CELL THERAPY PRODUCT (ORICELL Autologous Cultured Chondrocytes On Porcine Collagen Membrane) TO HOSPITALS

BY

MISS THANWARAT SRICHAMPA

AN INDEPENDENT STUDY SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF BUSINESS ADMINISTRATION (GLOBAL ENTREPRENEURSHIP) INTERNATIONAL MASTER IN BUSINESS ADMINISTRATION

FACULTY OF COMMERCE AND ACCOUNTANCY

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ABSTRACT

OriCell is the product that will use porcine collagen membrane to fix articular cartilage defect in the knee. It has not been launched in Thailand yet. OriCell is used for single lesion with full thickness cartilage. Those target patients are fall, sport injury or accident. This research is aim to investigate target market and potential market in Thailand. It is conducted by interviewing all relevant stakeholders. They are orthopedic surgeons, scientist in laboratories, health tech venture capital, pharmacist and expert in Thai FDA. The result shows that surgeons are interested in the product as long as it has efficacy over existing treatment. However, since the market size is quite small, it can be sold to patient based on case-by-case. The target hospitals that will use this product might be private hospitals or specialized hospitals. The clinical trial has shown its efficacy is better than existing operation procedure (microfracture).

Keywords: MACI, Articular Cartilage Defect, Orthopedic Surgery, Orthopedic, Knee Joint

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TABLE OF CONTENTS

	Page
ABSTRACT	(1)
ACKNOWLEDGEMENTS	(2)
CHAPTER 1 INTRODUCTION	1
1.1 Background	1
1.2 Patient Situation	2
1.3 The idea of OriCell	2
CHAPTER 2 REVIEW OF LITERATURE	4
2.1 MACI	4
2.1.1 Detail of MACI	4
2.1.2 Limitation of use	4
2.1.3 Important safety information	4
2.1.4 How it works?	5
2.1.5 Type of patients suitable with MACI	6
2.2 FDA Approval	6
2.2.1 FDA	6
2.3 Type of orthopedic surgery	7
2.4 Articular Cartilage and Articular Cartilage Defect	8
2.4.1 Articular Cartilage	8
2.4.2 Articular Cartilage Defect	9

CHAPTER 3 RESEARCH METHODOLOGY 10

3.1 Primary Research 10

3.1.1 Stakeholders 10

3.1.1.1 Suppliers 10

3.1.1.2 Buyers 11

3.1.1.3 Investor 11

3.1.2 In-depth interview questions 12

3.1.3 Challenges and Difficulties 12

CHAPTER 4 RESULTS AND DISCUSSION 14

4.1 Interview result with orthopedic surgeons 14

4.1.1 Orthopedic surgeons "O" 14

4.1.2 Orthopedic surgeons "Ni" 17

4.1.3 Orthopedic surgeons "Thanai" 19

4.1.4 Orthopedic surgeons "T1" 21

4.1.5 Orthopedic surgeons "T2" 22

4.1.6 Orthopedic surgeons "Phob" 23

4.2 Interview result with laboratory 24

4.2.1 KMUTT laboratory 24

4.2.2 Stem-Cell laboratory 26

4.3 Interview result with result with health tech venture capital 28

4.3.1 Ruckdee 28

4.4 Interview result with pharmacist 29

4.4.1 Pharmacist 29

4.5 Interview result with Thai FDA expert 30

4.5.1 Thai FDA expert 30

CHAPTER 5 CONCLUSIONS AND RECOMMENDATIONS 32

5.1 Conclusion on stakeholder 32

5.1.1 Orthopedic surgeon 32

5.1.2 Hospitals 32

5.1.3 Suppliers 32

5.1.4 Venture capital 33

5.1.5 Thai FDA 33

5.2 Suggestion 34

5.2.1 Location/Place 34

5.2.2 Procedure to sell this product 34

5.2.3 Approximate cost for laboratory and operation per 1 case 35

5.2.4 Capital Funding 38

5.2.5 Efficacy 38

5.2.6 Training to orthopedic surgeons 41

REFERENCES 42

BIOGRAPHY 46

CHAPTER 1
INTRODUCTION

1.1 Background

This research paper aims to identify how much of demand in the market for this new product in medical industry. In addition, it aims to find market potential for OriCell to set up apparently in Thailand.

Surgery for these type of knee defects is for athlete, especially football players, injuries from accident, and foreigners who are looking for good quality surgery in Thailand. Roughly estimated, there are over six millions of patients in Thailand who is above age 65 and suffering from Osteoarthritis.

Knee is one of the body organ. It is very important. Inside the knee, there are bones, cartilage, ligaments, and tendons. Specifically, cartilage is a thin, elastic white smooth tissue that protects the bone and reassures that the joint surfaces can glide over each other conveniently. It covers the ends of bones where they come together to form joints. Healthy cartilage in joints makes it easier to move.

The problems about knee is that people generally get injured easily in the knee from various reasons: a fall or severe sport injury, previous knee injuries or wear and tear over time and immobilization for long periods. People with previous surgical interferences face more chances of articular cartilage damage due to changed mechanics of the joint. Articular cartilage damage may also be found in the shoulder as well which will cause pain, discomfort and limited movement.

However, Cartilage has a very limited capacity for self-restoration. Articular cartilage does not usually regenerate (the process of repair by formation of the same type of tissue) after injury or disease leading to loss of tissue and formation of a defect. Because cartilage does not heal itself well, doctors have developed surgical techniques to stimulate the growth of new cartilage.

Surgical techniques to repair damaged cartilage are developing. As more is learned about cartilage and the healing response, surgeons will be better able to restore an injured joint. Restoring articular cartilage can relieve pain and allow better function. Most importantly, it can delay or prevent the onset of arthritis.

1.2 Patient situation

In 2010, there were roughly 10.4 million patients (US number) visits to doctors' offices because of common knee injuries such as fractures, dislocations, sprains, and ligament tears. Knee injury is one of the most common reasons people see their doctors.

Statistically, in Thailand, sport athletes mostly injure at knees. For instance, 47% of football player injuries come from knee. Likewise, many other sport athletes also suffer from knee injuries for most sport accident cases. Moreover, Thai people tends to have osteoarthritis more, approximately 6,000,000 people starting from middle-aged period. This number is based on year 2006 and the number of patients is expected to extend more due to higher number of elderly in Thailand and other risk factors such as weight, aging, habitual improper posture and chronic knee injuries and osteoarthritis. Provided this number of knee patients, this illustrate prospect of using MACI for knee cartilage surgery amongst Thai orthopedic surgeons.

1.3 The idea of OriCell

Why MACI (autologous cultured chondrocytes on porcine collagen membrane)?

MACI is the newest launch innovation to cure articular cartilage defect in the knees. It is recently approved by FDA in the US to officially use in human beings. My plan is to set up OriCell realistically in Thailand using Stem Cell Research Lab as an operator and import porcine collagen membrane from Vericel or ask from KMUTT

where they are experimenting on this project. Actually, before using this product with the Thai, it should be tested with Thai patients and should be approved by FDA Thai as well.

Firstly, demand side is the orthopedic doctors and hospitals. Usually, when any new medical material or equipment is launched into the market, the medical dealer will deal with the doctor and get the doctor impressed. If they agree upon the benefit of this material, then the doctor will suggest the procurement department of the hospital to buy this medical equipment or material. However, they have committee whenever they want to buy any new medical equipment to the hospital. Therefore, it sometimes takes lots of time to get the procedure finished.

On the other hand, the supply side consists of KMUTT where they are experimenting with this product similar to MACI, it can be potential source of material for supplying to the hospitals. Likewise, Vericel which is the origin of this MACI can be likely source of MACI for us.

CHAPTER 2
REVIEW OF LITERATURE

2.1 MACI

2.1.1 Detail of MACI

According to Vericel Company website, it states that "MACI (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product that is indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the adult knee, with or without bone involvement.

MACI is intended for autologous use and must only be administered to the patient for whom it was manufactured. The implantation of MACI is to be performed via an arthrotomy to the knee joint under sterile conditions.

The amount of MACI administered is dependent upon the size (surface in cm^2) of the cartilage defect. The implantation membrane is trimmed by the treating surgeon to the size and shape of the defect, to ensure the damaged area is completely covered, and implanted cell-side down."

2.1.2 Limitation of use

According to Vericel Company website, it states that "Effectiveness of MACI in joints other than the knee has not been established. Safety and effectiveness of MACI in patients over the age of 55 years have not been established."

2.1.3 Important safety information

According to Vericel Company website, it states that "MACI is contraindicated in patients with a known history of hypersensitivity to gentamicin, other aminoglycosides, or products of porcine or bovine origin. MACI is also contraindicated for patients with severe osteoarthritis of the knee, inflammatory arthritis, inflammatory joint disease, or uncorrected congenital blood coagulation disorders. MACI is also not

indicated for use in patients who have undergone prior knee surgery in the past 6 months, excluding surgery to procure a biopsy or a concomitant procedure to prepare the knee for a MACI implant.

MACI is contraindicated in patients who are unable to follow a physician-prescribed post-surgical rehabilitation program.

The safety of MACI in patients with malignancy in the area of cartilage biopsy or implant is unknown. Expansion of present malignant or dysplastic cells during the culturing process or implantation is possible.

Patients undergoing procedures associated with MACI are not routinely tested for transmissible infectious diseases. A cartilage biopsy and MACI implant may carry the risk of transmitting infectious diseases to healthcare providers handling the tissue. Universal precautions should be employed when handling the biopsy samples and the MACI product."

2.1.4 How it works?

The process can be broken down into 5 steps:

1. If your doctor thinks Autologous Chondrocyte Implantation may be an option for you, he or she will take a biopsy (a small sample of tissue) from your knee.

2. The biopsy is then shipped to the laboratory, where it will be stored cryogenically (frozen).

3. When you and your doctor decide the time is right for autologous chondrocyte implantation, cartilage cells (chondrocytes) from your biopsy will be grown and placed into a collagen scaffold (called MACI).

4. MACI is then delivered to your surgeon for the implantation procedure.

5. Once received, your surgeon will shape the MACI implant to your cartilage defect and affix it to the damaged area.

2.1.5 Type of patients suitable with MACI

Most candidates for articular cartilage restoration are young adults with a single injury, or lesion. Older patients, or those with many lesions in one joint, are less likely to benefit from the surgery.

2.2 FDA Approval

2.2.1 FDA

On December 13, 2016, There is an approval for MACI to use officially in human beings. It states that "The U.S. Food and Drug Administration today approved MACI (autologous cultured chondrocytes on porcine collagen membrane) for the repair of symptomatic, full-thickness cartilage defects of the knee in adult patients. MACI is the first FDA-approved product that applies the process of tissue engineering to grow cells on scaffolds using healthy cartilage tissue from the patient's own knee."

" Knee problems are common, and occur in people of all ages. Cartilage defects in the knee can result from an injury, straining the knee beyond its normal motion, or can be caused by overuse, muscle weakness, and general wear and tear."

"Different cartilage defects require different treatments, so therapy must be tailored to the patient." "The introduction of MACI provides surgeons with an additional option for treatment."

"MACI is composed of a patient's own (autologous) cells that are expanded and placed onto a bio-resorbable (can be broken down by the body) porcine-derived collagen membrane that is implanted over the area where the defective or damaged tissue was removed. Administration should be performed by a surgeon specifically trained in the use of MACI."

"Each MACI implant consists of a small cellular sheet containing 500,000 to 1,000,000 cells per cm2 (about 0.16 square inches). The amount of MACI

administered depends on the size of the cartilage defect, and is trimmed to ensure that the damaged area is completely covered. Multiple implants may be used if there is more than one defect."

"The safety and efficacy of MACI were shown in a two-year clinical trial designed to demonstrate reduced pain and improved function in comparison to microfracture, an alternative surgical procedure for cartilage repair. The trial included 144 patients (72 in each treatment group). A majority of the patients who completed the two-year clinical trial also participated in a three year follow-up study. Overall efficacy data support a long-term clinical benefit from the use of the MACI implant in patients with cartilage defects."

"The most common side effect reported by people who received MACI were: joint pain, common cold-like symptoms, headache and back pain."

"MACI is manufactured by Vericel Corporation, headquartered in Cambridge, Massachusetts."

"The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products."

2.3 Type of orthopedic surgery

According to orthopedic surgical method, there are many types of orthopedic surgery. " Many procedures to restore articular cartilage are done arthroscopically. During arthroscopy, your surgeon makes three small, puncture incisions around your joint using an arthroscope."

"Some procedures require the surgeon to have more direct access to the affected area. Longer, open incisions are required. Sometimes it is necessary to address other problems in the joint, such as meniscal or ligament tears, when cartilage surgery is done."

In general, recovery from an arthroscopic procedure is quicker and less painful than a traditional, open surgery. Your doctor will discuss the options with patients to determine what kind of procedure is right for patients.

The most common procedures for cartilage restoration are:

- Micro Fracture
- Drilling
- Abrasion Arthroplasty
- Autologous Chondrocyte Implantation
- Osteochondral Autograft Transplantation
- Osteochondral Allograft Transplantation

2.4 Articular Cartilage and Articular Cartilage Defect

2.4.1 Articular Cartilage

Articular cartilage, by definition, is " hyaline cartilage on the articular surfaces of bones. As such, it lies inside the joint cavity of synovial joints, bathed in synovial fluid produced by the synovial membrane that lines the walls of the cavity.

Though it is often found in close contact with menisci and articular disks, articular cartilage is not considered a part of either of these structures, which are made entirely of fibrocartilage.

Articular cartilage is the smooth, white tissue that covers the ends of bones where they come together to form joints. Healthy cartilage in our joints makes it easier to move. It allows the bones to glide over each other with very little friction."

2.4.2 Articular Cartilage Defect

Articular Cartilage Defect, by definition, is "Cartilage structures and functions can be damaged. Such damage can result from a variety of causes, such as a bad fall or traumatic sport-accident, previous knee injuries or wear and tear over time. Immobilization for long periods can also result in cartilage damage.

Articular cartilage damage in the knee may be found on its own but it will more often be found in conjunction with injuries to ligaments and menisci. People with previous surgical interventions face more chances of articular cartilage damage due to altered mechanics of the joint. Articular cartilage damage may also be found in the shoulder causing pain, discomfort and limited movement.

Articular cartilage does not usually regenerate (the process of repair by formation of the same type of tissue) after injury or disease leading to loss of tissue and formation of a defect. This fact was first described by William Hunter in 1743. Several surgical techniques have been developed in the effort to repair articular cartilage defects."

CHAPTER 3
RESEARCH METHODOLOGY

3.1 Primary Research

The propose of primary research is to find pathway to settle up OriCell as a medical cell therapy company and to find market feasibility of this product. In order to find that, I have to conduct in-depth interview and survey with relevant stakeholders. However, there is problems and challenges when I got into interview with orthopedic surgeon, scientist in the lab and other people. Hence, I also want to conclude this in the research as well.

3.1.1 Stakeholders

The question to ask in this section is to find whether there is possibility to operate cell therapy medical company in Thailand. There are many stakeholders related to my product, which I have to define how they are relevant to my work.

3.1.1.1 Suppliers

There are many potential suppliers which are King Mongkut's University of Technology Thonburi (KMUTT), Stem Cell Research Center in Thailand (Blind), Vericel (Analog of Oricell) and Medical dealer.

King Mongkut's University of Technology Thonburi (KMUTT) is experimenting this type of product similar to MACI and currently joining the experiment with Siriraj hospital. This piece of information is given by one of the orthopedic doctors. I would like to interview with KMUTT because it is probably possible to supply MACI by this institute instead of import from Vericel.

Vericel is originally the one who produces MACI, I would like to talk with them how they came up with this innovation and whether they plan to sell to other countries like Thailand. What will be their pricing strategy and whom are they

looking for to be their dealer? This is another case where I may import this product instead of producing it domestically.

Stem Cell Research Center in Thailand, in this case, I would like to interview with the research center in the big university hospital such as Siriraj and Ramathibodi hospital, however, the constraints, they do not want to be appeared publicly due to research ethics and secrecy, hence in the result part, I will blind the name of the institute and researchers. In addition, to interview with this stakeholders, I would like to know the feasibility of conducting this product when I need the scientist to grow chondrocytes on porcine collagen membrane (the scaffold) before the surgeon inserts back to patient.

For the medical dealer, I have a friend who had been working with pharmaceutical company as a medical detail or dealer, I would like to ask her about the process how the hospital considers buying any kind of medical material into the hospital.

3.1.1.2 Buyers

Normally, to bring the medical supply into the hospital, we need to get the doctor impressed first, from that the doctor can suggest the hospital to buy as a medical material in the future. So, my target group are orthopedic surgeons and hospitals. I plan to sell to private hospitals as B2B and for public hospitals I plan to sell it massively through medical dealer. However, before penetrating that I have to go to orthopedic surgery association where they gather all orthopedic surgeons there in which I plan to meet many surgeons who know and be able to suggest me further. One of the opinions from my advisor is to find the biggest professor in the big university hospital first to buy and use my product, after this other surgeon will follow him. Finally, I will be able to sell across all orthopedic surgeons.

3.1.1.3 Investor

Ruckdee intends to match the healthcare innovation with investment. They are a platform where healthcare meets business. Ruckdee specifically provides consultancy for healthcare projects regarding business and fund raising strategy while supporting the Health-Tech ecosystem in Thailand in which I think it is

really suitable with my project. I would like to know the feasibility of raising fund with this kind of product.

3.1.2 In-depth interview questions

The purpose of the in-depth interview is to find out deeper information regarding to each relevant stakeholders. Is that possible to set up OriCell realistically in Thailand? In this case, I plan to interview 5 orthopedic doctors, 2 stem cell centers, 1 medical dealer and 1 venture capital which is Ruckdee to see their opinion upon OriCell.

Here are questions:

1. Do you know MACI?
2. How do you use it?
3. How do you currently provide treatment to patients?
4. Do you think which one is better compared old way and OriCell?
5. Do you think OriCell will be able to use in other body cartilage rather than knee cartilage?

3.1.3 Challenges and Difficulties

Regarding to this survey and interview, there are many difficulties upon each stakeholders as followings.

For the orthopedic doctors, they lack of business knowledge. Sometimes, they do not want to talk because they may not have experienced MACI before in Thailand. In addition, the big concern is about training doctors to use MACI in Thailand. Finally, because of their limited time, they do not want to do survey because it takes time.

For the stem cell research center, they do not want to talk because sometimes it is under experimental or research period. They do not want to decide absolutely because it concerns lives of the people and basically in Thailand curing

people with stem cell is under research trial. And sometimes, they do not want to talk because it is their current research.

For the Vericel which is the origin of this product, they may not provide information because of trade secret and it is their trademark. Moreover, the importance is porcine collagen membrane which is the core innovation of the company in which they may not tell in detail. However, we can search some information from the company website.

CHAPTER 4
RESULTS AND DISCUSSION

4.1 Interview result with orthopedic surgeons

4.1.1 Orthopedic surgeon "O"

He specialized in ligament and cartilage surgery. He mentions about surgery this way using the product. Here are my questions and his answers.

1. What is your specialization?

I am specialized in doing osteochondral autograft transplantation and knee ligament repair.

2. Do you know the product before?

I think I have heard of the product before, it is the new way of surgery. I think it fits with those who suffer from sport injury. In the article, they mention about curing those who has full thickness cartilage damage with single lesion.

3. How many types of patients do you have?

They have two types of patients; the first type is OA (Osteoarthritis) of the knee. The other is sport injury. Most of them come to him with OA. However, the product is used to cure sport injury mainly. Currently, it is not for general treatment of OA.

4. How do you currently treat the patients?

For OA, we try to treat patients with conservative ways first, meaning that we try to first let the patient control his or her weight, second give patients medicines such as Analgesics, Nonsteroidal anti-inflammatory drugs, Corticosteroids and injecting Hyaluronic acid, third send them to do physical therapy or rehabilitation, and forth give them assistive devices such as scooters, canes, walkers, splints, shoe orthotics or helpful tools, such as jar openers, long-handled shoe horns or steering wheel grips. We provide different treatment according to severity. If all of them do not work,

then we will provide surgery. However, there are different types of surgery, so we need to consider which one is more suitable to severity of the disease of patients. Generally, OA, when cartilage has degenerative change, the whole or partial cartilage may get defected and it needs metal components to do knee replacement implants. Usually, those metal components are titanium.

For sport injury patients, they usually come with the symptom of pain because it occurred an accident. Hence, firstly if the pain is not too severe and the patients can be treated by medicines, they will not go for surgery. After some time, if the patients still have pain and more swollen knees, then they will let the patients go for X-ray, MRI or scanner to see where is the lesion or defect. From the doctor experience, most are football players who are suffered from being crashed or fallen during the game. Mostly, they are diagnosed of having tear in ligament and later they are found out of having cartilage defect or lesion. The surgeon will look for severity of the defect, if it is not severe or it is not at the position where it holds body weight, then surgeon will not bring patient to surgery. Only when patient is considered having severe lesion in cartilage where it holds body weight and it causes pain during daily life activities, then if that is the case, they will consider patients for surgery.

5. So, what surgery technique do you use for sport injury patients?

He is using Osteochondral Autograft Transplantation or mosaicplasty technique. The procedure is that he plugs out the healthy cartilage where it does not hold body weight and plugs in the healthy cartilage back to where it is damage, but before putting it in, he has to prepare the area around the damaged surface to be smooth first. The good thing about this technique is it opens the knee only once and it finishes within itself. Patients will not be operated twice, thus it reduces pain.

6. Do you think that by operating patients twice for the product implants (First is to do biopsy and second is to implant the grown chondrocyte on scaffold back to cartilage defect), it will be more risk of being infectious?

Well, he thinks that it would not cause any troubles as long as it sterilizes and no germ, bacteria or virus falls inside. But the thing is that it may be

troublesome during the transportation process from laboratory to hospital. The standard quality of operation may have too little risk of being infectious.

7. What do you think about laboratory for the product? Should it be opened in hospitals or outside hospitals as a central laboratory?

He thinks that it should be outside the hospitals because it needs to pull all resource at the same place and provide service to hospitals. For examples, the roles of laboratory are collecting piece of cartilage and grow the chondrocytes on the porcine scaffold until it is enough for the damage area in cartilage and then sending sterilized bottle that contains chondrocyte on scaffold back to hospitals and implanting back to the lesion on the cartilage by surgeons. It needs to control quality.

8. What do you think about porcine scaffold? Since it is made from pig, do you think it is compatible with human organs?

Personally, He thinks it would not affect the patients since it has been tested with 72 patients who are randomly chosen to test with the product. Moreover, porcine scaffold is designed to be biodegradable, hence it would not cause harm to patients. Yet, the chondrocytes are raised with gentamicin, so it might be harmful to those who are hypersensitive to these chemicals.

9. Do you think that for the product, the surgeons need technical skill or not?

It depends on each surgeon skill, however it does not go beyond surgeon knowledge or capacity, thus it should be possible to learn and operate this the product.

10. What do you think about training for surgeons?

He thinks that the company can bring the surgeons to learn at the US headquarter or the company sets some kind of workshop to provide technical surgery operation for surgeons.

11. Do you want to provide more information?

He has heard of some of the laboratories in Thailand, maybe King Mongkut's University of Technology Thonburi. They are doing similar product to the product.

4.1.2 Orthopedic surgeon "Ni"

1. Do you know about the product?

He has heard about it somehow but he has never used it in his operation.

2. What do you think about potential using this in Thailand?

Since this product is specifically using for sport injury, so he thinks the market size is quite small compared to osteoarthritis situation in Thailand. What he worries more about this the product is that the operation technique whether it requires complicated technique or not, otherwise surgeon will go for easier technique. Currently, he is mainly treating people who normally have osteoarthritis. Those who come to the hospital, they are treated with physical therapy and medicine first before being considered for big operation. He will treat those who have complete damage cartilage by replacing defect cartilage with titanium one. So in his view, if the product has more complex procedure, then surgeon might not consider using it.

Another point is that he thinks private hospitals might be interested in this product more but I have to consider how many patients each year who get sport injury at cartilage and need operation to repair. Otherwise, it would not be cost effective to set up lab and operate this the product. But suppose if I have to open this, I have to open as a central laboratory to share this facility to other hospitals as well. I cannot rely on laboratory within the hospitals, I must set it up as a shared facility.

3. What do you think about the riskiness of operation?

The riskiness level of operation twice (first biopsy and second insertion) is almost the same to other procedure. But what we need to concern is more about sterile process when bringing patients' bodies tissues to outside hospital area. The

company must be able to guarantee that there will not be contamination during the process. In addition, the laboratory must be certified according to world standard.

4. What is the process of bringing this to be used in public hospital system?

They should provide the evidence that it is under The Comptroller General's Department by going to Royal College of Surgeons of Thailand, they will provide committees to inspect the usage of the product. Then, if committees approve with provided evidence of research, treatment result and approval from Food and Drug Administration, the product will be listed on The Comptroller General's Department.

5. What do you think about providing trainings to surgeons?

They can provide training to the surgeons by giving them the sample product and let the surgeon uses. Suppose surgeons like it, they will continuously use it and order it more from dealer. However, the company needs to give surgeons training such as bringing surgeons to the US at headquarter to see operation procedure. Or else, the company or my startups should approach who has been trained at the center in the US before and try to spill over knowledge to other surgeons.

6. What are your concerns?

He concerns most about techniques that are required for operation. Suppose it is more difficult than previous operation procedure, surgeons will not choose this procedure. Moreover, the product itself must prove its efficacy in terms of cohesion with the lesion. In addition, the result of using this product implanted in patients must be proved to be better than existing procedures. Post-operation procedure must not be hard to maintain. Otherwise, surgeons will not choose this procedure. Cost effectiveness is also one of many factors that hospitals consider. It should be considered as well whether it requires sport orthopedic surgeons or general orthopedic surgeon.

7. What do you think about opening laboratory?

He thinks that it should be opened as a central laboratory. It should not be in particular hospitals.

4.1.3 Orthopedic surgeon "Thanai"

1. What do you think about the product? Have you ever heard of it?

He has heard of it for a long time. There is a European surgeon who already did this type of operation already. His name is Lars Peterson. He has conducted the so-called autologous cell implantation in cartilage.

2. What is the result of Lars Peterson?

His implantation yields effective result and this is since 2001.

3. What are your current procedure for operation?

It depends on size of cartilage defect. Suppose it is small lesion, then he will use microfracture, yet the result is unsatisfied because it produces fibrocartilage. If the lesion size is bigger, then he will do mosaicplasty or flesh autograft.

4. What do you think about MACI?

He thinks it might be better than Lars Peterson procedure because it has provided better material which is scaffold. It must provide structure for chondrocytes to be cultured which will indicate strength of the lesion.

5. What do you think about stem cells?

It goods but since there is no structure, it may not be that strong when you inject into lesion.

6. Have you ever heard of cell culture laboratory in Thailand? In addition, how much is the approximate cost?

Yes, there are two laboratories in Thailand. Basically, surgeons will send chondrocytes in foreign laboratory or domestic laboratory. The approximate cost of growing chondrocytes is roughly 300,000 - 400,000 baht.

7. What are requirements for opening laboratory in Thailand?

He thinks it is ISO.

8. What is approximate price of operation for private hospital?

He thinks for arthroscopy roughly is about 100,000 - 200,000 baht. For open surgery, the cost is roughly 100,000 baht. This is the price for public hospitals.

For private hospitals, the cost of arthroscopy would be 1,000,000 baht including chondrocytes culture in the laboratory. The open surgery for private hospitals would be 500,000 - 600,000 baht including chondrocytes culture in the laboratory. For using this product in operation, it requires open surgery procedure. The cost of using stem cell for cartilage defect would be 300,000 - 400,000 baht

9. Have you ever heard of stem cell center in Thailand?

Yes, there are many private stem cell centers in Thailand. They use stem cell extraction from placenta to duplicate and cure cartilage defect patients.

10. What do you think about patient reaction to the product and the riskiness of operation?

For the porcine scaffold, since it is scientifically proven. There should not be dramatic effect on human cartilage and human rejection. It must be able to be used in human body. He thinks that since the riskiness of operation is less than 1%, then it will be acceptable under medical condition.

11. What is your suggestion for selling the product in Thailand?

He thinks the market size is quite small since it is for sport injury only and it is only effective with one lesion without scattering. However, if I can find insurance company to cover this cost for patients who go for private hospitals, that will work too.

12. What do you think about the potential problems that might occur?

Since it is the small market size for sport injury, so it might be hard to find potential patients. They must go to MRI to scan for size of lesion and let the patients decide which procedure they want to go for treatment. Since the approximate cost of MACI might be high, maybe almost 1,000,000 baht. So, it is might be hard for the hospital to find potential patients who have willingness to pay for this. In addition, surgeons might choose better way with lower cost to operate for patients.

13. Suppose the company asks for approval from Food and Drug Administration, what would be advantages and disadvantages of this product?

Since this procedure autologous chondrocyte implantation done by Lars Peterson has long established for almost 20 years, so it is easy for Thai FDA to approve this.

14. What do you think about providing training to the surgeon?

There should be workshop provided for surgeons in Thailand or the company can bring expert from headquarter to exhibit how-to operation procedure for this product.

15. What are requirements for laboratory for this kind of product?

It requires sterile bottle and super cleanliness of the laboratory. The problem of carrying cell cartilage out of this hospital would not exist.

16. What type of hospitals that is suitable for this product introduction?

It should be suitable for private hospital since the cost is quite expensive and it needs patients with high purchasing power.

4.1.4 Orthopedic surgeon "T1"

1. Have you ever heard of this product?

He has heard of this product; however, it is more suitable with sport injury than osteoarthritis because the healing efficacy of this product is more suitable with sport injury than osteoarthritis. Since it is only one lesion in the cartilage, so it is more suitable with sport injury cartilage person.

2. What do you think about laboratory sterilization process?

If we send to outside laboratory, we need to destroy the leftover tissue. Moreover, the process of bringing tissue out of the hospitals must be accurate and transparent. There are many cell centers such as bone bank at Siriraj hospitals or tissue centers that collect cells from many patients.

3. What do you think about riskiness of the product?

The riskiness of the product is within acceptable range as long as you can make sure it is really sterile.

4. What do you think about potential patients?

Surgeons will normally diagnose patients with potential symptoms first, then they will be asked to go for rehabilitation. If rehabilitation cannot cure patients then patients will be sent to x-ray with computer scan to see how big is the size of lesion. Suppose lesion at cartilage is big enough then surgeons will consider using this product for operation.

5. What do you think about potential hospitals?

It will have potential in private hospitals since this product is easily trial in private hospitals more than public hospitals. Private hospitals must be interested in the product. However, I have to find the right hospitals who can treat patients with this product, or those who have lots of sport injury patients.

6. What do you think about patient reaction?

They must be tested in patients for certain amount. Suppose it has the research that can be certified its efficacy, then testing may not be needed. Yet, this must be considered case-by-case basis.

4.1.5 Orthopedic surgeon "T2"

1. What do you think about MACI?

He has not heard about it before. We must compare efficacy between the product usage and microfracture.

2. What are drawbacks of the product?

It must be many stages to use this product during operation.

3. What have you heard about the requirement of the product?

He has heard that it requires young patients.

4. What do you think about opportunity using this product in Thailand?

The product must be used in private hospitals because it can reach higher number of patients. For public hospitals, it can reach only those who has rights for treatment. The product may go to prototype hospitals first, such as Bangkok hospitals. Then after some time, other hospitals may follow this prototype hospital. Yet, those hospitals that the product approaches must have patients who have sport injury with ability to pay for the cost. The product must prove its efficacy given the cost, otherwise surgeons will not select this product to be used in human body.

5. What do you think about the laboratory?

The laboratory must be in good quality in the sense that it must be able to grow chondrocytes because chondrocytes is hard to grow.

4.1.6 Orthopedic surgeon "Phob"

1. Do you know about the product before?

He has heard about the product.

2. What kind of disease that your patients have?

Mostly, they get osteoarthritis, rarely found in sport injury. So, it is rarely to see those who get cartilage defect.

3. Suppose this product is used in the hospitals, what do you think about that?

It must have efficacy over previous other procedure, otherwise it will not be used. Moreover, the cost must not be higher than other procedure, otherwise it will not be used as well.

4. What are riskiness that you perceive?

Patients might feel frequent pain, since they must be operated twice.

5. Any other suggestion?

He has heard of other places who are doing this as well like Srinakharinwirot University and Chiangmai University. Maybe they have more information to provide.

4.2 Interview result with laboratory

4.2.1 KMUTT laboratory

1. What do you think about the product?

Since the scaffold is made from porcine, it must not have leftover inside human body, otherwise it might cause inflammation in human body. From the document, it has shown it is made from type ⅓ collagen membrane. It must not have side effect in human body.

2. What is your research about?

Callus bone is extracted from death body and cultured with chondrocytes sheet.

3. What do you think about patients who are going to use this product?

They must be sport injury patients, so the market size is quite small compared to osteoarthritis patients. The product must be developed until it is usable for osteoarthritis.

4. What do you think about drawbacks of the product?

It might cause pain to patients twice since we have to operate twice.

5. What do you think about laboratory location?

It must be outside hospitals, so the model should be central laboratory. The laboratory must have GMP approval. Yet, the concerns are high capital requirement, need some number of customers and logistics. Also, high cost for technician employment, chemical using inside laboratory and quality control cost. To

reduce total cost, it must be large scale production in order to gain economy of scale. Comparing with laboratory setting up in hospitals, the regulations might be less, however it still requires technician to operate in the laboratory. The laboratory must show timing, especially for the biopsy.

6. What do you think about using stem cell for treatment of cartilage defect?

In Thailand, scientist uses injection approach to insert stem cell inside cartilage defect. Yet, there is no guarantee that stem cell will differentiate itself to be chondrocytes.

7. What do you think about clinical trial for the product?

It must use 2 years for clinical trials and 3 years for follow up year. The sample size of patients must be 50-60 patients which is quite high.

8. Do you know the cost of current treatment procedure?

The current treatment procedure would be roughly 100,000 baht - microfracture.

Currently, for sport injury patients will be treated with microfracture and mosaicplasty.

9. What do you think about market trend?

She thinks people are more concerned about health, they go for sport more nowadays. So, people may get sport injury more easily.

10. What do you think about way to import this product?

Patent of the product from headquarter may be bought and brought to be used in hospitals.

11. What do you think about FDA approval process in Thailand?

It may take long time for Thai FDA to approve because no one has asked for approval from Thai FDA before using cell therapy product. Since the product is the first product asking for approval from FDA, it may take some time to proceed because regulator may not be familiar with this type of product.

4.2.2 Stem-Cell laboratory

1. What is your specialization?

She is specializing in research of stem cell. Stem cell that is used is from amnion. Normally, it will be thrown away, however we realize that we can make use of it. Now, she is focusing on using stem cell to cure cartilage defect but currently she is seeing better way to cure cartilage defect. Because it has been proved that stem cell cannot perfectly cure the cartilage defect. Since stem cell has no structure in itself and it tends to change according to surrounding cells, so when injecting stem cell it might not grow up to be chondrocyte as we expect and it might change into other types of cell which we cannot control that kind of result. She is trying to find other ways to solve the problem of not being able to use stem cell to cure cartilage defect. She mentioned that stem cell can be used to cure osteoarthritis but not in sport injury because for sport injury, it requires replacement of a piece of cartilage.

2. Do you know the product?

She mentioned that she does not know beforehand what is the product. Because she is currently conducting stem cell research.

3. What do you think about the product?

The product is good but it is made from pig, so her concern is that it might cause trouble to patients because it is non-human tissue. She worries that human body might reject the porcine scaffold. In case that human organ does not reject, it may not yield the best result as it might not be compatible with the cartilage. Moreover, surgeons have to operate twice, first is biopsy and second is inserting chondrocytes cultured on scaffold back to where it defects, thus it may not be convenient for surgeons and operation riskiness may increase.

4. What do you think about opportunity using the product in Thailand?

She thinks the product is suitable to use in private hospital. Since it is kind of fancy product. In her opinion, it is not good to cut cartilage from patient because in the future there may be more defect or lesion in those areas and it might

cause further fracture for the whole cartilage. She thinks that it might not cause interest to public hospitals since it may cause more complex surgery process than previous standard, the difficulty of setting up laboratory in the hospital or as a central laboratory. Generally, surgeons will treat patients with conservative first, meaning that they will try not to bring patients to operation, unless other alternatives are not effective, then they will go for operation. Otherwise, it would cause troublesome and pain to patients. For public hospitals or university hospitals, it may cause burdens to them because the product cannot be proved to have better success rate than other alternatives. Then, those hospitals will not consider because it may cause ineffectiveness and highly unnecessary cost. She also mentioned that public hospitals try not to increase steps or processes for operation due to cost, number of patient rooms available, manpower and capacity of surgeons and total hospital costs. Normally, public or university hospitals tend to reduce cost and time consumption as much as possible and they might not be interested in complex or fancy product. On the other hand, private hospitals tend to use effective product which can treat patients effectively, regardless of price or cost incurred.

5. What do you think about setting up the product laboratory in Thailand?

She said that it might not be attractive to public hospitals to setting up laboratory because it causes high cost. In addition, many hospitals are conducting substitute products such as stem cell or using distilled cadaver bone and chondrocyte culture on the distilled cadaver bone. She thinks that those hospitals may not be interest and they have to ask for authorization such as ISO and GMP. Unless I talk to private hospitals, they might be interest because it is a fancy product (in her view), they might decide to use the product much easier than public hospitals.

6. Are you interested in partnership with us as a laboratory who carry the product outcome?

She said that it might not be her specialization. She is also not interested in this field of the product. Equipment and materials in her lab are used for

stem cell experiment specifically, thus it would not be proper to use her lab as a recipient or pilot test for this project.

7. Can you compare the treatment effectiveness by using the product and stem cell?

Stem Cell is much better in terms of efficacy but she has never used the product MACI before, so she cannot tell whether it is much better. Since stem cell is from patient's cell body, it might be better because there is no antigen to body. However, this is just opinion, you have to prove it.

4.3 Interview result with health tech venture capital

4.3.1 Ruckdee

1. What are criteria that you are going to give fund to health startups?

It must be impact funding. That means the impact of health startups or products is spread to people and society. The project should not oppose the regulation. In addition, the startups should have concrete business plan that shows self-sustained business meaning that the business can earn profit and use profit to reinvest in itself. To show concrete business plan, it must include ability of the product to be sold at competitive price, cost, business idea. This is suggestion for startups at scaling stage. For the beginning stage, it needs NRCT, STI or TCELS to do preclinical and clinical trials.

2. What are your concerns?

The market size must be possible. In the future, there must be many people play sport, so the chance of having more sport injury people would be higher. Hence, the market size would be possible. Yet, the product must be cost effective and higher efficacy compared to existing product.

4.4 Interview result with pharmacist

4.4.1 Pharmacist

1. Can you tell the process of bringing medical equipment to the hospitals in the view of private medical company?

First, you have to define who are your competitors in the same range, market price and then the company can offer product price to the hospitals. To see market price, you need central price from Thai FDA to quote as reference price. For the offering price, the hospital will look for efficacy, price and Thai FDA approval. For the target group, the company must define what kind of doctors will be customers and in which hospitals. After that, the company must contact the doctors and submit relevant documents to them. Then the doctors will propose the proposal from the company to board meeting in the hospitals which will be held once a year for bringing new medical equipment to the hospitals.

2. Can you tell the process of bringing medical equipment to the hospitals in the view of doctors (users/customers)?

The doctors will send documents made by the product company to the hospitals, then the board meeting will ask the pharmacist to prepare information in terms of price, cost and product comparison with other brands. The selling price will base on agreeable price between hospitals and the company. The hospitals will consider cost effectiveness, number of patients that can use the product and price. This process is for public hospitals. But the process for private hospitals may be less complicated. If the private hospitals want to buy or use, they can buy according to their need.

3. Suppose the product is high price, will they buy?

The hospitals will buy case by case, if the product is needed for specific type of patients. The public hospital will buy if the doctor requests to use this product for specific disease.

4. What do you think about selling strategy of the product?

The company should approach the hospitals with high number of orthopedic patients such as Pramongkutklao hospital or Siriraj hospital. The representative of the company should approach potential orthopedic doctors and give sample product to use in specific patients. Key success is to give to the doctor that has patients for this product. After that, doctor will bring the medical equipment to board meeting of the hospitals.

5. Can you tell the process of giving training to the doctors?

Since the product is innovative, so the company needs to invite experts from head quarter or moderators which is the doctor who is the supreme positions in the medical schools, so that everyone follows him. The moderator can say about product, real usage case and medicinal property in order to attract other doctors to follow. This workshop or event can be held according to each hospital areas. The company can start from the medical schools or soldier medical school and spread to other hospital areas.

4.5 Interview result with Thai FDA expert

4.5.1 Thai FDA expert

1. What do you think about the product?

It must be defined in what type of medical material it is in the FDA category. Before bringing the medical material into the hospital, the company must have certificate of analysis and Thai FDA approval to show to the hospital.

2. FDA approval process in Thailand?

First, defining the category of the product and submit document to CSDT. Usually, Thai FDA listens more to EU medical approval side. The company should approach the doctor who conducts research about this product to set up protocol, then running pre-clinical test in mouse and clinical test in human beings. It will take 3-5 years to complete the process if the company has to run clinical trial. Yet, if the

product is already conducted the research, the result can be brought to Thai FDA to shorten the process. It may take less time, maybe only one year. Thai FDA will look for quality, safety and efficacy. The process for conducting product experiment in the first phrase may find funding from national science technology and innovation policy office.

3. Process to set up the company?

First, the company must be set up and register with DBD. Then, the company needs to ask permission from Thai FDA.

4. Suggestion for this product?

The product must be listed on national list of essential medicines in order to be sued by public hospitals. Key doctors must bring this to the hospital usage. Yet, if it is not listed on national list of essential medicines, the product must prove its efficacy over other brands given the price. In addition, the product can be used in specialized hospital, such as gene therapy hospital, holistic clinic or private hospital for specific patient. It may be imported case by case basis. The product may be used in Thailand and other countries, if we export to other countries.

5. What do you think about asking doctors to use it?

First, the product must be presented to the doctors who are going to have cases related to the product, then reminding doctors to use it frequently, until he asks the document from the company to be submitted in the hospitals. The product must solve pain point of doctors, patients and hospitals.

CHAPTER 5
CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion on stakeholders

5.1.1 Orthopedic surgeons

They are willing to use this product as long as the operation procedure is not too complex and not harder than previous surgical procedure. However, the product must prove its efficacy over other product or method. The riskiness of operation would be on average, yet the patients must be under operation twice, so it might cause pain to them.

5.1.2 Hospitals

Private hospitals might be more interested in this product since its cost is quite high. In addition, the process of bringing this product to public hospitals might be long. The specialized clinic or cell therapy hospitals might be interested in this product. Suppose if we want to bring this product to public hospitals, it should be listed on national list of essential medicines. In case of public hospitals, it needs to be first expanded to medical schools and soldier medical schools because they have lots of knee injury patients.

5.1.3 Suppliers

The product company should find capable laboratory to operate this. Many laboratories are doing their own research, so we may find those who are willing to corporate with us in order to produce. However, comparing other medical procedures, there is not much evidence to support that other procedures are more successful than this procedure. Others are doing the stem cell and callus bone from dead body. Both are in pre-clinical trial using animals during preclinical test.

5.1.4 Venture capital

Ruckdee is the health tech startups venture capital. They will give fund to those who are in scaling stage. For the preclinical and clinical trials, the company may need some other sources of fund such as STI, NRCT and TCELS.

5.1.5 Thai FDA

First, the product must belong to the company. Then, the company must be registered with DBD. Then, the product must ask approval from Thai FDA. The product must have research or clinical trial already. For this process, it needs 2-3 years for the clinical trial. However, if the product is imported and conducted the research already, it will shorten the time for Thai FDA approval. After having conducted the research, we can submit this to FDA to be reviewed by specialists or surgeons who have expertise in this field. Total time consumption would roughly be 1 year.

In the perspective of pharmacist, the process of bringing new medical material to the hospitals will take place once a year. However, with this new type of innovation, the medical dealer must go to the doctors or specialists in order to get them approved with the product first. Then, when the doctors approve this new product, the doctors will bring this product into board of directors of the hospitals in order to get the committees approved. Given this process, the product must be listed on Thai FDA already. For the inauguration, the new product like this might be introduced by medical professors who can influence other young physicians. In addition, medical professors might be able to tell their experience based on what they have done with in the treatment so far. This event can be held like workshop which can be started from medical schools at the beginning and spreading to other parts of Thailand. The beginning hospitals might be those who get lots of injured people in sports and accidents when it comes to sale strategy.

5.2 Suggestion

5.2.1 Location/Place

The location that we will sell the product will be based on case by case basis. Since the product is for injured people from sport or accident, it might be more suitable to let the doctor order by order. This strategy can go to public hospitals. Moreover, the starting points should be hospitals with these two kinds of patients in high number such as Soldier hospital or medical school with high number in sport or accident injury. Another approach is to go to private hospitals because they will be interested in this kind of product, given any price with higher efficacy compared to previous surgery methods. The last one is to go for specialized clinics who are specialized on cell therapy because they will be more interested in this product since it uses autologous chondrocytes from the patients themselves.

5.2.2 Procedure to sell this product

Before being able to sell the product, the product must belong to a company. Then, the company registers with DBD and then asking approval from FDA. Before taking approval from FDA, the product must already have supported medical research that can show its efficacy. Otherwise, the product must have research doctors to conduct the supported medical research in order to have protocol, toxicity, preclinical and clinical test. Approval from FDA alone after having supported medical research of the product is approximately one year.

5.2.3 Approximate cost for laboratory and operation per 1 case

Estimated cost per 1 case patient MACI					
Chondrocyte 500,000 cells per cm^2 on a resorbable type I/III collagen membrane					
Items	**Size**	**Price (Foreign currency)**	**Price (Baht)**	**Price/ml (Baht)**	**Cost per one time**
DMEM/F12	6*500 ml	$140.19	4678.08	1.56	38.98
pronase solution	5 g	SGD952.35	23557.14	4711.43	4711.43
collagenase P solution	100 mg	SGD952.35	3376.44	33.76	844.11
trypsin-EDTA	100 ml	SGD74.45	1841.58	18.42	460.40
FBS	500 ml	$500	16684.80	33.37	834.24
PBS	6*500 ml	$79.73	2660.56	0.89	22.17
Nutridoma-SP	100 ml	SGD19115.83	1200.00	12.00	300.00
		34658			7211.33
Related Equipment					
Items	Size	Price (Baht)	Price/Items (Baht)	No. of Items used	Total cost (Price/Item*No.)
tube 15 ml	500 tubes	4,280.00	8.56	6	51.36
superspeed tube	50 tubes	14,980.00	299.60	2	599.20
ultracentrifuge tube	50 tubes	22,470.00	449.40	2	898.80
flask 75	100 flasks	5,157.40	51.57	2	103.15
eppendorf 5 ml	500 tubes	3,798.50	7.60	3	22.79
eppendorf 1.5 ml	500 tubes	428.00	0.86	7	5.99
syringe filter 0.22 um	50 pieces	2,700.00	54.00	1	54.00
syringe filter 0.1 um	50 pieces	3,300.00	66.00	1	66.00
tip 1000 ul/rack	1 rack	224.70	224.70	1	224.70
tip 200 ul/rack	1 rack	160.50	160.50	1	160.50
					2186.491

Items	Number	Price/Item	Total Cost
Centrifuge tube 15 ml	2	9.00	18.00
Centrifuge tube 50 ml	6	10.70	64.20
Serological pipette 10 ml	8	10.00	80.00
Serological pipette 5 ml	2	9.00	18.00
Tip 1000 µl	5	2.25	11.25
Tip 200 µl	2	1.67	3.34
Tip 10 µl	2	1.67	3.34
Flask 75 NT	15	51.57	773.61
Flask 75 T	1	39.59	39.59
syringe filter 0.22 um	2	54.00	108.00
Syringe 20ml	2	11.40	22.80
syringe filter 0.45 um	2	54.00	108.00
			1250.13
Staffs (Master Degree)	8400	2.65/min	22,260.00
			22,260.00
Electricity Cost	Time	Unit	Total Cost
Centrifuge 760 W, 5 mins/times, 3 times	0.25 hour	0.19	0.26
Cabinet 2,200 W, 100 mins/process	1.67 hour	3.67	4.99
CO_2 Incubator 380 W, 24 hours/times, 4 days	96 hour	36.48	78.40
			83.6501

Tools	Number of Hours	Price	Price/No. of Hours in Five years	Total Cost
Centrifuge	0.25	200,000.00	4.57	1.14
Cabinet	1.67	176,500.00	4.03	6.73
Coulter counter	2	52,056.58	1.19	2.38
Microscope	2	408,777.60	9.33	18.67
Aspirator	3	66,426.10	1.52	4.55
CO2 Incubator	96	640,000.00	14.61	1402.74
				1436.203
Material				
Rubber Gloves	3	2.785	8.36	
Mask	3	1.4	4.20	
			12.555	
		Total Cost	**34,440.36**	

*electricity cost calculation no. of electricity unit = (W/1000) x no. of electric appliance x hours

**Electricity rate is based on government rate

Electricity Unit	Electricity cost (Baht/Unit)
First 10 units (0-10)	1.3576
unit 11 th onward	2.4482

Cost per one case operation

Items	Size	Price (Baht)	Cost per one case
MRI Bone/Joint/Extremity 1 part	1 times	8,900.00	8,900.00
Room, special type	4 nights	600.00	2,400.00
General Anesthetic (GA), first hour	2 times	900.00	1,800.00

General Anesthetic (GA), following hours	4 hours	700.00	2,800.00
Blood during operation	2 units		1,700.00
Operation cost (Biopsy)	1 times		90,000.00
Operation cost (Implant)	1 times		100,000.00
Resurrection	2 times	900.00	1,800.00
Total Cost for operation			209,400.00

Hence, total estimated cost would be 34,440.36+209,400.00 = 243,840.36 Baht. This is an estimated cost, so it might differ from this number. In addition, the best proxy price with this product is microfracture operation price which is not available on source.

5.2.4 Capital Funding

For the first stage, in the experimental stage, the product may find funding from the research support funding of Thailand like TCELS, NRCT and STI because it suits with beginning stage of pre-clinical trial and post-clinical trial but after the product has been conducted experiment and reliable research has been published, now they will be more ready to ask for approval from Thai FDA and be likely to be commercialized. At this initial stage of commercialization, with solid business plan, the product can be pitched to find other source of fund such as Ruckdee or other venture capitals who are interested in this kind of product or health startups.

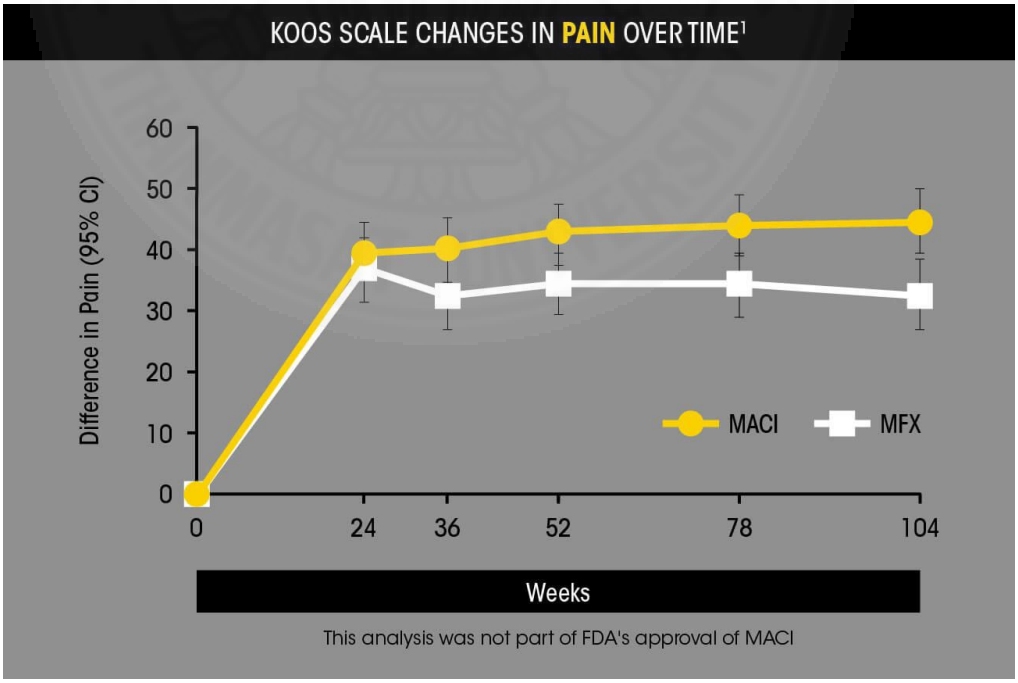
5.2.5 Efficacy

The American Journal of Sport Medicine, they mention about "Matrix-Applied Characterized Autologous Cultured Chondrocytes Versus

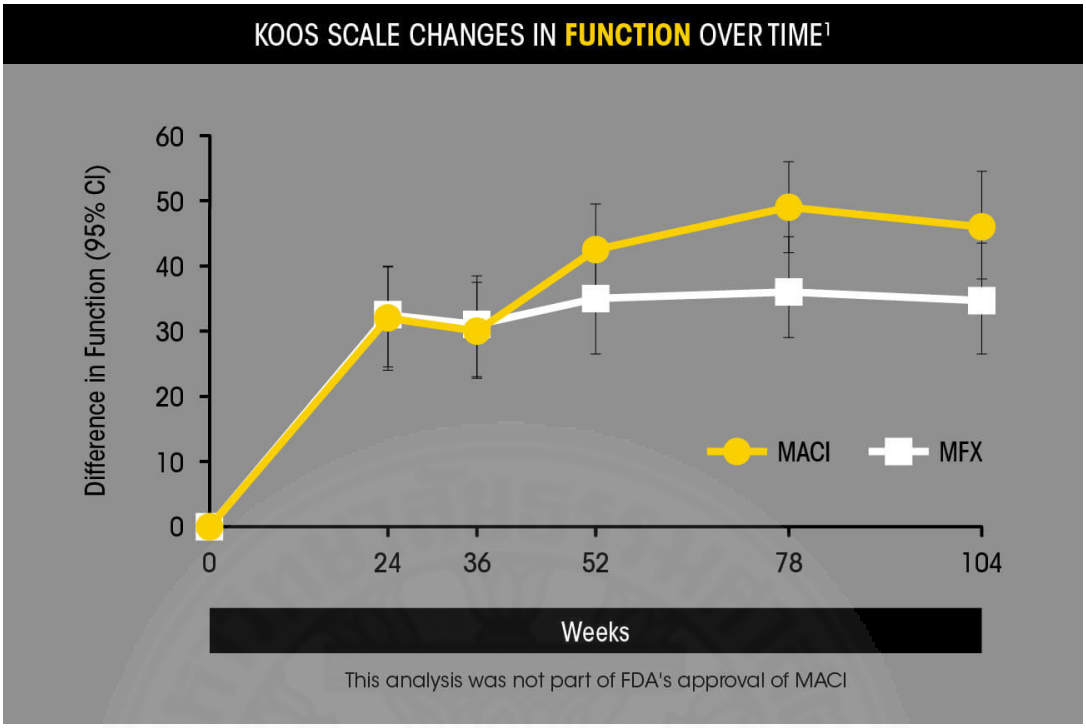
Microfracture" experiment. So the background is that "Randomized controlled trials studying the efficacy and safety of matrix-applied characterized autologous cultured chondrocytes (MACI) versus microfracture (MFX) for treating cartilage defects are limited". The purpose is "to compare the clinical efficacy and safety of MACI versus MFX in the treatment of patients with symptomatic cartilage defects of the knee". Their conclusion is that "the treatment of symptomatic cartilage knee defects 3 cm2 in size using MACI was clinically and statistically significantly better than with MFX, with similar structural repair tissue and safety, in this heterogeneous patient population. Moreover, MACI offers a more efficacious alternative than MFX with a similar safety profile for the treatment of symptomatic articular cartilage defects of the knee".

Pain and Function

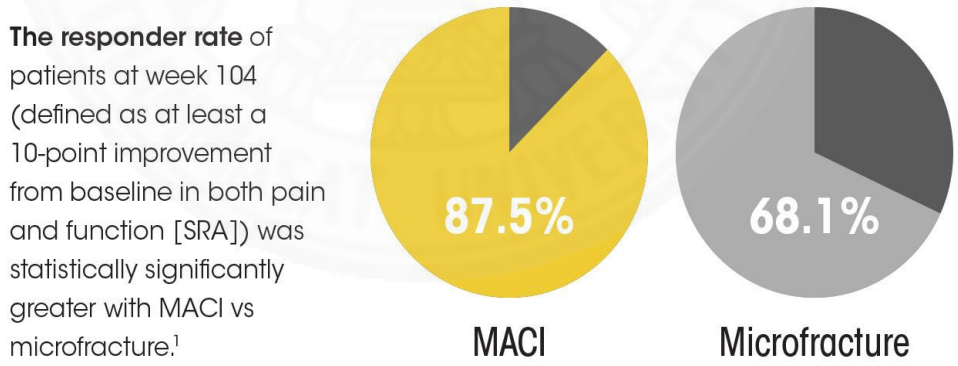
The product implant demonstrated statistically significantly greater improvement in both pain and function than microfracture at 2 years as shown in the graph below.



KOOS (Knee Injury and Osteoarthritis) showing that the product MACI is much better in terms of difference in pain compared to microfracture when time goes by.



KOOS (Knee Injury and Osteoarthritis) showing that the product MACI is much better in terms of difference in function compared to microfracture when time goes by.



Note. From *MACI*. (2017). *Maci.com*. Retrieved 14 August 2017, from http://www.maci.com/healthcare-professionals/the-maci-story/clinical-results.html

5.2.6 Training to orthopedic surgeons

The company can send surgeons to be trained in the US. This practice will give them incentives in order to be interested in this product more. In addition, they can directly learn from experts in this field. Another approach is to held events inviting our target groups such as medical schools or soldier medical schools who have lots of patients who got injured with sports or accidents with cartilage and inviting moderator from the headquarter to provide knowledge to surgeons or inviting medical professors who are specialized or familiar with the product already, then let them give medical information of the product, real case operation, efficacy, post-treatment result and the innovation itself. Telling overall story from honorable medical professor, other professors or surgeons who are unfamiliar with the product will trust this product more and be willing to use this product as the result shown to the public by medical professors. Yet, the problem is that the company must prove its efficacy over other procedure in order to gain customers' trust (surgeons) before they come to use this product, otherwise they will not change to the new one

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