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The IFMBE is a WHO accredited NGO covering the full range of biomedical and clinical engineering, healthcare, healthcare technology and management. It is representing through its 58 member societies some 120.000 professionals involved in the various issues of improved health and health care delivery.

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About IFMBE

The International Federation for Medical and Biological Engineering (IFMBE) was established in 1959 to provide medical and biological engineering with a vehicle for international collaboration in research and practice of the profession. The Federation has a long history of encouraging and promoting international cooperation and collaboration in the use of science and engineering for improving health and quality of life.

The IFMBE is an organization with membership of national and transnational societies and an International Academy. At present there are 52 national members and 5 transnational members representing a total membership in excess of 120 000 worldwide. An observer category is provided to groups or organizations considering formal affiliation. Personal membership is possible for individuals living in countries without a member society The International Academy includes individuals who have been recognized by the IFMBE for their outstanding contributions to biomedical engineering.

Objectives

The objectives of the International Federation for Medical and Biological Engineering are scientific, technological, literary, and educational. Within the field of medical, clinical and biological engineering it's aims are to encourage research and the application of knowledge, and to disseminate information and promote collaboration.

In pursuit of these aims the Federation engages in the following activities: sponsorship of national and international meetings, publication of official journals, cooperation with other societies and organizations, appointment of commissions on special problems, awarding of prizes and distinctions, establishment of professional standards and ethics within the field, as well as other activities which in the opinion of the General Assembly or the Administrative Council would further the cause of medical, clinical or biological engineering. It promotes the formation of regional, national, international or specialized societies, groups or boards, the coordination of bibliographic or informational services and the improvement of standards in terminology, equipment, methods and safety practices, and the delivery of health care.

The Federation works to promote improved communication and understanding in the world community of engineering, medicine and biology.

Activities

Publications of IFMBE include: the journal *Medical and Biological Engineering and Computing*, the electronic magazine *IFMBE News*, and the Book Series on Biomedical Engineering. In cooperation with its international and regional conferences, IFMBE also publishes the IFMBE Proceedings Series. All publications of the IFMBE are published by Springer Verlag. The Federation has two divisions: Clinical Engineering and Health Care Technology Assessment.

Every three years the IFMBE holds a World Congress on Medical Physics and Biomedical Engineering, organized in cooperation with the IOMP and the IUPESM. In addition, annual, milestone and regional conferences are organized in different regions of the world, such as Asia Pacific, Europe, the Nordic-Baltic and Mediterranean regions, Africa and Latin America.

The administrative council of the IFMBE meets once a year and is the steering body for the IFMBE: The council is subject to the rulings of the General Assembly, which meets every three years.

Information on the activities of the IFMBE can be found on the web site at: http://www.ifmbe.org.

Foreword

It is our great pleasure to welcome you at the 14th Nordic-Baltic Conference on Biomedical Engineering and Medical Physics – NBC-2008. The Conference is held every third year in one of the Nordic-Baltic countries under the auspices of the International Federation for Medical and Biological Engineering and traditionally brings together scientists not only from the Nordic-Baltic region, but from the entire world.

Modern Biomedical engineering is dynamic, boosting field of science, benefiting from its intrinsic interdisciplinary nature. That is why the Conference brings together scientists from medicine, chemistry, physics, engineers and computer scientists as well as people from education and business to enjoy the meeting under the motto ***"Cooperation for health"***.

Gratitude should be expressed to the members of the International Scientific Committee of the Conference. With the invaluable help from the International Advisory Committee they composed the Program of the Conference, ensuring its scientific quality and relevance to the up-to-date needs. Special thanks to the Local Organizing Committee and to our sponsors, that made Conference happen.

For the first time NBC comes to Riga – the capital city of Latvia, the city of crossroads, rich in its scientific and cultural traditions. During all its 800 year history, Riga connected people from North and South, East and West. By hosting NBC-2008, Riga made one further step on this way. In June, you will enjoy green parks and alleys of the city and feel charming spirit of close Baltic Midsummer.

We are sure you will enjoy NBC-2008 both scientifically and socially, and we do our best to make NBC-2008 an outstanding event.

We are looking forward to meeting you in Riga.

Associated Professor Alexei Katashev
President of the Latvian Medical Engineering and Physics Society,
Co-Chairman

Professor Yuri Dekhtyar
Riga Technical University

Co-Chairman

Professor Janis Spigulis
University of Latvia

Co-Chairman

Conference details

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Medical Imaging, Telemedicine and E-Health

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Building and Implementing an eHealth Strategy: is there a Good Recipe for Baltic Countries?

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Abstract — **eHealth is concerned as a sum of technological means for registration, storage, processing and management of health related information. Since Baltic countries are looking for an optimal directions for eHealth development, presentation is discussing harmonization with eHealth developments in the world and EU - main directives: WHO strategy "eHealth for health care delivery" and an action plan for e European eHealth area (2004), standardization efforts, countries – leaders, success stories, lessons learnt and possible examples to follow. Also problems of Baltic countries - commonalities (similar political, social and health care legacy, diversified local health IT systems, demands caused by ageing, social and economic transitions, free market of health services) and specifics. (Legislative and management principles and environment, intensity, targets and priorities of national pilot eHealth projects) are analysed. Facing eHealth development challenges the choice of appropriate strategy and implementation management becomes crucial. It was analyzed Baltic eHealth activities, including Lithuanian experience – recently accepted eHealth strategy and implementation plan (2007-2015). Alternatives of implementation concepts and standard based integration seeking to create a standard-based and citizen-centred architecture are discussed, action priorities by importance and by time sequence are analysed. Analysis leads to conclusion, that the effective Baltic way towards European eHealth area requires avoiding parallelism, sharing experience, providing of pilot cross-boarder trials between Baltic and Nordic countries, defining the role and contribution of biomedical engineering and medical physics.**

Keywords — **eHealth, Baltic countries, strategic planning, interoperability, collaboration**

I. Introduction

Importance of eHealth as a sum of technological means for registration, storage, processing and management of health related information is rapidly increasing. "eHealth" becomes an inclusive term integrating medical informatics, telemedicine and biomedical engineering, i.e. all methodical and instrumental tools for health information acquisition, management and applications in clinical practice, research and administration. Important feature of eHealth is it's scale reaching far beyond hospital environment or communication doctor-to-patient or doctor-to-doctor (such point to point communication is usually called telemedicine). EHealth is a new paradigm creating an integral environment for health services for all users. Clients here are connected to eHealth system, which is at least of region or national (in future – international) scale. Taking into account the complex character of healthcare (high costs, and the need for quality, patient safety, adequate organization and delivery, cross-border care, reimbursement, and liability), eHealth provides one of the most important solutions to address the cost and quality of healthcare. Therefore recently (from the year 2000) a pace of eHealth developments has dramatically risen in majority of countries. World Health Organization (WHO) has approved a strategy "eHealth for health care delivery" (2004) and announced the eHealth as a main instrument of health care improvement over the world, including developing countries [1]. European Union (EU) also issued an important political document "Health—Making Healthcare Better for European Citizens: An Action Plan for a European e-Health Area" [2] which emphasis the need of common EU effort and standard based integration and interoperability [3]. An Action Plan declares that in 2009 European Commission will define standard requirements for eHealth services, legal and security environment in member countries. EHealth conference in Berlin (2007) accepted a Berlin Declaration [4] which outlines six specific actions, including collaboration, setting common roadmap, standardization, certification and accreditation of eHealth systems, involvement of research and industry.

Baltic countries are facing an eHealth development challenges which originate from the specific national needs of the health care from one side and also the need to create common eHealth area in Europe – from the other side. Since national eHealth activities and projects takes the first steps it's highly important to choose a right strategic direction and implementation concepts.

II. Challenges of Baltic States

A. Facing global eHealth problems

Global health problems – ageing of population, rising of health service and medication costs, environmental risks, rising demands and expectations of citizens, consumptional attitude towards health services [5] – become a challenge

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also for Baltic countries. Countries are trying to solve those problems inter alia by development of eHealth systems. On this way countries are facing both problems caused by global changes [6] and also by specific environment of countries still under social and economical transition [7].

One of the main problems Baltic countries are facing in eHealth development is instability of eHealth standards [8]. Urgent need to manage effectively health information forces policy makers to take immediate development decisions, neither in conditions when standards are not fully accepted and stable nor in global nor in national scales. Pragmatic decisions still are taken locally and problems with integration of not compatible solutions are significant (for example integration currently takes about 20% of hospital IT spending).

Rising demands of health service consumers and relatively easy migration of citizens (especially within EU) causes first signs of "health tourism" – when people start moving across countries looking for high quality cost-effective health services. This challenge forces national health systems to be economically competitive from one side and also professionally compatible (taking into consideration international quality and information interchange standards) form another. EHealth instruments are potentially effective to cope with both of the above challenges. Therefore progressively thinking health officials are especially eager to implement immediately eHealth solutions into clinical and managerial practice. (EU recommends member states to spend for eHealth no less than 2,5 % of total annual health expenditures, i.e. to make significant strategic investments).

The situation causes a collision of global challenges and needs of eHealth implementations from one side and limited global experience of large scale eHealth developments from another. There is a lack of internationally recognized leading experts of eHealth standards, system developers capable to lead national scale eHealth projects. Even big companies and vendors are taking first steps in this way.

B. Specifically Baltic challenges

In the context of eHealth development Baltic countries have a lot of commonalities typical for all of them: similar political, social and health care legacy, diversified and underdeveloped local health IT systems, demands caused by social and economic transition, health reforms, privatization and emerging free market of health services.

Although Baltic countries are rapidly reaching the development level of EU average, some social and economic processes are still in transition. Rapid economic growth and democratization is accompanied by rather unequal social services, especially in rural areas, significant differences remain in quality and accessibility of health services across country. Health systems and especially IT solutions are underfinanced to compare with western countries. Allocations for eHealth are less than 1% of all health service expenditures (to be compared with EU recommendation – 2, 5%). Since eHealth is a quite new paradigm – not only a new technologies but a new way of thinking and working, there is a lack of deep understanding of the essence and possibilities of eHealth among political decision makers and in some extent among health specialists and managers. Health systems are experiencing the rising costs of services, medicine, equipment, also lack of specialists due to emigration of doctors, therefore attention of decision makers are directed towards this kind problems. This bias sometimes hampers investment, development of necessary legislative environment, and consequently – implementation of eHealth systems – important tools for all health care problems.

Starting position of Baltic states on the way of eHealth developments is rather favorite: penetration of internet and wireless communications is sufficient and rapidly increasing; broadband telecommunication networks - well developed; number and qualification of general profile IT specialists is high; health reforms in particular countries create a good motivation for eHealth implementations. In contrast with developed Western countries – Baltic countries have no heavy heritage of well functioning local old information systems. This creates a chance to start with modern concepts and advanced solutions without painful destroying of existing systems.

EHealth developments in Estonia [8, 9] Latvia [10, 11 Lithuania [12, 13] – in fact at the moment have no principal differences. However differences could arise due to different development strategies and implementation management. This could cause future problems of integration eHealth systems into common area, according to EU initiatives.

III. Leaders to follow and role of the strategy

A. eHealth lessons worldwide

The landscape of eHealth developments around the world is presented in [6], by permanently working Global observatory for eHealth [14]. In Europe respectively eHealth monitoring is provided by EHTEL organization [15] and EK portal [16]. Activity analysis shows that in fact there is no completed and implemented interoperable national scale eHealth system anywhere. However there are lot of projects

and organizations supported by big investments and having ambitious long term plans. Among leaders could be mentioned Canada with well established planning and implementation management [17], UK with heavy investments and governmental control [18], Australia with effective administration [19], and USA with pragmatic approach and realistic Enterprise Architecture planning [20].

In Europe Nordic countries are leaders - Denmark with heterogeneous and "bottom-up" built eHealth system; Sweden and Norway with effective telemedicine pilots and practical implementations, Finland with advanced technologies. Big European countries like Germany, France and Spain have difficulties with national scale eHealth system development because of highly diversified systems and complicated legislation. For example Germany as a federal state implements a patient health cards (mainly for insurance purposes) first and Electronic Health Record (EHR) is planned for quite far future.

Although countries are using different eHealth development concepts, implementation methods as well as different level of financial support of activities some common lessons could be extracted: 1) success is highly dependent on management and legislative environment created; 2) proper strategic planning and implementation roadmap is essential; 3) in the beginning physician acceptance is limited and additional time is needed to manage electronic records; 4) investments to eHealth give the high revenue in terms of economy, social and health factors; 5) lack of unanimously accepted standards and problems with information security hamper development.

B. Role of the strategy

In order to define the own way of eHealth development in the context of the great variety of concepts and approaches countries necessarily are developing particular eHealth strategies. 85 % of countries over the world plan to have eHealth strategies or other similar documents by 2008 [1, 6]. eHealth strategies differ by the level of abstraction and detalization, relation with implementation and by other features: from global WHO and EU strategies [1, 2] to particular strategies of countries and regions, dependent on strategic planning traditions, legislation, awareness and competences. But the importance of strategies in all cases lies in harmonization of efforts, setting goals and terms to achieve them and pointing to the benefits to all users from citizens to ministry level management.

Here possibly valuable Lithuanian experience could be mentioned – recently country approved national eHealth strategy (2007-2015) and implementation plan [12, 13].

C. Problems of implementation

Implementation planning is inseparable part of the strategy. Strategic plan of implementation should be not a list of actions to be taken, but rather set of goals to be reached, together with concrete measurable implementation indicators, benchmarks and terms. The way how strategic goals could be reached could be partly an object of initiatives coming "bottom up" from local socialists, researchers, vendors and users.

The main development problems arise at the phase of implementation. There is a lack of highly experienced local companies and vendors to run a big national scale projects in Baltic States. eHealth paradigm is quite new and financial support of the development was till now very limited. Big companies like HP, Siemens are using their existing products and offer purchases rather then support a creation of an advanced "bottom up" grown products which are expected.

Management and organizational difficulties also are evident: eHealth projects are typically national – the key is integration in the scale of country. There is a lack of adequate competences and managerial resources to plan lead and supervise such complicated projects. Difficulties are increased by the great variety of partners, their motivations, needs, qualifications.

Although problem of standards could be concerned as global (there are no ultimate world wide accepted standards) locally this makes long term implementation planning problematic. Legislative environment also is not suitable yet and its development lags behind other actions.

IV. Choice of the best way towards eHealth area

On the way from the strategy to implementation and evaluation of results lot of important decisions should be taken. Every decision is stipulated by the country specifics but in every stage a choice of best solution is a challenge.

In rapidly changing landscape of eHealth developments and standards two main trends are noticeable: systematic and pragmatic.

Systematic concept is provided by expert driven standard development organizations such as CEN TC251, OpenEHR initiative. It is based on thorough definitions of goals and aims, with emphasis to semantics, are patient – centered, oriented to continuity of care of individuals.

From the other side – *pragmatic* concept is driven mainly by vendors and users – (.g. IHE, HL7, EA) and is oriented to communication, exchange of documents provided by isolated health profiles (users), takes the diverse situation in health information as a starting point for simple communication with gradual extension of transactions towards

service oriented architectures, business process management and finally towards semantic interoperability.

In fact two above concepts have positive and negative sides and countries are deciding their best way, usually being a combination of both concepts. Countries usually are profiling existing pre-standards instead of inventing new standards. Industry and vendors are driving pragmatic standard developments process (IHE, HL7), since consultant's-driven standard development originations (CORBA, CEN) are rather not so effective (because of long term fundamental research, negotiations and limited responsivity to the current and rather urgent needs of market) [21].

Since health system needs for information management are quite urgent, a pragmatic way proposed for example by IHE [22] has been widely taken (70 vendors successfully passed the XDS validation testing at the recent Europe connectathon)

Good recipe in setting of strategic priorities and implementation planning (if there is a good recipe at all) could be probably oriented towards:

1) Integrated national wide and standard based system;
2) Patient centered and EHR based architecture of the system;
3) System ensuring health service continuity across institutions and in time (life-long), oriented towards early prediction and prophylactics;
4) Proper combination of systematic and pragmatic concepts;
5) Proper combination of top-down (standards, strategy) and bottom-up (implementation alternatives, local initiatives and motivation) concepts;
6) Special attention towards security and legislation;
7) From the very beginning care about integration and interoperability in semantic, information and technological levels;
8) Involvement of all users and actors, agile mode of software engineering.

V. Conclusion

The Baltic way towards European eHealth area requires coordination of strategies, merging efforts of countries with similar situations, avoiding parallelism, sharing experiences. Pilot cross-boarder integration and collaboration trials between Baltic and Nordic countries are essentially important. Biomedical engineering and medical physics here must contribute here by development of new methods and technologies of sensors; computer based diagnostic, information processing and decision support tools.

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Biomedical Engineering Program on the Internet for Worldwide Use

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Abstract — **Biomedical Engineering, which is a multidisciplinary and fast developing field of science, covers a large number of sub-specialties. Therefore, for any university, especially for the smaller ones, it is difficult to produce and update high quality teaching material in all aspects of the field. Creating a curriculum on the Internet helps universities and students worldwide in obtaining educational material in this field.**

Keywords — **Biomedical engineering, Internet education, *www.evicab.eu***

I. Introduction

Internet is more and more used as a platform for educational material and student administration. The use of internet makes the geographical distances to disappear.

Biomedical Engineering is needed all around the world and globalization encourages the students to mobility between universities. It is important that education in Biomedical Engineering is harmonized to facilitate the mobility. The BIOMEDEA project facilitates this within the study programs in European universities.

All this gives strong reasons to develop an education program on the Internet.

This is the basis for the project: European Virtual Campus for Biomedical Engineering – EVICAB. It was funded by the European Commission Education and Training for 2006-2007.

EVICAB offers high-quality courses prepared by the best international teachers. The courses include lecture videos and associated lecture slides. The courses are also associated with additional teaching material like full textbooks, exercises, laboratory exercises etc.

All courses offered by EVICAB are recognized by at least one university in the European Union. Thus it is easy for any other university in the EU to include EVICAB courses to their curriculum.

Because the teaching material in EVICAB is available free of charge and because it can be used via Internet form anywhere in the world, the BME program provided by the EVICAB is available for worldwide use.

EVICAB uses the Wiki-idea but is more strongly controlled by an Administrative Board. This ensures that the teaching material provided by the experts is of high quality and cannot be changed by anyone else than the author. In addition to the primary teaching material, the courses have windows with free access. These are used for providing additional teaching material by the users of EVICAB. In addition to helping the students, this Wiki material may be utilized by the course author for improving the course.

The teaching material for EVICAB is provided by the best experts free of charge. The benefit from this for the teacher is that his/her reputation as an expert will be strengthened worldwide and this will support his/her career as pedagogue and scientist.

Associated to the EVICAB education there is also developed a method for Internet examinations. This will further strengthen the worldwide use of EVICAB because the geographical location of the students and the teachers does not play any role anymore.

www.evicab.eu

II. Evicab project

The objective of the project is to develop, build up and evaluate sustainable, dynamical solutions for virtual mobility and e-learning that, according to the Bologna process,

(i) Mutually support the harmonization of the European higher education programs,

(ii) Improve the quality of and comparability between the programs, and

(iii) Advance the post-graduate studies, qualification and certification. These practices will be developed, piloted and evaluated in the field of biomedical engineering and medical physics.

Important goal is that these approaches and mechanisms for virtual e-learning can be extended and transferred from this project also to other disciplines to promote virtual student and teacher mobility and credit transfer between European universities.

III. Evicab consortium

EVICAB is coordinated by the Ragnar Granit Institute of Tampere University of Technology. Professor Jaakko Malmivuo serves as Director of the project and Assistant Professor Juha Nousiainen as coordinator. The other partners are:

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- Mediamaisteri Group Ltd, Tampere, Finland
- Department of Biomedical Engineering, Linköping University, Linköping, Sweden
- Biomedical Engineering Center, Tallinn University of Technology, Tallinn, Estonia
- Institute of Biomedical Engineering, Kaunas University of Technology, Kaunas, Lithuania.
- Department of Biomedical Engineering, Brno University of Technology, Brno, Czech Republic.

EVICAB welcomes interested institutes to join as associate partners. We hope that the associate partners active participate in producing teaching material to EVICAB.

IV. Idea of EVICAB

The fundamental idea of the EVICAB is that it offers an open platform for Biomedical Engineering curriculum on the Internet. The openness means the open access to and free right to use the resources of the EVICAB, and an open possibility for all experts in the field to contribute to the development of the content of the virtual curriculum.

Teachers, who are experienced and recognized experts in their field, are encouraged to submit full e-courses, course modules and other teaching material to EVICAB. The material may include many different formats like video lectures, PowerPoint slides, pdf-files, Word files etc.

EVICAB is not a university. The course and student administrations continue in the universities as usual: The teacher, responsible of the course/study program, may select from the EVICAB courses for the BME curriculum of the university. The students study the course either as ordinary lecturing course with the EVICAB material supporting the lectures or the course may be partially or solely studied from EVICAB. The students, or anyone even outside the university, may study EVICAB courses to add their competence in Biomedical Engineering. Thus EVICAB is important also for the persons in the working life to improving their professional competence.

The EVICAB has an Administrative Board which administers the EVICAB curriculum. The board accepts courses of sufficient scientific, pedagogical and technical quality. The board may also invite experts to provide course material to the EVICAB. Courses which apparently are of low quality, either out of date, lower quality than competing courses and not appreciated by the users of the EVICAB will be deleted. Active feedback from the users of EVICAB, both teachers and students, is essential. All this will be realized by utilizing a dynamical quality assurance system.

V. Impact of EVICAB on e-learning

In its completed form, EVICAB will have strong impact on all main levels of the education process:

For students it will provide virtual mobility as a complementary, preparatory, or even substitutive option for physical mobility. The increased number on e-courses for distance learning will give higher variety of qualified studies and degrees.

Teachers will substantially benefit from the open resources, teaching materials and e-courses available through the EVICAB. The support provided for design and development, as well as the good practices and high-quality e-courses will motivate and spur the teachers in the e-course development.

EVICAB will contribute to the harmonization process of BME curricula in Europe in co-operation with BIOMEDEA and will improve the quality of the curricula. Finally, the solutions and models developed for building the virtual BME curriculum can be applied to other disciplines.

VI. Internet examination

Another successful innovation and application in our e-learning activities has been the Internet examination.

In the Internet examination the students make the exam in a computer class. This may be performed simultaneously in several universities. Therefore the students do not need to travel to the location there the course was given.

The students open the Moodle program at the time of the examination and find the examination questions from there. We usually allow the students to use all the material available on the Internet. This requires that instead of asking “What is ...” the examination questions shall be formulated so that they indicate that the student has understood the topic and is able to apply this information. The only thing which is not allowed is communication with another person via e-mail etc. during the examination.

VII. Mobile course material

One of the key issues in the EVICAB is to reach the students anywhere and anytime. The learning process should not be dependent on the location of the student. Internet based material supports this idea and hence all the educational resources are provided in the EVICAB platform in the Internet. Not only is the Internet used for media for

learning process but also portable devices such as iPod and mobile phones can be used. In EVICAB project different media are supported. Students may choose the best media for his or her current lifestyle; busy student may, for instance, watch the lecture videos in a bus on the way to or from university.

VIII. Why to provide courses to EVICAB?

EVICAB is an important teaching and learning method only if it is available free of charge and worldwide. As a consequence, the learning material should be provided free of charge.

Why experienced and competent teachers should provide such material without charge and without receiving royalties? Acceptance of a course by EVICAB will be a certificate for quality. Worldwide distribution to all university students will give exceptional publicity for the author and his/her university. All this will facilitate the sales of traditional teaching material produced by the course author. This will also attract international students from other countries all over the world to apply to the home university of the material author. We already have experience which has proven these issues to be realistic.

The Internet has dramatically changed the distribution of information. Distribution is worldwide, real time and free of delivery costs. The technology also supports wide variety of attractive presentation modalities. All this ensures wide audience and publicity for the material on the Internet. For instance, the Wikipedia dictionary serves as a successful example of this new era of information delivery. On the basis of this publicity it is possible to create markets also for traditional printed educational material. In addition the EVICAB will provide the platform for all courses free of charge. Pedagogical evaluation and technical support for course design are also provided in request. This will ensure the high quality and up to date virtual learning environment.

IX. Conclusion

In future, the teaching and learning will mainly be based on Internet. The ideas and the technology of EVICAB are not limited only for application on Biomedical Engineering but it may be applied to all fields and levels of education. EVICAB will be the forerunner and show the way to more efficient and high quality education

Acknowledgment

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The Modification of Titanium Dioxide MOCVD Coating in TiAlNb after Immersion in Artificial Saliva

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Abstract — **The paper aim is to observed the modification of passive coating obtained on TiAlNb with a Metal-Organic Chemical Vapor Deposition (MOCVD) [1, 2] procedure after immersion in artificial saliva (Fusayama) with calcium content. Two temperatures [T] (400°C and 500°C), two pressures [p] (1 and 20 torr) and variable molecular fracetion [χ] from 76 to 5000 were used in MOCVD coating procedures. The X-ray spectrum confirms the dense and uniform deposition of TiO_2 film on TiAlNb alloy surface. The results of analyses used in the present paper contribute of the extended research in the biomaterial domain.**

Keywords — **TiAlNb alloy, MOCVD, artificial saliva, Scanning Electronic Microscopy, contact angle, infrared technique.**

I. Introduction

Implants are one of the great success stories of modern medicine. It is important to characterize the implant surface and to consider the interfacial phenomenon that occur between surface, biological molecules and cells since implant surfaces with different properties result in different responses at the cellular and consequently at the tissue level around the implant [3-6]. After was demonstrated that the titanium and titanium alloys are excellent implant biomaterial, now the research try to improve the performance of this biomaterials working to the process for the modification of the surface topography and biochemistry for a very good adhesion of the human cell and a better biocompatibility with the body. The use of titanium and his alloys for biomedical applications has increased dramatically in this century, being extensively [7-10] the choice in dentistry dental implants, dental crowns and partial denture frameworks. As titanium, TiAlNb alloy readeily passivates to form a protective oxide layer, which accounts for its high corrosion resistance. This protection capacity of the oxide depends on the obtaining procedure and environment [11], taking into account that in bioliquids various processes as adsorption and ions release are taken place.

II. Materials and methods

A. Materials

The biomaterial used in this research is a cylindrical form of TiAlNb alloy made from Bucharest Romania IMNR Institute with the following composition (Table 1):

Table 1 Composition of the implant biomaterial [%]

Al	Nb	Fe	C	O	N	H	Ti
5.88	6.65	0.03	0.10	0.20	0.07	0.02	87.05

This cylindrical form was divided in many pastille samples with 2 mm thickness and 1 cm^2 diameter and that represent the expose work sample.

The biometallic sample surface preparation involves: abrasion, chemically polished in 20% HNO_3 + 3% HF from 10 minutes, degreased in boiling benzene from 5 minutes and thoroughly rinsed with tap and distilled water.

The simulated bioliquid was Fusayama artificial saliva with important calcium content [12] as following (Table 2):

Table 2 Composition of the simulated Fusayama saliva

Substance	g/L
NaCl	0.400
KCl	0.900
$CaCl_2 \cdot 2H_2O$	0.795
NaH_2PO_4	0.690
Urea	1.000

B. Methods

To improve the biocompatibility resistance of the TiAlNb alloy on the surface samples the TiO_2 was deposition using the Metal-Organic Chemical Vapor Deposition method (MOCVD) [13, 14] at the Toulouse France Institute. In this technique it is mark the precursor (the vapor of a metal-organic complex = $[Ti\{OCH(CH_3)_2\}_4]$ titanium isopropyl oxide (TTIP)) to reactor with a heated surface which represent the substrate and in this case the solid reaction deposits and forms a thin film on the substrate surface. Pressure was regulated

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with a Baratron gauge connected via a pressure controller to a butterfly valve above a vacuum pump. 99.9992% pure N_2 (Air Products) was fed through two lines equipped with MKS mass flow rate controllers, one to sweep away the precursor, the other to dilute it. The deposition temperature was measured with a thermocouple K plugged into the reaction zone.

The used techniques for surface characterization were Scanning Electronic Microscopy (SEM) – [LEO-435 and FEI/Phillips XL30 ESEM with EDAX module], porosimetry and roughness – [interferometer optic Metro-ProTM Zygo New View 100] measurements.

The immersion test was performed in artificial saliva with calcium content. The modification of passive layer was evaluated with Contact Angle (CA) – [DIGIDROP Contact Angle Meter (BGX Scientific Instruments)] and structural infrared (FT-IR) [Perkin Elmer, Spectrum 100] analysis.

III. Results and Discussion

The modification of titanium dioxide MOCVD coating on TiAlNb alloy after immersion in Fusayama artificial saliva was observed and analyzed in comparison with the initial cases of TiAlNb/TiO_2 alloy.

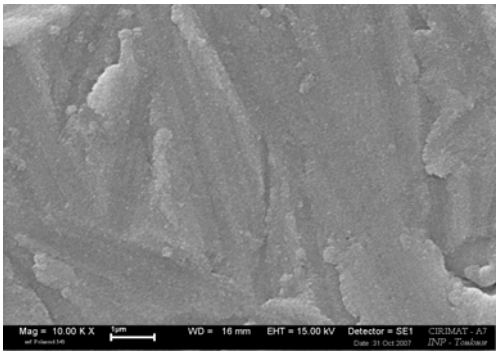


Fig. 1 ESEM image of TiAlNb/TiO_2 – T 500/p 20/χ76

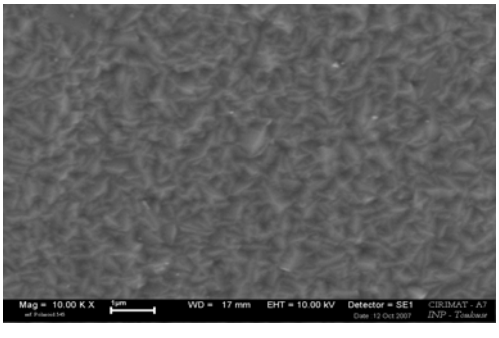


Fig. 2 ESEM image of TiAlNb/TiO_2 – T 400/p 1/χ5000

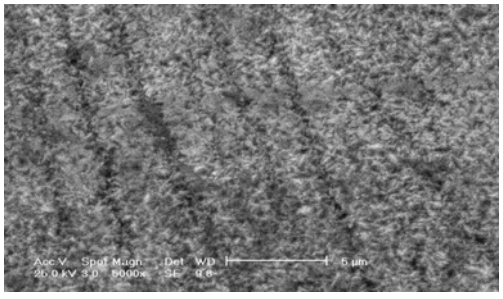


Fig. 3 ESEM image of TiAlNb/TiO_2 – T 400/p 1/χ5000after immersion one month in artificial saliva

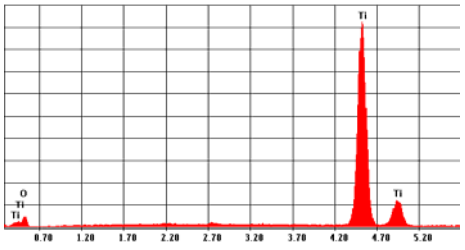


Fig. 4 Spectrum for emission in X-ray from TiAlNb/TiO_2 – T 400/p 1/χ5000

The passive titanium layer is a mixture of oxides with composition and morphology depending on the experimental MOCVD deposition conditions.

One of the biometallic alloy surface characterization was the ESEM method which present the modification on the surface. Figures 1 ÷ 3 present a dens and uniform coating of film TiO_2 on the TiAlNb surface before and after immersion for one month in artificial medium (Fusayama).

The ESEM image is completed by X-ray spectrum which confirms the good deposition of thin films TiO_2 using MOCVD technique (Figure 4).

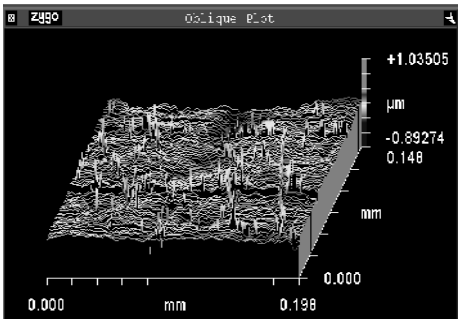
The surface porosity and roughness values for the TiAlNb/TiO_2 alloy are presented in Table 3 and Figure 5.

Depending on deposition condition, the roughness varies from micro to nano scale as can be seen in the following table. Regarding porosity, this parameter is not a function of deposition condition in this case.

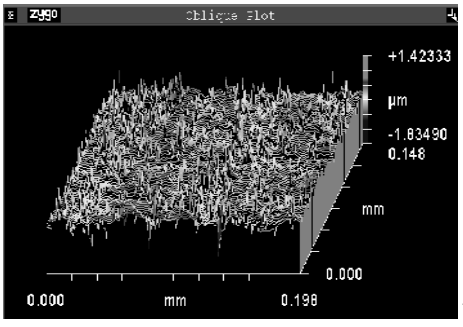
The good wettability of the treated biomaterial surfaces is an interesting aspect in order to obtain chemical interaction with the physiological fluids surfaces and also to avoid cell growth and protein adsorption. It was demonstrate that for a

Table 3 Characterization of surface porosity and roughness

Titanium alloy	Porosity [%]	R_a [μm]
TiAlNb/TiO_2 – T 400/p 1/χ5000	90	0.066
TiAlNb/TiO_2 – T 500/p 20/χ76	90	0.160



a)



b)

Fig. 5 Roughness 3D images of samples TiAlNb/TiO_2 a) T_d=400ºC (χ = 5000 ppm), b) T_d=500ºC (χ =76 ppm)

successful osteointegration is better to have a lower contact angle value [15, 16].

The quality of titanium dioxide deposition on TiAlNb alloy showed the influence on the wettability of the surfaces. Distilled water put on coated samples with TiO_2 formed a regular drop, with a hydrophilic character (Table 4). After immersion of the same samples for one month in artificial medium (Fusayama), the TiAlNb samples covered / uncovered with TiO_2 are a little bit easily wetted.

FT-IR analysis, in the absorbance mode, shows the presence of phosphate and hydroxyl groups formed after immersion of the sample in Fusayama saliva.

After immersion of TiAlNb/TiO_2 alloy – T 400/p 1/χ 5000 sample in artificial saliva, the phosphate bonded appears at 1083 cm^{-1} in the IR spectrum, probably due to the presence of $(H_2PO_4)^-$ on Fusayama composition. The νOH band obtained

Table 4 The contact angle values for studied sample

Titanium alloy	Contact angle [º]
TiAlNb	78
TiAlNb/TiO_2 – T 400/p 1/χ 5000	70
TiAlNb/TiO_2 – T 500/p 20/χ 76	68
TiAlNb – Fusayama	78
TiAlNb/TiO_2 – T 400/p 1/χ 5000 – Fusayama	72
TiAlNb/TiO_2 – T 500/p 20/χ 76 – Fusayama	69

is supposed to be involved in the formation of the species like $Ti(OH)_2$ or hydroxo-complexes such as $TiO(OH)_2$.

The $H_2PO_4^-$ ion existent in the composition of Fusayama solution is adsorbed on the titanium surface oxide (1):

$$TiO(OH)_2 + H_2PO_4^- \rightarrow TiO(H_2PO_4)_2 + 2OH^- \quad (1)$$

It is known from literature [17] that phosphate ions are preferentially taken up in the surface film during repassivation and calcium ions are adsorbed on the surface, according to the reaction (2):

$$TiO(H_2PO_4)_2 + Ca^{2+} + 2OH \rightarrow CaTiO(H_2PO_4)_2(OH)_2 \quad (2)$$

The titanium alloy implant biocompatibility increases if the calcium phosphate will form, and that is a very important biointerface process, which helps osteointegration.

IV. Conclusions

The microscopy images present a dens and uniform MOCVD coating TiO_2 film on the TiAlNb surface before and after immersion for one month in artificial saliva (Fusayama). The MOCVD deposition condition determinate a change of the roughness values (from micro to nano), but not also in this case for the porosity value.

For all studied samples before and after immersion in artificial saliva the contact angle determination indicated a hydrophilic character. A decrease in contact angle value is associated with MOCVD deposition condition. Immersion in Fusayama does not change significantly the balance hydrophilic-hydrophobic.

FT-IR analysis, in the absorbance mode, shows the presence of phosphate and hydroxyl groups formed after immersion of the TiAlNb/TiO_2 alloy in Fusayama saliva.

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Osteogenesis on Surface Selective Laser Sintered Bioresorbable Scaffolds

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Abstract — **In this study we have used a novel surface selective laser sintering (SSLS) technique to develop CAD/CAM designed scaffolds for bone tissue engineering. SSLS polylactic acid scaffolds were evaluated *in vitro* and *in vivo* as templates for human fetal femur-derived cell and adult human bone marrow stromal cell osteogenesis. Both cell types were cultured successfully on SSLS scaffolds with an increase in expression of alkaline phosphatase activity. Cell in-growth and Alcian blue/Sirius red positive staining of matrix deposition were observed on SSLS scaffolds in vitro in basal medium and osteogenic culture conditions. Similar results were observed in vivo with type I collagen expressed by cells on the scaffolds. In the critical sized femur segmental defect, SSLS scaffolds seeded with the cells enhanced significantly bone tissue regeneration.**

Keywords — **Tissue engineering, laser sintering, scaffolds.**

I. Introduction

Recent tissue engineering advances based upon porous polymer scaffolds, which act as a delivery vehicle for cells, have led to the possibility of successful repair and restoration of function in damaged or diseased tissues [1]. This involves seeding highly porous biodegradable scaffolds with donor cells and/or growth factors, culturing and then implanting the scaffolds to induce direct growth of a new tissue. The manufacturing of such scaffolds still presents both materials and technical problems. These scaffolds must be biocompatible to minimise adverse inflammatory reactions, augment cellular in-growth and fit anatomically within the bone defect. The imperfection of current techniques (e.g. mold casting, injection molding, foaming, particulate leaching, etc.) has encouraged the development and use of a Rapid Prototyping (RP) approach for reliable fabrication of scaffolds with controlled architecture satisfying a range of requirements related to their strength and toughness, osteoinductivity and osteoconductivity, controlled rate of biodegradation and inflammatory response [2].

We previously reported the development of a new RP method - Surface Selective Laser Sintering (SSLS) [3] enabling precise fabrication of scaffolds even from thermosensitive biodegradable polymers such as polylactic acid (PLA). In SSLS we can fuse the polymer particles, which do not absorb near infrared (λ ~1.0μm) laser radiation, by controlled melting of the particle surface only (Fig.1). This is achieved by homogeneously distributing a small amount (≤ 0.1 wt.%) of carbon black (CB) nanoparticles over the PLA surface. Carbon absorbs laser energy allowing localized melting and fusion of the PLA particle surface. This controlled melting prevents significant overheating of their internal domains [4]. We have demonstrated that this sintering process does not damage the polymer chemical structure. Moreover, the most of the activity of the enzymes incorporated into individual PLA particles can be retained following SSLS processing [3].

In this study we have used our SSLS poly-(D,L)-lactic acid scaffolds for their *in vitro* and *in vivo* evaluation as templates for human fetal femur-derived cell (HFFDC) and adult human bone marrow stromal cell (HBMSC) osteogenesis.

II. Materials and methods

Poly (D,L)-lactic acid (M_w=108kDa, polydispersity =1.4) was purchased from Alkermes (Boston, MA, USA) and was ground to a fine powder (mean particle diameter of around 100μm) using a pestle and mortar. A small amount (ca. 0.1wt.%) of furnace carbon black (CB) with surface area ≈ 100m^2/g was added to this powder by thorough mixing covering all of the PLA particles.

PLA scaffolds with desired architecture (Fig.1) were fabricated using an experimental prototype of SSLS machine designed and produced by ILIT RAS. It based on continuous wave fibre laser "LS-1.06" (IRE-Polus Ltd, Moscow, Russia) emitting at λ=1.06 μm with a maximum power of 10W.

Laser beam was delivered to the powder bed using a silica fiber, magnifying objective, focusing lens and X-Y computer controlled scanner resulting in ca. 125μm diameter laser spot onto the polymer particles. Only CB particles absorb radiation at this wavelength allowing specific surface melting and powder fusion. Laser power

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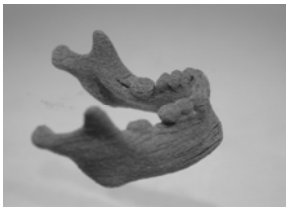

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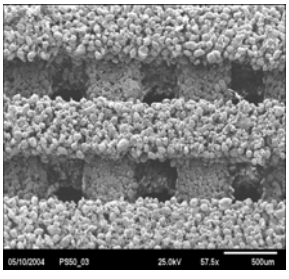


c

Figure 1. SSLS scull and mandibular biomodels based on NMR data (a, b) and PLA scaffold (c).

density on the focal plane used for reliable sintering of PLA/CB particles at the scan velocity 6 mm/s was $\mathbf{I_t} \approx 1.2\pm0.2x10^4$ W/cm^2.

Fetal Calf Serum (FCS) was purchased from Invitrogen, Scotland. α-MEM, dexamethasaone and alkaline phosphatase kits and all other tissue culture reagents were purchased from Sigma-Aldrich, (UK) unless stated. Adult human bone marrow samples were obtained from hematological normal patients undergoing routine elective hip replacement surgery. Cultures were maintained in basal medium *(α-MEM* containing10%FCS) at 37°C in humidified air with 5% CO_2. Human fetal femurs were obtained following termination of pregnancy according to guidelines issued by the Polkinghome Report. Femurs were dissected and plated into T25 flasks in 2ml basal medium. Cells were cultured for 7 days from explants before passage and scaffolds seeding.

SSLS scaffolds were individually seeded with HFFDC and adult HBMSC, and cultured for 7 and 28 days. 10μg/ml Cell Tracker Green™ CMFDA and 5μg/ml Ethidium Homodimer-1 (CTG/EH-1) (Molecular Probes, Leiden, NL) have been used to label viable and necrotic cells respectively. Prior to fixation, cells were bathed in α-MEM containing CTG/EH-1 at 37°C for 1 hour. Samples were washed with α-MEM, and then rinsed in PBS before fixing in 70% ethanol. Samples were visualised on Carl Zeiss Axiovert 200 microscope with software package to capture fluorescently labeled cells. Following culture of cells on SSLS samples, scaffolds were washed in PBS before 1 hour fixation in 3% gluteraldehyde/4% paraformaldehyde in PBS (pH=7.4). After rinses in PBS, scaffolds were dehydrated though 10 min washes in ethanol and transferred to hexamethyldisilizane (Agar Scientific Ltd, UK) for two 10 min washes then excess was allowed to evaporate. Scaffolds were then analysed at FEI Quanta 200 scanning electron microscope with FEI imaging software.

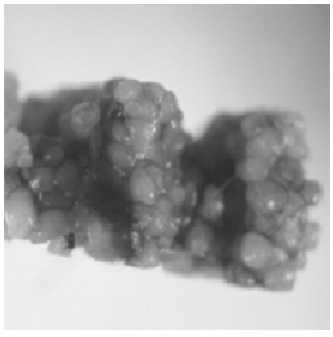
For *in vivo* studies female MF-1 nu/nu immunodeficient mice were purchased from Harlan (Loughborough, UK). The animals were anaesthetised with fentanyl-fluanisone (Hypnorm) (Janssen-Cilag Ltd) and midazolam (Hypnovel) (Roche Ltd) in sterile water at a ratio of 1:1 and a dose of 10ml/kg intraperitoneally. HFFDC seeded and unseeded SSLS scaffolds were cultured in osteogenic medium (α-MEM/10% FCS with 100μM ascorbate and 10nM dexamethasone) for 24 hours prior to subcutaneous implantation into mice. Control cultures of fetal cell-seeded SSLS scaffolds were maintained *in vitro* in basal conditions. After 28 days mice were killed and parallel cell cultures stopped. Samples were explanted for histological analysis.

III. Results and discussion

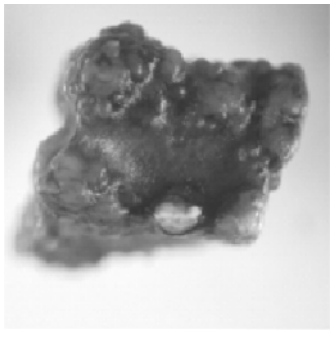
Following seeding onto the SSLS scaffolds, extensive cell adhesion was observed within 24 hours. In extended culture over a period of 7 days, adult HBMSC and HFFDC were observed adhered and viable (Fig.2) HFFDC were observed to cover the scaffold completely forming a sheet of cells in contrast to the adult HBMSC populations. Both types of cells grown on the SSLS scaffolds expressed high activity of alkaline phosphatase.

SEM analysis of HFFDC ability to differentiate in basal and osteogenic culture conditions has showed a progressive proliferation of cells over the scaffolds with complete coverage occurring after 7 days in culture. No significant differences were observed between cells grown in basal and osteogenic medium. Positive staining for Alcian blue and Sirius red staining indicative of proteoglycans and fibrous collagens respectively of HFFDC grown on SSLS scaffolds

a



b



c

Figure 2. *In vitro* cell growth on SSLS scaffolds**.** (**a**) Bare SSLS-PLA scaffold, (**b**) HBMSC seeded and (**c**) HFFDC seeded scaffolds expressed high activity of alkaline phosphatase. Magnific. 100X.

was observed after 28 days in culture. Cells grown in basal and osteogenic culture medium showed good growth and penetration within the SSLS scaffold assessed by histological examination

To evaluate the ability of these scaffolds to provide a platform for differentiation and mineralisation *in vivo,* basal and osteogenic stimulated HFFDC were seeded onto SSLS scaffolds and subcutaneously implanted into nude mice for 4 weeks. PLA alone was served as negative control. Angiogenesis evidenced by blood vessel growth developed in and around SSLS scaffold (Fig.3).

SSLS scaffolds promoted cell adhesion, proliferation and differentiation with extensive evidence of new bone matrix

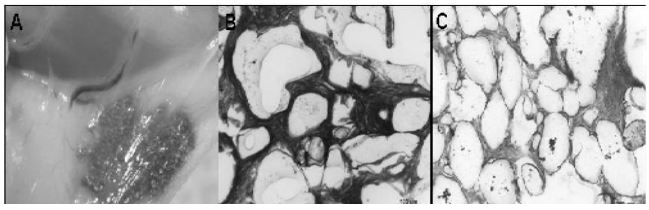


Figure 3. A - Blood vessel growth developed in and around the SSLS scaffold. B - Alcian Blue/Sirius red staining of matrix deposition by HFFDC after 28 days. C - Immunocytochemistry of HFFDC growth on SSLS scaffolds at day 28 *in vivo*, demonstrating type I collagen. Bars = 100 μm.

deposition as detected by Alcian blue/Sirius red staining for cartilage and bone. Furthermore, evidence of type I collagen staining was also observed with enhanced expression occurring in osteogenic induced HFFDC seeded SSLS scaffolds.

New bone formation was also examined in a clinically relevant mouse segmental femur defect. Radiological and histological analyses were conducted at 4 weeks post surgery to compare the healing of the implanted SSLS scaffold with and without the addition of HBMSC and HFFDC. There was no detectable repair of the resected bone region over the 4 weeks period in the control group in the absence of a SSLS scaffold. Substantial bone formation and bridging of the defect gap occurred in the groups that contained SSLS scaffolds with enhanced mineralization present in the SSLS scaffold seeded with adult HBMSC group.

IV. Conclusion

Our studies demonstrate that HBMSC and particularly HFFDC, can grow and survive on SSLS PLA scaffolds and provide a template for osteogenic differentiation *in vivo*. These scaffold implants containing bone marrow derived cells seeded onto them, proved successful in the reparation of a critical sized bone defect. Modifications in the structure of these scaffolds may improve the strength of these scaffolds to match up or surpass the gold standard of bone allograft. Addition of small concentrations of factors such as hydroxyapatite to the PLA/CB mixture would provide the strength to the defect area to allow not only bone growth and repair, but critically, bone remodeling. In fabricating SSLS-PLA scaffolds we have the ability to create structures that can fit anatomically into a bone defect providing the right size, strength and porosity for osteogenesis and the development of a vascular supply for the important nutrient and gaseous exchange needed for tissue regeneration. Moreover, this mild processing route opens up the possibility of incorporating bioactive species such as growth