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Procedia CIRP 125 (2024) 90–95

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CIRP BioM 2024

Virtual Surgical Planning for Point-of-Care Manufacturing

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Abstract

Two factors motivating the achievement of safe and effective Point-of-Care Manufacturing (POCM) are (1) to provide personalized medical devices to patients with short treatment windows (e.g., trauma, advanced stage cancer) and (2) to ensure that those devices improve outcomes and reduce revision surgery rates. In-hospital use of Virtual Surgical Planning (VSP) now commonly includes the production of surgical models and procedure guides (e.g., cutting, drilling, or placement guides and tool jigs). As this technology becomes widely available, we envision the FDA approving VSP software with tools for personalized, implantable, medical device design and POCM. Indeed, VSP for local optimization of device shape (external surfaces and internal pore geometry), placement (anatomical location), materials (via interactive simulation of postoperative device performance), and the fabrication process engineering plan can be executed in real time. This is nothing short of a paradigm shift from manual personalization of off-the-shelf devices or the factory-based fabrication of personalized medical devices. As an example of this new paradigm, we present here a hypothetical VSP pathway for the design and POCM of personalized mandibular graft fixation devices where optimized performance avoids both stress shielding-induced bone loss as well as stress concentration-induced device failure.

 Peer-review under responsibility of the scientific committee of the CIRP BioM 2024

Keywords: Biomanufacturing, Point-of-Care Manufacturing, Virtual Surgical Planning, Skeletal Fixation Device, Computer Aided Design.

1. Introduction

At this time, reconstructive skeletal, and other organ the study reported here, we focus on VSP for reconstructive restorative, surgeries are often simulated virtually (i.e., on surgery of the craniomaxillofacial (CMF) complex that computer), referred to as Virtual Surgical Planning (VSP), to obtain the target shape of tissues that are to be reconstructed. In

Peer-review under responsibility of the scientific committee of the CIRP BioM 2024 10.1016/j.procir.2024.08.016

includes the design of skeletal fixation hardware. However, commercially available surgical simulation software and services do not provide the surgeon with biomechanical properties of the post-operative anatomy (i.e., functional outcome) nor do they inform the surgeon's choice of fixation hardware geometry, material, or location. In many cases the virtually reconstructed bone is 3D printed, and fixation plates are manually bent to those models to provide optimal fit. It is known that reducing any plate-to-bone gap, so that the plate is flush to the bone, increases fixation stability.[1,2] However, beyond flush plating, predicting outcomes is left to the surgeon's experience and medical judgement. Today's personalized CMF reconstructive surgery can involve more art (of medicine) than (data-driven) science. However, if biomechanical information were available, it could be used by the surgeon to choose optimal fixation plate shape, thickness, length, footprint, and location, as well as fixation plate screw location, type, and length. All of these variables play a biomechanical role in bone healing as well as the healed bone's function and homeostasis after healing has been completed.

Nomenclature

3D three dimensional
CAD Computer Aided Design
CAE Computer Aided Engineering cGMP current good manufacturing practices CMF craniomaxillofacial
CT Computed Tomography (x-ray slice image)
FDA United States Food and Drug Administration
FEA Finite Element Analysis
FEM Finite Element Model
GPa Gigapascals
IACUC Institutional Animal Care & Use Committee
IRB Internal Review Board
LPBF Laser Powder Bed Fusion (3D printing)
NiTi nickel titanium
POCM point-of-care manufacturing
Ti64 Surgical Grade 5 titanium alloy (Ti-6Al-4V)
VSP virtual surgical planning

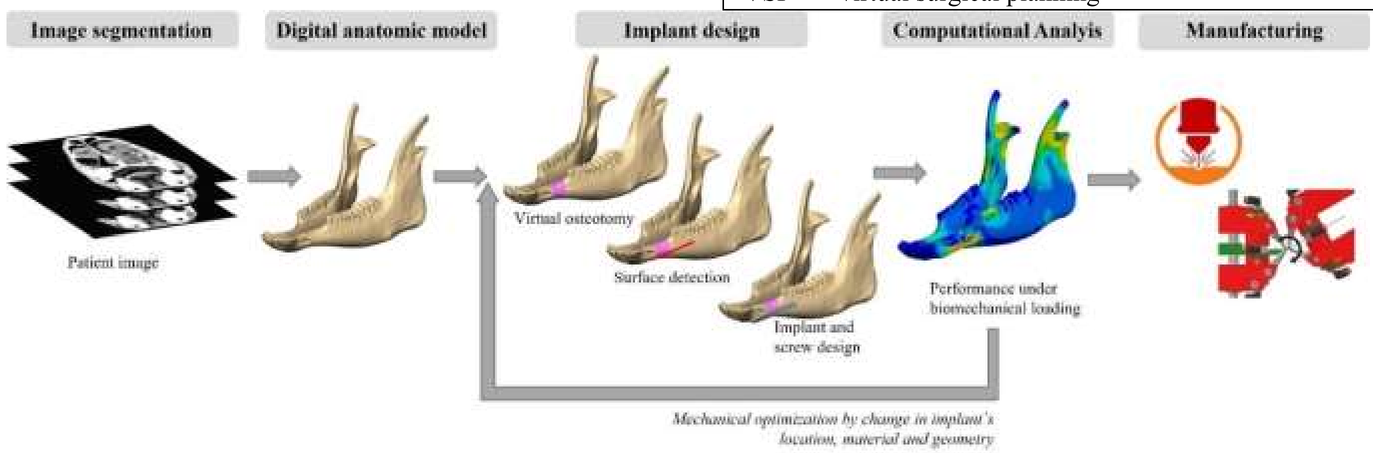
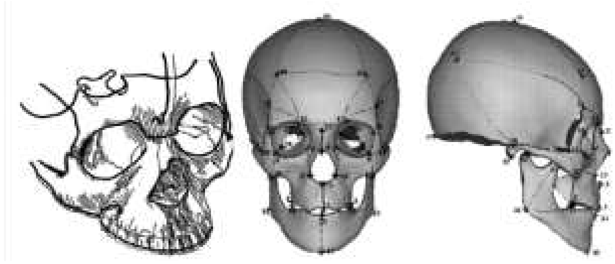


Figure 1. *Virtual Surgical Planning and Device Design Simulated in a Sheep Model*: A 3D CT scan is used to create a 3D model of a sheep mandible. Potential surgical plans and bone fixation plans are compared with biomechanical outcome (i.e., optimization reduces stress shielding of bone and reduces stress concentration in the fixation device). Fabrication process engineering (e.g., robotic plate bending [shown], 3D printing, etc.) for the manufacture of a mandibular

graft fixation device.

One deterrent to incorporating the attending surgeon's assessment of the biomechanical performance of a personalized medical device into a VSP workflow (Fig. 1) is the fact that this process, VSP, mostly occurs offline and offsite (i.e., outside the hospital). Lengthy preparation is required for headquarterbased manufacturers of personalized medical devices to follow HIPAA requirements to obtain a patient's 3D CT (Computed Tomography) scan, conduct a VSP session which is usually an online viewing of a technician's prior work designed to obtain physician approval and possibly minor requests for offline adjustment, fabricate the approved device, and ship the device. Thus workpath, not FDA-approval, is likely the cause of limiting options for device personalization. Unfortunately, many large, tertiary care medical centers do not currently utilize any of these services. With or without personalization, because there is virtually no biomechanical aspect to the planning process, high levels of mechanical failure are considered "acceptable". Failures may be attributed to medical experience and judgement or the use of overly stiff materials.[3,4] Overly stiff materials "stress concentrate" and may cause implant loosening or device failure (breakage). Because overly stiff materials collect and conduct load, formally loaded segments of bone may resorb due to stress shielding potentially leading to revision surgery. However, the lack of biomechanical information makes it impossible to avoid stress shielding or, another possibility, stress concentration. Stress concentration, especially in work-hardened "crimp" (i.e., thinned areas for plate bending) zones, may lead to device failure. Indeed, 3639% of hemi-mandibular graft fixation devices can be expected to fail and require revision surgery[5-7] with 8-10% of all CMF fixation plates having been observed to break,[8] loosen,[9] or in other ways fail during normal activities. In addition to the painful emergency caused by unexpected failure of these devices, typical re-operation costs average $50,000 in the United States.[10] While it usually takes longer to manifest than CMF fixation failure, stress shielding of hip implants commonly results in aseptic loosening. To avoid this, there have been attempts at modulating mechanical properties using



A B C

Figure 2. *Deformable Templates*: Surface curvature-mapped 3D CT images (A) are the source for our crestline and geodesic line tile wireframe deformable templates of the skull. We will fit the skull template to new patient images by matching high curvature anatomical landmarks. The average surface images (B, C) have a grid of points on each surface tile and a tetrahedral mesh for the skull which, along with the CT density data, are used to set up a biomechanical model of the skull.[12]

multimaterial devices.[11] In cases of cancer or trauma, having design and fabrication resources available at the point-of-care would facilitate personalization without delaying reconstructive surgery. By providing CMF surgeons interactive biomechanical information during point-of-care VSP, we expect to allow them to choose a graft fixation device's geometry, material, and location that avoids bone stressshielding and device-stress concentration, thereby optimizing patient outcomes.

2. Virtual Surgical Planning, Device Design, and Device Performance Simulation

2.1. Homology mapping for device design and mechanical performance modeling during virtual surgical planning (VSP)

Our approach to VSP begins with an established map of 3D CT-imaged skull surface anatomy that locates biologically homologous features in regions of high surface curvature (Fig. 2A).[12] We would then use this homology map to superimpose a normative shape as a guide to the reconstruction of a defect seen in a patient's 3D CT-based image (Fig. 2B, 2C) that may be due to trauma or cancer. These two conditions, trauma and late stage cancer, that may have a treatment window of less than a week, a difficult request for headquarters-centered professional services, possibly in different time zones or on a different continent, to accommodate. Our POC (Point-of-Care) VSP surface template breaks down the patient's 3D CT surface image into a series of homologous landmarks, crestlines, and tiles (i.e., shapes found in all normal skulls). Once mapped, osteotomies would be performed in VSP software, and 3D CTimaged bone grafts would be placed to fill segmental defects (full gaps). To ensure these grafts heal with the adjacent host bone, it would be best to form personalized CMF fixation devices. This personalization can be done by manual or robotic bending, or by 3D printing. Preoperative forming of fixation plates saves OR time bending fixation plates in the operating room during an open surgical procedure.

2.2. Performance optimization of personalized fixation hardware within VSP

A VSP biomechanical model that includes normal bone, bone grafts, fixation, and chewing forces would aid in the selection and location of fixation hardware to be personalized (bent) and provide the surgeon information that should help avoid harmful stress shielding of the bone and stress concentrations in the device. Current surgical simulation software is silent in terms of information that can help the surgeon choose a fixation strategy from among FDA-approved devices. The map described in Fig. 2 defines the anatomy of the outer surface of the skull, providing a grid of regularly spaced surface landmarks which can be used to create a tetrahedral mesh with valid mechanical properties (i.e., finite element model).[13] The assigned mechanical properties of the skull can be directly derived from 3D CT data (Fig. 2). The mechanical model of chewing seen in Fig. 3, for a sheep, is based on the same model we established for humans.[14] As

noted in that report, the estimation of force in any potent or sheep has been proven to correlate with the muscles' physiological cross sectional area. Our model of human chewing begins with segmentation of the maxilla, mandible, and the three relevant muscles of mastication (i.e., masseters, medial pterygoid, and temporalis). From this scene we extract the individual muscle vectors (i.e., direction with force of pull) based on the force parameter's known relationship to the maximum cross-sectional area of each muscle) and overall chewing strength. Based on expected loading, the finite element mesh is assigned mechanical properties and a loading model is initially generated from average biomechanical templates. The finite element model is personalized with that person's muscle vectors (i.e., direction and force magnitudes) to determine chewing strength.

Fixation of large bone grafts placed in the upper or lower jaws, such as the one shown in Fig. 3, may require 2-3.5 mm thick reconstruction bars that can be bent and cut to fit bone

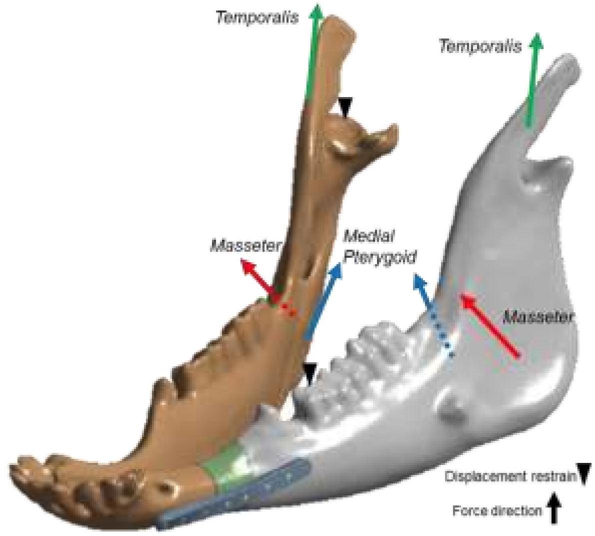
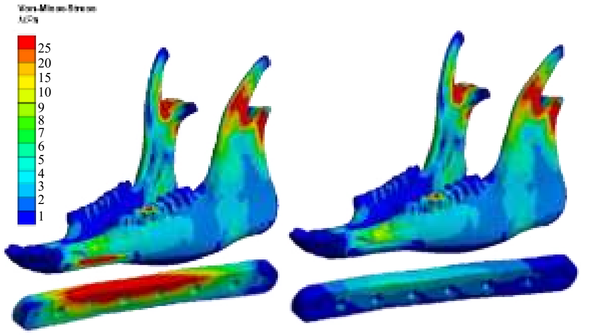


Figure 3. *Mechanical Model of the Masticatory (Chewing) Apparatus*: The maximum cross-sectional area of the three muscles of mastication and their directions of pull are used to model chewing forces in the fixation hardware and the bone.



(A) Ti64 (E=112 GPa) (B) NiTi (E=23 GPa)

Figure 4. *Fixation Hardware Material*: Above is the most common location for mandibular graft fixation (i.e., inferior border of the mandible). Ti64, Surgical Grade 5 titanium alloy, is the most common material used for skeletal reconstruction hardware. Note that in (A) much of the load is concentrated (red) in the fixation plate, effectively stealing the compressive load from the unhealed bone. That does not bode well for future load transfer from the fixation plate to the newly healed bone. A simple change to the less stiff but sufficiently strong, biocompatible, and superelastic material, NiTi in (B) places less load in the plate (green to blue) and more load in the overall unit (i.e., the reconstructed mandible, bone graft, fixation plate, and fixation screws).

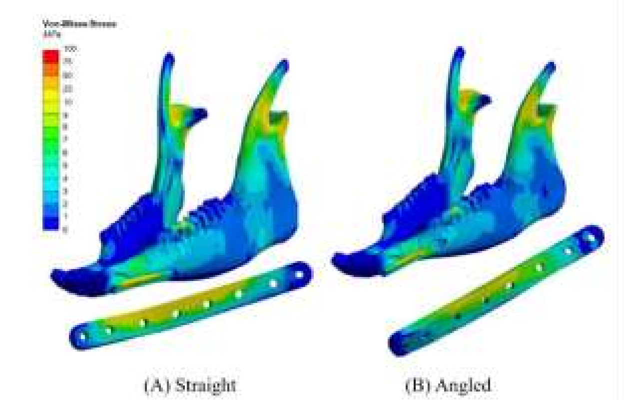


Figure 5. *Fixation Hardware Location*: These simulated fixation plates are formed from NiTi and sit on the healed bone. Note that the load in the fixation plate goes down (i.e., less yellow, more green and, especially, blue) when the plate is angled upward (superiorly) in the anterior to posterior direction (i.e., towards the molars). The overall chewing load on the whole masticatory apparatus (i.e., mandibular bone, muscles, fixation plate, and screws) is the same. However, now the load is transferred to the bone bringing about more compressive load on the grafted bone.

adjacent to, as well as over, mandibular or maxillary grafts. The screw holes may accept locking screws (i.e., threads on screw head). However, it would be helpful if one could model normal stress-strain trajectories and confirm that after healing they will be uninterrupted by CMF fixation stress concentrations.

2.3. Optimization of fixation device material

If attending surgeons could be provided biomechanical modeling of fixation plates, they would likely have the following goals:

1. Have all loading conditions, especially maximum load, result in compression of the bone osteotomies (bone cuts) between the graft and adjacent host bone.
2. Avoid or minimize interruption of the normal (posthealing) stress-strain trajectories (i.e., avoid stress shielding).
3. Avoid over-concentrating load (i.e., avoid stress concentrations) in any region of the fixation hardware that could potentially fail due to fatigue (i.e., cyclic loading) prior to load transfer to the healed bone.
4. Adjust the external shape and internal porous regions (if any) of the fixation plate to provide just enough strength and stiffness to accomplish goal #1.
5. Adjust the plate location and the screw location and depth to best accomplish goals #1 and #2 (i.e., avoid stress shielding and stress concentration).
6. Adjust the fixation plate material to ensure it is consistent with goals #1, #2, and #3.

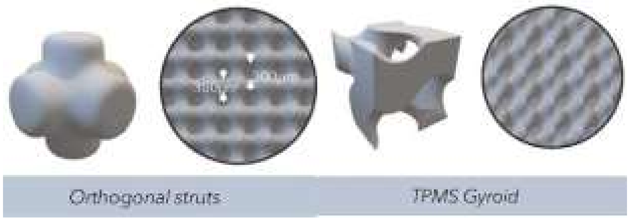
Adjustment of fixation plate material is currently limited to primarily the standard-of-care alloy Ti64 and a few other similar titanium alloys, all with a stiffness over 100 GPa. The stiffness of the strongest portions of the mandible and maxilla rarely exceeds 25 GPa and more commonly is in the range of 18-22 GPa. Our group has been studying NiTi as an alternative to the predominant titanium fixation plate alloys.[15] All that changes in Fig. 4 between the two simulations is the material. It is changed from Ti64 to NiTi. The loss of red (highest) stress concentrations in the fixation plate shows the dramatic effect that can be had by switching from a highly stiff to a more flexible material. It must also be said that our model shows that the NiTi fixation device can maintain fixation during the highest loads the device can be expected to experience.

2.4. Optimization of fixation device location

The location of the mandibular graft fixation device seen in Fig. 4 is a common choice of surgeons in the absence of mechanical analysis information. Fig. 5 shows that by tilting the plate up posteriorly (i.e., near the molars), it gains some leverage based on summed direction of the masticatory muscles and the geometry of the mandible. That leverage manifests as less load in the fixation plate and more compressive load between the host and bone graft segments. The loading regime in this and all simulations in this paper involves maximum load at M_1 (first lower left molar, note red on top of that molar in Fig. 4).[16]

2.5. Optimization of fixation device shape

The external shape of the mandibular graft fixation plate in Fig. 3-5 is basically the same as a tongue depressor or a popsicle stick with eyelets (holes) for fixation plate screws. As the load that the fixation plate increases to a high level, such as the load in the fixation plates shown here are expected to encounter, the plates can made thicker, the screw eyelets and screw heads can be threaded (i.e., “locking head screws”), and the screw heads can be countersunk into that threaded region. Off-the-shelf fixation plates provide screw eyelets at a regular pitch (i.e., inter-eyelet distance is constant). Not all eyelets must be filled with screws. The area between the eyelets is usually a thinned crimp zone, which can be manually bent to bring the plate flush to the surface of the bone. The entire plate



(A) (B)

Figure 6. *Internal Porosity*: The two pore geometries shown here represent the extremes. (A) Orthogonal (90 degree) strut intersection angle, by definition, concentrate stress at their intersection. This will make them prone to fatigue failure (i.e., cyclic loading failure). (B) TPMS (Triply Periodic Minimal Surfaces) spread curvature out uniformly, thereby reducing strut intersection angle. Schoen's gyroid algorithm also allows simultaneous modulation of strut diameter, pore diameter, and overall porosity (i.e., percent by volume of internal air space. In Schoen's gyroid the struts come together in a helical pattern at angles less than 35 degrees.[17] There also gradient and adaptive gyroids, geometries which improve control over stiffness.

is solid with mechanical properties differing most affected by the thickness of the plate.

When fixation plates are 3D printed, the location of the screw eyelets do not have to be at a regular pitch. They are usually positioned on either side of an osteotomy. Moreover, it is possible to modulate the stiffness of a 3D printed fixation plate by including internal porosity in the design of the plate. As mentioned, porosity is not currently incorporated into mandibular fixation plates, while it is available commercially in intervertebral spinal fusion cages. The smallest (highest resolution) of strut diameter and pore space diameter rendered by LPBF (laser powder bed fusion) 3D printing (metal powders) is usually 200 micron, but can easily be 300 microns, a useful dimension for these devices. When stiffness of the dense material is close to that of bone, modest changes in pore geometry and porosity will make it easier to stiffness-match the device to best serve the needs of fixation (i.e., bone healing) without the subsequent interruption of normal loading patterns.

Strut intersection angle can strongly affect stiffness. Fig. 6 shows the two opposite ends of the spectrum of pore geometries. Orthogonal struts, the highest intersection angle for isotropic struts, by definition will stress concentrate at the strut intersection. Alternatively, TPMS (Triply Periodic Minimal Surface) pore geometries spread curvature out uniformly over the porous region's surface. This is partly due to reduced strut intersection angle. In Schoen's gyroid the struts come together in a helical pattern at angles less than 35 degrees.[17] Schoen's gyroid algorithm also allows simultaneous modulation of strut diameter, pore diameter, and overall porosity (i.e., percent by volume of internal air space). There are also gradient and adaptive gyroid geometries which also can be used to improve control over stiffness.

2.6. Automated bending of off-the-shelf fixation plates

As mentioned, current workflows that send patient 3D CT data to corporate headquarters, likely multiple time zones apart, are not conducive to providing personalized 3D printed fixation devices within the 2 day to one week time windows often available to trauma patients or late stage cancer patients, respectively.

Where available, 3D printed VSP models of a desired CMF surgical reconstruction can be used as a target substrate for preoperative, manual fixation hardware bending. These models often provide better access to the surface of interest than the anatomy as seen through the surgical window. With reconstructive surgery following major trauma, a surgeon may spend hours bending plates to that VSP model, or more commonly, to the patient's exposed bony anatomy. Only at the most advanced tertiary care centers are able to design personalized CMF fixation devices and 3D print them locally. Research by our group, and funded by the NSF at the new HAMMER Engineering Research Center (website: hammer.osu.edu) aims to provide a VSP environment where surgeons could visualize the shape of fixation plates available at their institution (i.e., off-the-shelf), virtually bend and locate the fixation plate flush to the bone, and then run a real-time mechanical analysis to see if it is performing as well as their experience tells them it should or to continue modifying the fixation plate's location, shape, and material to improve the fixation plate's performance until it is judged to be optimal. Currently we are in the process of moving VSP tools we have created for use in the Amira (Thermo Fisher, Waltham, MA) to the open source 3D Slicer (website: www.slicer.org) environment. In regards to biomechanical modeling and analysis, our primary environment is Ansys (Cannonsburg, PA).

Once the simulated fixation plate's performance has been fully optimized, we proposed determining the optimal fabrication process (i.e., via a digital twin) using either LPBF or robotic fixation plate bending of commonly available offthe-shelf fixation plates. To this end the HAMMER team has created the "Bendy Bot" (Fig. 1, far right), a fixation platebending robot which is being tested for clinical utility. Another paper in this issue references our current progress on developing that prototype "Bendy Bot" system.[18] As currently configured, the Bendy Bot bends standard, off-the-shelf Ti6Al-4V fixation plates. While professional services exist, as mentioned, 3D printing is not an option at most hospitals for the local fabrication of personalized skeletal fixation devices. Were it available, clean room cGMP (current Good Manufacturing Practices) would need to be employed. We do not anticipate those types of services being widely available by 2025, but do expect they will begin to be regionally available, especially in regions with the largest populations.

3. Conclusions

This study postulates that, if available, an attending skeletal reconstruction surgeon, in this case a CMF surgeon treating patients who are to receive maxillary or mandibular grafts, would benefit from the availability of procedure planning where the biomechanical performance outcome was displayed prior to committing to a particular graft fixation strategy. If the surgeon were sufficiently informed of the biomechanical outcome, fixation device performance, and long term prognosis based on that simulated performance that avoids stress shielding-induced bone loss or stress concentration-induced device failure by achieving stiffness-matching.[19]

The performance criteria that are most critical to model are fixation plate location, shape (external and internal), and material. Once those parameters are optimized in a static mechanical modeling simulation, it would be useful to produce an optimized fabrication process via a digital twin of the effects of the fabrication process (e.g., robotic bending, LPBF 3D printing) has on the material properties of the resulting fixation plate so that it performs as simulated during the design process. Static mechanical simulation should be sufficient to model the maximum loading conditions. However, dynamic modeling would be needed to simulate cyclic loading situations that may lead to fatigue failure.

Finally, in most cases currently, manual bending of fixation plate hardware is based on the surgeon's assessment of the anatomy seen in the operating room. We envision widely available robotic bending of fixation plates (next 5 years), or LPBF printing of fixation plates, to be available to the majority of tertiary care medical centers worldwide within a 2-5 day window. We also anticipate POCM of fixation plates to become widely available in the largest urban centers. We draw the line on POCM at overnight delivery. Indeed, the POCM of medical implants is just beginning.

Acknowledgements

The authors wish to acknowledge a President's Research Excellence (PRE) Catalyst grant, titled "Hybrid Autonomous Point-of-Care Manufacturing", from The Ohio State University and a United States National Science Foundation Engineering Research Center grant (EEC-2133630), titled "Hybrid Autonomous Manufacturing: Moving from Evolution to Revolution" (https://hammer.osu.edu). Partial support was also provided by an Ohio State University James Comprehensive Cancer Center (CCC) grant for the Biomedical Device Initiative. Partial support for this project was provided by a Technology Validation Startup Fund (TVSF) Phase II grant, #TECG20170372, from the Third Frontier (Development Office), State of Ohio. Partial support for this project was provided by a grant from RegenFix, LLC (Toledo, OH). Partial support was provided by the Departments of Materials Science and Engineering and Plastic and Reconstructive Surgery, The Ohio State University.

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