growth of this market, as well as understand in more depth the distribution of companies in this industry and their area of activity. The country currently has 11 companies and startups operating in the area, mostly providing training, with a distribution of almost 60% of these establishments in the southeast region of the country, justified by being a tech hub and research investments center.

Therefore, it was possible to analyze the data concerning the scientific contribution and development in the area of 3D bioprinting today, as well as to observe the context of the Brazilian market in the global panorama. Thus, it is concluded that this is a branch with a significant potential for expansion and great impact on the biomedical sector for the coming years, and it is essential to emphasize the attention and encouragement that research institutions need, especially analyzing the Brazilian scenario.

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