Chapter 11
Hospital Factory for Manufacturing Customised, Patient-Specific 3D Anatomo-Functional Models and Prostheses

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Abstract The fabrication of personalised prostheses tailored on each patient is one of the major needs and key issues for the future of several surgical specialties. Moreover, the production of patient-specific anatomo-functional models for preoperative planning is an important requirement in the presence of tailored prostheses, as also the surgical treatment must be optimised for each patient. The presence of a prototyping service inside the hospital would be a benefit for the clinical activity, as its location would allow a closer interaction with clinicians, leading to significant time and cost reductions. However, at present, these services are extremely rare worldwide. Based on these considerations, we investigate enhanced methods and technologies for implementing such a service. Moreover, we analyse the sustainability of the service and, thanks to the development of two prototypes, we show the feasibility of the production inside the hospital.

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11.1 Scientific and Industrial Motivations, Goals and Objectives

The significant increase of life expectancy over the last decades [1], which was made possible thanks to the progress of medical sciences, generated as a counterpart a higher demand for health care services, as elderly people generally need more intensive medical assistance [2, 3]. In addition, the modern possibilities to treat patients affected by severe diseases are generating new classes of chronic patients who need specific and highly qualified treatments [4]. This new demand for more intensive, advanced and personalised care services is clearly in contrast with the limited budget of national and regional health care systems. Consequently, new models are necessary to guarantee adequate care treatments to each patient.

In parallel, new production technologies are boosting the manufacturing of patient-specific solutions. On the one hand, personalised prostheses tailored on the specific patient are becoming crucial for the development of several surgical specialties; on the other hand, patient-specific anatomic models for preoperative planning are essential in the presence of customised prostheses, as also the surgical treatment must be optimised.

However, in the common practice, most of medical products are produced in standard sizes and shapes, and then stocked in hospitals, where the product to implant is chosen as the one closest to patient's anatomy. Thus, it is often necessary to manually adapt the product to the anatomic characteristics of the patient, with the risk of damaging the product and not reaching the optimal size and shape for the patient. This may also determine longer surgery times, with higher costs per patient.

Just recently, we may notice a significant growth of rapid prototyping services dedicated to the medical field, which are mostly provided by external companies that established a medical division.[1] However, the presence of a prototyping service inside the hospital would be a benefit for the clinical activity. The location inside the hospital would allow a closer interaction with clinicians during the model development, leading to significant time and cost reductions, and to a higher effectiveness of the products.

At present, to the best of our knowledge, there are only four services located inside the hospital worldwide: 3D Print Lab@USB (Basel, Switzerland)[2]; RIH 3D Lab (Rhode Island, Providence, RI, US)[3]; Austin Health 3D Medical Printing Laboratory (Austin, Melbourne, Victoria, Australia)[4]; 3D and Quantitative Imaging Laboratory (Stanford University School of Medicine, Stanford, CA, US).[5] However, though they

[1] Materialise—www.materialise.com/en/industries/healthcare.
Zare—www.zare-prototyping.eu/en/medical-division.

[2] 3D Print Lab@USB—www.unispital-basel.ch/das-universitaetsspital/bereiche/medizinische-querschnittsfunktionen/kliniken-institute-abteilungen/departement-radiologie/kliniken-institute/klinik-fuer-radiologie-und-nuklearmedizin/3d-print-lab.

[3] RIH 3D Lab—www.brown.edu/Research/3DLab.

[4] Austin Health 3D Medical Printing Laboratory—www.austin.org.au/page?ID=1839.

[5] 3D and Quantitative Imaging Laboratory—http://3dqlab.stanford.edu/.

are located inside the hospital, these laboratories have several limitations in terms of available technologies, as they are equipped with low cost machines and rely on outsourcing for the complex cases that require high-resolution 3D printers. Moreover, their work is confined to the orthopaedic and maxillo-facial specialties, which are the easiest to manage.

In this context, the project *Hospital Factory for Manufacturing Customised, Patient-Specific 3D Anatomo-Functional Models and Prostheses* (Fab@Hospital) proposed an innovative paradigm, i.e., the production of personalised medical products (e.g., prostheses) in an environment closely integrated with the hospital, through new design approaches and technologies, to guarantee a direct interaction between patients, medical personnel, and product manufacturers. This may improve the quality of life for patients, the performance of the health care system, and the competitiveness of manufacturers.

The Fab@Hospital paradigm consists of:

- advanced mathematical tools and modelling technologies tailored to manufacture personalised products;
- location of a *hospital factory* inside or near the hospital;
- production of personalised products (e.g., prostheses) at the *hospital factory* in a short time, thanks to the combination of innovative technologies and processes.

Besides the products, the hospital factory would produce personalised anatomic models (e.g., reconstructions of vascular districts), which may help the surgeons in studying the treatment in advance by simulating different strategies.

To meet these goals, the following scientific and technological objectives were identified:

1. Define new mathematical methods and approaches to build accurate anatomo-functional models from medical images.
2. Define improvements to the existing technologies for personalised products, e.g., additive manufacturing and micro Electrical Discharge Machining (EDM).
3. Propose innovative process combinations to reduce the production costs, thus supporting a wide diffusion of personalised medical products.
4. Demonstrate the applicability of the new technological approaches and process combinations through the development of two prototypes.
5. Propose new business models for the production of personalised medical products inside or near the hospital.

The rest of the chapter is organised as follows. Section 11.2 overviews literature related to the addressed problems, which are stated in Sect. 11.3. The developed technologies and methodologies are detailed in Sect. 11.4, while the outcomes of the work (in terms of two prototypes, several mathematical tools and a business model structure) are shown in Sect. 11.5.

11.2 State of the Art

Some medical specialties have started to benefit from rapid prototyping in the last few years, especially for preoperative planning purposes [5, 6]. In fact, clinicians may obtain more information from physical objects than from computer virtual models only. Moreover, their educational value to train new surgeons is also recognised [7].

Among the others, maxillofacial and orthopaedic specialties currently employ physical models to test different solutions, e.g., for the implant of bone fixation plates.

Vascular surgery has seen the development of a dedicated rapid prototyping sector [8]. In fact, the benefit of a physical vascular model for planning the implant of stents or vascular prostheses is linked not only to its morphological characteristics, but also to the mechanical properties of the reproduced vascular district. As the surgeon tests the placement and the release of the prosthesis, and he/she evaluates the prosthesis-vessel interaction, the vessel is required to have a behaviour as consistent as possible with the real pathophysiology; thus, compliant models with controlled elasticity are needed. However, vascular applications are mainly at the research level, and very few companies deal with patient-specific silicone vascular models.

In all cases, the current production scheme in factories not linked to the hospitals has some drawbacks:

- *Anatomo-functional properties*. Clinicians do not have the expertise to retrieve functional properties from the common medical imaging. At the same time, manufacturers do not have the expertise to translate these properties into suitable production specifications. Consequently, sending the production request to an external factory without a discussion between clinicians and manufacturers about the specifications may reduce the effectiveness of the personalised medical product.
- *Production times*. The direct interaction between clinicians and manufacturers would avoid loss of information and the need to correct the product, thus speeding up the process. Moreover, the production inside or near the hospital would significantly reduce transportation times.
- *Costs*. Even though the prices of the anatomic models for visualisation purposes are lowering, thanks to the progressive spread of prototyping technologies, moving the production inside the hospital would significantly reduce the costs. Moreover, compliant functional models with proper elasticity are still extremely expensive (thousands of euros even for very small vascular districts) and the production inside the hospital would make them more affordable.

Our literature analysis focuses on the four topics addressed in this work, i.e., patient-specific anatomo-functional cardiovascular models, patient-specific fixation plates, mathematical tools to support their design, and business models to make their production more efficient.

- **Cardiovascular models**. In vitro analyses of the vascular fluid-dynamics may help clinicians in understanding the impact of specific pathologies and devices. In this context, additive manufacturing is playing a crucial role, allowing the production of highly complex geometries at lower costs and in lower times than with standard subtractive technologies. Thus, additive manufacturing is rapidly spreading in the medical field to produce patient-specific anatomic models. In particular, 3D printed anatomic models have been used to test different operative approaches [9–12], or to improve the design process of endovascular devices. In fact, in vitro fluid-dynamic analyses are useful to identify the interaction between the device (e.g., valves, endo-prostheses, stents) and the human vascular system [13–16].

- **Fixation plates and screws**. Patient-specific fixation plates and screws are not widely adopted, due to the difficulties in the small-scale production of 3D complex components, usually made of stainless steel (ASTM F-55 and F-56), pure titanium and its alloys (ASTM F-136), and cobalt-chromium-tungsten-nickel alloy (ASTM F-90). In this context, micro-EDM could be a suitable technology for producing customised plates, due to the ability to perform complex and high-precision machining on electro-conductive materials [17]. Being a thermal process, it can be used with considerable success also for the machining of extremely hard and strong materials [18], including conductive ceramics [19, 20]. Also techno-polymers, like the PolyEther Ether Ketone (PEEK), have been recently introduced for the manufacturing of fixation plates. In this case, 3D printing technologies such as Fusion Deposition Modelling (FDM) and Stereo Lithography Apparatus (SLA) can be applied.
- **Mathematical models**. Tools for reconstructing the geometrical features of some districts from medical imagining are nowadays widespread and widely used in clinics. However, as for the mechanical properties, commercial tools do not generally include this possibility, which still represents an open research issue.
- **Business models**. There are very few works investigating the business and managerial sides of manufacturing customised medical products. The existing studies, which have been conducted only recently, mainly address the problem from an economic perspective. Some works investigated the economic implications of 3D printing in general [24], while others focused on evaluating the cost structure and developing cost models for additive manufacturing [25–27]. Lindemann et al. [28] developed a business model for evaluating the cost of additive manufacturing. Schröder et al. [29] investigated the manufacturing of customised medical devices from a business model perspective with a specific focus on value chain; they emphasised that interoperability is a significant driver for the efficient manufacturing of customised medical devices, as customisation is not a single-stakeholder process but a multi-actor process that includes suppliers, surgeons and patients.

11.3 Problem Statement and Proposed Approach

Our work includes two main applications. On the one hand, we employ additive manufacturing (3D printing) to produce anatomo-functional models for the cardiovascular specialty; on the other hand, we exploit micro-EDM and additive manufacturing to produce fixation plates for the orthopaedic specialty. Moreover, our work also involves two supporting activities, i.e., the development of mathematical models and tools for the design of patient-specific products, and the development of appropriate business models to suggest the best management strategies and to prove the benefits of the Fab@Hospital paradigm (i.e., the production inside or near the hospital). All these activities are detailed in the next subsections.

11.3.1 Additive Manufacturing for Cardiovascular Models

The goal is to manufacture deformable vascular models, with realistic mechanical and geometrical properties, to be employed for in vitro analyses. In particular, we focus on benchmark aortic models to test innovative endovascular devices and new surgical procedures.

The proposed production approach is based on additive manufacturing in combination with a moulding technique, to produce silicone models featuring both mechanical and geometrical properties of the vessel.

Ideally, the highest adherence to reality is possible through a full patient-specific approach, in which all mechanical and geometrical information, along with flows and pressures, are acquired from the specific patient. In the absence of all information, a less specific approach can be pursued by combining patient-specific information and general knowledge common to several individuals (retrieved from the literature or measured on a significant number of patients).

11.3.2 Micro-EDM and Additive Manufacturing for Fixation Plates

Although customised implants are occasionally used for surgery, they are not oriented to traumatic pathologies. In fact, the treatment of traumatic pathologies requires

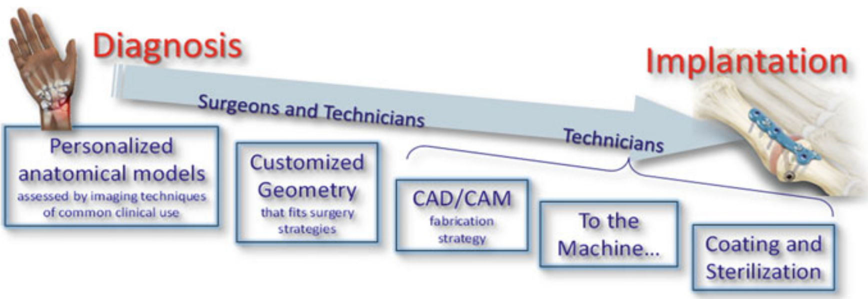

Fig. 11.1 Procedure for fabricating customised fixation plates

manufacturing the fixation plate in less than seven days, thus requiring a strong interaction between clinicians and manufacturers (see Fig. 11.1 for the fabrication procedure).

The rapid production and the clinicians-manufactures interaction could be easily achieved if the prototyping station were inside the hospital. However, to make such prototyping station available, the fabrication technology for customised devices should fulfil several constraints, due to the confined space and the controlled environment. Additive manufacturing and micro-EDM fulfil these constraints. On the one hand, complex 3D shapes can be manufactured with micro-EDM on every electro-conductive material (e.g., titanium and surgical steel); on the other hand, FDM and SLA are suitable for the fabrication of polymeric objects with complex shape at low cost and low environmental impact.

11.3.3 Prediction Models for Patient-Specific Functional Properties

Stochastic tools may support the estimation of patient-specific mechanical properties in several districts, based on non-invasive measurements and patient's characteristics. This is of particular importance in case of soft tissues (e.g., for the cardiovascular specialty). Thus, we focus on two cardiovascular applications: (i) the estimation of the aortic stiffness and its spatial variations; (ii) the estimation of the ultimate mechanical properties and of the stress-strain characteristics in patients with ascending aorta aneurysm. Moreover, due to the lack of effective tools to support Finite Element Analysis (FEA) under uncertain parameters and Structural Topology Optimization (STO), which are common problems when dealing with patient-specific problems, we propose an approach for efficiently solving FEA problems in the presence of stochastic parameters or within iterative optimization algorithms.

11.3.4 Business Models

As mentioned above, there are no appropriate business models that can be employed to support the additive manufacturing of patient-specific medical devices. The gap in the literature is even larger when considering the role of the hospitals in manufacturing individualised medical products, as hospitals are usually perceived only as end-users of the products. Also Product-Service System (PSS) oriented business models pay very little attention to apply the concept in health care, and even less to extend the practices of PSS to increase the integration between hospitals and manufacturers of customised medical products.

Thus, our goal is to develop a reference structure for business models that can support the Fab@Hospital paradigm.

11.4 Developed Technologies, Methodologies and Tools

In the following, we present the technologies, the methodologies and the tools developed to address the four problems presented in Sect. 11.3. Moreover, as for additive manufacturing and micro-EDM, we describe the features of the associated prototypes. The first prototype (described in Sect. 11.4.1) is a preoperative model for the cardiovascular specialty, while the second prototype (described in Sect. 11.4.2) consists of a set of fixation plates for the orthopaedic specialty.

11.4.1 Additive Manufacturing for Cardiovascular Models

We relied on a moulding technique to create an aorta benchmark model, where the mould is produced by means of 3D printing technology. We built up a flexible and completely parametric model, which is able to adapt in a consistent way to the modifications of the structural parameters. In particular, for the prototype, we considered geometrical and mechanical parameters retrieved from the literature; in addition, in the absence of literature data, some geometrical data were obtained from several Computed Tomography (CT) images.

The mould is composed of three parts: two outer shells and an inner part that creates the inner lumen of the vessel (Fig. 11.2). The thickness of the model, given by the distance between inner and outer moulds, was selected according the desired

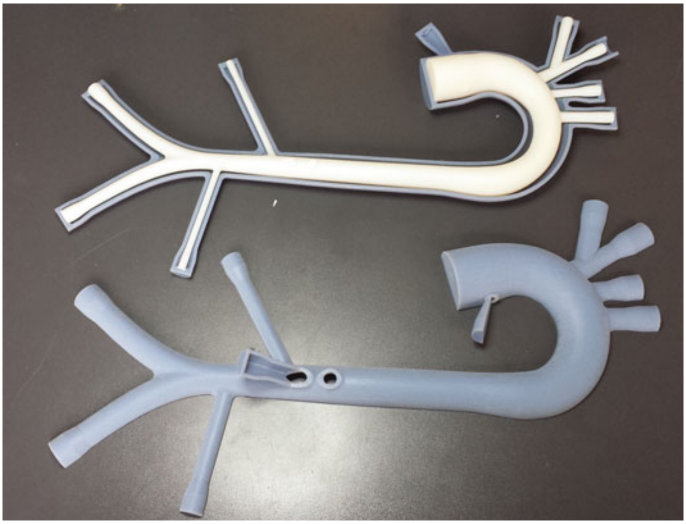

Fig. 11.2 3D printed mould of the aorta model, composed of an inner lumen (white) and two outer shells (blue)

punctual compliance. Indeed, starting from the inner lumen geometry, we computed the thickness in order to get the desired compliance.

The mould was manufactured using the 3D printing technology. We employed the Objet 30 Pro printer (Stratasys, MN, US), which is based on the *Material Jetting* technology, where layers of photopolymer resin are deployed on a building tray and cured by means of ultraviolet light. We employed the commercial photopolymer VeroWhitePlus RGD835 and the support material FullCure 705, which is necessary to support the parts of the model that do not lay directly on the tray or the underlying layer. After printing, a fine post-processing was performed to ensure a smooth finishing of all surfaces of the mould that will be in contact with the silicone, and the mould was finally assembled.

To create the aorta model, we employed the two-part Sylgard 184 Silicone Elastomer (Dow Corning, MI, US) in a ratio of 10 parts of silicone base to 1 part of curing agent by weight. The silicone mixture was poured into the mould, placed into a vacuum chamber to eliminate air, and then left curing at room temperature (about 23 °C) for 48 h. Such two-part ratio and curing temperature were chosen in order to tune the mechanical properties of the silicone [30]; the selected combination leads to a final elastic modulus of 1.32 ± 0.07 MPa. After curing, the mould was removed to get the final silicone model.

The resulting prototype, which can be considered a benchmark deformable aortic model, is shown in Fig. 11.3. It is endowed with terminations that can be connected to in vitro circuits by means of pipe junctions. Moreover, the use of transparent silicone allows inner visibility, which is fundamental for several experiments, e.g., endograft deployment or particle tracking. Transparency is also fundamental to exploit the model to train beginner surgeons and clinicians; allowing inner visibility, the student is able to look through the vessel at the movements of the endoscopic instruments.

11.4.2 Micro-EDM and Additive Manufacturing for Fixation Plates

Three manufacturing technologies (namely, micro-EDM, FDM and SLA) were tested for manufacturing several prototypes made of different materials (metals and polymers). The two additive manufacturing technologies were studied using two geometries and different polymers.

The two most appropriate micro-EDM approaches (i.e., milling-EDM and wire-EDM) were tested in terms of material removal rate, to minimise the machining time. Two materials were investigated: titanium, which is largely employed in the medical sector due to biocompatibility and mechanical characteristics, and the ceramic composite Si3N4-TiN, which is currently used for dental implants. Several tests were carried out to find the best strategy and parameters to achieve the typical features of fixation plates, such as holes and bores. Holes are necessary on plates both for temporary and permanent fixture because, according to the anatomy of the patient

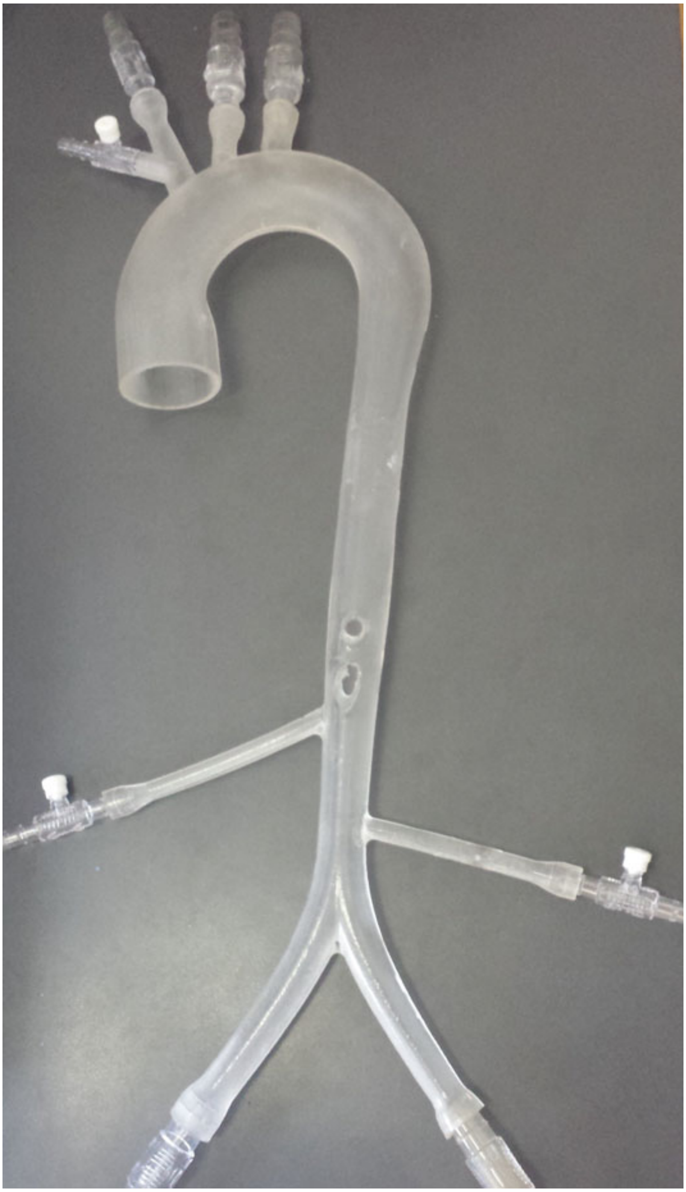

Fig. 11.3 Silicone aorta model after mould removal

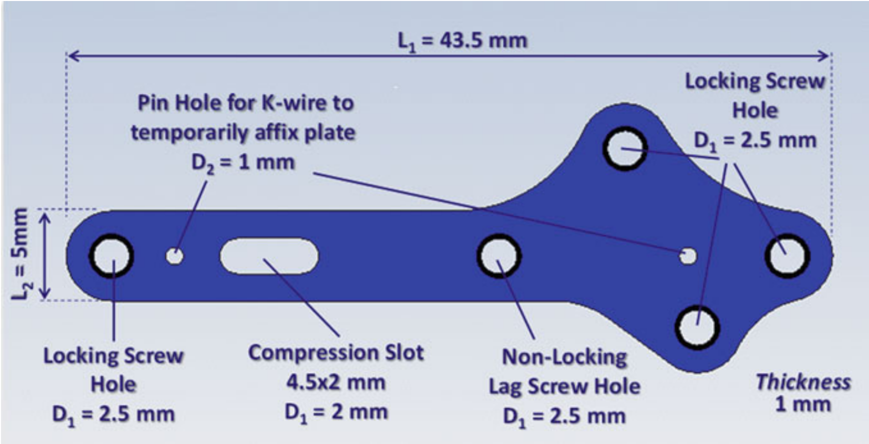

Fig. 11.4 Fracture plate for osteotomy and arthrodesis in the foot

and the fracture, different fixation points are required; bores lighten the plate and help assembling during the surgery.

The FDM process was tested with engineering polymers and composites. Tests were carried out to correlate the FDM process parameters with the highest resolution achievable. They were conducted on both ad hoc designed samples and on a few designs of commercial fixation plates, using the printers Sharebot Next Generation (Sharebot, Italy) and S2 (Gimax 3D, Italy). Moreover, to tailor the mechanical properties of the biocompatible polymers, carbon nanotubes (CNT) were added as filler in several polymeric matrixes, e.g., Polymethyl Methacrylate (PMMA), Polyoxymethylene (POM) and Polyamide (PA). The mechanical characterisation of these composites was carried out using FDM 3D printing and SLA dog-bone tensile specimens. SLA technology, with the equipment Form 1+ (Formalabs, MA, US) was finally selected as alternative additive process, in order to compare its performance with the FDM in terms of production time, mechanical strength and surface quality.

As for the prototype, the micro-EDM was tested on the prototype shown in Fig. 11.4, which is inspired by a fixation plate commercialised by Vilex (McMinnville, TN, USA). The plate includes four holes for the screws, to lock the plate to the bone, a non-locking lag screw hole, one compression slot and two smaller holes for temporary fixing. Samples were manufactured to prove the customisation methodology, the machining performance and the process ability.

A commercial fixation plate for the *Rolando fracture* (i.e., a fracture to the base of the thumb, see Fig. 11.5a) was selected as test specimen in order to assess additive manufacturing capabilities. The prototype was fabricated in several polymers (both commercial and internally developed) using FDM and SLA. As expected, the two technologies have different potentialities. FDM allowed the use of a greater variety

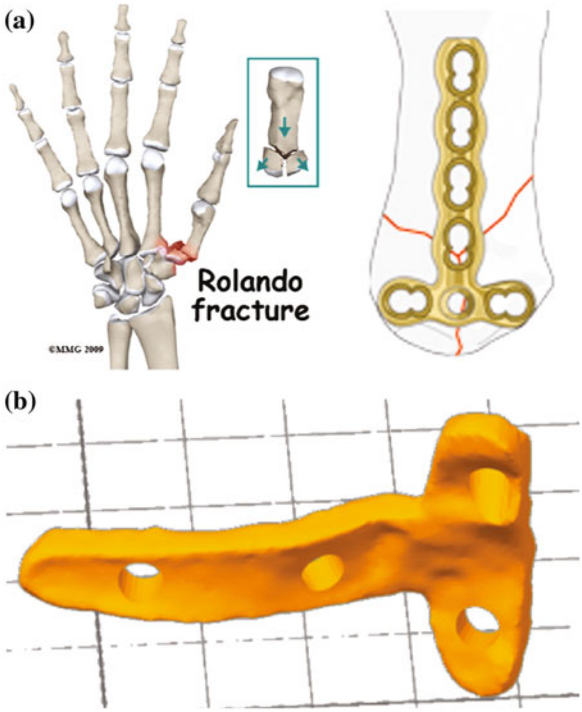

Fig. 11.5 Rolando fracture and commercial fixation plate (**a**); proposed patient-specific plate (**b**)

of polymers and composites with tailored properties, while the selection of materials for SLA was much reduced.

Finally, a patient-specific fixation plate for the *Rolando fracture* was designed and fabricated with different polymers (Fig. 11.5b). Figure 11.6 shows some of the produced plates, made using FDM in PA-CNT4% and SLA. SLA samples present very smooth surfaces due to the higher resolution of the technology.

11.4.3 Prediction Models to Identify Patient-Specific Functional Properties

As mentioned in Sect. 11.3.3, we focused our activity on three applications, for which an adequate solution in the literature was still lacking.

The first one deals with a Bayesian estimation approach to assess the stiffness and its spatial variations in a given aortic region, based on CT Angiography (CTA) images acquired over a cardiac cycle [21]. The arterial stiffness was derived by linking the kinematic information from the CTA images with pressure waveforms, generated by a lumped parameter model of the circulation [22]. The proposed approach includes

Fig. 11.6 Rolando fracture fixation plates made using FDM (**a**) and SLA (**b**)

the uncertainty of the input variables and exploits the entire diameter and pressure waveforms over the cardiac cycle.

The second application deals with the ascending aorta aneurysm, which is a severe life-threatening condition with asymptomatic rupture risk. We developed an approach to estimate the patient-specific ultimate mechanical properties and the stress-strain characteristics based on non-invasive data [23]. Through a regression model, we built the response surfaces for the ultimate stress and strain, and for the coefficients of the stress-strain characteristics, all in function of patient data commonly available in the clinical practice.

Moreover, due to the lack of effective tools to support Finite Element Analysis (FEA) under uncertain parameters and Structural Topology Optimization (STO), which are common problems when dealing with patient-specific problems, we propose an approach for efficiently solving FEA problems in the presence of stochastic parameters or within iterative optimization algorithms.

Finally, a relevant issue for studying the mechanical behaviour of biological tissues and structures with computational tools (e.g., FEA) is the uncertainty associated with the model parameters. We addressed the problem of solving the FEA in the presence of uncertain parameters by exploiting the functional principal component analysis to get acceptable computational efforts [31]. Indeed, the approach allows to construct an optimal basis of the solutions space and to project the full FEA problem into a smaller space spanned by this basis. The same approach was also used to reduce the computational effort of iterative optimization algorithms for STO [32].

11.4.4 Business Models

A general structure to configure potential business models for customised manufacturing in health care was developed. The proposed structure is based on the Product-Service System (PSS) concept, considering the morphological box defined by Lay et al. [33]. At the same time, it entails some modifications on the role of hospital and machinery supplier.

In particular, the proposed model consists of a set of building blocks, i.e., characteristic features that define the main aspects and decision points to be set (Fig. 11.7). For each feature, a number of options were defined, which describe the potential alternatives that can be selected to configure the business model. The features consider six relevant perspectives for a PSS-oriented business model: (i) *Location*, which refers to the physical production location of customized medical device; (ii) *Operational personnel*, which refers to the workforce allocation for production; (iii) *Equipment ownership*, which describes the property right to use the manufacturing equipment and machinery; (iv) *Maintenance*, which describes the party responsible for carrying out the maintenance of the equipment; (v) *Payment mode*, which define whether the payment is made in a traditional or an alternative way; (vi) *Target segment*, which clarifies whether the fabricated devices are produced only to serve the internal use of the hospital, or also to be offered and sold to other potential external customers [43]. Business models are thus configured by selecting different options for each characteristic feature; obviously, each configuration defines a particular strategy for the customer and the supplier.

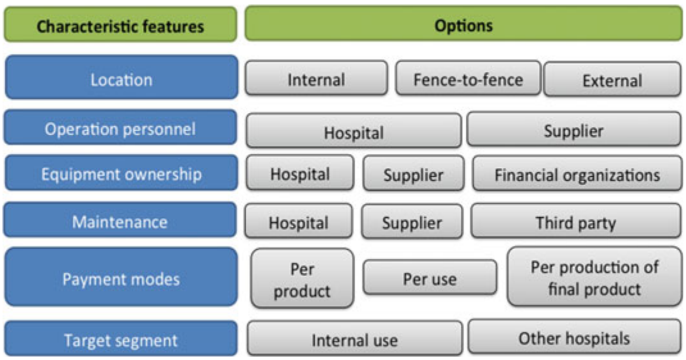

Fig. 11.7 Structure of the proposed PSS-oriented business model [35]

11.5 Outcomes

We present the outcomes and the results separately for each addressed problem. In particular, we refer to the prototypes, the mathematical models and the business model.

11.5.1 Aorta Silicone Model

The model was first analysed from a macroscopic point of view: surfaces are smooth, homogenous, even if slightly damaged only in the subtlest parts. Also the transparency is guaranteed.

For a quantitative analysis, the silicone model was tested to assess the actual compliance of the mock aorta. A series of CT scans of the model were performed at different inner pressures, using a 64 slice Definition AS CT (Siemens, Germany). To do so, all branches were closed and an inner pressure was imposed by means of a sphygmomanometer, ranging from 40 to 220 mmHg. Then, all acquisitions were post-processed, performing the segmentation of the air in the aorta lumen with the open source software ITK-Snap. At the end of the segmentation process, a set of labels was obtained, one for each slice of the CT scan, which were interpolated to create the inner volume rendering. Through the inner volume at different pressures, we identified the compliance of the model, expressed as the slope of the volume-pressure curve, here equal to 0.2008 cm^3/mmHg. Results show a linear volume-pressure relation that properly replicates the physiology of the aorta, even though the slope of the curve is slightly lower than expected, meaning that the model is more rigid than a physiologic aorta [34].

This small mismatch can be explained by the amount of factors that may impair the properties of the silicone mixture. Actually, a fine tuning of the mechanical properties can be performed by acting on the ratio between base and curing agent, i.e., the elastic modulus can be significantly reduced by lowering the amount of the curing agent. Moreover, lowering the curing temperature leads to the same result, even if the decrease is less significant.

11.5.2 Fixation Plates

The SX200 HP micro-EDM machine (Sarix, Switzerland) was equipped with different electrode tools according to the manufacturing strategy. A tungsten carbide cylindrical rod and a copper cylindrical tube, both with nominal diameter 0.4 mm, were used for the milling and the drilling operations, respectively. The overall machining time to complete a fracture plate in Titanium was equal to 375 min.

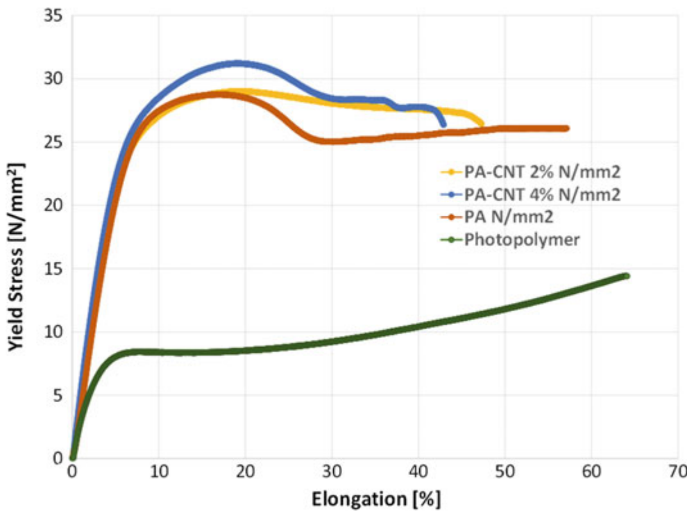

Fig. 11.8 Tensile tests for PA, PA with different CNT concentrations, and photopolymer from SLA

The same plate was made in a ceramic composite (Si3N4-TiN) using micro-EDM. Due to the higher material removal rate, the total machining time was reduced to 245 min. Unfortunately, the machining time is a severe drawback for this technology, which might not be suitable for more complex devices with a higher number of holes and bores.

Concerning the additive manufacturing, Fig. 11.8 shows the results of the tensile tests performed on different polymers by using dog-bone tensile specimens manufactured using FDM 3D printing and SLA. It can be noticed the poor mechanical performance of the photopolymer with respect to PA. The PA-CNT composites slightly increase the maximum yield stress, while they do not seem to influence the Young modulus.

11.5.3 Prediction Models

For the Bayesian estimation of the stiffness and its spatial variations, efficiency and accuracy of the proposed method were tested on some simulated cases and on a real patient [21]. The proposed approach showed to be powerful and to catch regional stiffness variations in human aorta using non-invasive data. The obtained estimates can also be used for producing patient-specific prostheses and preoperative tools that respect the estimated mechanical properties.

As for the estimation of patient-specific ultimate mechanical properties and stress-strain characteristics, we applied the approach to a dataset of 59 patients. The approach was validated, as accurate response surfaces were obtained for both ultimate properties and stress-strain coefficients [23]: prediction errors are acceptable, even though a larger patient dataset would be required to stabilise the surfaces, making it possible an effective application in the clinical practice.

Finally, considering the reduced basis approach to solve FEA problems in the presence of uncertain parameters [31] or for STO [32], results are promising. We assessed the applicability of the proposed approach on several test cases, obtaining satisfactory results. On the one hand, solving the problem in the reduced space spanned the functional principal components is computationally effective; on the other hand, very good approximations are obtained by upper bounding the error between the full FEA solution and the reduced one.

11.5.4 Business Models

The generated configurations of business model were defined by combining different options for each characteristic feature. Three main configurations were developed [35]:

- *Product-oriented business model*, in which the hospital buys the production machinery from a supplier with additional services. In this scenario, the hospital is the manufacturer and the production can take place either inside or near the hospital.
- *Use-oriented business model*, in which the hospital does not acquire any production machinery and the supplier retains the ownership of all equipments. In this configuration, the hospital rents or leases the equipments, and installs them in an internal production lab. While the ownership is not transferred to the hospital, the equipment is run by operating personnel of the hospital.
- *Result-oriented business model*, in which the hospital takes a step forward toward collaboration and integration with the supplier. While the fabrication place remains inside or near the hospital and the production takes place under the supervision of the hospital, the supplier is responsible for running the production. The supplier owns the equipments, provides additional maintenance services, and is responsible for running the production through its own personnel. The hospital provides the physical space for the production, and pays for the production of each final product.

Figure 11.9 shows the three different configurations.

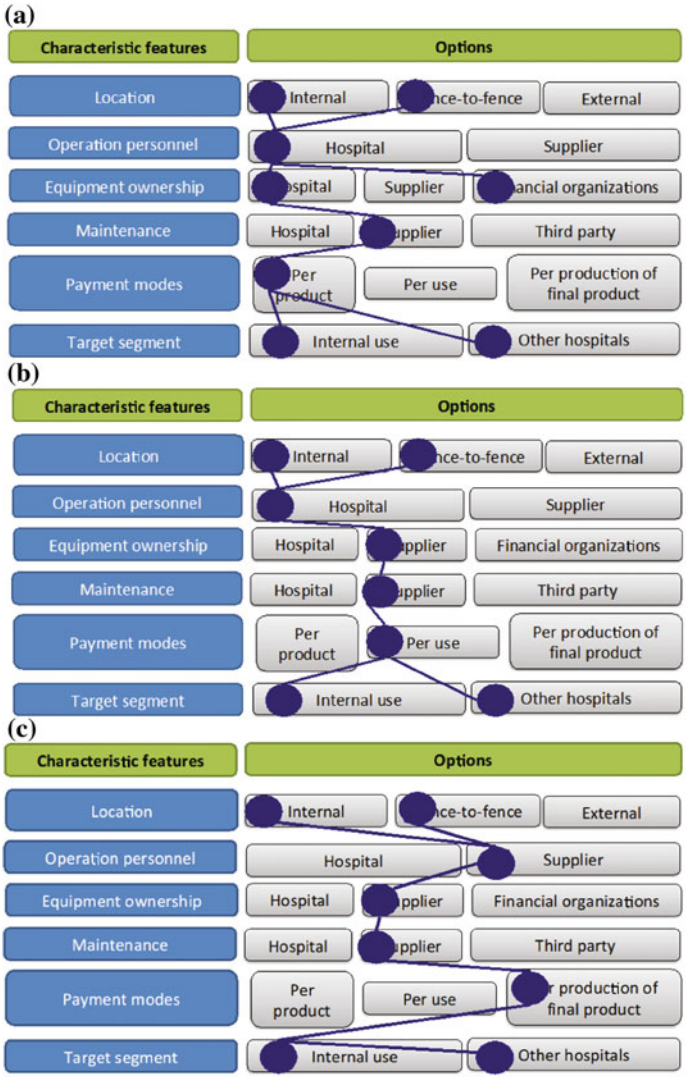

Fig. 11.9 Three possible business model configurations [35]: product-oriented business model (**a**); use-oriented-oriented business model (**b**); result-oriented business model (**c**)

11.6 Conclusions and Future Research

In this work, we propose a new paradigm to bring the production of personalised products (e.g., prostheses) inside or near the hospital, i.e., the Fab@Hospital paradigm.

Through some relevant examples, we proved the possibility to produce patient-specific products in small factories with production processes that may easily involve clinicians. Moreover, we also validated the approach by interacting with clinicians of several specialties.

The major scientific contributions can be summarised as follows:

1. A novel insight on the role of entry tears in type B aortic dissection: pressure measurements in an in vitro 3D printed model [36].
2. Stent graft deployment increases aortic stiffness in an ex-vivo porcine model [37].
3. Changes in aortic pulse wave velocity of four thoracic aortic stent grafts in an ex vivo porcine model [38].
4. A compliant aortic model for in vitro simulations: design and manufacturing process [34].
5. Micro-EDM studies of the fabrication of customised internal fixation devices for orthopedic surgery [39].
6. Process capability and mechanical properties of FDM in micro manufacturing [40].
7. Bayesian estimation of the aortic stiffness based on non-invasive computed tomography images [41].
8. A clinically-applicable stochastic approach for non-invasive estimation of aortic stiffness using computed tomography data [21].
9. A regression method based on noninvasive clinical data to predict the mechanical behavior of ascending aorta aneurysmal tissue [23].
10. Efficient uncertainty quantification in stochastic finite element analysis based on functional principal components [31].
11. Applying functional principal components to structural topology optimization [32].
12. Proposal of an innovative business model for customized production in healthcare [42].
13. Development of a PSS-oriented business model for customized production in healthcare [35].
14. A new perspective of product-service business models for customized manufacturing in healthcare [43].

Items 1–4 refer to the additive manufacturing for cardiovascular models; items 5–6 to the fixation plates made using micro-EDM and additive manufacturing; items 7–11 to prediction and mathematical tools; items 12–14 to the business models.

Future work will consider the implementation of the Fab@Hospital paradigm in a small hospital factory, to simulate the entire production process from the clinical request up to the final product.

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