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REVIEW ARTICLE

Workflow for Robotic Point-of-Care Manufacturing of Personalized Maxillofacial Graft Fixation Hardware

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Abstract

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As of this writing, Point-of-Care Manufacturing (POCM) occurs at a handful of advanced tertiary and quaternary care medical centers. These services are mainly limited to 3D printed anatomic models whose shapes derive primarily from CT or MR imaging. In far fewer cases, Virtual Surgical Planning (VSP) and 3D printed surgical guides are manufactured and surgical models are used to pre-bend fixation hardware, produce osteotomy guides, or in the fewest cases, fabricate personalized implants. Ensuring safe and effective POCM is highly relevant to rapidly emerging and time-sensitive personalized interventions for cardiac, trauma, cancer resection/radiosurgery, and neurological surgery. These rapidly emerging cases may not have time for current centralized production services to respond or the return on investment is insufficient motivation. However, patient awareness of the rise of POCM has put a premium on determining design and fabrication workflows that would be needed to provide these patients with personalized procedure planning, surgical guides, and implantable devices. This opportunity could also leverage Metamorphic Manufacturing (MM), Hybrid Autonomous Manufacturing (HAM), and the benefits of Integrated Computational Materials Engineering (ICME). The overarching goal of MM is to design a personalized device's shape simultaneously with its function and a fabrication strategy that uses manufacturing modalities and device materials that can ensure the output of a device with optimal shape and mechanical performance. As an initiative in this discipline, we report here on preliminary design and early-stage, partial testing of a workflow that embraces the benefits of MM, HAM, and ICME for the design and fabrication of personalized mandibular graft fixation hardware.

Keywords Metamorphic manufacturing · Distributed manufacturing · Robotics · Virtual surgical planning · Stress shielding · Stress concentration · Stiffness matching

Introduction

History and Approach to Point-of-Care Manufacturing

Point-of-Care Manufacturing (POCM) has dominated recent discussion at several national and international annual medical and manufacturing meetings that have been historically dedicated to 3D printing in medicine such as ASME (American Society of Mechanical Engineers) AM Medical, SME (Society of Manufacturing Engineers) RAPID + TCT, CIRP BioM (International Academy for Production Engineering), and the RSNA (Radiological Society of North America) 3D Printing SIG [1–3]. POCM Workshops have also recently been held at the US FDA and elsewhere [4]. Currently, POCM services usually begin with the need for personalization of medical devices for a patient´s medical condition. 3D Computed Tomography (CT) or 3D Magnetic Resonance Imaging (MRI) scans are obtained for diagnostic purposes and then, used to create 3D anatomic models. Following segmentation of the anatomy of interest, the isolated 3D surfaces are then used in a Virtual Surgical Planning (VSP) environment. VSP is the process of taking patient-specific data to design a surgical intervention and often to create 3D models of a surgical reconstruction. Those surgical models can be 3D printed for use in planning and as an intra-operative reference. Additionally, the surgical plan created in VSP software can be employed in stereotactic intra-operative image guidance systems. These strategies have demonstrated many benefits including Operating Room (OR) time reduction, improving surgical outcomes, and decreasing hardware failure rates [5].

Currently, a limited number of tertiary care medical facilities have the advanced manufacturing and quality control capabilities needed for pre-operative production and qualification of 3D printed sterilizable guides (i.e., reference, biopsy, cutting, drilling, placement), radiation custom boluses, jigs (i.e., equipment orientation and stabilization), and, much more rarely, point-of-care fabrication of implants or to provide robotic procedural assistance. In regard to the POCM of personalized implants, VSP-designed reconstructive skeletal fixation, percutaneous prosthetics, cranial reconstruction plans, segmental defect-filling plates, external airway stents, personalization of vascular and cardiac devices with patient-specific data are available at very few centers of excellence. In some cases, these devices are the result of a vendor-hospital collaboration [6]. While some of these personalized therapeutic devices or aids are also available from vendor-based centralized production facilities, most are only available if manufactured at the point-of-care as they result from local research in collaboration with surgical departments and/or private companies. Nevertheless, the lag time for manufacturing personalized devices can be too long to treat many rapidly

emerging conditions (e.g., trauma, cancer, neurological, cardiac) when manufactured at private company headquarters.

Limitations of Current POCM and VSP Strategies for Fixation Hardware

Despite recent advances in POCM and VSP strategies for medical device manufacturing, there are still gaps in most design engineering, decision-making based on expected mechanical performance, selection of materials, and fabrication workflows, including for craniomaxillofacial (CMF) fixation hardware (e.g., fixation plates) to treat trauma, cancer, or other rapidly emerging serious conditions. Some areas of opportunity are the limited shape variation of hardware provided by vendors, which are approved based on medical judgment rather than a mechanical optimization report for choice of material, shape, fixation hardware location, and screw depth and location. Therefore, the lack of design and personalization of these devices with optimized function and fit might compromise their performance.

What is also missing in current POCM strategies is the identification of the anticipated physiological load, such as chewing forces for the maxilla or mandible [7]. In addition, in most cases simulated loading regimes are neglected. They could be used to: (1) design and test fixation to confirm that grafted bone is only under compression (i.e., so as to bear all loading during healing) avoiding wound healing site damage by placing healing sites under tension, (2) reducing micromotion during healing to lower the risk of failed bone healing and insufficient vascularization, and (3) ensuring that the wound healing fixation does not interrupt normal stress–strain trajectories of the healed bone [8].

An approach to unify such design and manufacturing efforts could be achieved by means of Integrated Computational Materials Engineering (ICME), where the design of a product is based on its manufacturing processes, material microstructure, and engineering properties at different length scales [9]. Its applicability, for example, has proven to be beneficial in the prediction of microstructure evolution in metals during hot rolling processes. By using different design variables and process parameters during modeling, great flexibility can be obtained in the tailoring of material properties, and thus, subsequently, in the performance of fabricated parts [10]. The same concept could be adapted to develop a methodology that considers relevant information from the fabrication process of skeletal fixation plates to anticipate changes in their microstructure, as well as input data on the patient's chewing biomechanics for personalization. By also incorporating the use of Metamorphic Manufacturing (MM) as an approach to rely on closed-loop forming methodologies and Hybrid Autonomous Manufacturing (HAM) to bring together materials and processes with sensing, Artificial Intelligence (AI), and Machine Learning (ML), personalized fabrication of fixation plates with the required quality and desired engineering properties for optimal performance would be supported [11, 12]. With these approaches, the medical device design and manufacturing systems would provide the surgeon with a computational graphical rendering of how critical choices in device materials and geometry will affect the performance and durability of the component, post-healing, and how the period of highest restored function might be achieved earlier and sustained longer. The ICME framework integrates length scales and process to performance [13]. In a very simple example, it is well known that residual stress is a dominant factor in component performance with respect to fatigue and stress corrosion in susceptible materials [14]. Further, the detailed sequence of bending operations will affect the distribution and magnitudes of residual stresses. Simple ICME-inspired calculations may locate compressive residual stresses at locations of maximum repeated tensile stress to improve component performance. At a more ambitious level, modeling implant and biological materials in a full rendering–planning–tracking cycle graphical environment might allow the attending physician to track the patient's recovery more fully and determine whether the planned restoration will be achieved.

It is these activities that have inspired us to propose a solution in the work reported here. Additional inspiration is not only research to optimize care, but to reduce production time for personalized services and devices to make them available for patients with emergent or low-volume unique conditions (e.g., trauma, oncologic surgery, and cardiac, or neurosurgical interventions). Measuring and tracking restoration and failure rates and combining those with other known failure risks (e.g., radiation, poor nutrition, smoking, body mass index, operative time, vasculopathies, chemotherapies that inhibit wound healing) in a patient-specific manner could lead to improved VSP and device design, and potentially, become "standard-of-care." The knowledge that some failures, through tracking, could be anticipated and avoid secondary surgeries, inspires us to see if the initial procedure could be reinforced by ICME, MM, and HAM to assist the manufacturing engineers and the attending physician with optimizing fixation design and noting risks that should be tracked in the event of weak or non-union. The planning, fabrication, and tracking process could all be accomplished at the point-of-care in real-time. Equally inspiring would be research into local fabrication (i.e., distributed manufacturing) methods that make continuous improvements in these procedures as well as treatment outcomes [15].

Challenges Facing Integration of Device and Fabrication Process Optimization for CMF Fixation Hardware

The cutting-edge practice to personalize off-the-shelf CMF reconstruction fixation plates to fit the patients´ anatomy is currently an iterative process of manual bending of a plate by the attending surgeon to fit a 3D printed model derived from VSP. This operation is time-consuming, less effective, and lacks precision (repeatability), which can ultimately lead to sub-optimal plate shape and placement. Additionally, repeated bending might provoke metal hardening, fatigue, and reduction in the mechanical properties of the bent areas [16]. To solve these problems, the attention of medical research has focused on Additive Manufacturing (AM), better known as 3D printing, for pre-operative treatment planning. This set of techniques is commonly associated with increased freedom of design of personalized devices or device components where personalization is known to improve outcomes. Since the final form is generated, no bending is needed. However, relative to manual personalization, 3D printed personalization is significantly more expensive. Despite the expense, 3D printed plates are now the standard-of-care for many CMF surgeons whose clientele can reimburse the high cost, and most importantly, whose care can accommodate the 3 weeks to 3 months of production time. Some of the most interesting advantages of 3D printing over traditional manufacturing methods include the potential reduction in manufacturing times, and the variety of materials that can be used [17–19]. However, those cost reductions are not yet available and are not anticipated for years to come.

Future AM systems are likely to allow the design engineer to optimize mechanical properties weighing the benefits of engineered porous structures, a strategy being explored for light weighting in the automotive and aerospace industries [20, 21]. Also, relevant is the ICME approach to link the underlying properties of the material with its intended performance [22], which could be an approach to selecting appropriate materials for the demands of the patient's local anatomy. With large CMF graft fixation, such capabilities would enable the modulation of personalized skeletal reconstruction hardware to avoid bone stress shielding and/or device stress concentration. This phenomenon occurs when there is an elastic mismatch between the bone and the adjacent metallic implant, causing the transfer of biomechanical load to the implant [23]. The reconstructed tissue may heal but subsequently receives less stress than is needed to maintain the bone, leading to mass loss and possibly mechanical failure [24]. Similarly, extreme surface roughness, mismatched mechanical strength, and chemical composition of the final 3D printed part may lead to a cytotoxic and inflammatory response, as well as anticipated failure within the body [25, 26]. Moreover, the adoption of 3D printing technology must comply with fabrication standards and regulatory agency oversight, such as the FDA [27]. In addition, the limited availability and high cost of 3D metal printing limit its use at this time at most medical facilities.

It is currently considered state of the art at tertiary and quaternary care medical centers, to 3D print models of the patient's reconstructed anatomy for use as a target substrate for pre-operative manual fixation hardware bending [28]. At very few advanced quaternary referral centers, such as the Mayo Clinic, it is possible to produce 3D printed anatomic models for bending plates, 3D printed fixation trays for osseous reconstruction, and also perform real-time VSP and directly 3D print personalized Ti-6Al-4 V fixation plates for CMF reconstructive surgeries [28–30]. However, as mentioned, manual bending can be imprecise (i.e., leading to gaps with the bone), make plan screw depth planning difficult, work harden crimp points, which may lead to future fatigue failure, and be time-consuming.

The work reported by Zhang et al. has shown a workflow to use a custom robot to manually bend CMF fixation plates based on what a human would opt for [31]. The main purpose of their reported study is to robotically reshape medical titanium alloy strips in 3 Degrees Of Freedom (DOF), according to the physician's needs. Results showed an improvement in fit accuracy and pre-operative efficiency [29, 31]. Nevertheless, the method they present does not link the planning for robotic bending of a strip of metal that will become a fixation plate relative to the effect of that bending on the mechanical performance of the plate once installed. How would it respond to the chewing forces it would undergo (e.g., risk of stress shielding)? What are the biomechanical needs of the fixated bone that must transition from the healing loading pattern to one where the bone regains capability and must, once again, receive a full load in order to maintain itself long-term via standard remodeling?

Considering the vast majority of CMF fixation hardware, which is prepared by manual bending, from the perspective of industrial metal forming, one would identify a lack of flexibility and modularity to generate personalized plates with both optimal shape and mechanical performance determined via VSP. For instance, current workflows utilizing standard manufacturing processes, such as incremental sheet forming, multi-point roller-bending, and reconfigurable or rapid forming dies, allow a high degree of relatively low-cost modularity in current industrial production of customized metallic parts [32–34]. The limitations of these processes derive from the need for generic tooling geometries and the associated manufacturing costs. However, we propose to translate the advantages of these many forming processes to a feasible workflow in the

CMF fixation hardware manufacturing process that also results in optimally performing devices.

Need for an Integrated Computational Materials Engineering Strategy for CMF Fixation Hardware

Reportedly, 36–39% of hemi-mandibular graft fixation devices can be expected to fail and require revision surgery [35–37], and 8–10% of all CMF fixation plates have been observed to break [38], loosen [39], or in other ways fail during normal activities. In addition to the painful emergency caused by the unexpected failure of these devices, typical re-operation costs average $50,000 [40]. This is an example of current procedures not having sufficient (1) mechanical input into the selection of off-the-shelf devices or materials, (2) no way for the attending surgeon to visualize the mechanical performance given available choice of where to place the device, its material, or its shape, and to use their medical judgement to determine what is best for their patient, and (3) the simple limitation of manually not being able to bend a fixation plate sufficiently to achieve a flush fit to the underlying bone.

Today's options for personalized CMF reconstructive surgery by-in-large involve more a combination of art (of medicine) and surgeon experience. Such work is based more on the medical judgement than it is model-driven science [41, 42]. To go from the gold-standard manual plate bending based on prior experience with fixation devices and attempts at best-fit to an ICME approach that considers a model-based definition of design optimization, materials, and manufacturing processes, POCM would benefit from a MM and HAM workflow that includes software-driven decision-making to assist the surgeons with design and fabrication optimization. The latter would be guided via VSP software and implemented by a MM-HAM system as an approach to bring together materials and processes with novel sensing and artificial intelligence [11, 43]. That conceptual approach could begin with the design, in our test case of mandibular graft fixation, of an optimal fixation plate that could be fabricated with flexible and automated metal forming processes. This latter part mimics what an experienced artisan or surgeon might do in the OR, but because the process would be automated, it can better adhere to a device design derived from work in VSP software based on the surgeon's best judgement and rules of best practice and considering the biomechanical modeling of healing outcomes irrespective of surgical experience. In addition, by using MM to control and record the exact manufacturing sequence by means of sensors and robotic manipulation systems, the fabricated parts would better adhere to quality standards [11] (see Fig. 1).

The accuracy that can be achieved on existing robotic bending machines by integrating bending sensors to support angle correction, spring back compensation, or material thickness variation is an example that demonstrates the robustness and benefits of integrating sensor systems into metal forming processes [44]. Other sensor systems

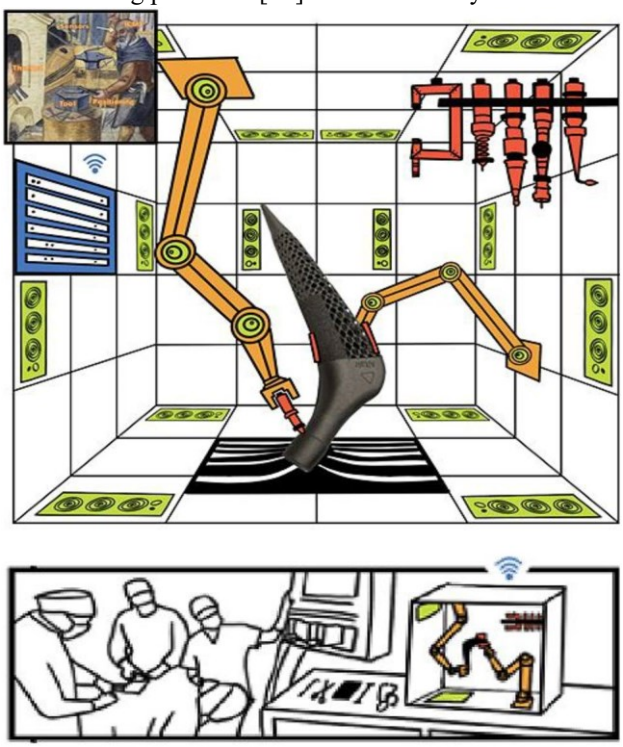

Fig. 1 Hybrid Autonomous Manufacturing (HAM): POCM of a hip implant via robotic machining with sensors (upper). Schematic of POCM HAM robots near OR (lower)

available commercially include optical, infrared, and x-ray imaging devices to measure residual stress or texture, which could be incorporated in a feedback loop with an environmental control system to achieve the desired material properties and geometry [11]. The key to these advances will be developing algorithms or procedures, likely enhanced with AI and ML, and controlling both the immediate process and the process sequence, for the automated fabrication of fixation plates, which may reduce manufacturing times, procedure cost, risk of re-operation, and near-term risk (e.g., by reducing OR time and procedure precision).

Thus, the motivation of the present work is focused on presenting a hypothetical POCM workflow that could improve the manufacture of CMF fixation hardware considering the approach of ICME, and embracing HAM and MM. In addition to workflow development, the physical challenges encountered in the hybrid (i.e., multi-method) fabrication of fixation hardware will be discussed here as a proof of concept. Finally, the challenges that the full realization of the workflow will take will be discussed. Our example will focus on mandibular graft fixation. However, the following could be quickly generalized to skeletal

reconstruction devices of many kinds and the approach to other medical device POCM.

Materials and Methods

Design of a Framework for Robotic POCM of Mandibular Graft Fixation Plates

In order to propose a workflow that considers the approach of ICME and in a VSP environment, relevant aspects related to the requirements for the design of fixation plates were obtained from close consultation with stakeholders (e.g., surgeons, manufacturing engineers, and VSP software providers). One of them was selecting strategies focused on the bone gap reduction to ensure that the plate is in close contact with the underlying bone to increase fixation stability [45, 46]. The tools envisioned for the workflow should also consider biomechanical data to choose the optimal fixation plate shape, thickness, length, footprint, and location, as well as fixation bone screw location, type, and length. All these variables play a biomechanical role in bone healing as well as the healed bone's subsequent ability to fully restore function.

The model for most commercially available services maintains confidentiality of the workflow used between obtaining a CT scan of the patient and then, presenting the fixation hardware to the physician for approval. While the physician must approve, it is not usual for them to request comparative results based on varying location, material, shape of the fixation plate or screw depth, and location. Standards used by FDA panels for these devices include ASTM F382-17. This standard establishes consistent methods to classify and define the geometric and performance characteristics of bone fixation plates [47].

With this information, we then proceeded to design a feasible workflow for the POCM of fixation plates. Here, we devised a workflow that would facilitate the local manufacture of mandibular fixation plates starting with reliable metal forming techniques and a plan to move to more sophisticated equipment that is accessible to our research group. Our workflow considers the use of (a) VSP to guarantee an implant design that is flush with the bone surface and with optimal biomechanical performance during bone healing, (b) process engineering for a stepwise ICME approach, and (c) uniform deformation strategies to reduce localized work hardening (e.g., at thinned crimp points in current off-the-shelf devices) that risk subsequent fatigue failure of the fixation plate. The closed-loop fabrication (*i.e.*, feedback between design, fabrication, and functional outcome) would be made possible by considering the above-mentioned approach of HAM and MM. Also, fabrication strategies that most efficiently reach the intended shape, while maintaining desired mechanical properties would be considered.

Results

Hypothetical Framework for Robotic POCM of Mandibular Graft Fixation Plates

Our hypothetical workflow consists of four stages, as shown in Fig. 2. The process starts with the CT scan of the region of interest and segmentation of the anatomical surfaces to be reconstructed. Then, the bone model is processed in a VSP environment as in surgery (i.e., cut, reconstructed, engrafted). In this virtual environment, it would be possible to design a personalized implant to fit the original or reconstructed anatomy. Afterward, the mechanical performance of the reconstructed, and fixated, bone graft would be computationally assessed (i.e., applying a static load) via Finite Element Analysis (FEA) and further optimized to enhance the surgical outcome. While most relevant studies consider the design of patient-specific implants and cutting guides, herein, we include the personalization of a medical device based on the mechanical requirements. Finally, the manufacturing process would be based on metal forming strategies, which would be previously validated via process engineering, to ensure personalized devices with desired mechanical properties as an outcome.

It is important to mention that in these stages we will consider the use of a quality management system (QMS) not only for the fixation plates that would be manufactured, but also for the hardware and software considered in the workflow and the manufacturing process. In this sense, design and fabrication processes would be documented to maintain their effectiveness according to the requirements of international standards, such as ISO 13485:2016 (i.e., Medical Device Good Manufacturing Practice) for medical devices [49].

Stage 1 (Patient Data Acquisition)

CT scan images of the patient's head are usually obtained and archived in the Digital Imaging and Communications in Medicine (DICOM) standard file format [50]. Several imaging techniques specific for 3D printing and VSP can be deployed to allow decreased segmentation time and CAD manipulation, such as metal artifact reduction, dual energy techniques, and bite blocks separating the maxilla and mandible. In our case, these images would be exported to Amira 3D software (Thermo Fisher Scientific, Waltham, MA, USA) for visualization, segmentation, and analysis. Here, a segmentation process would be conducted to differentiate the bone tissue from soft tissue, according to its density represented in different values of gray and the segmenter´s understanding of the anatomy. Segmentation operator precision would also be documented. It is important to note that significant inroads have been made toward automated CMF segmentation [51]. Finally, a volume reconstruction of the region of interest, the mandible in our test case, would be done and a Standard Tessellation Language (STL) file of the patient's anatomy be exported for further implant design and computational simulation.

Stage 2 (Medical Device Shape and Mechanical Personalization)

Patient-specific mandibular graft fixation would be designed in Geomagic Freeform (3D Systems, Rock Hill, SC, US) software. The software allows the detection of the mandibular surface. A generic straight fixation plate design would be used to create a bent plate that is fully in contact (flush) with the mandibular and graft surfaces. The Geomagic digital tools also facilitate a virtual surgery simulation that considers the location of the mandibular resection, geometry, and length of the bone graft during implant design. Within our conceived workflow (shown in Fig. 3), we would draw a line on the mandibular and bone-graft (i.e., osteotomy) surfaces which represents the midline of the desired fixation plate's location. Then, a series of operations would be used to create the personalized plate with the desired external dimensions (i.e., length, width, and thickness) based on the mechanical needs of the healing process as well as consideration toward not interrupting future normal loading of the healed bone. This mechanical modeling includes planning screw location and length. Finally, cutting guides would be designed. If useful, the host mandible, bone graft, screws, and implant could be exported for testing and optimization, by computational and/or in-vitro mechanical analysis, of the overall reconstruction's mechanical performance during mock chewing.

The mechanical behavior and strength of the fixation plate, fixated bone graft, and host mandible would be simulated during mastication via static FEA for two scenarios of interest: (1) during the healing period to evaluate the implant's stiffness and stability, and (2) after bone healing and muscle force restoration is complete to avoid stress shielding of that newly healed bone. To this end, it would be necessary to create a volume mesh of the 3D CT or CAD-derived components (fixation plate, host bone, screws, and bone graft), set the boundary conditions (displacement restraints and forces), material properties, establish the interaction between components and solve the model. Furthermore, preliminary mesh quality and mesh convergence studies must be performed to increase the accuracy of the FEA results. Boundary conditions simulate chewing for maximum occlusal force at the right first molar (M_1) by restraining the movement in all directions of the buccal cusps of the teeth when they are inside the two rows of upper cusps (i.e., centric occlusion). The mandibular condyles would be constrained to prevent movement as well. Each masticatory muscles' force magnitude, direction, and area of attachment would be defined according to previous work [52, 53]. However, 60% of the maximum value would

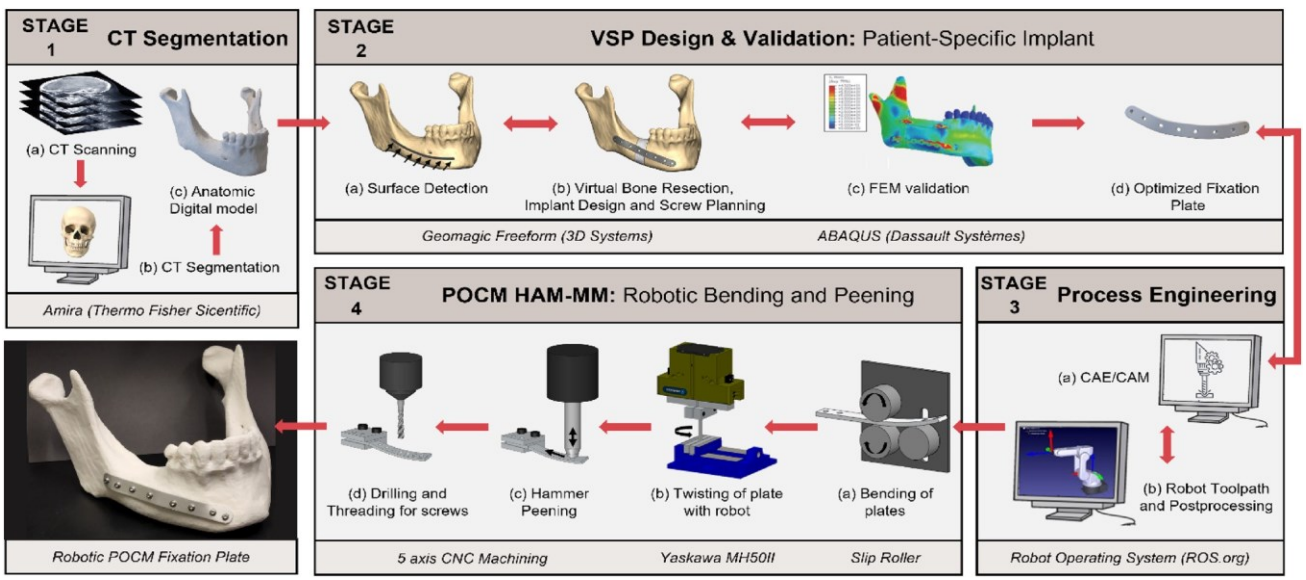

Fig. 2 Hypothetical robotic POCM workflow: Stage 1: Segmentation (identification) of patient 3D CT surfaces of interest; Stage 2: Implant Design and Mechanical Modeling: Validation of plate location, fit, and screw paths; Stage 3: Manufacturing Process Engineering coded robot toolpaths; Stage 4: Bending, Twisting, and Peening leads to a flush-fitting fixation plate. Note: Stage 2C is derived from Fig. 1 in Moghaddam NS, Skoracki, Dean D, et al. [48]

be used during the before-healing computational analysis as chewing power decreases after mandibular reconstructive surgery and is slowly regained [54].

The contact between the host bone and the graft bone would be simulated as well for two scenarios: before-healing (no union) and after-healing (union). Other authors have analyzed the pre-healing state of engrafted bone by assigning a friction coefficient of zero between components to allow free motion [55]. After computational analysis, the host bone-graft bone interface micromotion and reaction force, as well as the resulting Von-Misses stress distribution in the bone and implant, would give feedback to the plate design stage for implant optimization. With these results, it could be assured that the bone graft is in compression and the maximum micromotion value (300-400 um) is reached, both being critical for successful healing. Additionally, the stress distribution results would show the location of stress concentrations and thereby potential areas of failure to optimize (remove) in the design of the skeletal fixation plate. Thus, the process of iterative design of the plate, screw depth and location planning, and validation by mechanical testing would ensure prior to implantation that the performanceoptimized plate was obtained by the optimized POCM process. The capabilities for after-healing performance simulation of CMF fixation plates have been addressed in a related work by our group [48].

This pre-operative mechanical model of chewing could be used to interactively change the size, shape, or location of the fixation device, properties which have been demonstrated to have an impact on the reduction of stress shielding in implants [48]. These variations are all done to accomplish three things simultaneously: optimal healing outcome; post-healing lack of stress shielding; and fabrication process engineering designed to achieve both the personalized shape and mechanical function of the fixation plate. In the ideal situation, the patient's surgeon would have input into these decisions. That rarely occurs in current commercially available service workflows. When personalized plates are ordered from commercial vendors, the physician's input may be limited to approval of the device's final shape for delivery.

Stage 3 (Process Engineering)

Once the optimized design of the fixation plate is obtained, we would proceed with manufacturing planning (process engineering, see Fig. 2). At this point, the curvature ranges and twisting angles of the plate would be determined from the optimized design and mechanical simulation performed in stage 2. To fabricate the fixation plates, the deformation strategy to obtain the primary shape could be performed by roll bending. Inspired by the performance of automated and flexible metal forming techniques [56], we would apply specific deformations or twisting on the plate with a robotic system to achieve the shape determined in the previous stage.

This back-and-forth stage would also serve to validate the optimization of the fixation plate's performance and optimization of the fabrication process to produce a fixation plate with that performance. This would be accomplished by using an ICME validation model to help predict the microstructural evolution of the plate´s material based on the design variables and forming process parameters. This data would also help determine, through computational simulations of the metal forming process, the forming loads, spring back, or specialized fixturing for the available plate bending equipment. The simulation and validation of robot trajectories and forces for the fabrication of fixation plates would be translated to Robot Operating System (ROS) process controls. This would allow us to have a digital twin to validate the manufacturing of the plates obtained from the design stage.

Stage 4 (POCM: Fabrication Modalities and Sequencing for Deformation of Graft Fixation Plate)

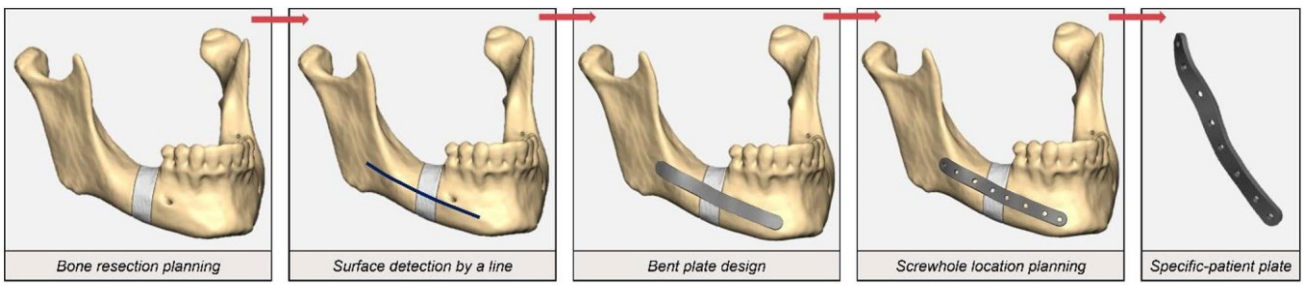

Fig. 3 Workflow for designing a patient-specific mandibular fixa- warped based on that line. Finally, the screw holes are planned. The tion plate. A line, which would be the undersurface centerline of the main purpose of the fixation plate is to hold in close contact the graft implant, is drawn over the bone surface. Next, the implant design is bone with the host mandible and to offer stability to the graft union

This stage consists of 4 sequential strategies based on a HAM-MM approach that would produce the final fixation plate to design specification and considering the forming

loads determined in the previous stage. The first step would consider bending straight plates by employing a slip roller of varying diameters according to the curvature ranges determined in the design phase. Then, the plate would be delivered to a station and fixed in a vise press, so the robotic system can apply the determined loads and angles to twist it. The final rough tuning of the surface contacting the bone (to adapt the surface of the plate to that of the mandible) would be made by peening. This operation should minimize the space between the two surfaces for proper fixation. The eyelet for fixation screws would be threaded (i.e., either standard threading or locking head threading) using 5-axis CNC machining. The location of each hole is determined by the previous VSP. In addition, air gas will be used for chip removal during the process to prevent the cutting tool or plate from cracking due to material entrapment. Finally, the ends of the plate would be cut and polished to achieve the final geometry. It is important to mention that sensory systems and control algorithms (MM approach) would be used to track the fabrication process to ensure that the plates adherence to quality standards and performance requirements identified in the VSP stage.

Discussion

The hypothetical workflow envisioned here may lead to significant challenges for designing and fabricating personalized CMF fixation plates at the point-of-care. Thanks to a brief, and still in progress, series of experiments where we used a 3D printed 2X scaled model of a jaw to exemplify the fitting of a fixation plate, we have begun to address some of the challenges that the real-world application of the proposed workflow would have to overcome. Figure 4 shows the stages of the plate fabrication process. For our demonstration case, we use a highly malleable strip of aluminum. Up to this point, we accomplished basic tasks with roll bending. Simultaneously, our work with robotic bending, peening, drilling, and threading is in progress.

Starting with VSP stage 2 for fixation plate design and fabrication planning, some of the challenges identified would be related to the iterative nature of the design and simulation software. For clinical cases with sensitive timelines, implant optimization could take considerable time. This stage also depends on the complexity of the case being handled. In addition, the computational processing required in FEA operations demands high resolution meshes for both shape and mechanical optimization of the fixation plate. Such challenges must be considered to ensure the optimized design of a plate occurs in time for the surgery.

In addition to our current workflow (Fig. 3), obstacles exist in implementing a planned fabrication procedure that would prevent removal of undesirable gaps between the fixation plate and the underlying bone (see Fig. 5). For example, one obstacle might be the quantitative assessment of the required torque to deform the plates at different angles while predicting spring back. This is especially necessary when working with materials with high stiffness, such as medical titanium or stainless-steel alloys. To achieve this, future work would address the development of an ICME model validation to predict microstructural changes during the forming process that might affect the performance of the plate, as well as computational simulation that offers a realistic environment of the manufacturing processes in our POCM workflow.

Furthermore, real-time tracking of shape evolution and mechanical properties during machining, forging, and bending will be incorporated with a camera and tactile systems as a MM approach. Indeed, kinematic sensors in the robotic manipulation arms and a relatively few points that are tracked on the evolving fixation plate should be sufficient. In this way, the desired final mechanical properties can be conserved during fabrication. Experiments are also underway to ensure a flush fit of the fixation plate to the underlying bone.

These processes will require further experimentation as the kinematic adjustment of deformation and torque control strategies for 3D contours might become too complex to initially implement during metal deformation [56–58]. Even though the goal of this effort is to manufacture, handle and

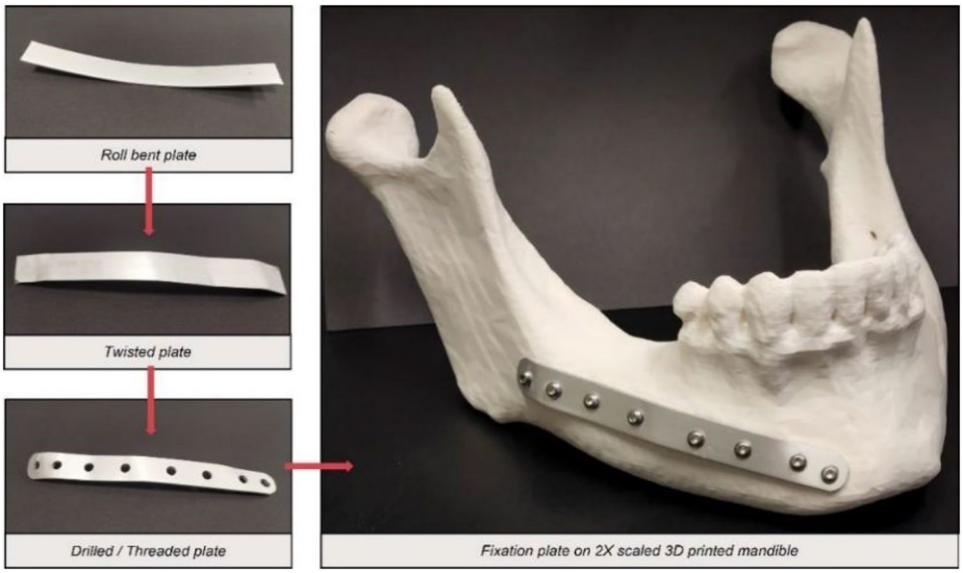

Fig. 4 Step-by-step sequence to manufacture an aluminum fixation plate. First, by means of roll bending, the deformation is done to match a preliminary shape approximating the mandible. Second, the robotic twisting is based on the angles determined in the design stage. Finally, peening, drilling, and threading will be done on the plate for bone fixation

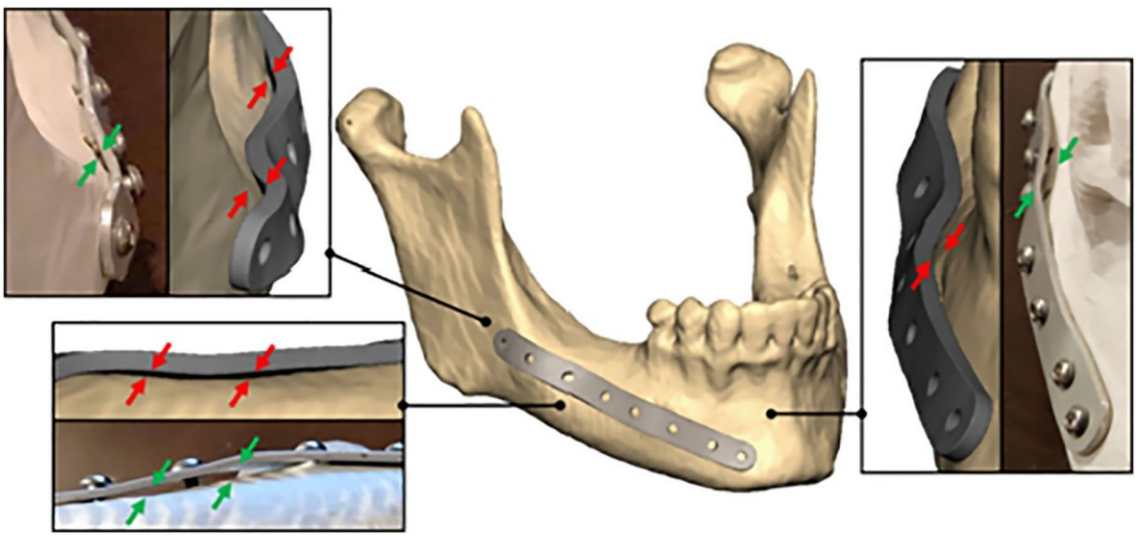

Fig. 5 Gaps between the fixation plate and host bone found in the designed and the proof-of-concept manufactured plate

deform surgical grade titanium alloy (Ti-6Al-4V) fixation plates, we used relatively plastic (easily deformable), large format, aluminum plates to test our design and manufacturing workflow. Ti alloys show higher hardness, stiffness, and strength than Al alloys. Furthermore, the deformation of Ti by a forming process can induce the development of texture deformation and changes in its mechanical properties. However, related work on cold roll bending of Ti has shown that it does not reduce the ultimate tensile stress or the hardness of the material, on the contrary, it would increase it [59]. Other work has computationally demonstrated the alteration of the stress–strain path, hence the reduction in stress-shielding, by changing the material [48], location or the geometry of the implant. To get a better understanding of the resulting properties, forces and torque that will be required for plate shaping and performance, computation and experimental studies that offer data for accurate deformation modeling (particularly in the process engineering stage 3) will be needed and demonstrated in a future study. This strategy would allow us to determine in advance the required changes to the manufacturing or fixturing process at stage 4.

Our group is developing a framework for component design and manufacturing based on a new National Science Foundation (NSF) Engineering Research Center grant on Hybrid Autonomous Manufacturing Moving from Evolution to Revolution (HAMMER) [43]. A long-term goal of the HAMMER project is to develop general rules for product and process design and execution and to extract the salient features so that they can be used with varied equipment suites to instantiate workflows such as the mandibular graft fixation design and fabrication presented in this paper. This decision-making and learning process is the essence of what human artisans do, and if this can be accomplished digitally for instance by robots, it will be an approach of reinforcement learning [60]. The designing of personalized medical devices and fabrication with a suite of computer-controlled machines would be complex but may be aided using ML and AI in stages 2–4 in our workflow. For complex open design problems that may have multiple valid solutions, appropriate AI and ML algorithms can quickly arrive at a valid fabrication solution that fulfills all design requirements [61]. As algorithms are presented with more data for learning, they may produce designs faster, require fewer computational resources, and create more generalized designs, not rigidly constrained to a single use case [12]. Understanding generalized designs may allow future creation of billets that work well in POCM systems. The use of limited design procedures for well-documented billets will allow the creation of an FDA-approvable design envelope that can be tied to well-defined, quantitative medical indications.

After the optimized design process is complete, AI and ML could also be utilized to create a manufacturing schedule and coordinate the necessary machines to produce the required design quickly and efficiently. When leveraging complex machines with several degrees of freedom, AI and ML can calculate forward kinematics and move a workpiece from initial stock, through each manufacturing process, to the final geometry [62]. Investing in the integration of AI and ML into POCM may improve the efficiency and efficacy of manufacturing personalized medical devices.

Authentication of raw materials and quality assurance of the final parts will also be a challenge for the widespread adoption of POCM. Each step will need to be accomplished under professional verification and validation (e.g., ISO 13485). For many products, quality assurance is performed on stock material and the manufacturing method is certified. By measuring the quality of stock and certifying the process, it is possible to predict quality and deliver components that meet safety and performance standards. While producing high-mix low-volume components, the necessary high variability of POCM processes used to produce each unique component will be incorporated in an FDA-approved Quality Management System.

Conclusion

The current standard-of-care practice of manual bending an off-the-shelf skeletal fixation device to fit a patient's anatomy in the OR, or a VSP-generated model usually requires multiple bending steps that are concentrated at given locations in commonly available fixation plates. The ability to smoothly curve a plate and gain a flush fit can be extremely challenging. Fatigue resistance may be compromised by excessive loading (i.e., stress concentrations) at gaps between the implant and bone, tensile residual stress at the maximum tensile region in the implant, and stress concentrations caused by kinks in bending. These factors increase the risk of failure for fixation devices in patients.

All of these problems may be minimized by the integration of an engineering approach on design, mechanical optimization based on expected performance, and an automated fabrication process. It also would be useful to provide surgeons and engineers an FDA-approved design and manufacturing environment that allows them to optimize device location, material, and shape. Thus, the objective of this work was to present a hypothetical POCM workflow that could improve the manufacturing of CMF fixation hardware considering the approach of ICME, MM, and involving HAM. This approach would also leverage MM to design a personalized device's shape simultaneously with its function and a fabrication strategy using manufacturing modalities

and device materials that can insure the output of a device with optimal shape and mechanical performance [11, 12].

The proposed workflow, which consists of CT segmentation, VSP design and validation, process engineering, and POCM fabrication, would consider biomechanical data to choose the optimal fixation plate shape, thickness, length, footprint, and location, as well as fixation bone screw location, type, and length. All these variables play a biomechanical role in bone healing as well as the healed bone's subsequent ability to fully restore function and maintain itself long-term. We envision a process that begins with an interactive VSP derived from pre-operative patient 3D CT imaged surfaces. In the future that environment would allow a comparison of various mechanical outcomes driven by FEA and the physician input on: (1) fixation plate shape, (2) materials, and (3) performance. Once optimized, a fabrication process involving multiple (hybrid) metal forming methods could leverage technology that is significantly less expensive and more easily distributed than current 3D metal printing technology. This new data-driven POCM workflow would provide physicians and engineers confidence that they were optimizing therapeutic outcomes and would begin to close the loop between VSP and patient outcomes.

In a brief and still in-progress proof-of-concept discussion, we have addressed some of the challenges that the real-world application of the proposed POCM workflow would imply, such as the need for high power computational processing for design and fabrication validation of fixation hardware for time-sensitive clinical cases. Although our workflow is focused on hardware for mandibular graft fixation, it could be quickly generalized to skeletal reconstruction devices of many types and the approach to the POCM of other types of medical devices. The POCM of personalized (i.e., shape, location, or material) fixation plates would benefit patients with rapidly emerging conditions such as skeletal reconstruction due to tumor or trauma who otherwise are unlikely to receive a personalized fixation device at most medical centers due to the need to surgically intervene in real-time.

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Declarations

Conflict of interest Four of the authors (MG, SN, GD, and DD) have filed a pending patent application on some of the subject matter of this paper.

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