

Fabrication and Functionalization of BioMedical Microdevices

FaBiMed

Grant Agreement n° 608901 – FoF.NMP.2013-11



FINAL REPORT

Publishable Summary

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement No 608901



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0) EXECUTIVE SUMMARY:

The medical device sector is a dynamic, innovation driven industrial sector with a huge growth potential, facing the change of paradigms in health care policies and uses as a constant demand for new diagnostic and therapeutic solutions. This is a huge opportunity for device makers, particularly small companies with strong knowledge base and innovation capacity, but at the same time poses a strong challenge particularly for small companies to manufacture said parts.

FaBiMed project has as main objective to provide solutions for manufacturing disposable components of novel medical devices, enhanced by micro and nanoscale geometrical features, at low cost and with short time to market and development cost compared with all current alternatives.

The philosophy applied throughout the project is to produce with low cost, high productivity methods (based on replication) to produce the parts, which include functional micro and nanostructures which are directly generated during the replication. The project developed and demonstrated several advanced toolmaking techniques which enable improved production and replication of micro and nanostructures at lower development and fabrication cost.

In particular, direct laser writing of elastomeric moulds allowed high aspect ratio microstructures to be produced in ceramics. This was used to produce ceramic drug delivery microneedles with nanoporous structure which absorbs and deliver antibiotics, and to produce enhanced miniature Ultrasound Transducers for medical image, which could not be produced by standard machining of ceramics.

Micromachining, combined with DLC coating and subsequent nanostructuring (technology patented by ADAMA) allowed to create steel inserts which can be used for replication of thousands to hundreds of thousands of polymer parts with functional nanostructures. This technology allows to shorten the development time of replication moulds with functional surfaces.

Inserts produced with this approach were used to produce surfaces with wettability control, enhanced capillarity, cell fixing and filtering abilities, all produced as passive components fully produced in a single polymer part.

As demonstrators for the technology, disposable plastic microfluidic strips were produced with unprecedented combination of cost effectiveness and integrated functions, thanks to the embedded high aspect ratio micro/nanostructures, through simple Hot Embossing on a PMMA film.

Ultrasharp (micron range tip diameter) polymer microneedle patches were also produced using the combination of cm² moulds and micromachined inserts, to produce the disposable component of a novel programmable drug delivery patch. This microneedle patch, comprising a number (9, 16, 25...) of microneedles, is produced in a single shot of injection moulding, with no need for further

welding or postprocessing, making the solution particularly efficient. The mould design allows to population groups specificities (like skin thickness and similar parameters affecting microneedle design) with substitution or rework of only part of the mould.

In this sense, the project developed methodologies for partial rework of the mould mini-inserts, without affecting the complete cavity, thus reducing the development time and cost, and making the replication process much more flexible than usual. These include hybrid additive-subtractive reconfiguration, multimaterial moulds with selective etching-redeposition, and models to assess the best solution for each case and assist in the design of the part and the moulding tools.

The project demonstrated the economical feasibility and sustainability of the proposed technology, by adapting the LCCA and ecoefficiency methodologies to the microstructuring scenarios and moulding.

The project focused on generation and fostering of exploitable results, and is strongly market oriented, and four key results were identified and analysed in terms of their market potential, leading to detailed business plan for short term (1 to 3 years) implementation of products and services, resulting in a positive leveraging effect on the investment both in the short term, and after the required internationalization and strategic partnership.

1) PROJECT CONTEXT AND OBJECTIVES:

FaBiMed (Fabrication and functionalization of biomedical microdevices) was a three years collaborative project, aimed to provide novel manufacturing paths for cost effective and flexible fabrication of disposable medical micro/nanostructured components for therapeutic and diagnostic medical devices. The main enabler for this goal is the use of novel concepts in tool making to produce nanostructured inserts for microreplication moulds.

The project develops a concurrent engineering approach, integrating innovations from three key areas: flexible and cost effective tooling fabrication, precision replication technologies and inspection techniques. This project is funded by the Seventh Framework Programme, in the Factories of the Future (FOF) theme related to the European Call for manufacturing of highly miniaturised components. The consortium is formed by 12 members from 7 different European countries, half of them being SMEs, and the others are RTD centres, one university and one public health provider. The coordinator is the Technology Centre AIMEN, from Spain.

The specific technical results that are targeted and achieved for this project are:

- Masterless microreplication manufacturing routes, for production of cost effective disposable medical microdevices, under the mass customization paradigm.
- New mould concepts on different materials, and development of effective and economic methods to realize them directly from the CAD data.
- Novel optical inspection technologies, for real time monitoring of the replication process, and for assessment of the geometrical quality of the produced part, down to the microfeatures.
- Improved microreplication processes by integrating the previous innovations.

These project outcomes have been demonstrated by developing the manufacturing route for three disposable components of already designed medical devices. The three of them, with different characteristics, share important requirements. They are innovative concepts which rely on miniaturization and micro/nano-features to improve their performance with respect to competing products. They are disposable and have strong economical constrains, and they need a new, appropriate manufacturing process to produce the required features at the maximum allowed production cost.

These three demonstrators are listed below:

- a) Microneedle array for painless transdermal drug delivery with programmable pharmacokinetics. The needles are small enough to avoid the pain sensors under the skin, and programmable because they are connected to electronically driven drug microinjectors.



Figure 1 – Prototype of microneedle drug injector, to be miniaturized during the project. (source: Crospon)

b) Compact disposable lab-on-chip microfluidic device, for a point-of-care diagnosis reader. The device uses polymer microfluidic chips with embedded micro and nanostructures for detecting complex parameters, like glycated haemoglobin, through a fast and direct blood test which could be usable for home care (readout in under 2 minutes). This kind of parameters normally take an overnight analysis in a specialized lab.

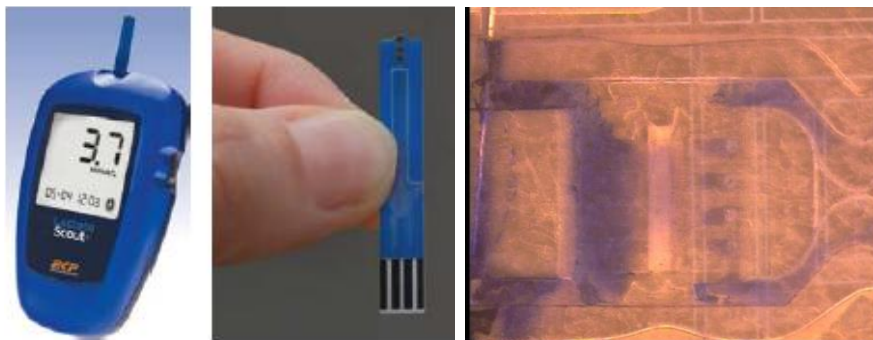


Figure 2 – Current functional device, lactate reader and microfluidic analysis plastic strip

c) Miniature high resolution ultrasound transducer microarray, which emits sound waves that are reflected by body tissues and are detected as echoes, for catheterism. The device is based on a matrix of micropillars made in a piezoelectric ceramic. The extremely small lateral dimension of the pillars allows improving the image resolution, and its small size allows its use for vascular surgery navigation (IVUS, intravenous ultrasound).

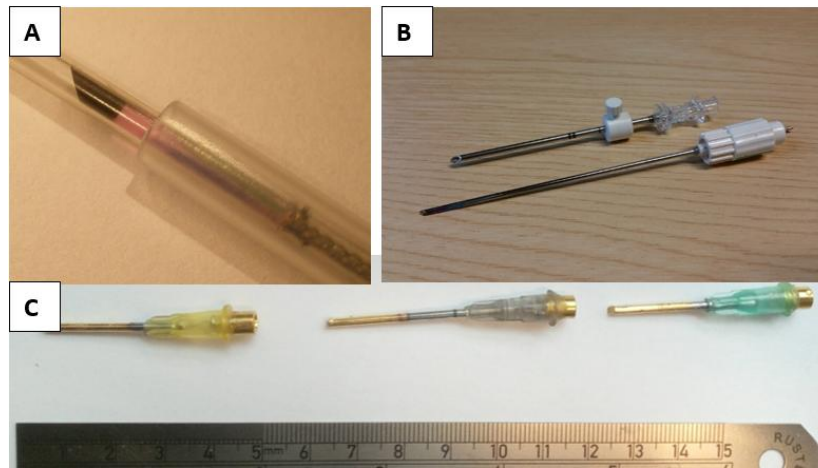


Figure 3 – A) US transducer in an intravascular catheter. B) Surgical needle demonstrator: Inserter cannula 2mm diameter (top) and transducer in a 1.8mm needle (bottom). C) Actual manufactured demonstrators in 1.8 mm stainless steel housing and with a mcx electrical connector.

These devices have demonstrated the ability of the manufacturing techniques developed by FaBiMed to simplify the process of bringing the product to the market. During the project, functional demonstrators of these products were produced and their geometrical, mechanical and functional characteristics tested, stating also the first steps for further certification after the project completion.

The manufacturing route was assessed from the technical, economical and resource efficiency point of view, using production as well as eco-design indicators.

2) MAIN S&T RESULTS/FOREGROUNDS

Since the very beginning, FABIMED has been a strongly application driven project, analysing the best options to optimize the proto-ideas about replication processes and manufacturing of functional medical devices by functionalization of the three demonstrators, together with the characterization and validation procedures for all of them.

The development of the manufacturing technologies was guided by the indications of the industrial partner on the specific needs for the design of the final devices, expected batch sizes, flexibility demands, and cost objectives.

The main goal is the development of cost effective and reconfigurable moulds for high throughput microreplication. The first approach is the improvement of existing toolmaking techniques based on metal substrates and micromachining. A combination of conventional and high accuracy machining, together with laser machining was used.

During the first part of the project, the main efforts were devoted to the development of maskless and masterless techniques for micro and nanostructuring of moulds and dies, with the objective of fabricating micro-nano-featured inserts for hot embossing, casting or injection moulding.

A method for optimization of the interaction between mechanical and laser removal methods was developed, including a vision based technique for automatic location and alignment.

An innovative method was tested to incorporate ultrafine and controlled nanofeatures on the surface of 3D micro or macroparts, by plasma assisted structuring of a DLC (Diamond Like Coating) coating applied on the metallic mould. DLC provides wear resistance and easier demoulding, and allows producing high aspect ratio (up to 1:10) structures. Besides, the DLC can be removed and recoated without affecting the rest of the mould.

This unique combination of technologies was tested and used to produce moulds with hierarchical multi-level geometries (from cm to nm sized structures), which were used for embossing and injection-moulding polymer parts. The capability to generate functional surfaces, like micro-filters or hydrophobic surfaces, has been demonstrated.

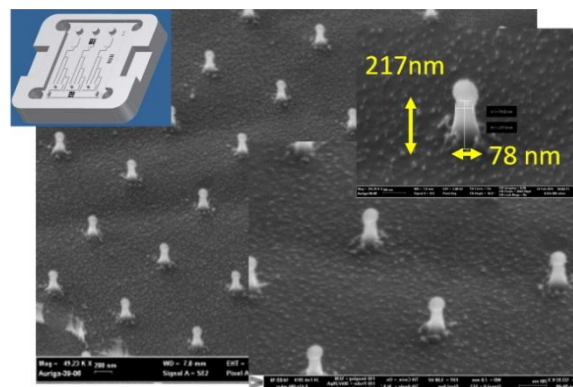


Figure 4 - Nanopillars from a specific section of the DLC coated mould for Injection Moulding.

The technology to produce multilevel, functional nanostructured surfaces in the mould cavities, is complemented with development of complex mould concepts to fabricate functional microparts like the hollowed microneedle arrays.

Beyond the use of conventional metallic moulds for replications, other novel concepts using new mould materials and replication technologies have been developed in the project, for processing polymers and ceramics. For ceramic microreplication, the best option was found by gel casting, using soft moulds (like PDMS), where a mix of a ceramic slurry and epoxy hardener is casted for later baking and sintering.

For the first time, direct laser 3D structuring on PDMS blocks was used for direct fabrication of gelcasting moulds, able to produce structures with up to 1:50 aspect ratio, like micropillars for ultrasound transducers.

During the second part of the project, the main activities were focused in the integration of solutions and results from tooling and replication, together with online inspection tools, to assess the technical feasibility of the FaBiMed manufacturing route, by identification of interdependences between the three main constrains: mould, replication and inspection.

For the characterization of the fabricated microstructures, optical technologies find the difficulty of trying to measure dimensions on transparent or highly reflecting materials. During the project, SEM microscopy is used as a powerful tool for microstructure observation, but an industrial method for 100% inspection is needed and two technologies were studied in the project: OCT (Optical coherence tomography) and LUS (Laser ultrasound). The LUS system is intended for fast detection of defects and inhomogeneities in large and dense micro-nanostructure arrays. Its principle of operation is based on the modifications of the spatial distribution of the Fourier amplitudes when the structures vibrate around the resonance frequency of their matrix. The actual image of the structures is not needed, but only the deviation of Fourier amplitudes with respect to a model, making the detection of inhomogeneities very fast and consuming low computational resources.

OCT (Optical Coherence Tomography) provides 3D information on the surfaces and volumes, and full geometrical information of complex structures. Two research lines were developed within the project regarding OCT: product inspection, and process monitoring.

For product inspection, an innovative OCT hybrid system was developed with extraordinary results. The system performs automated location of critical features and high resolution 3D reconstruction and metrology, only where needed, to reduce inspection time, and maximize the relevant data extraction. This allows 100% inspection of replicated parts, at only few seconds per square cm, saving time, data and computational resources.

For process monitoring, the project developed an optical probe to be integrated in the replication mould, a groundbreaking technology which provides real time information on the replication process at microscale.

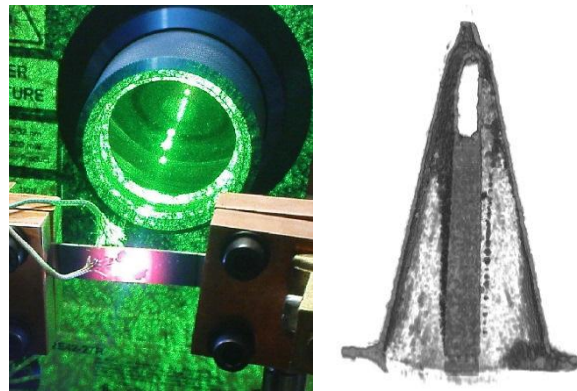


Figure 5 –LUS excitation and detection; OCT image of a microneedle

FABIMED also aims for economically sound and sustainable manufacturing and mouldmaking. Life Cycle&Cost Assesment (LCCA) methods have been adapted and applied to validate in which extent the new manufacturing paths are feasible according to pre-defined production, environmental and economic targets. The environmental impact and eco-efficiency metrics which allow to compare the FaBiMed fabrication alternatives with current benchmarks, where defined and thanks to the obtained results, the appropriate methods for design of flexible micro-manufacturing paths and performance analysis were adopted for the selected customized products/markets.

In the last months of the FABIMED project, the fabrication and validation of the three functional demonstrators have been completed:

- microfluidic lab-on-a-chip on polymer films, with micro and nano embedded features which allows an improved performance (higher functionality) of the device at lower cost.
- Hollow microneedles array, manufactured in a single Injection Moulding step, resulting in low cost and high functionality, thanks to its sharp edge and low volume delivery channel.
- Ultrasound transducers, with higher resolution thanks to the high aspect ratio microfeatures, and reduced manufacturing cost due to the application of cheap, reusable moulds.

Demonstrator 1: microfluidic chip

The first demo-line of the FaBiMed project is a compact disposable microfluidic device developed by Senslab. The microfluidic device, comprised by a sensor device (micro-patterned and nano-patterned polymer films, electronics and housing) aims the detection of different blood substances with a disposable microfluidic sensor made from two polymer films.

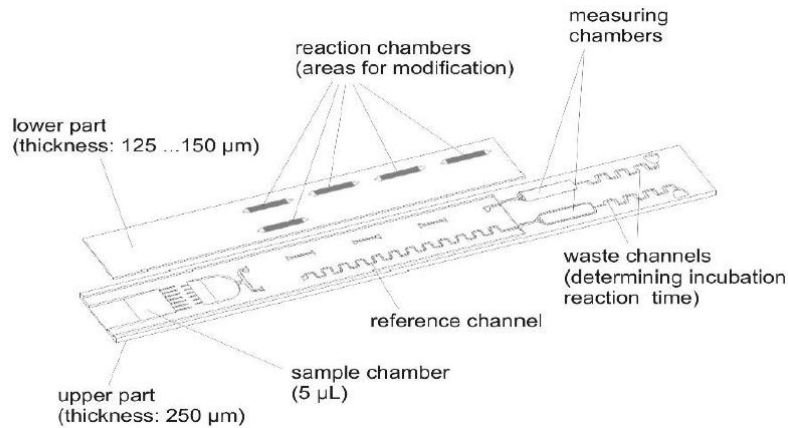


Figure 6: Prototype design.

The microfluidic chip, has been designed for the transportation of the sample of whole blood (less than 5 μl) by capillary forces alone. In order to obtain the value of the complex parameter the sample has to be hemolysed, proteolysed and measured with respect to four different measurands within the microfluidic system.

The FaBiMed microfluidic chip was successfully integrated into the demonstrator prototype and has been shown to perform properly in the capillarity forces for the blood analysis.

A crucial functional part of the developed micro fluidic arrangement is the separation of blood cells in the sample chamber.

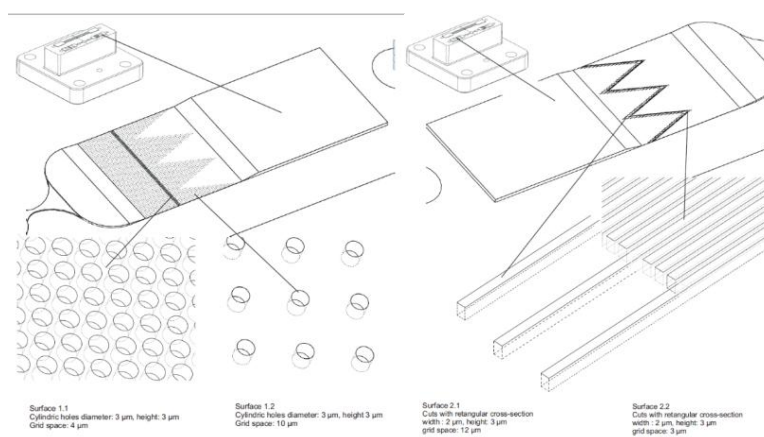


Figure 7: First construction concepts of blood separation in the sample chamber

The primarily design was simplified in agreement with the project partners. In the hot embossing tool, micro squares were manufactured after a micro milling process on the surface. The formation of these square rows should prove a filter function for fluids.

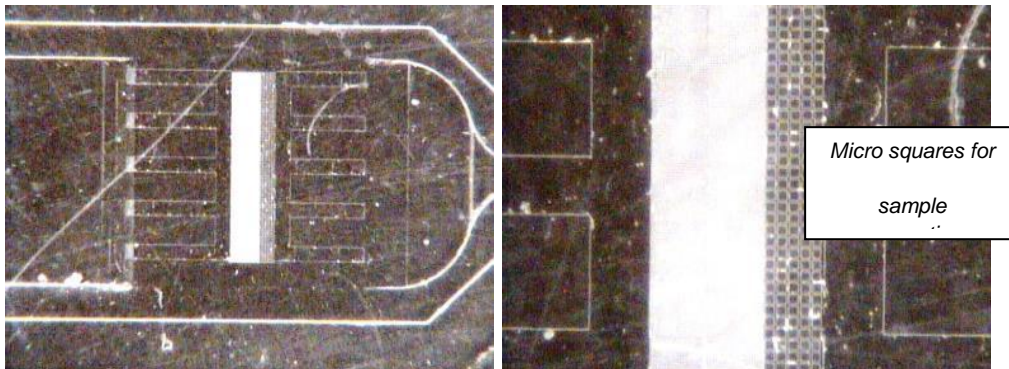


Figure 8: Simplified micro fluidic separation chamber

The simplified structuring of the microfluidic chips showed partial functional failures, mainly with blood because of sealing problems between the functional foils that could not be foreseen during the design process. Therefore, the design and manufacturing of the mould inserts had to be optimized in an additional iteration to prevent these overflow defects that impede the filtering of the whole blood. This proceeding was covered by our risk management but did imply a delay in demonstrator completion and evaluation.

A suitable substrate with electrodes for the integration of the micro fluidics in the sensor development is essential. To avoid any fluidic failure of the bonded micro separation chamber, a plane surface is required. Therefore, a polyester foil is nano-coated with an inert metal. The structuring of the metallic layer was done by laser treatment to create micro-electrodes < 50 μm width.

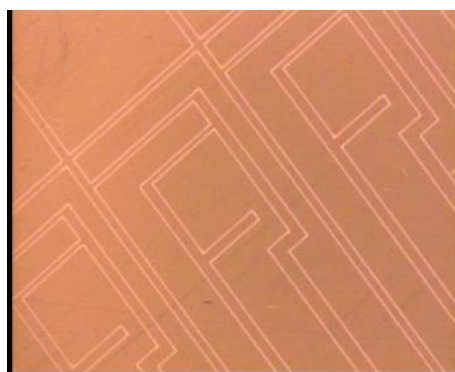


Figure 9: Laser structured electrodes on metal-coated polyester substrate

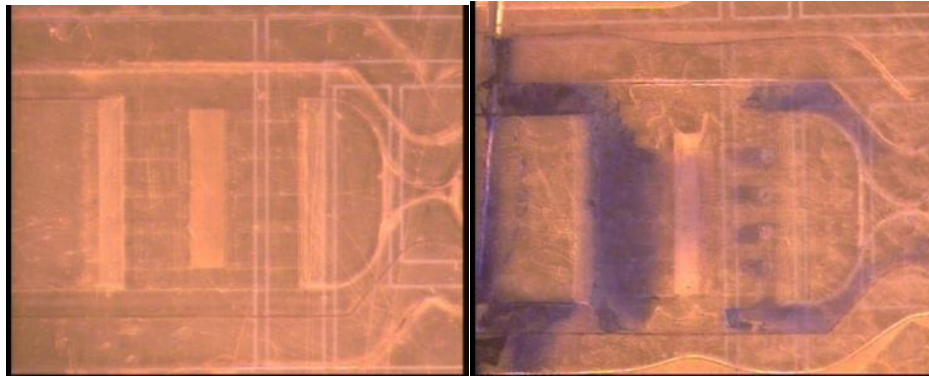


Figure 10: Application of a micro filter chamber with model fluid on laser manufactured electrodes

Demonstrator 2: Microneedle array

A programmable drug delivery platform, incorporating an injection moulded polymeric hollow microneedle array, is to be developed in the project. The aim of this platform is to enable painless controlled delivery of one or more drugs in a single patch applied to the skin. Such a system is intended to deliver medication intradermally and enable precise control of dosage timing, access to dosage history, patient activation mechanisms and inherent safety protocols for preventing adverse drug reactions (programmable pharmacokinetics).

The prototyped has been designed as two distinct components; the disposal drug delivery cartridge and the reusable housing which contains all the communication and control electronics, as stated in deliverable D1.4 (Demonstrators definition and demonstration protocol).

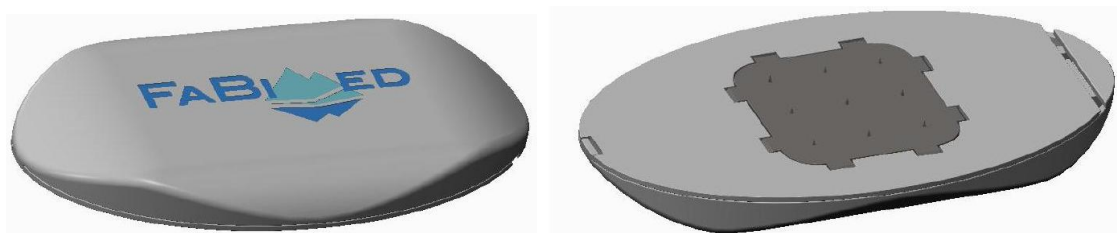


Figure 11: Prototype design and housing

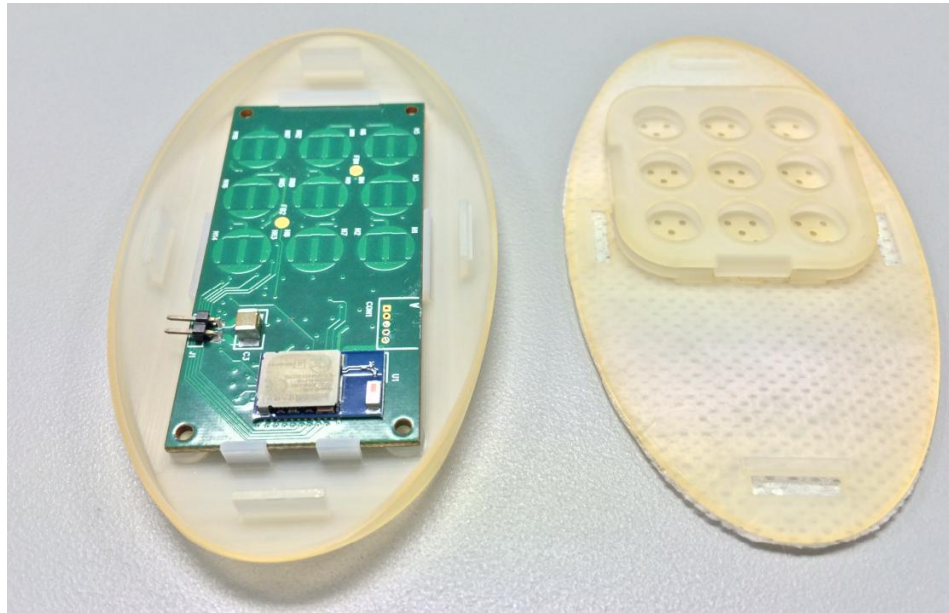


Figure 12: Actual prototype and housing.

The microneedle array, the subject of the FaBiMed project, has been designed with 9nr. Microneedles 1mm in height on the underside of the device. These are the drug delivery microneedle and will be in contact with the patient. On the upper side of the microneedle array, there is an additional “burst needle” and a taper to maximise the efficiency of the drug flow.



Figure 13: Actual microneedle array and external features to facilitate alignment.

The FaBiMed microneedle array was also successfully integrated into the demonstrator prototype and has been shown to eject liquid once the relevant microinjector is activated. Porcine skin substitute was also used to demonstrate that the microneedles can penetrate and inject drug into the dermis of the patient.

Polymeric microneedle arrays used with this drug delivery technology in the past were produced using a combination of injection moulding and laser post processing. This manufacturing method is expensive and would not be feasible for use in the large volume manufacturing required for a single use component. The FaBiMed microneedle array was produced by a single injection moulding shot, which is much more economical and results in a feasible route to market for this component.

Demonstrator 3: ultrasound transducer

The third demo-line of the FaBiMed project is an ultrasound transducer which emits sound waves that are reflected by body tissues and are detected as echoes. Images of tissues can be obtained by either scanning or rotating the transducer in combination with a data acquisition system.

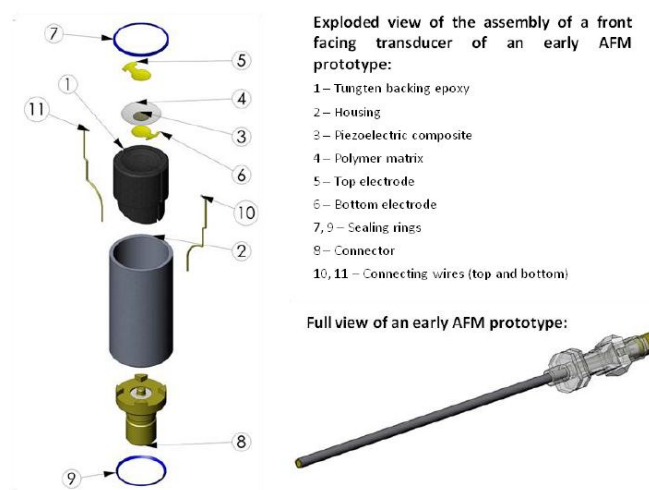


Figure 14: Prototype design

The FaBiMed route consisted of the following manufacturing steps.

1. Laser drilling of elastomeric moulds.
2. Gel-casting of PZT ceramic slurry with a high solids loading (~45%).
3. Drying and de-moulding green piezoelectric pillar structures.
4. Sintering of piezoelectric pillar structures.
5. Epoxy encapsulation of pillar structures to form a 1-3 piezoelectric composite.
6. Lapping of the piezoelectric composite to a defined thickness.
7. Application of electrodes and poling.
8. Laser cutting of composites.

9. Device integration (composite, backing layer, electrical connections, housing).

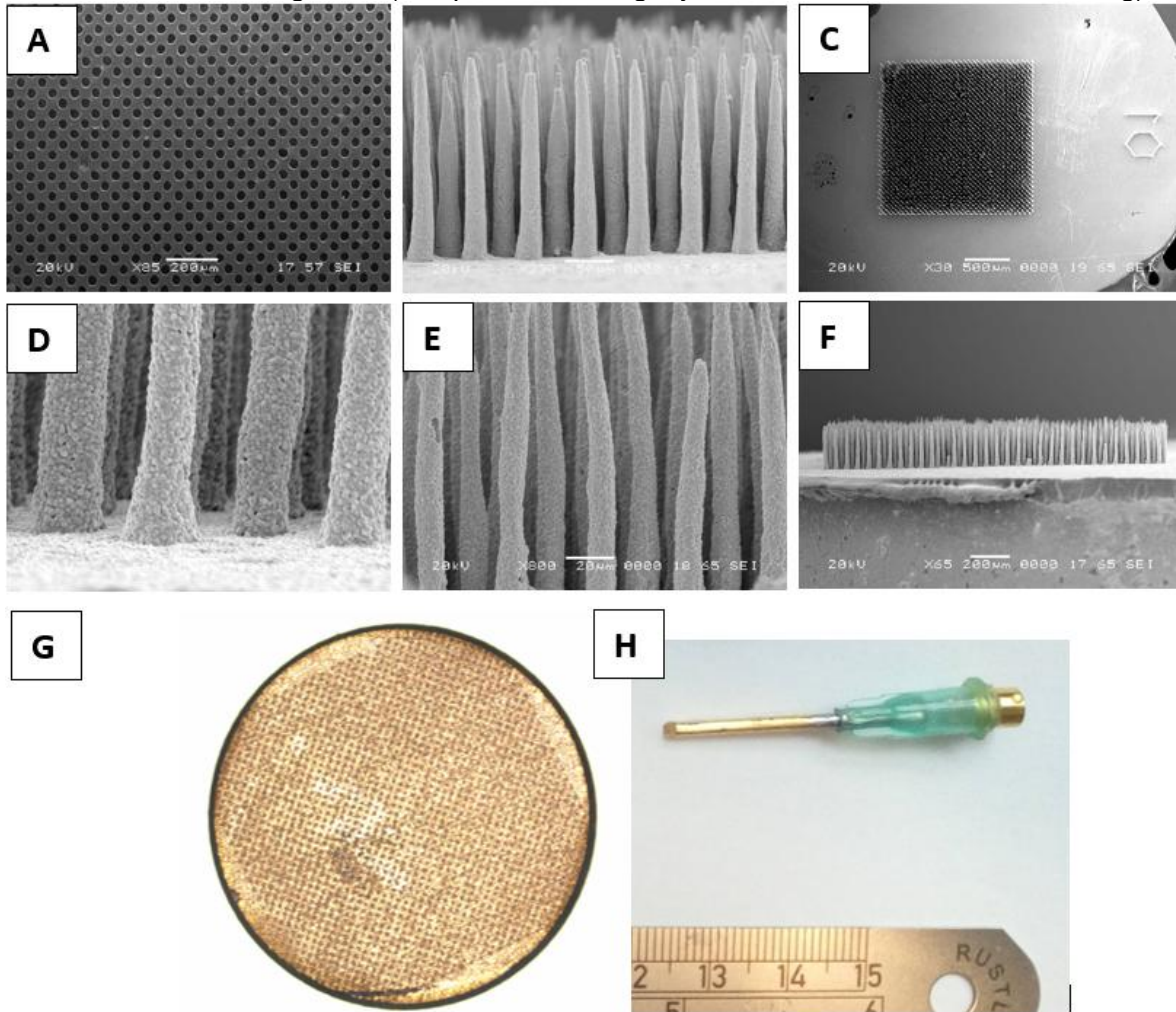


Figure 15: A) Actual laser-drilled elastomeric moulds. B & C) De-moulded green PZT pillar structures. D, E & F) Sintered pillar structures. G) Actual piezoelectric composite laser cut to 1.6mm diameter. H) Actual demonstrator integrated in a 1.8mm diameter housing with an MCX connector. The piezoelectric element has been curved to a 6mm ROC and mounted on a 45 degree chamfered tip which would enable ultrasonic imaging by linear scanning and rotation of the transducer.

The FaBiMed US transducer was also successfully integrated into the demonstrator prototype and has been shown to give similar results as transducers of the same design manufactured with the VPP route.

The demonstration of the FaBiMed ultrasound transducers can be deemed successful from a technical point of view. The piezoelectric composites and ultrasound transducers were fully characterised using a range of characterisation techniques (Scanning electron microscopy (SEM), Optical computing tomography OCT, Impedance analysis, Laser vibrometry, pulse echo, imaging of phantoms and imaging of tissues).

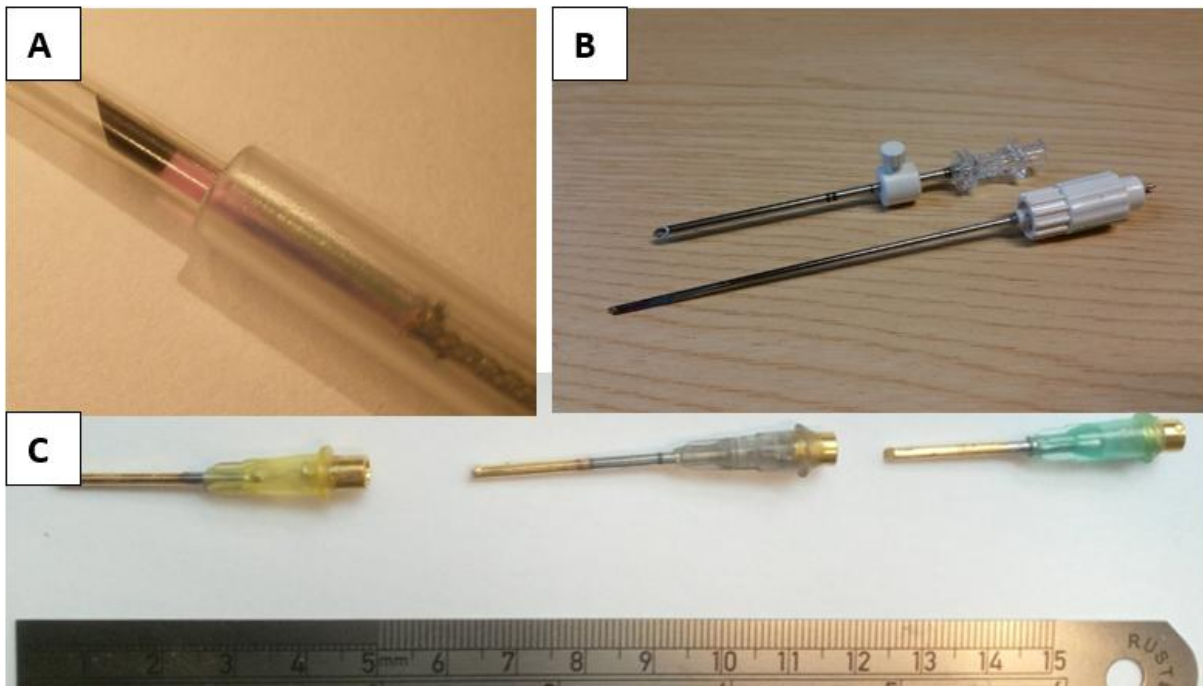


Figure 16: A) Prop depicting demonstrator inside a catheter for intravascular applications. B) Prop depicting demonstrator for ultrasound in needle applications. Inserter cannula 2mm diameter (top) and ultrasound mounted in a 1.8mm needle (bottom) which could be inserted inside the cannula. C) Actual manufactured demonstrators in 1.8 mm stainless steel housing and with a mcx electrical connector.

Image quality obtained with the project resulting prototype was as good or better than the benchmark solution fabricated with a more expensive production technology.

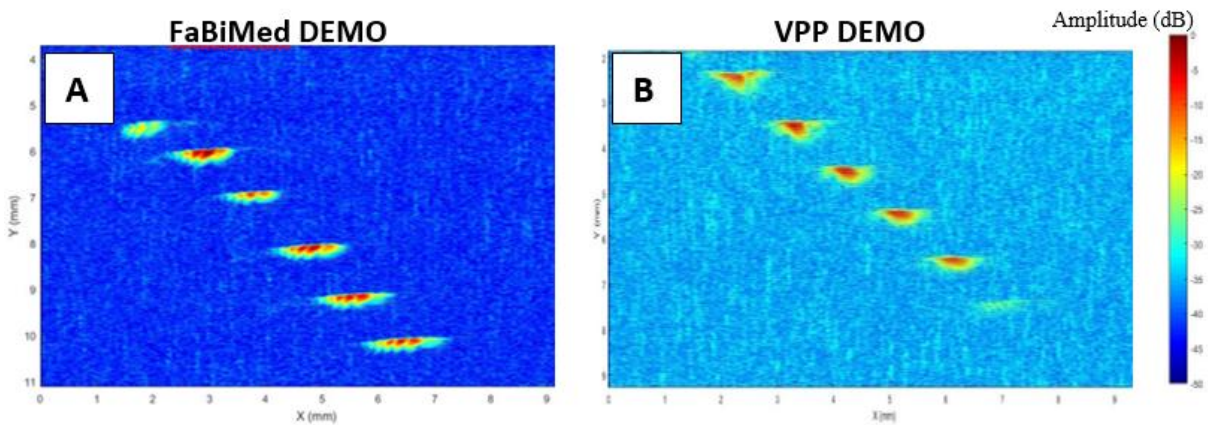


Figure 17: Backscattered scan images of a of a 25 micron diameter tungsten wire array with 1mm horizontal and vertical steps immersed in water obtained using both FaBiMed and VPP needle transducers.

3) POTENTIAL IMPACT AND USE

The societal, economical, and technological potential impact of developments in medical devices is dramatically growing, due to ageing of population, improvements in healthcare, personalized medicine, e-medicine, early diagnosis and POC (Point of Care) analysis.

The feasibility demonstration, and low cost manufacturing, brought by FaBiMed to the three case study devices, will bring significant impact to the European medical device sector and health care system, as well as economic impact to the medical device industry. These results are divided in outputs for technology transfer of concepts, systems and techniques developed and optimized during the project, and the complete operational demonstrators of the three medical devices.

The transfer will be related to the different routes that have been improved for being efficient in time and in the identical replication of the whole details of every component, even at nanometre scales. The particular achievements will be:

- Intelligent, adaptable tooling systems for hot embossing and injection moulding, expected to be available at the end of the project for medical device manufacturer and/or injection moulding companies. In addition, the reusable/reconfigurable moulds will improve the flexibility of injection and embossing, and will lower their tooling costs.
- Accelerated replication process with high accuracy for macro-micro-nano scale features, just exploitable after the end of the project and oriented to medical device manufacturer and OEM industry.

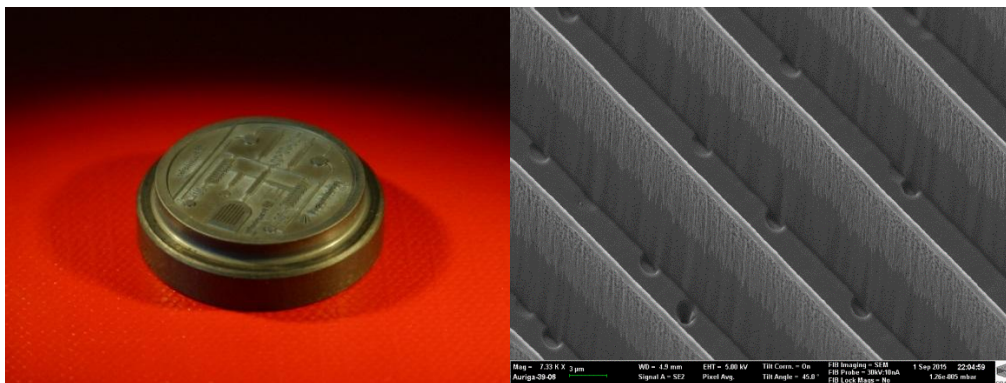


Figure 18 - Steel cavity for microfluidic fabrication by hot embossing (Source: FhIWU). Nanofeatures for wettability control on the surface of the hot embossing mould (source: ADAMA)

- Low cost microfabrication of ceramic components by gel casting with masterless production of elastomer moulds, available six months after the end of the project and oriented to the ceramic microdevice industry. The new elastomeric reusable moulds will lower the total cost dramatically from current methods (over 40% estimated cost reduction).

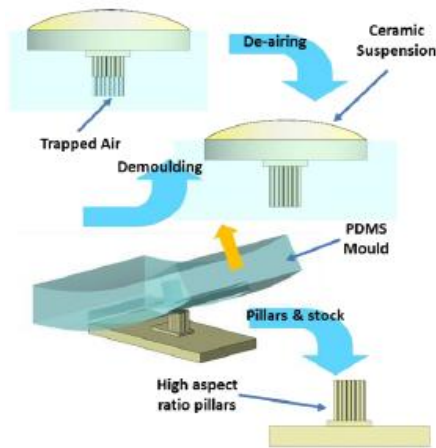


Figure 19 - Processing steps for the gel-casting micro-moulding of ceramic composites

- Injection moulding of nanostructured functional components using DLC nanostructured coating on steel, fully operational after 1 year from the end of FABIMED, and it will be addressed to diverse industries that work on flexible electronics, wearable electronics, toys, etc...



Figure 20 - Manufactured injection moulding tool and mould inserts before replication experiments.

- Micro-nanostructuring of glass by implantation and high energy plasma, to be exploitable right after the project end, and targeted to various sectors like Optics, optoelectronics, photonics or photovoltaics.

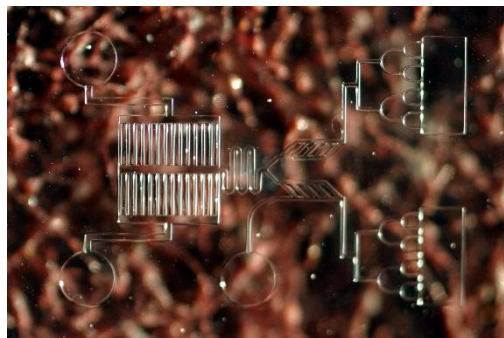


Figure 21 - Microfluidic structure on glass

- In-Cavity Optical Coherence Tomography system for real time monitoring of microrreplication, ready around 18 months after the end of the project and interesting for the micromoulding industry.

The previous results in terms of technology, also have direct impact in applications. All the demonstrators, available at the end of the project, are planned to become commercial products after 1-2 years after the end of the project, after fulfilling the specific regulatory approval procedures (“In Vitro Diagnostic Devices (IVDD)”, “Active Implantable Medical Devices (AIMD)” and “Medical Devices Directive (MDD)”). They final devices will be:

- A low cost, multiparametric POC test system, based on disposable plastic microfluidic chip. The main targeted applications in short term will be glycaemia control, and high performance sport. In long term, this technology can enable more complex, multiparametric essays from a single nanolitre sample of blood, effectively realizing the concept of Point of Care laboratory.

- A miniature piezotransducer for High Resolution IntraVascular Ultrasound Sound Imaging (IVUS), will be used for diagnosis and guidance during vascular surgery. Further development will enable the integration of this kind of piezotrasnducer as navigation aid for a variety of surgical procedures, from cardiovascular interventions to spinal and neuro-surgery, where the avoidance of vital nerves and precise placement of the surgical procedure can not only improve the procedure effectivity, but also increase the survival rates in critical or high risk interventions and cut their side effects.

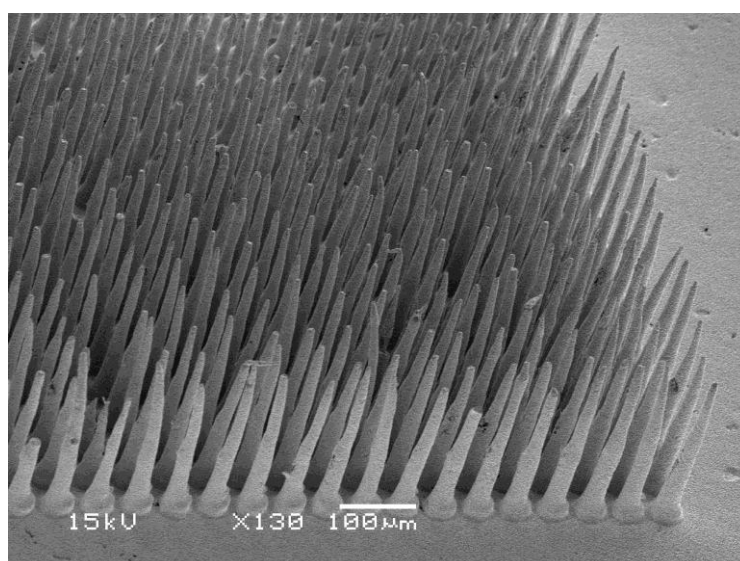


Figure 22 – SEM image of the pillar array for the US transducer

- A disposable microneedle array patch for transdermal drug delivery with patient specific geometry, to be used together with CROSPON patented multi-injector. Available in less than 2 years after the project, and valid for a wide range of drugs and chemicals, including large molecules like hormones. Painless, automated and monitored drug delivery can be a high impact solution for many long term, complex multi-drug treatment, especially for special target groups like elderly patients. More effective drug administration and use is then combined with enhanced safety as all the deliveries are measured and monitored electronically.



Figure 23 – Hollow microneedles made on plastic by injection moulding

These devices will obtain a competitive advantage from FaBiMed project (in particular the ability to be produced at low cost even for medium-low batches), and a support to commercialization thanks to the demonstration of the product, but also the qualification and assessment of their economical, commercial and industrial feasibility.

Fabimed micromanufacturing approach contributes to fulfil several of the European priorities for advanced manufacturing, as collected in the Factories of the Future Roadmap:

- **High-precision manufacturing:** Miniaturisation of products and production equipment are identified as key issues for future manufacturing. FABIMED provided solutions for effective production of complex microparts, and the design of the moulding tools is an integral part of the project. The results might affect future manufacturing approaches outside of the medical realm.
- **Customisation:** Europe identified customization as a strong added value. In case of medical product it's a must, due to patient/drug/analyte specificities. The medical market can be considered as lead users for mass customized products. FABIMED has provided strategies to combine mass production (replication) with individualization (insert reconfiguration).
- **Competitively affordable customized production, especially for small and medium-sized companies:** FABIMED has addressed this issue from the beginning. All the industrial partners of FABIMED are innovative SMEs with strong market pressure and changing environment conditions (costs, volumes and mix). Besides the flexibility of the mould making technologies themselves, FABIMED provided methodologies and decision-support tools to assess the different production scenarios and decide the appropriate strategies.
- **Service-oriented manufacturing paradigms:** FABIMED has developed toolmaking methods and technologies which serve finalistic objectives within a traditional manufacturing value chain, but the opportunity has been detected for the nanostructuring of coatings as a manufacturing service, both for components of manufacturing equipment and for final parts. Nanostructured moulds for microfluidics in FABIMED has been itself a case study of this new business model.
- **Sustainable production:** The processing technologies (laser micromachining, plasma etching, etc...) proposed in the project are inherently material and energy efficient, as they substitute large area surface treatment with selective processing. Normally, the use of selective processing result in slow production, but in this case this is solved by the combination of energy and material efficient toolmaking with high productivity replication. Beyond that, FABIMED puts a special focus on sustainability assessment by the use of a Life Cycle/Cost evaluation methodology which helps in the design of the most sustainable manufacturing path.

4) FaBiMed WEBSITE:

<http://www.fabimed.eu/>

5) FaBiMed CONSORTIUM:

Nº	Name	Acronym	Country
1	ASOCIACION DE INVESTIGACION METALURGICA DEL NOROESTE	AIMEN	Spain
2	FRAUNHOFER-GESELLSCHAFT ZUR FOERDERUNG DER ANGEWANDTEN FORSCHUNG E.V	FhIWU	Germany
3	APPLIED FUNCTIONAL MATERIALS LIMITED	AFM	United Kingdom
4	ADAMA INNOVATIONS LTD	ADAMA	Ireland
5	SENSLAB - GESELLSCHAFT ZUR ENTWICKLUNG UND HERSTELLUNG BIOELETRONISCHER SENSOREN MBH	SENSLAB	Germany
6	UNIVERSIDADE DE AVEIRO	UAVR	Portugal
7	INSTITUTO DE ENGENHARIA MECANICA E GESTAO INDUSTRIAL	INEGI	Portugal
8	Research Center for Non Destructive Testing GmbH	RECENDT	Austria
9	PROMOLDING BV	PROMOLD	Netherlands
10	CROSPON LIMITED	CROSPON	Ireland
11	TWOPTICS SYSTEMS DESIGN SL	TSD	Spain
12	SERVIZO GALEGO DE SAUDE	SERGAS	Spain