Adoption and Diffusion of Disruptive Technologies: The Case of 3D Printing in the Medical Device Industry

White paper I: Opportunity Areas, Stakeholder mapping and Road Mapping

Enabling Capability Platforms
Dr Sam Tavassoli and team members
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Ethics Declaration

This report is a result of project number 21946 and was granted ethics approval by the RMIT University Human Research Ethics Committee.

Foreword

A Commonwealth Scientific and Industrial Research Organisation (CSIRO) report titled 'Medical Technologies and Pharmaceuticals Roadmap - A Roadmap for unlocking future growth opportunities for Australia' (2017) identified various opportunities for growth which can potentially add $18 billion to the Australian economy and produce about 28,000 new jobs within the next eight years. One of the opportunities for growth listed, aligning with the global megatrend of precision and personalised healthcare, was patient-specific implants enabled by 3D printing.

Australian firms and hospitals have been responsible for many world firsts in the 3D printed medical device industry, such as the world first usage of a patients' CT scan data to manufacture a custom shoulder arthrodesis plate, the 3D printed patient-specific acetabular hip reconstruction from the Royal Perth Hospital, and patient-specific heel by Anatomics. Despite these impressive innovations, there are only a handful of firms in Australia, which are active in the implant sector of the medical device industry.

This white paper investigates the opportunity areas within the 3D printed medical device industry, identifies the barriers that the industry faces and provides road-mapping to reach the opportunity areas through iterative steps. Four opportunity areas were identified: technology, material science, regulatory framework, and business models. In the second white paper, we dug deeper into business model areas. These investigations were done by collaborating with representatives from all stakeholder categories, them being surgeons, medical device manufacturers, researchers, the medical device regulations branch of the TGA, health insurers, 3D printer and software manufacturers, patients and hospitals.

The white paper is a result of a two-year project titled 'Adoption and Diffusion of Disruptive Technologies: The Case of 3D Printing in the Medical Device Industry' and was fully funded by the Enabling Capability Platforms Opportunity Fund by RMIT University. I would like to sincerely thank the following individuals for their for their support, namely Professor Calum Drummond AO, Professor Swee Mak, Alex Kingsbury (RMIT University), Andrew Batty (LCG), and all the participants in the RMIT workshops on 3D Printed medical devices during 2018 and 2019.

I would also like to thank the interdisciplinary research team for their excellent contributions which includes Professor Anne-Laure Mention, Professor Ivan Cole, Professor Pia Arenius, Professor Milan Brandt, Professor Ma Qian, Mr Aly Elghitany, Mr Leon Pope (RMIT University) Professor Olaf Diegel and Mr Babak Kianian (Lund University).

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Executive Summary

This report investigates the adoption and diffusion of 3D Printing (3DP) technology in the Australian Medical Device industry. This is done collaboratively with active stakeholders in the industry who identified barriers that inhibit the widespread adoption of medical 3DP and drafted industry roadmaps that forecast the progression of the technology in the medical space. This process has involved contributions from 55 stakeholders who participated in a workshop event hosted by RMIT on May 2018. There were a wide range of stakeholder involved, i.e. small and large manufacturers, researchers, surgeon, patients, insurers, and regulators.

3DP as a technology is considered an opportunity for growth in Australia's evolving manufacturing industry. Utilising 3DP in the medical sector shows potential benefits for patients and industry growth, however, widespread adoption and diffusion of the technology is slow. There are only a handful of firms in Australia that are active in the implant sector of the industry. This is partly due to fierce competition from overseas companies, but also market, technological, and regulatory-related barriers in the medical device industry. Such barriers are amplified by inefficient coordination between various stakeholders in the industry.This report entails the investigation of the adoption of 3DP in the Medical Device industry.
This is done by providing the following:

i. The process mapping of the medical implants, from raw materials all the way to patient implantation.
ii. Stakeholder mapping of the industry in Australia.
iii. Identifying the top four major opportunity areas, which can foster the adoption of 3DP medical devices.
iv. Developing the industry road map, in four nominated applications, by identifying the barriers in realising such four opportunity areas.
v. Recommending solutions based on the discussion and understanding of the proposed barriers that are hindering the wide spread adoption and diffusion of 3DP medical implants.

The process mapping entailed designing a process map that depicted the six overall stages involves in the process of turning a raw material into an implanted device in the patient. The six main steps are material production, powder production, collaborative powder development process, implant and design manufacturing, hospital process and manufacturing, and regulation and reimbursement process. Currently, the first three stages primarily occur outside of Australia, with the latter stages occurring in Australia once the powder and printers are imported. The purpose of stakeholder mapping is to depict how each stakeholder category affects and/or gets affected by the wider adoption and diffusion of 3D printed medical device. The types of the relationship between each stakeholder category and the ultimate goal varies, depending on their positions in the industry and their interest in the ultimate goal. Each stakeholder category can act as one or simultaneously several of the following three types:

(i) Beneficiary: that gets benefit by wider adoption and diffusion of 3D printed medical devices, i.e. SMEs, large firms, patients, surgeons, hospitals, research centres and insurer
(ii) Enhancer: that can purely support the wider adoption and diffusion of 3DP medical devices, i.e. SMEs and research centres.
(iii) Influencer: that can make both positive and negative effects on the wider adoption and diffusion of 3DP medical devices, depending to their actions, i.e. large firms, patients, surgeons, hospitals, and insurers.

The top four major opportunity areas within medical 3DP are: Material Science, Technology, Business Models, and Regulations. Within each opportunity area there are a multitude of barriers that inhibit widespread adoption of the technology. Major barriers include:

Technology	Future Developments	Barriers
Material Science	• Improved Mechanical Properties • Increased Bio-Compatibility • Cross-class (or hybrid) materials • Tissue Engineering	• Cost of developing novel materials for implantation • Regulation validation
Technology	• AI Integration • Repeatability • Computer Modelling • Advanced Surface Finishing	• Manufacturing Process & Post-process approval • Technology standardisation • Quality Control
Business Models	• Centralised and Decentralised business model viability • Just-In-Time Manufacturing	• Medical Professional Endorsement and Adoption • Staff Training (for hospital on-site printing) • Legal Liability concerns • Medical Device Reimbursement • Lack of cost Modelling
Regulations	• Custom Medical Device Regulatory Process Revision • Global Harmonisation of Regulatory Requirements	• Alternate methods of TGA validation • Absence of international technical standards for 3D Printing

By remedying these barriers, future developments could be realised, leading to superior patient-specific medical devices, streamlined healthcare and highly integrated businesses selling services worldwide. Such future development can be illustrated in industry road maps. Four industry roadmaps were drafted collaboratively together with industry stakeholders, one for each opportunity area focusing in a specific application. For material science, we developed the road map for novel biomaterials with superior mechanical and biocompatible qualities. We focused on the application of cross-class or hybrid biomaterial with a metal scaffold and a bio-active coating.

For technology, we developed the road map for super-fast metal 3D printers to increase productivity and enable implant sterilization in batches, instead of the current inefficient method of sterilising one-off devices. For business model, we developed the road map for exploring the decentralised manufacturing of medical devices on a global scale. For regulation, we developed the road map aiming toward regulatory pathways for cross-category devices. At the end of the report, we also raised remaining concerns noted by industry stakeholders to be tackled in near future in order to foster the adaption and diffusion of 3DP in medical device industry.

1. INTRODUCTION

1.1. Background

The Australian medical device industry comprises about 500 companies employing over 19,000 people [1]. The majority of the companies are small to medium sized enterprises (SMEs) with less than 20 employees and revenue of less than $2 million [2]. Australia's market for medical devices was valued around $12 billion AUD in 2016 [1]. A recent report by CSIRO shows how the industry can potentially add $18 billion to the Australian economy and create about 28,000 new jobs within the next eight years through the development of technologies that are identified as opportunities for growth [3].

One of the technologies listed are 3D Printing (3DP) orthopaedic implants, which can significantly lead to expansion of the industry. It also could provide benefits for patients. A recent Belgian report provides systematic literature review on medical, economic and legal studies of the implementation of 3D printed implants [4]. It concludes that 3D printed implants may reduce surgical complication rates, pre-operation time, hospital length of stay and total cost, however more evidence is required.

Australian medical device companies are exploring the disruptive technology of 3DP to aid surgery planning and manufacturing of orthopaedic implants. However, there are only a handful of firms in Australia that are active in the implant sector of the industry. This is partly due to fierce competition from overseas companies, but also market, technological, and regulatory-related barriers in the medical device industry.

For example, due to the Australia's low population and the highly regulated maze associated with 3D printing implantable medical devices [5], they are expensive to develop and especially difficult to commercialise in Australia. Such barriers are amplified by inefficient coordination between various stakeholders in the industry.

There is a clear need to bring various stakeholders in the industry together, as it seems people and institutions are not collaborating efficiently. For instance, an invited keynote speaker in a workshop on 30th of May at RMIT stated:

> "I think that the critical thing we need to do in Australia is to come together but everybody tries to do the same thing across the cities and we need to cognate and fill in each other on what we're doing across the country. We also need to cultivate an environment that produces entrepreneurs that are willing to take the risk to start businesses in the personalised medicine area"

Bringing a wide range of stakeholders in the industry, which sometimes have conflicting interest, can facilitate the wider adoption and diffusion of 3DP in medical devices among Australian businesses, hence leading to expansion of the industry. This can pave the way to identify opportunity areas in the industry, pin point barriers embedded in those opportunity areas, and draft a road map for variety of opportunity areas within the industry. This has not been done before and the main aim of this report is to do so.

1.2. Description of the overall project

This report is part of a bigger project which investigates the adoption of disruptive technologies and emergence of entrepreneurial opportunities by focusing on the case of 3D Printing (3DP) in the Medical Device industry, particularly in implants application.

The expected outcome of the project is a comprehensive guideline for the adoption and diffusion of implants applications of 3DP. This is done by developing solutions to remove technological, market, and regulatory barriers for both patent-specific and off-the-shelf implants.

The impact will be to unlock the potential of 3DP applications in the medical device industry, which will benefit potential new entrants to the industry, incumbent firms, health care system, and patients in Australia. It will also offer a benchmark in University-Industry collaboration via RMIT's leadership.

Project members are Dr Sam Tavassoli, Prof Pia Arenius, Prof Milan Brandt, Prof Ivan Cole, Prof Anne-Laure Mention, Prof Ma Qian, Mr Aly Elghitany and Mr Leon Pope (RMIT University), Prof Olaf Diegel and Mr Babak Kianian (Lund University, Sweden) and Mr Rob Wood (Stryker Asia Pacific).

The project runs through October 2017 to the end of 2020 and is funded through the Enabling Capability Platform Opportunity Fund at RMIT University. Internally, it is led by the Global Business Innovation ECP and is supported by Advanced Manufacturing & Fabrication ECP.

Externally, the project has Lund University as the academic partner and a variety of industry in-kind contributors, such as Stryker, OMX Solutions and Innovative Manufacturing Co-operative Research Centre (IMCRC).

Moreover, the project has also consultations from a wider range of SMEs in medical device industry in Australia, the Therapeutic Goods Administration (TGA) as the regulatory body for therapeutic goods in Australia, regulation consultants and 3DP economics experts.

The scope of the project primarily encompasses 3DP medical devices (particularly metal printing), but it also touches upon biopinting briefly.

1.3. Aim of the report

The aim of this report is to reflect the outline and preliminary findings of the newly granted project, outlined above in Section 1.2. This is done by providing the following:

- The process mapping of the medical implants, from raw materials all the way to patient implantation.
- Stakeholder mapping of the industry in Australia. This incorporates various stakeholder categories, such as manufacturers, researchers, regulatory bodies, industry associations, surgeons, patients, hospitals and medical device consultants.
- Identifying the top four major opportunity areas, which can foster the adoption of 3D printing medical devices, them being improvements in Material Science, Technology, Business Models, and Regulation.
- Developing the industry road map, in four nominated applications, by identifying the barriers in realising such four opportunity areas.
- Recommending solutions based on the discussion and understanding of the proposed barriers that are hindering the wide spread adoption and diffusion of 3-D printed medical implants.

1.4. Structure of the report

This report has seven sections, in which the first is the introduction. Section 2 provides an overview of the A-to-Z process of 3D printing of metal medical device, starting from titanium ore and showing the stakeholder interactions involved to create a device for implantation in a patient. Section 3 includes a current stakeholder map and the relationship of each stakeholder with the widespread adoption of 3D printing in medical device industry. Section 4 contains results from a major workshop that was hosted at RMIT on the 30th of May 2018.

It includes key opportunity areas where developments can be made to further the widespread adoption of 3D printing in medical device industry, as well as barriers that currently inhibit adoption and recommendations to overcome said barriers. Section 5 includes the preliminary draft of four industry roadmaps that were drafted by stakeholders the same workshop. Section 6 provides open questions and concerns about the four identifies opportunities areas and associated barriers with them. Section 7 concludes the report.

1.5. Methodology

Most of the data for the purpose of this report was collected in a major workshop held at RMIT on 30th of May 2018.
Prior to the workshop, we mapped the process of 3D Printing medical devices from A-to-Z to get the holistic understanding on the whole process and stakeholders involved. Then, we mapped various categories of stakeholders that affect (or get affected by) the adoption of 3DP medical devices in Australia. In order to do these pre-workshop activities, industry experts and researchers were consulted. The systematic stakeholder mapping of the Australian 3DP Medical Device industry has been an ongoing task and has resulted categorising members into SMEs, Large Manufacturers, Government Regulators, Industry Associations, Research Centres, Hospitals, Surgeons, Patients, Health Insurers and medical device consultants.

From the stakeholder mapping, a total of 112 representatives from all identified categories of stakeholders were invited to a one-day workshop that was held on the 30th of May. From the 112 invitations, 55 stakeholders attended and were represented as follows: 20 researchers, 14 manufacturers, 8 representatives of industry associations, 8 regulations specialists, 3 health insurance representatives 2 surgeons, and one patient.

The workshop had a morning session which started at 9:15 AM and ended at 1:30 PM and an afternoon session that went from 2:00PM until 5:00 PM.

The entire day was facilitated by Andrew Batty, an established industry consultant, who also co-developed the content of the workshop. The morning session consisted of an introduction by the project leader and 8 panellists' talks from different stakeholders, followed by a question-and-
answer discussion between the audience and 8 panellists. Each panellist had a shared theme in which they stated the benefits that 3DP brings to their patients, products or customers, followed by the barriers that they face in their sector of the industry. The goal of the morning session was to bring all attendees to a shared baseline of knowledge and instigate ideas for the afternoon session which had specific data-gathering activities.

In the afternoon session, we split the participants into 5 tables where each stakeholder category could be represented. All tables had one dedicated Dictaphone, which recorded all the discussions. This was with the consent of the participants, while keeping the anonymity. We then transcribed the discussions into the text and prepared the current report. The afternoon session content consisted of three activities.

The first activity was a roundtable discussion addressing one major question on each of the four opportunity areas.

The question for the opportunity area of Science and Materials was: “Where and how does science need to progress to improve medical device performance?”

For Technology; “What are the greatest technological challenges limiting the widespread use of 3D printing for the manufacture of medical devices?”.

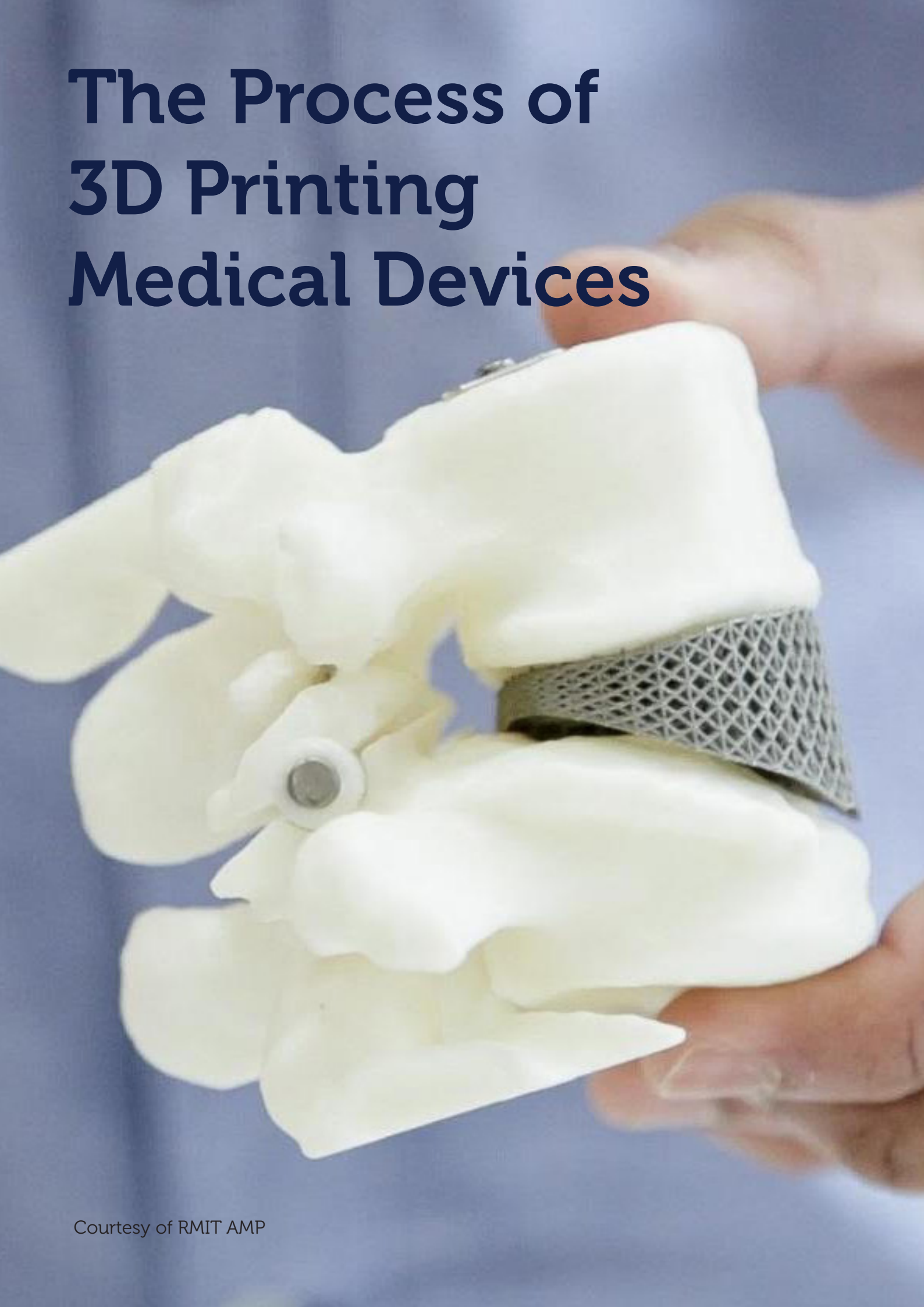
For Business Models; “As adoption increases, how do we anticipate business models changing and affecting the manufacturing of medical devices?”

And for Regulation; “What are the key regulatory and quality issues (including risk) that need to be considered and actioned to provide improved adoption and patient healthcare?”

The second activity was a survey where the most influential potential barriers to the adoption of 3DP implants in medical devise were ranked by participants. The ranking was on the basis of whether stakeholders agreed or not on what was a potential barrier. Barriers were defined as systematic blockages that inhibit the widespread adoption of a technology. Based on systematic review of scientific literature, a list of 21 potential barriers were proposed (see Section 4.2).

And finally, the third activity involved merging the participants into four tables and each table being responsible for drafting industry roadmaps in one of the opportunity areas. The objective of drafting industry roadmaps was to produce a visual, chronologically ordered guide to identify the industry drivers, identify barriers that prevent adoption and systemically suggest methods of overcoming the barriers. Before participants drafted roadmaps, they were given the definition of key terms in industry road-mapping, i.e. trends, opportunity areas, technology and capabilities, enablers and barriers in the context of the activity. Then they were provided an empty roadmap template, which had specified time-periods, with short term indicating a two year period (2018-2020), medium term (2020-2024), long term (2024-2028), and vision (2028 onward). Once a table had selected a specific opportunity area, they were asked to brainstorm industry trends, enablers, technology & capabilities and barriers and write them into the roadmap according to where they would fit in the timeline. The activity went for one hour before a representative from each table presented their roadmap to the room.

The Process of 3D Printing Medical Devices



Courtesy of RMIT AMP

2. THE PROCESS OF 3D PRINTING MEDICAL DEVICES

We designed the process map which shows the journey of raw materials all the way to patient implantation. There are six overall stages involves in the process of turning a raw material into an implanted device in the patient. Figure 1 below illustrates the six stages and their relationships. There are three main material types that are acceptable for implants (class 3 medical devices). These three material types are titanium, polymers (PEEK) and ceramics. Titanium has been regarded as the current standard for 3D printed implants, especially amongst metals. Therefore, in this report we will mainly focus on Titanium implants.

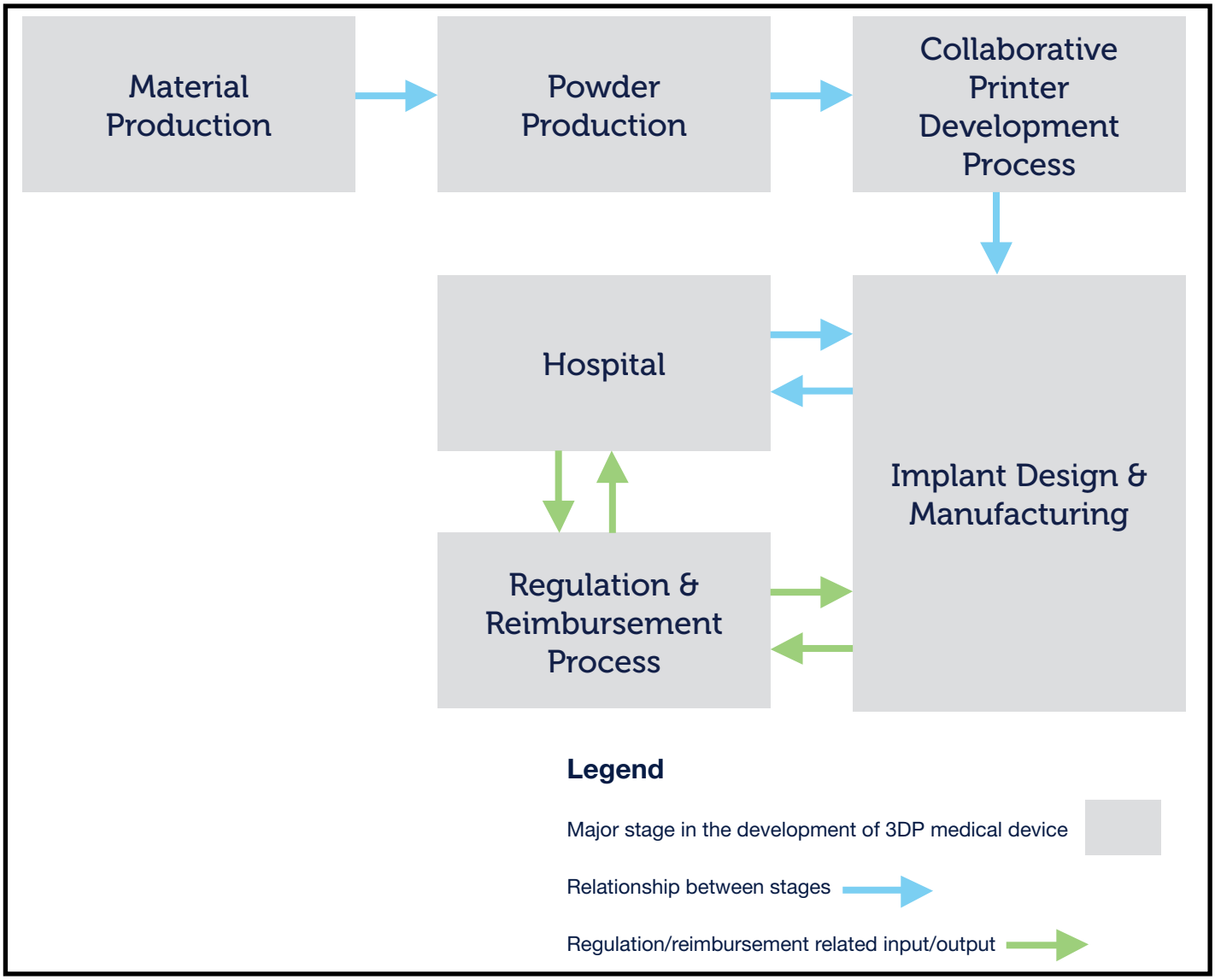


Figure 1: The Aggregate Process Map of 3D Printed Titanium Implant

Currently, the first three stages primarily occur outside of Australia, with the latter stages occurring in Australia once the powder and printers are imported.

We also dig deeper in each of the above six stages and provide detailed steps in each of the stages of the development of 3DP titanium medical devices from an Australian manufacture's perspective. This is depicted in Figure 2.

The description of each of the six overall stages and their detailed steps in the process map.

Material Production

Initially, the titanium is obtained as an ore and typically can go through numerous steps being acquisition of the titanium ore, refining the ore to a sponge and then further refining the sponge to an ingot. Commonly, the ore is refined to a sponge and then sent to powder production but conversely, the ingot stage is a subsequent stage of further refining the titanium sponge. These steps are what prelude the powder production by having the titanium prepared to be broken down into the fine particle size that 3D printers demand. However, increased adoption of 3D printing has driven powder manufacturers into optimising the sponge stage, thus reducing production costs, which is also reflected in the cost of titanium powder.

Powder Production

Once the titanium is ready to be powdered, it is then subjected to either one of three processes to break down the titanium down into a powder. These processes being mechanical breakdown and shaping, spheroidisation or atomisation. Through either process of production, the powder is refined, and the size of each particle decreases. Presently, 3D printing for medical purposes requires the quality that is given by the atomisation process, although as spheroidisation should theoretically be suitable as long as the particle sizes are consistent, and a thorough post-processing system is conducted on the printed devices. Consequently, atomisation may be bypassed with a more affordable powdering method for powder production in 3-D printed titanium implants. This stage does not apply for non-metal powders or filaments.

Collaborative Printer Development Process

After the titanium is powdered, it must be refined to the properties it needs to possess in order to perform the desired function. Alongside the reined power, the printers and their software is also optimised for numerous purposes including consistent output and to meet the product's (e.g. implant) needs. Overall, every aspect of printing is optimised to ensure the most promising outcome. The extent of collaboration between institutes varies on materials. Materials other than titanium demand more attention and time in this stage.

Implant Design & Manufacturing

Currently, the vast majority of 3D printer and titanium powder manufacturers are international, and their products are imported to local SMEs and large manufacturers. Once imported, local SMEs and large manufacturers design and produce varying aspects (or entirely) of the implant. The active role of manufacturers begins once they receive the patient's DICOM file to make the corresponding implant through numerous steps. These steps generally involve 3D file design and preparation, 3D printing, post-processing and then sterilisation. Large companies design and manufacture everything in-house mainly because of having tight control over the process. SMEs typically do not have facilities to do the manufacturing and sterilisation in-house, hence they design the CAD files and then outsource the rest to the bureaus. In this stage for ceramic and polymer-based powders, further refinement to the sought-after properties and output is also made collaboratively within local companies and research facilities. It should be noted that in this stage that manufacturers also do a quality assessment check to ensure any new product is patient ready.

Hospital Process

In parallel to the Australian manufacturers, hospitals contain some of the other key stake-holders within the supply chain. In order to have a 3D file (STL file) created for printing, a device is digitally modelled, which is based on a patient's CT scan. When the patient checks in the hospital, scanning typically takes place through computed tomography (CT). Once that they are scanned, a 3D file (DICOM file) of the body part needing the implant is rendered and can be sent to the manufacturer. The manufacturer then converts it into an STL, performs some digital pre-processing and prints the implant, which is then post-processed and sterilised. Finally, it is sent back to the hospital for surgery.

Regulation and Reimbursement Process

In Australia, the TGA is the regulatory body involved in ensuring that the manufactured implants pose minimal risk to the patient. This is performed through establishing and upholding regulatory framework in which each stakeholder in Australia complies with. This stage overarches the other stages as it shapes the outcome (through regulation) while also acting as a feedback system in detection of need for updating regulations. The TGA's two-way nature entails that it receives feedback and is in constant communication with both hospitals and manufacturers to evaluate current regulation and update it when it is required. Specifically, with the 'Implant Design and Manufacturing' stage, the manufacturers submit the new implant documentation and results (e.g. performance, failures, biocompatibility, etc.) to be evaluated and eventually approved by the TGA, if the TGA's standards are met. If a manufacturer's device achieves that approval, they can be enlisted on the Department of Health's Australasia's Register of Therapeutic Goods' (ARTG). Being enlisted on the ARTG allows eligibility for that the manufacturer to have that device reimbursed by health insurers. To be reimbursed, the device must be evaluated for eligibility for the prosthesis list. Once approved to be on the prothesis list, insurers then proceed to reimburse the manufacturer for the new device. This is illustrated in the 'Regulation and Reimbursement process' (Figure 1 and 2) which demonstrate a symbiotic and distinct relationship to the other five processes. For this reason, the regulation and reimbursement interactions are coloured green and the other stage interactions are coloured blue.

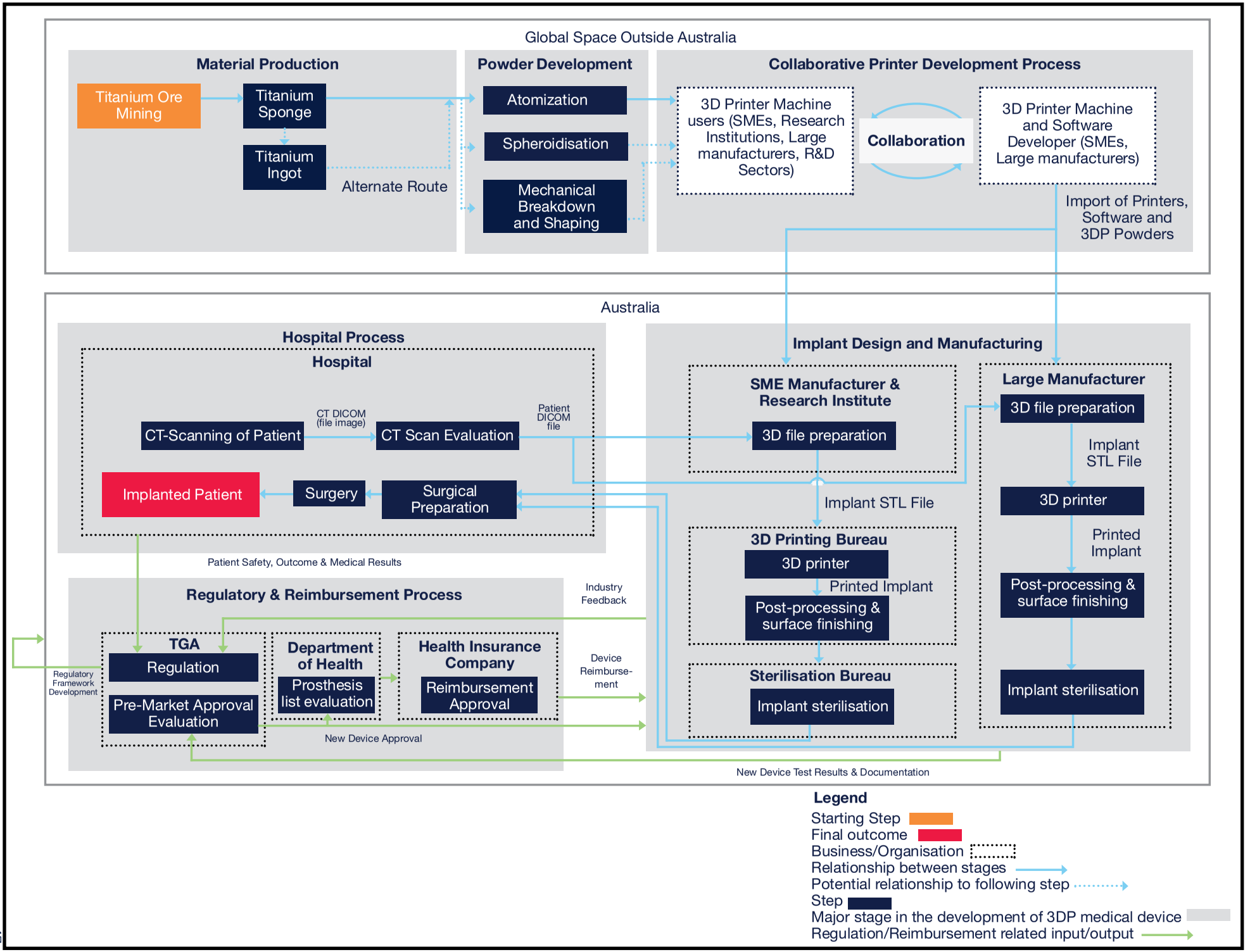


Figure 2: The Process Map of 3D Printed Titanium Implants

Stakeholder Mapping

Courtesy of RMIT AMP

3. STAKEHOLDER MAPPING

The purpose of stakeholder mapping is to show how each stakeholder category can affect (and/or get affected by) the ultimate goal of this project, which is the wider adoption and diffusion of 3D printed medical device. The types of the relationship between each stakeholder category and the ultimate goal can be different from each other, depending on their positions in the industry and their interest in the ultimate goal. Each stakeholder category can act as one or simultaneously several of the following three types. They can be:

Beneficiary — Refers to a stakeholder that gets benefit (including monetary or non monetary) by wider adoption and diffusion of 3D printed medical devices.

Enhancer — Refers to a stakeholder that can positively enhance and foster the dynamics of 3DP medical devices and support the wider adoption and diffusion of 3DP medical devices, through financial endowment, human resources or intellectual support. It is about a pure positive effect.

Influencer — Refers to a stakeholder that can make both positive and negative effects on the wider adoption and diffusion of 3DP medical devices, depending to their actions.

The stakeholder mapping is reported in the Figure 1 and the explanation of each stakeholder and their relationships with the ultimate goal of wider adoption and diffusion of 3DP medical device is explained in the following. Under each stakeholder category, the list of organizations that are currently active in Australia are reported. The list is close to be comprehensive, but not necessarily so.

Industry Associations

Enhancer — Industry associations play a supportive role by funding companies, research centres, research projects, eliminate some of the market entrance barriers for start-ups, and builds networks between companies and governmental agencies.

SMEs

Beneficiary — There are a variety of roles for SME's throughout the supply chain of 3D printed medical devices, particularly the design part of the process. A wider diffusion of 3D-printed medical devices, can naturally provide SMEs to have more market growth opportunities in this industry, particularly when it comes to export of design (we will elaborate on this when we will have decentralised business model later in the report).

Enhancer — The engagement of SMEs in R&D of 3D printed devices can increase innovation, the adoption of 3D printing in medical device industry and further diffusion of the technology. This is because SMEs usually engage in niche and costume made devices that are typically out of realm of larger firms in the industry.

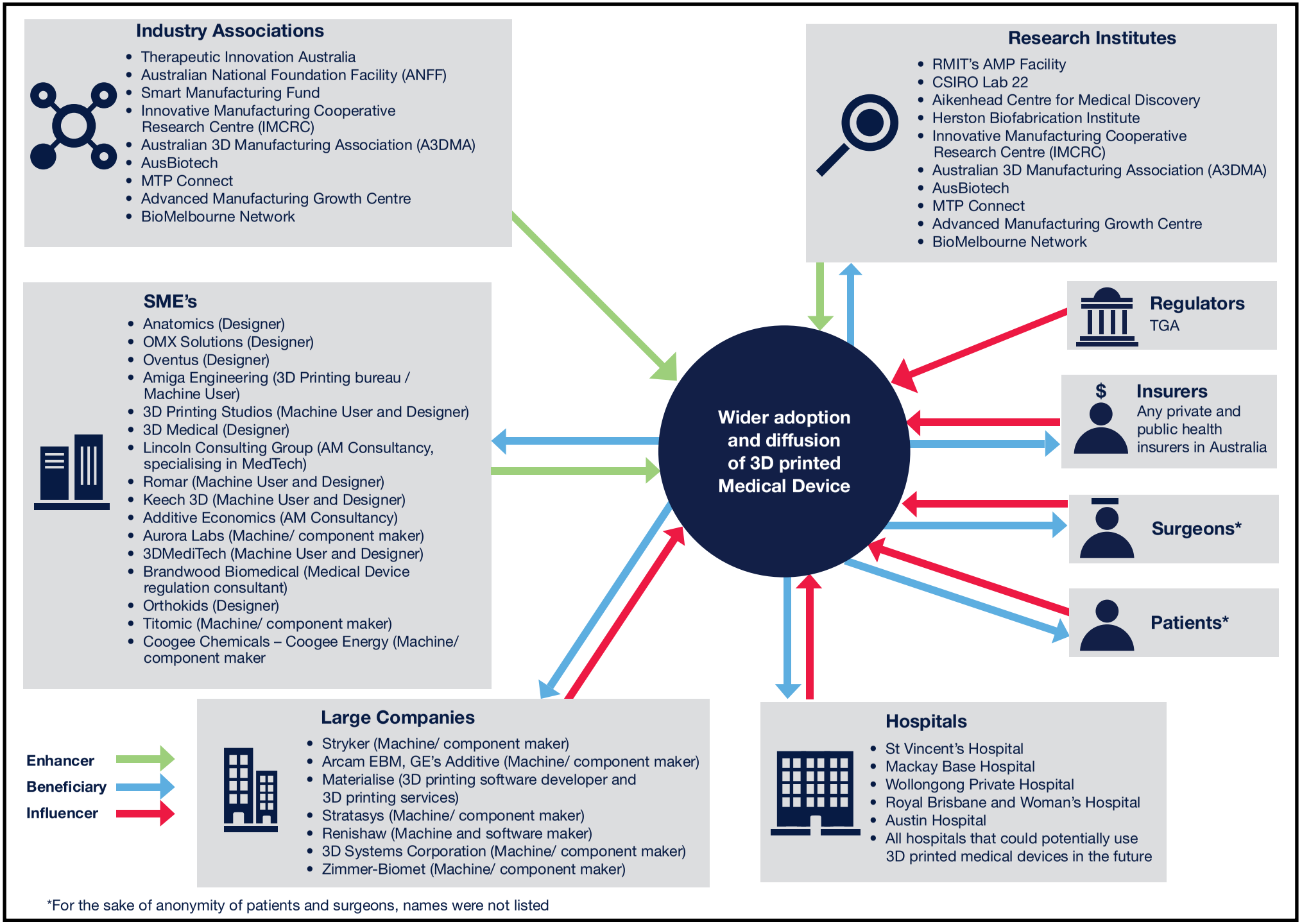


Figure 3: Stakeholder Mapping of Australia's 3DP Medical Device Indstry

Large Firms

Beneficiary

The growth of 3D printed medical devices increases demand toward large manufacturers' products. This enables broadening their business but also further investment through R&D and production and hence increasing their long-run competitiveness. They similarly have the chance to follow foreign markets, as we discussed it for SMEs, and in larger scale.

Influencer

Large firms typically undertake the heavy lifting majority of stages in supply chain of 3D printed medical devices, from design all the way to manufacturing. From patient-specific to mass-produced 3D Printed medical devices. Therefore, they can clearly drive the wider spread adoption of the innovation and expansion of the industry. On the other hand, they might impose some risks and challenges to the wider adoption of the 3D Printing medical devices by lobbying with regulators and make some barriers for SMEs market entrance. This can have negative impacts on the overall innovation of the industry.

Patient

Beneficiary

The 2018 KCE report [4] suggests a reduction of surgical complication rates, reduced pre-operation time, hospital length of stay and total cost as benefits to patients. 3D printing can also manufacture obscure medical cases such as sarcomas, which would be impossible or difficult with non-3D printing methods.

Influencer

Patient satisfaction levels are the ultimate influencer and could have both positive and negative effects on the industry. Endorsement can encourage more research, investment and production of new and innovative 3D printed implants, along with support of surgeons and insurers. Negative experiences can result in the rejection of the technology, hence lowering the pace of adoption and diffusion of the technology.

Hospitals

Beneficiary

Hospitals can benefit by providing more personalised healthcare to patients, resulting in the increase of their reputation.

Influencer

To fully take advantage of the customisation of personalised devices that 3D printing enables, hospitals will need to have some level of partnership with device designers, whether that be SMEs, large manufacturers or having a design team on-site. If hospitals do not collaborate, this could decelerate the adoption of the technology. On the other hand, if they collaborate, it leads to acceleration.

Research Centers

Enhancer

The advancement of medical 3D printing requires research and development in material sciences, 3D printing methods and industry collaboration with research centres.

Beneficiary

Since 3D printing is one the new advanced manufacturing technologies that Australia is investing in, research centres can inherit more grants and financial support (Governmental or private) for conducting research projects in the 3D printing in the industry. Findings in these areas could increase their reputation nationally and globally.

Insurers

Beneficiary

If customised devices leads to less rehabilitation time, less revisional surgeries and a reduction in hospital stay, 3D printed implants can reduce the cost for insurers and their clients who can return to the workforce faster.

Influencer

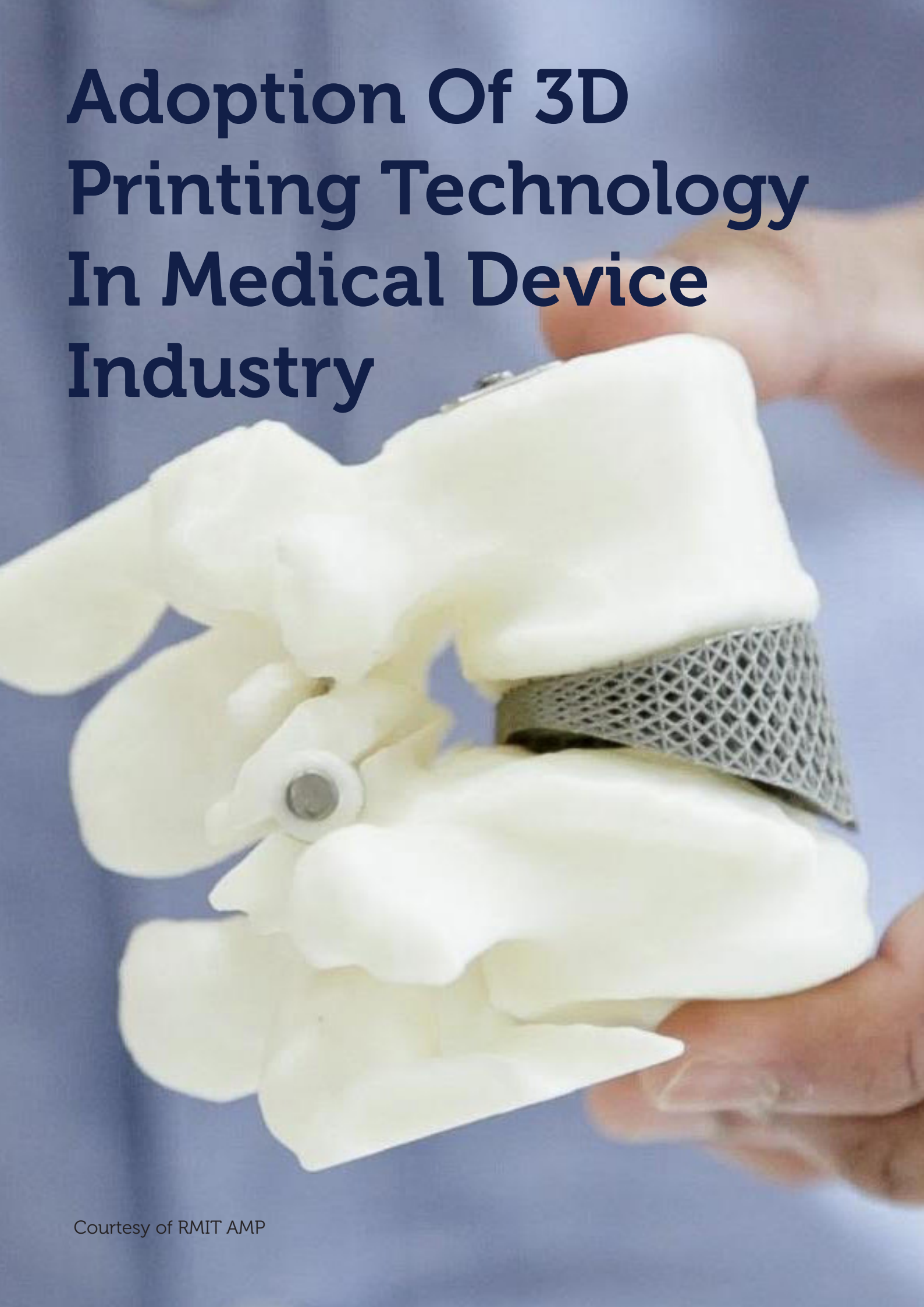
The support of insurers by considering the reimbursement of 3D printed devices and patient insurance coverage could encourage patients, device manufacturers, surgeons and hospitals to use 3D printed devices. The lack of coverage and reimbursement could also decelerate the adoption of the technology as it could reduce incentive of manufacturing the devices, leading to less clinical evidence being available.

Regulatory body (TGA)

Influencer

The regulatory framework administered by the TGA has a vital impact on the actions of implant manufacturers. If regulatory concerns that are associated with custom devices (section 4.1.4) are addressed and a clear regulatory pathway process is developed, this could motivate innovation and investment in 3D printed devices. Without this documentation, the risk involved with class III medical devices does not match the regulation protocol and could discourage investment

Adoption Of 3D Printing Technology In Medical Device Industry



Courtesy of RMIT AMP

4.1 OPPORTUNITY AREAS

The four main opportunity areas proposed for the adoption of 3DP in the medical device industry are: Material Science, Technology, Business Models, and Regulations.

Material Science

Technology

Business Models

Regulations

Each determined to be a key area in the fruition of adoption and diffusion of 3DP for medical device industry. See Figure 4 for a brief outline on how each of the following opportunity area relate to each other and the ultimate goal.

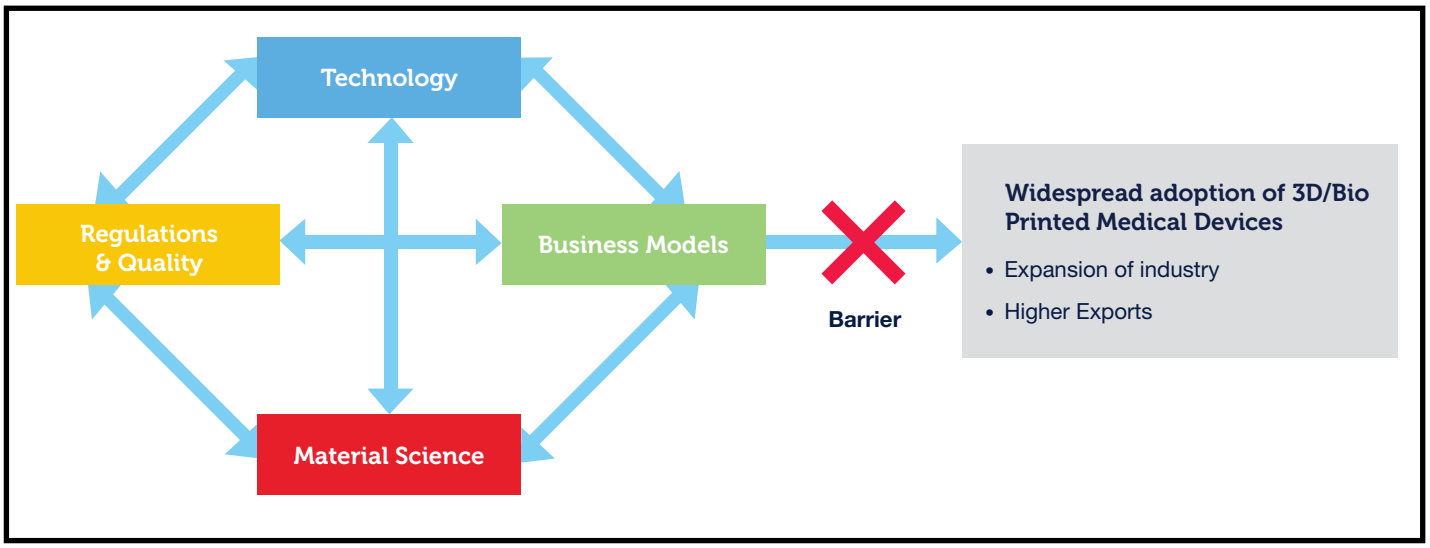


Figure 4: The relationship between opportunity areas for the outcome of widespread adoption of 3D/ Bio oprinter medical devices

4.1.1 Material Science

The ability to replicate the function of healthy human tissue is considered the “holy grail” of medical implant design. 3D printing as a technology enables the fabrication of implants with accurate, specific dimensions for the intended patient, and therefore improving a patient’s life. However, there is a constrained selection of materials that inhibits the technology’s adoption and its vast potential.

Currently, the most common materials being printed for medical implants are Ti-6Al-4V (Ti64), polycaprolactone (PCL) and polyether ether ketone (PEEK), all of which do not identically match the mechanical properties and physiological needs of human tissues and do not stimulate the recovery process for the surrounding tissues post-implantation.As stated by a participant in the afternoon session of the workshop:

> “ Ti64 is a great material for now. For another material to be considered, it must be not only having better mechanical properties, but be clinically trialled and tested, regulation certified with the cost being factored ”

Areas for Improvement in Material Sciences

The four main areas of improvements as proposed are Mechanical Properties, Bio-Compatibility, Cross-class (or hybrid) Materials, and Tissue Engineering.

• Mechanical Properties
The mechanical properties are integral to address in order to avoid stress shielding and unfamiliar strain on surrounding tissue. Mechanical properties also need to encompass fatigue cycles, torsion and other mechanical forces that an implant experiences.

• Bio-Compatibility
The biocompatibility, ensuring no adverse reactions can happen in the body. The bioactivity, which can stimulate recovery, promote osseointegration. It is not only an inert implant in the body, but also it can enhance the overall cost-effectiveness of the materials.

• Cross-class (or Hybrid) Materials
Another area to improve is 3D printing cross-class materials, for example, being able to print a titanium-alloy scaffold with a bioresorbable ceramic or polymer that is seeded with drugs that can stimulate osseointegration.

• Tissue Engineering
If the penultimate goal is to produce implants that completely replicates human tissue, a patient’s own stem-cells for tissue engineering may be the key.

Examples of Materials to be Developed

The progression from current Ti64 printed implants to future materials to be used for implants that are analogous to human tissue will not be instantaneous. Suggestions from stakeholders in the workshop included three major steps in science development that can occur, i.e. further developments in Advanced Alloys, Biodegradable Materials, and Bio-Printed Tissue.

• Advanced Alloys

To further advance the current state of material choice, it was discussed that other metals and alloys show promise and better characteristics for implantation. For example, an immediate successor to Ti64 implants could be titanium-tantalum (45%/55%) which provides a lower elastic modulus that better matches bone and therefore reducing stress shielding.

• Biodegradable Materials

The next milestone in science development could be biodegradable materials that facilitate the patient's innate rehabilitative process to construct tissue around and within the implant, eventually replacing it or providing superior osseointegration than strictly metal implants. Specific areas of development include the integration of morphogenic proteins, which promote bone growth, into biodegradable 3D printed constructs such as manganese-zinc ceramics.

• Tissue Engineering

Australia has become a hotspot for tissue engineering and regenerative medicine research. The process of tissue engineering involves seeding a patient's stem cells into a hydrogel scaffold, bioprinting the intended structure and culturing functional adult-tissue in bioreactors. Manufacturing large-scale functional human tissue with vascularisation will be a difficult task, but the potential of implanting a patients' own tissue can reduce inflammatory complications, revisional surgeries and eliminate stress-shielding to name a few of the potential benefits.

4.1.2 Technology

The opportunity area of technology concerns all equipment involved in producing a 3D printed implant. This includes CT and MRI machines, 3D scanners, 3D printers, post-processing equipment, sterilisation equipment and all software involved. Stakeholders contended that there would be a case for patient-specific devices that could be accepted by regulation if the manufacturing processes could be validated. This entails the main areas of opportunity proposed by stakeholders, which are quality control, repeatability and surface finish.

Quality Control

Entails the output of a printed device that would be acceptable to use. Real-time monitoring and AI implementation would be deterministic to ensuring high quality devices being printed

• **Real-Time Monitoring** was discussed by stakeholders as a technology related opportunity area. It was agreed that the integration of real time imaging during printing withthe application of artificial technology (A.I) to predict upcoming flaws based on what is detected in the images would minimise unacceptable devices being produced.

• **AI application** was also discussed to be implemented as quality control. With the increase of computational power and image processing techniques, application of AI now has a role it can play in the quality control for the technology-related opportunity area. It would serve the purpose of evaluating each layer for more efficient error prediction during real-time monitoring.

Repeatability

Is the capacity to consistently produce a device with the same quality. To ensure reproducibility, stake holders contended, in tandem to quality control, having strict guidelines on the manufacturing process to ensure a device can be repeatedly printed to the same quality. It was also repeated mentioned that computer modelling with performance simulations would be key to repeatable prints.

Computer Modelling

Stakeholders mentioned that computer modelling, alongside better controlled printers, would be paramount for a consistent high-quality output. With more computational power and software capacity being on offer to research institutes, universities and industries (including manufacturers), computer modelling is becoming more accurate in the prediction of an implant's performance.

Surface Finish

Surface Finish plays an integral role in the uptake of a medical implant into the body. Depending on implant type and what it is needed for, the surface properties must be made in correspondence. This includes the surface treatment (e.g. sterilisation).

4.1.3 Business Model

The business models for major actors in the industry (large firms as well as SMEs) will change in near future. Such changes are not the same for SMEs (who have niche in low-volume custom devices) and large firms (who primarily target a larger percentage of the public). Such changes in the business model for SMEs and large firms will be affected by the role that two other actors play, i.e. service bureaus and hospitals.

Centralised vs. Decentralised Manufacturing

There is a strong consensus among the participants that decentralised (distributed) manufacturing will be one of the dominant business models in the industry in near future. In its simplest form, such decentralised manufacturing can be described as a two-step process for a company. First, designing a CAD (and Print-ready) file locally, which can be done by SMEs or large firms. This is the time-consuming but less capital-intensive step. Second, sending the file to be printed close to the customer (i.e. patient). The file can be sent to a service bureau close to a hospital (where patient is waiting for an implant) or directly to the hospital. It can be sent nationally or globally to overseas locations. This is the faster but more capital intensive step, as most of the cost of the process is associated with printing and post-processing.

Such two-step process can lower the price of finished medical devices in several ways. First, it can lower logistic costs to almost zero. Second, it can lower the labour cost, if it is being made in low-labour-cost countries, like China. Third, it can also lower the energy cost, if again it is made in low-energy-cost countries. Moreover, the two-step process of decentralised manufacturing also implies a faster lead time of production, which is particularly critical in medical device industry, in which, for example, a patient is waiting for an implant. As a participant pointed out:

> "This (Two-step process of decentralised manufacturing) is especially practical for cancer patients that want custom implants. If the manufacturer is in another country, by the time it is sent overseas the cancer has spread and more bone needs to be removed than anticipated initially."

The exact implication of decentralised manufacturing depends on the size of companies. The smaller companies are naturally more prone to go for decentralised model, as they typically lack in-house printing machines. In adopting the decentralised model, they will face how they manufacture (including contracting of outsourced manufacturing) and also how they handle the cost of regulatory hurdles. The bigger companies are typically more resistant to go for decentralised business model. This is because of two reasons: first, they do not want to forfeit the existing control that they have over the centralised manufacturing of having devices manufactured in-house.

Second, decentralised model would lead to the complication on liability on a broken implant. However, large companies might be affected by competitive pricing of smaller companies that are naturally more willing to go for decentralised model and hence lower prices, even in the absence of economies of scale. Therefore, there are potential motives for large companies to go for the decentralised model too. This can be only realised if large companies can sort out the quality & control as well as liability concerns around the decentralised business model. In such case, they would not need warehouse spaces for shelved products thus would experience logistical and warehousing cost saving.

Two Types of Decentralised Manufacturing: Service Bureau-Based and Hospital-Based

One type of the decentralised manufacturing is outsourcing the printing to service bureaus which are located close to hospitals. This is crucial in most patient specific implants, as currently the cost is typically for these devices. Printing, heat treating and sterilising of one-off metal devices is not economically optimal and companies need to do these processes in batches to make them cost competitive. The report elaborated already in this type of decentralised manufacturing in the above section.

The second type is hospital-based, where the printing occurs directly in the hospital. An example of hospital based manufacturing the Just-In-Time project, by RMIT, Stryker, IMCRC, and UTS. Basically, what this project is trying to do is what the automotive industry did 20 years ago regarding business models with just in time manufacturing. The inventory previously held for implants will no longer be needed and can be printed prior to a surgery. Usually these surgeries are well planned and booked in advance, not really emergency, and therefore no need for a storage of different sized implants.

However, it is only possible to do so if a model of “cluster of hospitals” is arranged. This model is opposed to printing in individual hospitals, and rather is about having certain major hospitals that dedicatedly print certain medical devices. This is simply because of very high overheads due to lack of economies of scale in a single hospital, where it is required to have a printing process which is repeated often enough that can fill a 3D printer’s build-plate with enough parts, with enough value, that will cover the build costs and machine processing costs.

For example, a Metal 3D printing equipment is roughly $750,000 and the resources for one knee replacement might cost $6,000. The question here is: will a hospital create enough knee replacements to justify that purchase? As a participant called it:

> “If we had the economies of illness, i.e. if everyone broke their leg frequently, it would be easier to advocate 3D printers in hospitals individually. But that is not the case and we do not want that anyway”

The model of cluster of hospitals requires coordination between hospitals.

Hospital-based manufacturing model might be ideal for patients, but in the current healthcare system it is not feasible, at least for high risk devices like implants. This is due to the QMS system that will be required by the hospital and they will need to be the licensed manufacturer of the device with 3D printers, post processing and sterilizing equipment. There is also concerns about the lack of trained personal in hospitals as well as complications associated with liability of failed devices. Particularly concerning the liability, they would not be liable for the product in current regulatory framework. The liability is on the designer of the part, i.e. companies like Stryker or OMX, and they will be required to conduct post-market surveillance.

Hospital-based manufacturing is currently only suitable for low risk devices (not class 3). Having hospitals print their own anatomical models and using them for diagnosis and planning (i.e. low risk devices) is fairly doable and desirable.

For example, if an anatomical model of a patients' skull was printed, a preformed orbital floor plate can be pre-emptively moulded before surgery, simplifying the surgery, reducing the time in theatre and making it less invasive. Nevertheless, before it can be adopted in hospitals, the level of quality that anatomical models will require must be established, as well as what medical device category they fit in.

Decentralised Manufacturing Enables Globalisation of Australian Manufacturing

In principle, companies can do all of the CT imaging with patient, do the design work and then hit the send button to the bureau somewhere else across the globe. This is particularly crucial for local SMEs that typically aim for the niche market of patient-specific devices, which however, has a small market nationally in Australia. As a participant pointed out:

> "Medical cases that can benefit from personalized devices are less than 5% in Australian market, which is simply not enough to make profit". Going global, however, would require bureaus in other countries, such as China, to be up to the quality needed. So far, those countries aren't but could in the future, mainly thanks to the current movement towards the harmonisation of regulatory frameworks globally"

4.1.4 Regulatory

Regulation and innovation are vital for the development and adoption of a technology, especially in the medical device industry. However, they are not necessarily hand-in-hand. As a stakeholder mentioned: “Innovation always occurs first, then regulation follows.”

The key regulatory and quality issues that were identified by stakeholders are the revisions to the TGA’s regulatory process for custom medical devices, the Global Harmonisation of Regulatory Requirements, and the Legal Liability of the Device Manufacturer.

Revisions to TGA’s Custom Medical Device Regulatory Process

The bottom line issue is that “Regulatory processes need to be matched according to the risk associated with the medical device” (A stakeholder). Currently, high-risk class 3 medical devices such as implants can be regulated under TGA’s custom-made provisions and require no QMS certification. It was unanimously pronounced by stakeholders that this process is dangerous, with high risk devices requiring a “new intelligently structured form of approach from the beginning to allow for a way to assess and regulate a patient-specific device” (Stakeholder).

TGA has a consultation paper out for this matter, however, this is yet to be a regulation. The current method of verifying the quality of the device prior to release for supply involves testing on a statistical basis or a 100% sampling rate. For patient-specific devices, where only one or two devices are made, this will likely be impractical. During the workshop event, two recommendations were proposed by participants. They are discussed in section 4.3.4 of the report.

Global Harmonisation of Regulatory Requirements

Australia is said to be a good launchpad for medical device companies to build case studies for commercialisation, however, due to the low population, many SMEs are looking to go offshore as quickly as possible to define markets on a global scale.

3D printing utilises the strengths of digital technology, enabling the possibility for devices to be digitally designed in Australia and manufactured around the globe, if partnered with an ISO certified manufacturer.

To realise this potential, “we have to harmonise regulatory requirements (and definitions) so there is a global standard” (A stakeholder).

The TGA is currently leading an international harmonisation initiative for the definitions of personalised medical devices through chairing an International Medical Device Regulators Forum (IMDRF) working group.

Legal Liability of a Device

If a medical device is digitally designed by a company with the physical manufacturing responsibilities outsourced to a 3D printing bureau or hospital, “legal liability of the device needs to be discussed” (stakeholder) between parties and explicit contracts must be in place to outline responsibilities.

Under current legislation, the party that is liable for the device is effectively the company whose “name is on the box”. If, however, the physical manufacturer does not abide by the QMS or current ISO industry standards and/or edits the digital STL file, they could be subject to potential litigation.

4.2 GENERAL BARRIERS

In tandem with the opportunity areas, comes the barriers that pose a possible impedance into the adoption and widespread use of 3DP medical devices. Through consultation with numerous stakeholders before the workshop, a number of possible barriers were proposed and listed. We then specifically asked stakeholders to rank the barriers for wide spread adoption of 3DP implants in the medical device industry in the form of both a survey and discussion as part of the workshop (see Methodology section for details of the survey and discussion). The proposed barriers mostly fell under the four categories of the opportunity areas and therefore were material science, technology, business models and regulation. It is worth mentioning that there were some proposed barriers in the survey that did not specifically fit into one of these four opportunity areas as well as few barriers that overlapped between several opportunity areas.

The main proposed possible barriers for material science category were ‘material issues’ and ‘powder issues’. The proposed possible barriers for technology were ‘manufacturing process and post-process approval’. The proposed possible barriers for business models included ‘staff training’, ‘shifting costs from traditional manufacturing to AM’, ’hospital costs’, ‘health insurers’, ‘medical device reimbursement’, ’hospital adoption’, ‘integration of non-medical AM companies into medical device technology’ and ‘medical professional endorsement and adoption’.

The proposed possible barriers for regulatory included ‘TGA cooperation with manufacturers’ and ‘TGA regulatory requirements’. Moreover, there are two barriers that overlapped between several opportunity areas, which are ‘material regulations’ (Material Science and Regulation) and ‘device regulations (Technology and Regulation). At the end, there were also barriers that did not necessarily fall under the other categories were ‘education on AM & 3-D Printing in Universities’, ‘awareness in schools primary, secondary and tertiary)’, ‘education platform on a global gcale’ and ‘knowledge sharing between universities’.

After collecting results of the survey, the top five barriers out of the proposed twenty presented barriers have been found. The top 5 barriers that raised by stakeholders are (percentage of surveyed stakeholders is reported in the parenthesis):

- ‘Manufacturing Process and Post-Processing Approval’ (85%)
- ‘Medical Professional Endorsement and Adoption’ (85%)
- ’Medical Device Reimbursement’ (77%)
- ’Material Issues’ (73%)
- ‘Staff Training’ (73%)

Observing the top five results, roughly each one corresponds to one of the four opportunity areas discussed above and therefore is an obstacle to achieving each opportunity area.
For the entire graph of the barriers, refer to Figure 5.

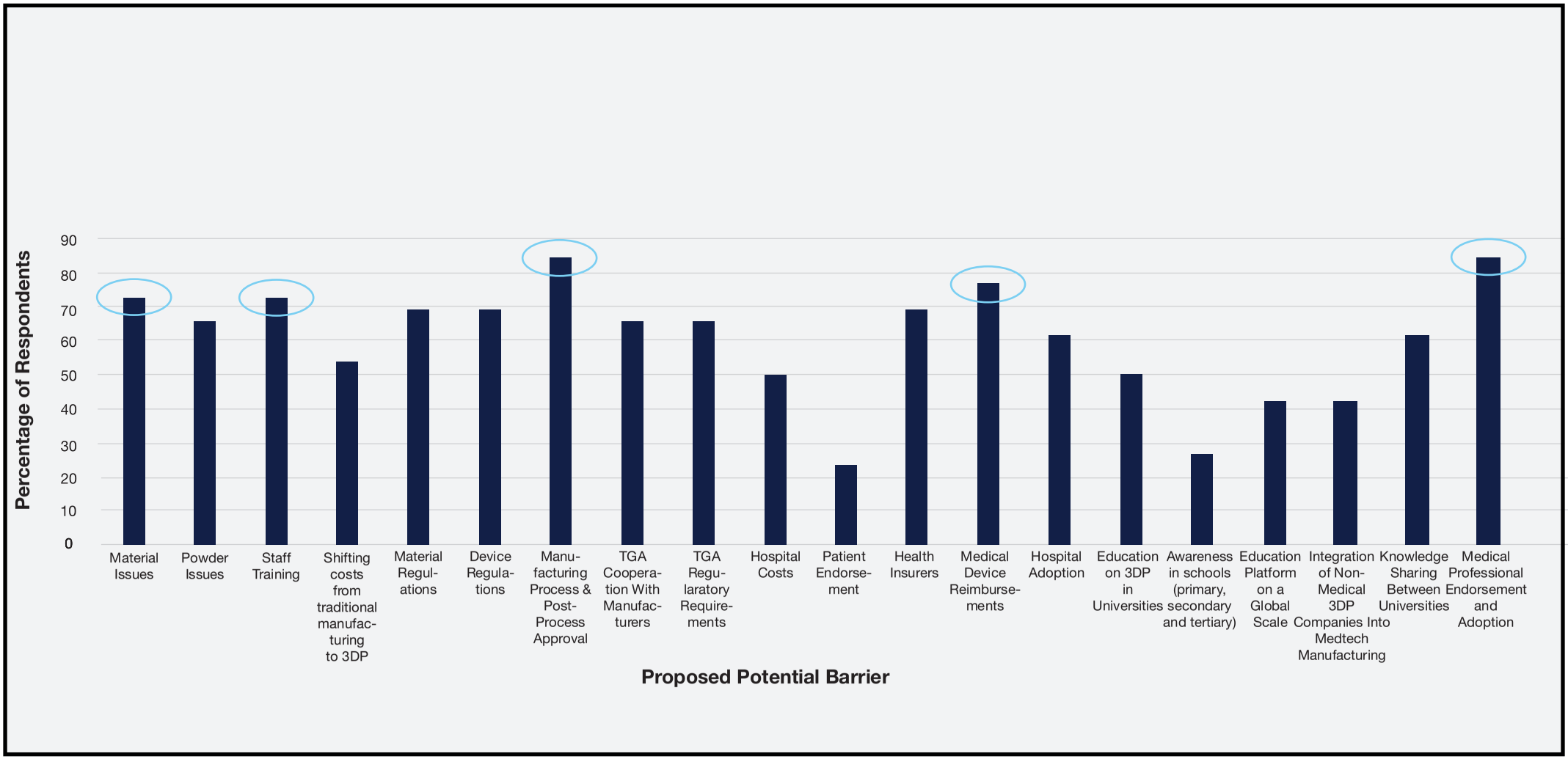


Figure 5: Agreed Upon Potential Barriers for Adoption and Diffusion of 3DP Medical Devices

4.2.1 Material Science Barriers

- ‘Material issues’ is considered as one of the top 5 barrier by stakeholders during the workshop. During the workshop’s discussion, it was mentioned that:

> “There is a huge hole in our understanding of the science of biomedical 3D printing. An RMIT study showed that the angle on which a titanium printed caused variation in outcome of cell-metal interaction. There is an underestimated biological complexity to the current understanding of 3D printing for implants”.

This reflects the **lack of full utilisation of current materials**, and hence lack of optimal results for patients.

- In addition to full utilisation of current materials, many potential materials are not being used due to cost of development and regulation validation. One stakeholder stating,

> “The process of regulating novel materials probably will not get any cheaper than the estimated 10 million (accounts for all of the studies required)

Moreover, the costs involved in conducting the necessary studies to satisfy ISO 10993 (Biological evaluation of medical devices) for an implantable material and submit an FDA/ TGA master file is deemed to be the most immediate barrier. As another stakeholder noted:

> “Developing a novel biomaterial in the lab might be feasible but making a biomaterial for clinical use is not as simple. The studies required for the regulation process will, on average, take 10 years and 100 million dollars

4.2.2 Technology Barriers

- 'Manufacturing Process & Post-Process Approval' is considered as **the most prevalent barrier** for adoption and diffusion of 3DP medical devices. This is clearly a technology-related barrier.

- 'Manufacturing Process & Post-Process Approval' entails quality control, repeatability, validation and surface finish (as elaborated in section 4.1.2). Quality control involves the concern of outputting a printed device that would be acceptable to use. Repeatability was the ability to reproduce a device and its quality. Surface finish is how the produced device has its surface prepared for application and implantation.

Quality Control

The foremost concern of stakeholders had regarding the technology opportunity areas was quality control and alongside the raised concerns were the proposed solutions.

- **Local heat shrinkage**
  During the printing of devices, heat warping occurs, and it causes local temperature differentials that cause shrinking in that locality. That local heat shrinkage (i.e. distortion threatens the mechanical integrity of the printed device and therefore the quality.

  Reproducibility has been discussed as a major barrier due the fact that there needs to be assurance that each device made will be upheld to the same quality. This is ultimately for safety reasons and therefore why regulatory bodies would demand manufacturers have guaranteed reproducible devices.

Surface Finish plays an integral role in the uptake of a medical implant into the body.

> "Depending on the application of the device, a rough surface finish might be advantageous as bone and other tissues can integrate with the device. Having methods of creating smooth and rough surface finishes enables diversity in device design." (Stakeholder)

This can include areas of high roughness and porosity for increased tissue attachment or smooth surfaces to reduce wear in joint applications.

- **Surface evaluation**
  Stakeholders have expressed the current level of resolution of CT scans, which are used to scan surfaces of a printed device, are not sufficient and "not economically viable in the long term".

- **Changes to traditional manufacturing techniques**
  Another issue raised regarding surface finish is that not all surface finishing techniques ar applicable to new structures made with 3D printing. For example, stakeholder said "Ethylene oxide sterilization might not be suitable for lattice structures due to residuals potentially being present in the lattice, causing cytosis or a carcinogenic effect in surrounding tissues". This signifies even though the desired surface finish may be achieved, other post-processing methods may have to be modified.

4.2.3 Business Model Barriers

- Both ‘Medical Professional Endorsement and Adoption’ (85% and as high as Manufacturing Process & Approval) and ‘Staff Training’ (73%), which are on the top five barriers (number two and five respec tively), are the business-related barriers.

- During the discussion in the afternoon, it was specifically expressed that out of all medical professionals, it is the surgeon’s willingness to adopt that is paramount. A surgeon’s input plays an important role in hospitals adopting on-site 3D printing as they are responsible for the implantation of the device into the patient.

- The other top barrier candidate, ‘Staff Training’, was discussed to be a key factor in the hospital on-site printing. Since liability and quality assurance was a concern, whomever is printing must be fully competent.

- This also ties in with a frequently mentioned barrier discussed, which was the issue of liability. If hospitals are to print on-site in the future, the question of “who is liable? The surgeon, hospital or part designer?” was raised. Different stake-holders contended different nominees are responsible if a 3D printed implant was to fail.

- ‘Medical device reimbursement’ came ranked third place with 77% contending it needs to be addressed. For manu-facturers, developing custom-made devices can be expensive due to the manufacturing and engineering costs that are specific to one device. “Sterilisation cost is also enormous, as you pay for the entire volume of the machine and if you cannot sterilise multiple devices at once, each sterilisation process is $5000.” There is limited financial incentive to design, manufacture and go through the regulation process for a novel device that will be produced in low volume. Making healthcare affordable for patients, device manufacturers and health insurers is one of the major challenges. The costs saved through the reduction in rehabilitation time and hospital stay must be a factor when evaluating the reimbursement of a medical device.

4.2.4 Regulation Barriers

Revisions to TGA's Custom Made Medical Device Regulatory Process

As mentioned in 4.1.4, regulatory processes need to be matched with the risk associated with the medical device.

> " High-risk products cannot be exempt under the current [custom made exemption] loophole (Stakeholder) "

In addition to this major barrier, the current method of regulating a custom-made device via the Australian Regulatory Guidelines for Medical Devices (ARGMD) is also not ideal. As a stakeholder identified:

> " Custom devices are mostly unique, with limited testing, most of which is virtual or simple mechanical tests, not fatigue testing. Traditionally manufactured implants undergo rigorous pre-market assessment evaluation. "

Stakeholders mentioned that there needs to be alternate methods of TGA validation for custom made devices that are produced in low-volume.

In addition to verifying the manufacturing technique, a new method of verifying clinical outcomes of the patient must also be established. The current gold standard is randomised trials, however, that is not suitable for devices which are personalised and yield different results.

Global Harmonisation of Regulatory Requirements

Stakeholders identified that to achieve the global harmonisation of regulatory requirements, definitions of patient specific, personalised and custom-made medical devices must be unified. The TGA is currently leading an international harmonisation initiative for the definitions of personalised medical devices through chairing an International Medical Device Regulators Forum (IMDRF) working group.

Another barrier encountered is the current absence of international technical standards including device evaluation methods, printing processes and materials. The American Society for Testing and Materials is currently investigating 3DP standards.

In a 2010 published paper [6], additional barriers to medical device regulatory harmonisation included:

- Differing regulatory capacity, expertise, infrastructure and finance.
- Government restrictions regarding subsidy reduction.
- Difficulties for stakeholders to reach consensus on harmonisation efforts.
- Countries having long established regulatory systems which are difficult to change.

The differing regulatory capacity between international regulatory bodies is a major barrier to global harmonisation as systems that are applicable for large regulatory bodies with more resources, might not be suitable for smaller bodies. An example of this is the difference between the FDA who have an estimated 1827 full-time employees in the medical devices and radiological health branch [7] compared to the "TGA's medical device branch [who] have about 100 people"(A stakeholder).

4.3 RECOMMENDATIONS FOR ADOPTION & DIFFUSION OF 3DP MEDICAL DEVICES

Based on the workshop's afternoon discussions, in this section, we raise several recommendations, in each of the opportunity areas elaborated above, to remove or remedy barriers and hence foster wider adoption and diffusion of 3DP medical devices.

4.3.1 Material Science

- As noted in the Barriers section, a major barrier concerning the material science is indeed the cost of the development and regulation of a new material. In this regard, one suggestion is to fast-track the regulation process by working with regulatory bodies' right from the beginning of the required studies. This is being initiated by CSIRO's Biomedical Materials Translational Facility (BMTF) which aims to help medical device companies develop their product at pilot scale. Overall this will save a minor amount of money as material science studies will still need to be conducted, however it could save SMEs time in their product design phase.

- Moreover, to incentivise material science development, government and industry associations need to continue to make grants (specifically targeted grants) in additive manufacturing and overcome the costs involved with material regulation, which is a clear burden for SMEs and even larger firms.

- Another major barrier concerning material science is material properties required for optimal results in patients. In this regard, it is recommended to target for the Biodegradable 3D Print-ready Materials. In order to adopt biodegradable 3D printed implants, there needs to be studies on what mechanical properties are needed for the 3D printing process and degradation studies to show a degradation rate equal to patient tissue integration and generation.

4.3.2 Technology

Quality Control

- **Utilising Electron Beam Printing**
  Titanium, the current implant material of choice, can be printed with "essentially zero" distortion when an electron beam printer is used to print it. It was stated by a stakeholder that "electron beam printers are what are used for metal printing as opposed to laser printing for this reason". Implementation of Electron Beam Printing for metal implants.

- **Real-time monitoring**
  It was agreed that the integration of real time imaging during printing with the application of artificial technology (A.I) to predict upcoming flaws based on what is detected in the images would minimise unacceptable devices being produced.

- **AI monitoring error prediction**
  It was cited that real-time AI monitoring during the printing process could compliment the "current (evaluation) procedures which use a CT scan to verify device dimensions before use". AI monitorisation could also be programmed proactively, to adjust printer parameters in real time in response to any irregularities that might occur. This could improve quality control during the printing process, saving money and time.

- **Alternative surface evaluation strategies**
  Alternative methods to CT scanning are laser-based surface evaluations. Researchers are also currently exploring various optical methods to better image the surface of a printed device.

Reproducibility

To ensure reproducibility, stakeholders proposed addressing quality control as that is one of the root factors of this barrier. Stakeholders also contended, in tandem to quality control, having strict guidelines on the manufacturing process to ensure a device can be repeatedly printed to the same quality.

- **Computer modelling**
  Computer modelling, alongside better controlled printers, would be paramount for a consistent high-quality output. More consideration into digital models of an implant was proposed by stakeholders to compensate for lack of large testing numbers needed as part of the validation process. Given the patient specific implants, being only one made in a batch (instead of scores in traditional manufacturing), computer modelled life cycle, fatigue, mechanical testing, etc., would be a counter offer to the regulatory bodies for quality assurance.

- **General upkeep**
  The final point contended for ensuring reproducibility was general diligence of using the same materials (e.g. powder quality), consistent printer maintenance and servicing.

4.3.3 Business Model

Decentralised manufacturing is the future. Decentralised manufacturing will be one of the dominate business model in the industry that will affect both small and large firms. It can be realised in two types: service bureaus-based and hospital-based. The former is the short terms pathway and the latter can be potentially the long-term pathway.

Decentralised service bureau-based manufacturing. Considering the decentralised service bureau-based manufacturing, the following business model seems to be superior, mainly for SMEs, but also for larger firms:

- First, design the Print-ready file in-house.
- Second, identify certified printing service bureaus nationally and globally. Such service bureaus typically provide the validation, quality control, and packaging. These service bureaus should be located close to "hot spot" of customers (e.g. patients in major hospitals).
- Third, pair with them either through ownership, partnership, or contracting, depending on the size of the focal medical device provider company.
- Fourth, simply send the design to the nearest bureau and print it near target location.

Decentralised service hospital-based manufacturing. If in the long run businesses are aiming for hospital-based manufacturing, then barriers such as hospital staff training and legal liability must be addressed.

Legal Liability of a Device. Other liability issues can arise when the device design is based on a CT or MRI scan of a patient, as defective scans must be considered. If device designers, manufacturers, doctors or hospitals are concerned, indemnification documents should be discussed and agreed upon between various stakeholders along the supply chain.

Having a universal framework of a device. In pursuing the decentralized model and keeping the design in-house, having a universal framework of a device is very important. Such framework then can be printed for customization, which alleviates the necessity of storing many types of the same part per implant. Much of the regulatory process stays the same, so it is easily integrated into the current healthcare system.

Sometimes Centralized business model is the way to go. It means having manufacturing in-house, which is mostly practiced by larger firms but also can be potentially pursued by SMEs. Specially for SMEs, it should be pursued only if having it creates, or enables, value, which go beyond financial matters and includes intangibles values such as: knowledge & knowhow (trade secret for example), enables to capture new opportunities or create a unique value proposition to clients. If no such intangible values are created through adoption, then outsourcing and decentralised manufacturing will most likely be the better course of action for companies.

SMEs target. For SMEs, rather than aiming to grow into large businesses, they should shift from the micro to the medium scale operating within niche markets that supply multinational organizations as well as being exporters in their own right, maintaining their agility and adaptability. This will allow Australian SMEs to continually meet customer demands.

Consideration for Insurers. Insurers are currently hesitant in covering patient-specific implants. They demand further evidence of the reliability of the device. A circuit breaker will be surgeons seeing the potential of the technology and how it can benefit the patients, then conducting independent trials. It does not need to be in Australia. Moreover, insurers need to look at the costs saved more holistically, e.g. rehabilitation time and hospital stay reduction.

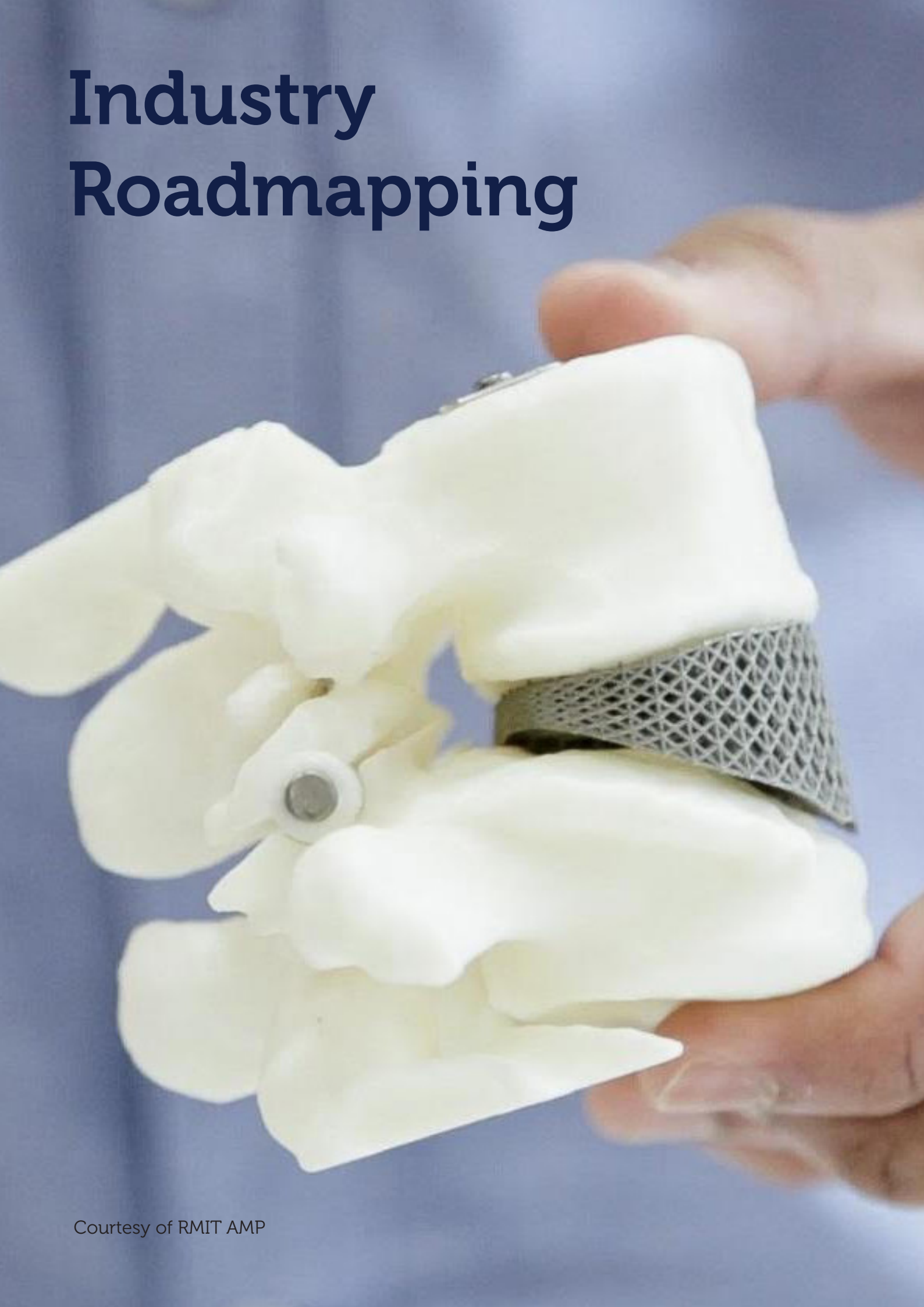
4.3.4 Regulation Barriers

To overcome the impractical method of statistical testing for low-volume produced custom devices, two recommendations were made by stakeholders; embracing long-term post-market follow up registries and regulating the manufacturing process.

Post-market follow up registries. One suggested method of device validation is to embrace a long-term post-market follow up registry, being flexible in regard to clinical studies, with most pre-market data being based on empirical, lab-based and digital simulation studies.

Regulating the manufacturing process. Another suggestion that will hasten regulation is to regulate the manufacturing process. This is not currently viable without harmonised 3D printing standards to enhance the repeatability. These standards are currently under development by the American Society for Testing and Materials (ASTM). However, a potential flaw that was identified in regulating the manufacturing process is that it can dilute competition (and consequently innovation) in 3D printer development if each machine model and associative software must be regulated by the TGA, delaying updates which will have to be re-evaluated. Therefore, a balanced trade-off is crucial when developing standardized processes.

Industry Roadmapping



Courtesy of RMIT AMP

5. INDUSTRY ROADMAPPING

Four industry roadmaps, one for each opportunity area, were drafted collaboratively by workshop participants. For each opportunity areas, we picked one specific example (application) to as the “goal” to reach for. Such specific application of the opportunity areas was obtained based on the consensus of wide variety of stakeholders (See Methodology Section for details of how this was crafted). It is shown in Blue boxes in Figures 1 to 4.

Then, we identify Enablers (Orange boxes in Figures 1 to 4), Technologies & Capabilities (Turquoise boxes), Trend (Pink boxes), and Barriers, which are specific to that application, as opposed to general barriers elaborated above (Grey boxes). Then we design each roadmap in a way that Enablers in principle drive the technologies & capabilities, and consequently technologies &
capabilities leads to the specific application of the opportunity areas. Of course, in such a pathway, we also identified Barriers that impede the smooth translation of technologies & capabilities into the final goal of the desired application. Below, we will elaborate on four roadmaps, each corresponds to a prominent application per four opportunity areas.

5.1 Material Science Roadmap for Novel Hybrid Biomaterials

Starting with the Material Science roadmap (Figure 6.1), the identified application is the development and adoption of novel biomaterials, particularly metal-based implants with bioactive coatings. There was a consensus among participants that this is a worthy example (application) to focus on, when it comes to the opportunity area of Material Science. Bioactive coatings can include a variety of drugs with immediate-release and modified-release dosage over time and the incorporation of a patient’s stem cells for accelerated rehabilitation. Stakeholders raised five specific barriers that inhibit novel biomaterials adoption which are reported in figure 6.1. Below are the descriptions of the elements of the roadmap.

Trends

- The trend of researching multifunctional materials is ongoing as it can enable faster patient recovery time and less revisional surgeries. The relatively inert materials that are being currently used are a solid baseline, but are not ideal for patient recovery and rehabilitation.

- In the development of multifunctional materials, many alloys and hybrid materials will be made giving a wide selection of material properties suitable for different medical applications. Having the choice from these materials will grant better control and enable bioactive materials that promote tissue growth.

Enablers

- In the short term, the existence of critical mass in the 3DP medical device industry can promote a good research and education sector.

Technologies and Capabilities

- With a strong research and education sector, key studies that can promote the adoption of novel biomaterials can be conducted efficiently.
- Studies involve mechanical, biocompatibility, cytocompatibility and 3D printability testing, and if the biomaterial is suitable it can overcome the barrier of material-to-cell interaction studies.

- With successful studies, public and government awareness of regenerative medicine will be improved.

- Current metal 3D printers are exploring surface finish modifications, however, being able to achieve sufficient 3DP resolution (i.e. specific surface profiles) is seen as a barrier.

- In combination with governmental support and the necessary evidence that satisfies ISO 10993, novel biomaterials can meet TGA standards and overcome the regulatory barriers.

- The final barrier is the high cost of materials. As a stakeholder stated: “Morphogenic protein [as an example of bioactive coatings] studies go back as far as 20 years, but the cost is extremely high to implement, let alone the manufacturing costs”. Ultimately, the additional expense should translate to more novel biomaterials, which in turn would result in the reduced recovery and rehabilitation time of patients.

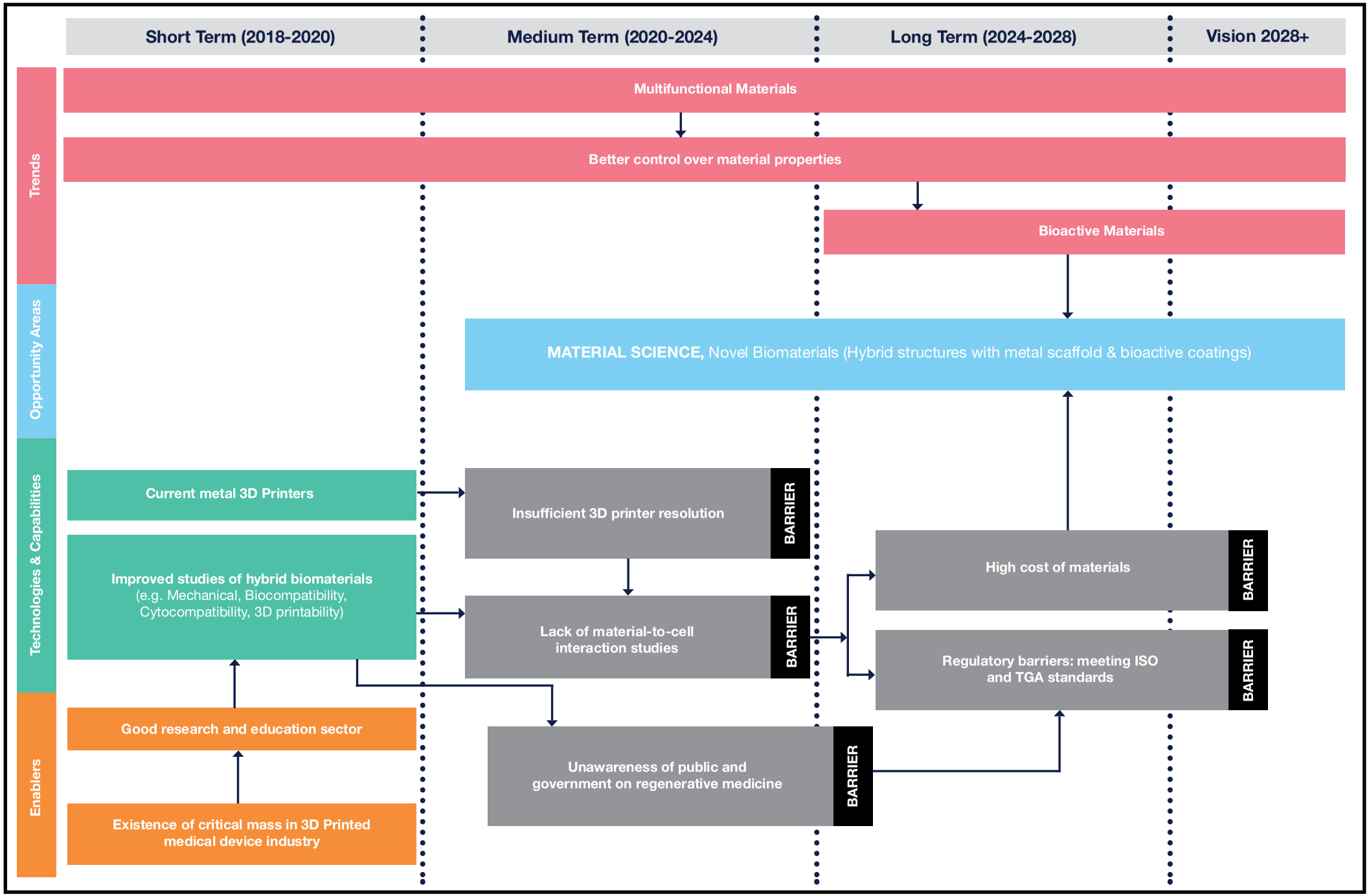


Figure 6.1: Material Science Roadmap for Novel Hybrid Biomaterials

5.2. Technology Roadmap for Super-Fast Metal 3D Printers

The technology roadmap (figure 6.2) has the objective of developing super-fast metal 3D printers which will increase productivity and enable implant sterilisation in batches, instead of the current inefficient method of paying for the entire volume of a sterilisation chamber per device. As said by a stakeholder:

> **"Printing, heat treating and sterilising one-off metal devices is not the way of the future and we need to do these processes in batches to make things cost competitive"**

Trends

- Stakeholders' noted the ongoing trend of informed surgeons, patients and device manufacturers of the capabilities of 3D printing.
- More medical device companies are also exploring the use of 3D printers for mass manufacturing as they provide more personalised goods.
- The increased adoption of 3DP medical devices was placed as a short-to-medium term trend, which will primarily be driven by successful clinical evidence over time.
- Although production in isolation is overall a niche requirement, 3D printing enables the unique ability to manufacture custom devices in remote locations.
- This could lead to the most viable method of manufacturing for space exploration, with the International Space Station already adopting a plastic 3D printer.

Enablers

- The short-term enablers that can lead to super-fast metal 3D printers in the future are trained staff and graduates and government & industry funding.
- Targeted government and industry funding incentives can lead to further AI development and directly help remedy the immediate technological barrier of real-time process monitoring.
- The medium-to-long term enabler of regulating novel alloys could lead to reduced material costs and more specialised alloys for the industry.

Technologies and Capabilities

- To achieve super-fast metal 3D printers, AI integration into real-time process monitoring will be advantageous by automating the process and reducing error and time.
- To have AI integration, the barrier of insufficient real-time process monitoring must be overcome.
- After addressing that barrier, utilising multiple CO2 sintering lasers was proposed in addition to printers with larger build-plates for increased productivity by printing larger batches of devices.
- Parameter identification for optimal AI integration was deemed a barrier as there are many parameters that influence the quality of 3D prints as stated in section 4.1.2.
- Once the parameters are identified, AI should be able to modify the printer settings to optimally calibrate the machine such that the physical device accurately matches the digitally modelled device.
- With the addition of more compatible alloys, that do not exhibit for example heat-warping in reaction to laser-sintering, the development of super-fast metal 3D printers can be achieved.

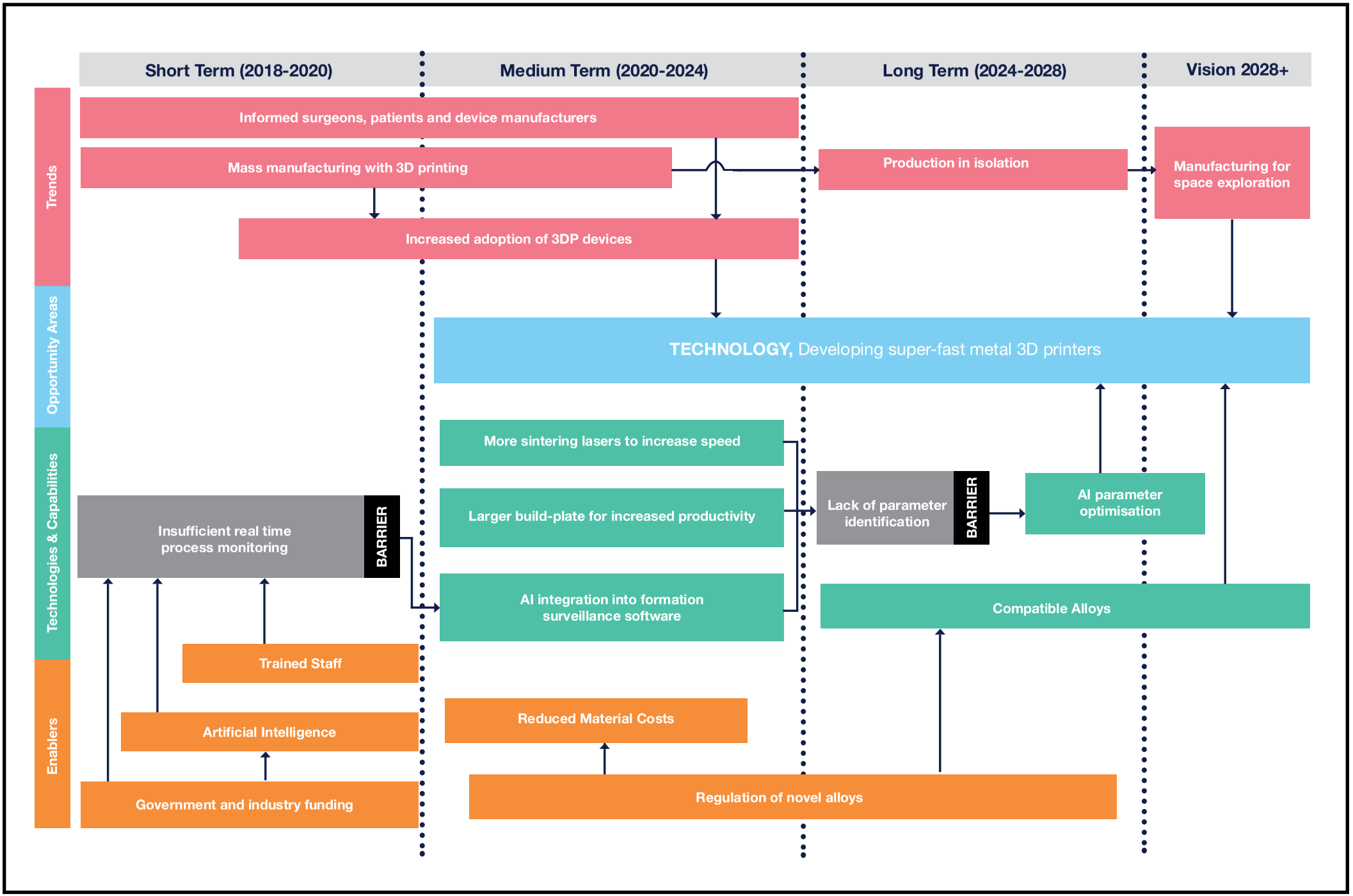


Figure 6.2: Technology Roadmap for Developing super-Fast Metal 3D Printers

5.3 Business Model Roadmap for Decentralised Manufacturing National and Global

The business model roadmap (figure 6.3) explores the decentralised manufacturing of medical implants on a national and global scale. Australia's manufacturing industry is evolving and looking to export customised high-margin solutions. This can happen by outsourcing manufacturing to 3D printing bureaus or hospitals around Australia to reduce a patients' waiting time as well as logistic costs. It can also happen by exporting digital designs and/or selling software IPR overseas to ISO certified 3D printing bureaus. In order to increase the viability of these business models, four barriers need to be overcome i.e. liability issues, quality concerns, the **lack of medical professional endorsement and adoption and lack of global regulation harmonisation.**

Trends

- As competition in manufacturing increases, this could lead to increased economic viability of 3D printed products in the short-term.
- Technological developments, increased economic viability and manufacturing closer to patients could also drive faster manufacturing and production speed.
- Personalised health care is an emerging trend and will inevitably trigger the cross-pollination of technological capabilities – one of which is 3D printing for health care.
- Having fast manufacturing and production speed in addition to the trend of personalised health care could lead to a market-niche being established. One of the suggestions was revision surgeries in the aging population.
- From establishing a market-niche in conjunction with the cross-pollination of specialised technological capabilities such as regenerative medicine, further innovation can occur to treat additional ailments.

Enablers

- In the short-term, cost-benefit analysis needs to be conducted on manufacturing methods and the viability of decentralised manufacturing. Clinical evidence and data could enable knowledge transfer from research institutes to hospitals and 3D printing bureaus.
- In the medium term, as the viability and competition of 3D printing increases, material costs could decrease. This could motivate large manufacturers of implants to adopt print-to-order products and the reduction of storing implants of many sizes.
- Stakeholders' identified CAD models becoming the IP holders' product, especially if digital files are not regulated as medical devices.
- The adoption of new biomaterials for implantation is identified in the long term, which associates with the trend of expanding the candidate of ailments 3D printing can treat.

Technologies and Capabilities

- Preparing skill capability in hospitals is essential for the adoption of 3D printed implants whether the 3D printing will be done nationally or globally, in hospitals or in 3D printing bureaus.

- In conjunction with quality monitoring as part of manufacturing, preparing the skill capability in hospitals could lead to consistent, high quality devices and the adoption of using universal framework models of implants and scaling them accordingly to a patients' specifications. This could streamline the method of designing custom devices.

- The increased viability of 3D printing could then address quality concerns and the highest-ranking barrier from figure 3, the lack of medical professional endorsement and adoption.

- Liability issues between all members of the supply chain can arise and explicit contracts must be in place to outline responsibilities. By addressing these barriers, businesses that outsource manufacturing to Australian 3D printing bureaus could be economically viable.

- Pursuing decentralised manufacturing globally, is obstructed by the lack of global regulation harmonisation, with class 3 medical devices requiring premarket approval under the jurisdiction from whichever country the device will be sold in.

- If regulations are unified globally, this could enable designers to outsource the 3D printing and post-processing of their medical devices to international 3D printing bureaus and hospitals, hence opening the global market for Australian businesses.

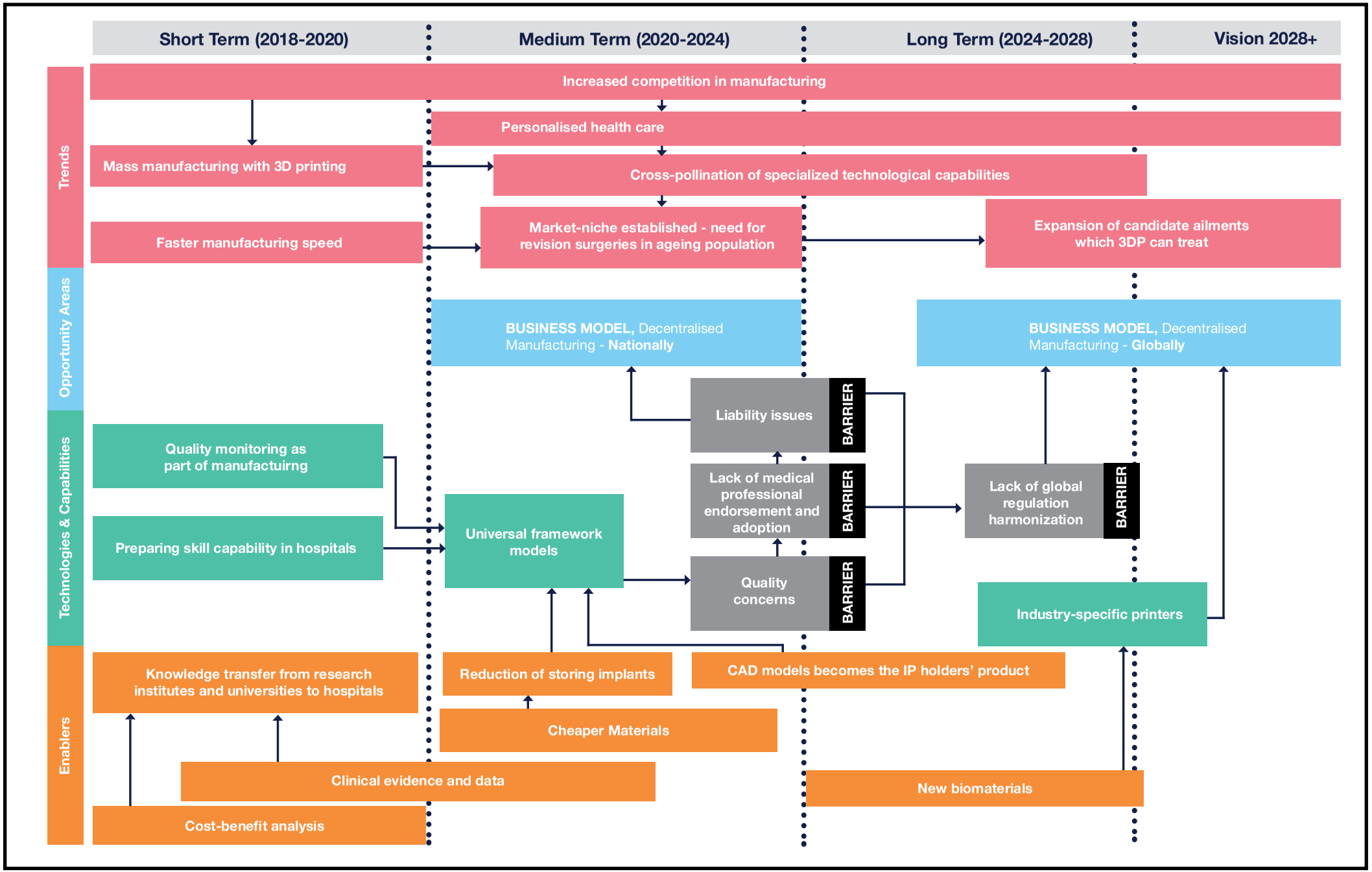


Figure 6.3: Business Model Roadmap for Decentralised Manufacturing (Nationally and Globally)

5.4. Regulatory Roadmap for Cross-over technology guidance document

The regulations roadmap (figure 6.4) looked at creating regulatory guidance documentation for cross-category devices, particularly combination of biological, medicine, and medical devices. A therapeutic good is regulated according to its primary mode of action. A document that guides companies that produce cross-over technologies such as bioprinted implants and drug-delivery scaffolds, could save the TGA and companies additional resources. As said by a stakeholder below:

> **"If the primary mode of action is an implant, it will likely fit best under the medical device framework. The proposed changes by the TGA is implementing that principle"**

Trends

- The harmonisation of global regulation standards initiated by the IMDRF is ongoing and will influence all regulatory documentation over time. A current example of that is class I medical devices that have CE accreditation, which can be regulated by the TGA via a fast-tracked method.
- Social awareness of patients and the availability of hospital and surgeon complication rates are other increasing trends.
- Medical tourism could influence the adoption of new science as patients are willing to travel overseas for treatments, which are not regulated in their home countries.
- The uptake of registries and global clinical trials could be a significant driver towards custom medical devices, as clinical evidence is not in abundance.

Enablers

- Government and Industry funding will be a significant enabler as the TGA will need to organise a taskforce to create the new documentation. Industry engagement can also help to educate all stakeholders involved on the necessary changes that need to be made.
- The revision of the custom-made medical devices guidelines and the new modifications made that will stem from the harmonisation of global regulation standards is another enabler.
- Biotech accelerators from industry associations and government could also enable an education institute for stakeholders involved, such as IMDRF, doctors, engineers and scientists.

Technologies and Capabilities

- Specialised hospitals, research and education institutes can promote the further development of cross-over biomaterials. Currently, most therapeutic goods can be categorised between medical devices, medicines (drugs) and biologicals, however when science and technology advances, bioprinted implants could contain all of these three categories.

- The development of cross-category devices will facilitate the need for regulatory guidance, however regulatory bodies need to accept the development of such new devices.

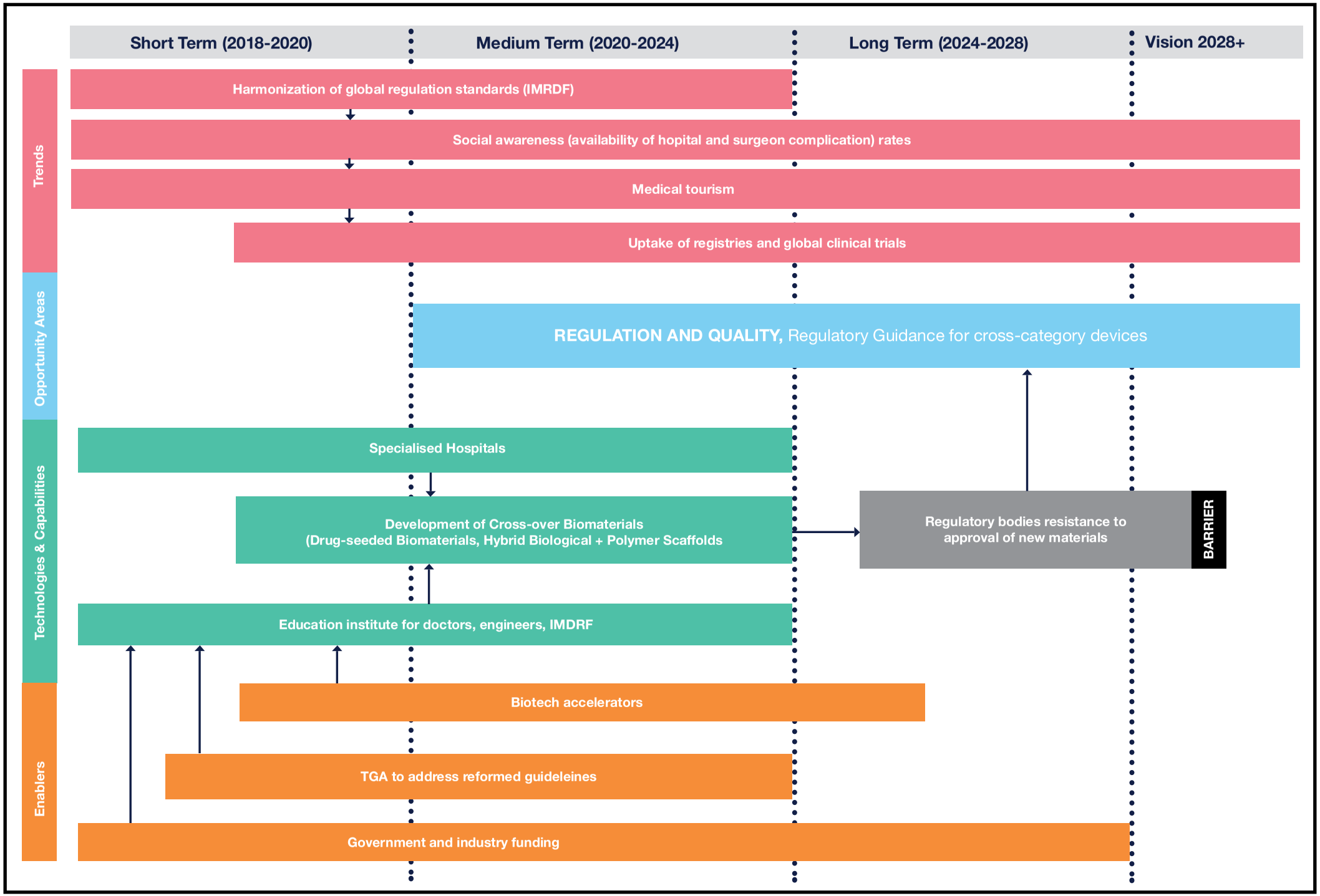
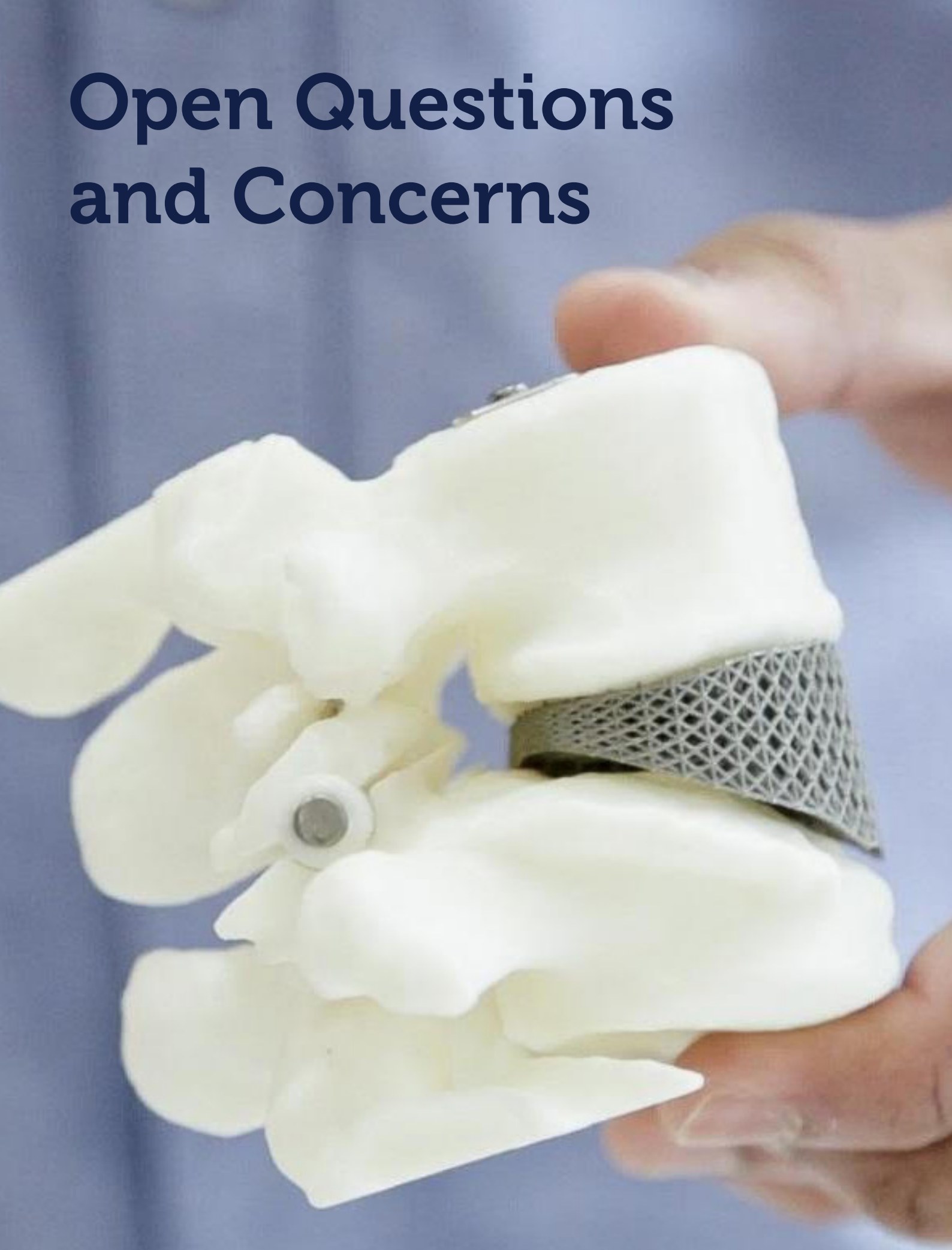


Figure 6.4: Regulatory Roadmap for Developing Guidance Document for Cross-Category Devices

Open Questions and Concerns



Courtesy of RMIT AMP

6. OPEN QUESTIONS AND CONCERNS

Based on above discussions and recommendations, there are still open questions and concerns in each opportunity areas. They need to be further investigated, and hence ideally should be turned into explicit recommendations.

6.1 Material Sciences

1. Bioactive coatings of materials that promote osseointegration and reduce infection rates show promise, but are expensive to develop and manufacture. Are there targeted grants going towards key steps in material science advancement?

2. How will novel materials that cross-over into different categories (Medicines, Biologicals, Medical Devices) be regulated as a therapeutic goods?

3. How can regulators and researchers work together to facilitate the adoption of novel materials?

6.2 Technology

1. One of the 'Circuit Breakers' discussed was surgeons seeing the potential of the technology. What can be done to increase medical professional endorsement? The majority of 3DP medical devices manufactured are in some way affiliated with surgeon who implanted them. Other independent surgeons need to be engaged and implant the devices to increase the medical data available and stimulate adoption.

2. As 3D printing is considered a 'special process' much like welding, can industry standards be established for 3D printing parameters (printing settings, maintenance and calibration of the printer)?

3. What considerations to the design process can be made to facilitate the integration of surface finish and quality throughout the design process and not at the end of manufacture?

6.3 Business Model

1. A main concern with de-centralisation is quality and control. How would quality be maintained by outsourcing the manufacturing to either service bureaus or hospitals?

2. Another concern is on liability. Who would be liable if a device fails? The company that owns and designed it or the certified manufacturer?

3. There is also concerns about "How do you make money?". It is not very clear that in the case of decentralised/distributed manufacturing, how does all of the company that has done all of the part design work get compensated?

4. Larger companies are more resistant to go for decentralised manufacturing due to willingness to keep tighter control over their manufacturing process in-house. But what will they face in near future where more and more smaller companies are going toward decentralised manufacturing, even globally speaking? In this case, they would have to think about their logistical and warehousing change.

5. In hospital-based decentralised manufacturing model, who would be the manufacture? A company representative, particularly in the case of larger firms (e.g. Stryker), or a hospital department/personnel? There are both cost and liability issues associated with this decision.

6. Sterilisation is a major cost. A proper cost modelling is needed to consider the best pathway, whether it is centralised manufacturing or decentralised, and in the latter case, whether it should be service bureau-based or hospital-based in order to minimise such cost.

7. How do we robustly decide whether to utilise 3DP technology or not to produce a particular devices? And if we decide so, how do we decide to produce it in-house or outsource it through decentralisation? And if we decide for decentralisation, where to outsource the manufacturing? Service-bureau or directly to hospital? Answering these questions requires a thorough cost-modeling analysis at the industry level per particular device.

6.4 Regulation

1. What are the steps that need to be taken to achieve the global harmonisation of regulatory requirements?

2. To change the regulatory process for 3D printed and bioprinted devices, an amendment to the TGA act of 1989 has to be made, which is a 5 to 6-year process. Can the process be expedited or if not, how do we future-proof the regulatory process?

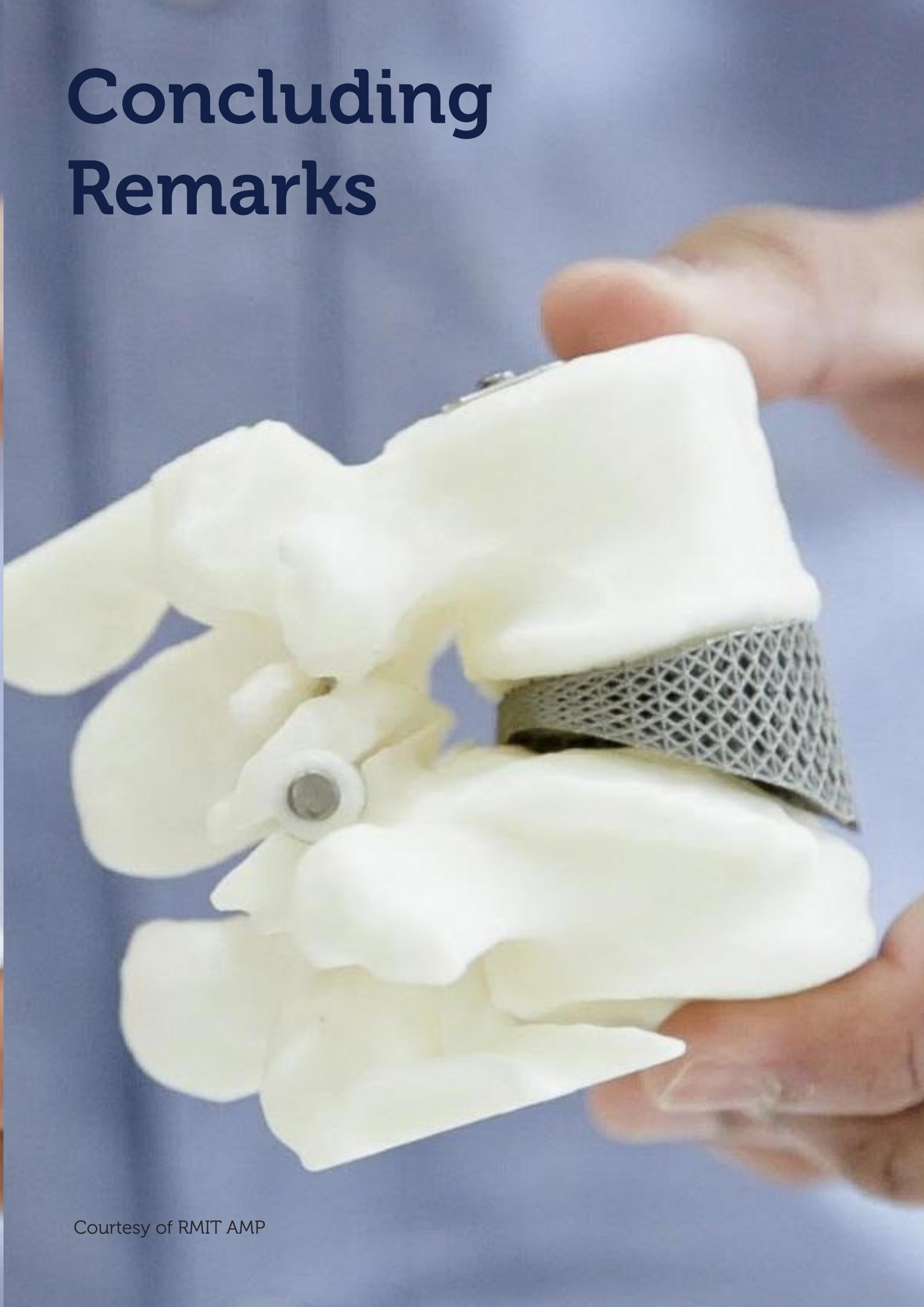
3. General Data Protection Regulation could potentially be breeched if patient data is circulated through the manufacturers' network. What are the quality systems that need to be in place to appropriately manage data and data integrity practises?

6.5 Root-Cause Analysis of Barriers

Conducting a root cause analysis of targeted complex barriers could provide a structured methodology to overcome the barrier. For example, according to the survey reported in section 4.2, medical professional endorsement and adoption is one of the key barriers that need to be addressed. There could be multiple reasons for existence of such barrier. First, it can be because of lack of clinical evidence, which makes surgeons hesitant to adopt 3DP medical devices, such as implants. If this is the case, then it can be remedied by existence of more clinical evidence in near future. Here the endeavour of research institutes can be helpful.

Second, it can also be because of the lack of training and education about the capabilities of 3D printed implants, as well as the mentality of "resistance to change" among medical professionals. If this is the case, it is harder to see the wider adoption of 3DP medical devices in near future. Conducting such Root-Cause analysis on the entire spectrum of the identified barriers can shed further light on ow to overcome the barriers fore wider adoption of 3DP medical devices.

Concluding Remarks



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CONCLUDING REMARKS

The aim of this report was to shed light on preliminary findings of a newly granted project by RMIT University in collaboration with a wide range of stakeholders in medical device industry in Australia. The project explores the adoption and diffusion of 3DP medical devices. In doing so, we developed the following:

- The process mapping of the 3D Printing medical implants, from raw materials all the way to patient implantation.

- Stakeholder mapping of the industry in Australia. This includes large and SMEs manufacturers, researchers, regulatory bodies, industry associations, surgeons, patients, hospitals and medical device consultants.

- Identifying the top four major opportunity areas, which can enable the adoption of 3D printing medical devices, them being developments in Material Science, Technology, Business Models, and Regulation.

- Developing the industry road map, in four nominated applications, by identifying the barriers in realising such four opportunity areas.

- Recommending solutions based on the discussion and understanding of the proposed barriers that are hindering the wide spread adoption and diffusion of 3-D printed medical implants.

This report was the first ever effort to comprehensively identify opportunities areas, barriers, provide preliminary recommendations to overcome those barriers, and draft industry roadmaps for nominated and prominent applications of 3DP in medical device industry in Australia. Nevertheless, there are still open questions and concerns in this high potential industry, which we also raised in this report. This report will be beneficial for industry actors (SMEs, large manufacturers, service bureaus) in order to get a holistic and multi-stakeholder perspective of the prospect of the industry and its opportunity areas. It is also beneficial for governmental research agencies, such as IMCRC and CSIRO to design targeted grants for areas where there are market failure blockages, which requires third party interventions. Last but not least, it can be helpful for regulatory bodies, to get insight on a wide range of opportunities areas in the industry that can be explored through smoother, faster, and more transparent regulatory pathways, particularly for SMEs.

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