Proceedings of the 2017 Industrial and Systems Engineering Conference
K. Coperich, E. Cudney, H. Nembhard, eds.

Patient Decision Making for Traditional Vs. 3D Printing-Based Meniscus Transplantation

Abstract ID: 2503

Zimeng Zhang[1], Shiren Wang[1*]
[1]Department of Industrial and Systems Engineering, Texas A&M University
College Station, TX 77843
Corresponding Authors: Email: S.Wang@tamu.edu

Abstract

Every year about 1.5 million people have surgery to treat meniscal tears across the US and Europe. Traditionally, meniscus transplantation is the primary treatment in the long term. 3D printing is a substitute to the traditional transplantation method. With its previous contribution to tooth crowns, hearing aids and other life science industries, 3D printing has shown to be successful. In this article, we would like to investigate the feasibility of adopting 3D printing on meniscus in terms of supply chain cost and patient cost. We use data collected from online resources, literature citations and making assumptions where necessary. The analysis is carried in two directions: first, cost models for traditional transplantation and 3D printing-based transplantation in patients' perspective are developed. Second, a hypothesized pathway model is created to analyze post-transplantation cost and risk for patients. Simulation based on the pathway model will be done to estimate parameters of the model. Meanwhile, we use a Markov model to study the potential post-transplantation risks which may induce additional cost to patients. Our results will help hospitals in making decisions on the introduction of 3D printing systems.

Key Words
Meniscus transplantation; 3D printing-based transplantation; cost analysis; decision making

1. Introduction:

Meniscus is a wedge-shaped piece of cartilage that plays an important role in knee function and provides joint congruency, shock absorption, load distribution, and stability [1]. Every year about 1.5 million people have surgery to treat meniscal tears across the US and Europe [2-5]. Meniscus treatment includes removing, repairing as well as transplantation of discoid meniscus, among which transplantation is the favored treatment because it can reduce pain and improve function more effectively and prolong the time of entering to the period of Total Knee Arthroplasty (TKA) [1]. Though meniscal allografts transplantation is the ideal option, this treatment has the limitation of shortage of donors, the risk of disease transmission and failures caused by donor-recipient shape mismatch. In the view of supply chain management of the meniscus transplantation system, the complicated operation procedures which involve meniscus allocation, procurement, testing, and transportation has the potential of increasing the surgery cost on patients.

The advent of 3D printing technology provides a promising solution to conquer the current problem encountered in the allograft transplantation. This technology can be used to manufacture artificial meniscus. One advantage regarding 3D bioprinting is that the complicated and customized geometries can be fabricated which solves matching problem in traditional transplantation [6-10]. With 3D-printing, the matching problem can be interpreted as a parameterization of patients' meniscus, surrounding bones and soft tissues. With the measurements exactly taken from the recipient, a 3D printable model of meniscus can be produced which will fit the patient's knee joint perfectly. To solve the parameterization problem, A.C.T.Vrancken et al. [11] give a geometry analysis of medial meniscus. In this article, the donor based transplantation cost and the estimated 3D printing-based meniscal prostheses cost will be studied and compared from patients' perspective.

Donor based meniscal transplantation, which is also called meniscal allograft transplantation, is a traditional method to deal with meniscus injury. We refer to [12,13] as comprehensive reviews of this method. The costs, success rates and long-term follow-ups of donor based treatment are mentioned in [1, 14-20]; among them, [1] studies the cost effectiveness of meniscal allograft transplantation and partial meniscectomy; [16] conducts a survey of American Association of Tissue Banks; [17] studies the survival probability and reoperation probability of meniscal allograft transplantation using a 2-year follow-up.

However, donor based meniscal transplantation have faced with great challenges nowadays, including increasing costs and long waiting periods. For the meniscal allograft implant, it had increased 490% in the year of 2007 [16] in comparison with the cost of average $643 in 1996 [14]. Latest data [1] shows a price of $4750 in the year of 2014. The cost of meniscal allograft implant is still increasing with the growing competency, and the waiting time for the suitable meniscus will also be increased. In 2004, 1400 meniscus transplantation was performed with an estimated 4-week waiting period [16]. 3D printing technology is a potential solution to deal with these challenges.

3D printing has been broadly used in printing human tissues [21]. However, among numerous number of studies on applications of 3D printing, very few have mentioned the issue of cost. In [22], a method of fabricating low cost soft tissue prostheses with desktop 3D printer is provided, where the cost of fabricating ear prosthesis can be as low as $30. This indicate the promising future of applying 3D printing technology in meniscal treatment.

The proposed research will conduct a comprehensive cost and risk analysis while the risk has been transferred in the form of cost for the traditional donor-based meniscus transplantation. Meanwhile, the estimated cost of 3D printing-based meniscus is also studied. All the data used in both analysis is collected from a variety of online sources, including literature citations.

2. Model and Methods:

In this work, a decision analytic Markov Model is generated to evaluate the cost of traditional meniscus transplantation treatments as well as the cost of 3D printing-based transplantation treatments in patients' perspective.

- Decision Analytic Model

A decision analytic Markov Model is generated by studying the procedure of meniscal allograft transplantation of a symptomatic, torn discoid lateral meniscus. Four states are introduced in this model, which are specified as "No Issue (NI)", "Need Repair (NR)", "Need Reoperation (NRO)" and "Need Total Knee Arthroplasty (NTKA)". NTKA is the most severe state a patient can be, where Total Knee Arthroplasty (TKA), a surgical procedure that replaces part of the knee joint, need to be performed. The initial state of the model is defined as NI immediately after the meniscus allograft surgery. Then the state will transfer to next state depending on the occurrence of different actions.

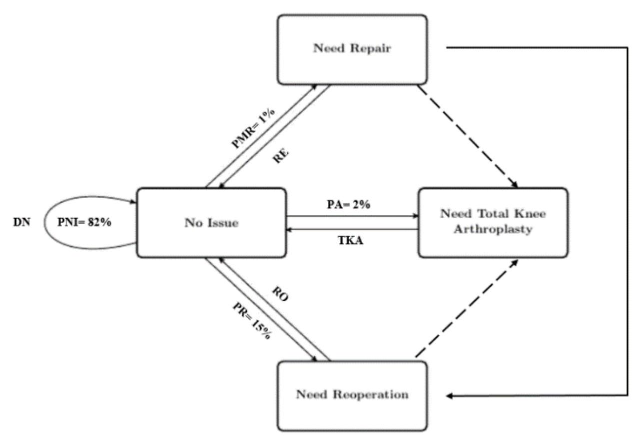

Figure 1. State Transition Diagram of the Designed Markov Model

These actions include "Repair (RE)","Reoperation (RO)", TKA and "Do Nothing (DN)", which again lead to one of four states NI, NR, NRO or NTKA. NI, NR are determined as intermediate state.NTKA is referred to as the "final" state, where TKA need to be performed with a considerable cost; after TKA, the patient enters state NI and stays NI for the rest of years simulated, and no further costs will be associated. On top of these transitions, one assumption is made in this model: the intermediate states are restricted to occur at most three times prior to proceeding to the final NTKA state. This assumption makes the survival rate of the implants close to the data in the literature.

Risk analysis is also conducted in this work which has been transformed to treatment costs. Treatment costs are treated as the primary outcome for the model. It varies when patients enter different states. Even the patient ends at the same final state, the cost varies for different pathways after the surgery for each patient. In this case, probability of transition is introduced into the model. Probabilities are considered for each transition period as “Annual Probability of Meniscal Repair (PMR) after meniscal allograft”, “Annual Probability of Arthroplasty (PA) after meniscal allograft”, “Annual Probability of Reoperation (PR) after meniscal allograft” and “Annual Probability of ‘No Issues’ (PNI) after meniscal allograft”. For each patient, we take a 20-year timespan with a 1-year cycle length to simulate the final treatment cost. We simulate 10,000 patients’ pathways after the meniscus transplantation and calculate the average treatment costs as our resul

Item	Cost	Range
Meniscus Allograft Transplantation Operation Fee	$8,880	$100-5000
Reoperation Procedure Fee	$1,770	-
Repair Procedure Fee	$2,760	-
Total Knee Arthroplasty Procedure Fee	$14,167	-

Table 1: Input Parameters Definitions and Values for the Markov Model of Traditional Meniscus

The data collected in this article is from a variety of online sources. The values of costs are from Austin J. Ramme ’s work [1]. The probability values are integrated from different works [1, 13, 17]. For the inputs in Markov Model, the total cost has been divided into four subjects, which include meniscal allograft transplantation fee, reoperation fee, repair fee and total knee arthroplasty fee. In each subject, the cost consists of two or three subdivisions including therapy and operation fees. Meniscal allograft implant cost is included in the meniscal

Item	Probability	Probability Used in Markov Model	Source
Probability of Meniscal Re-injury (PMR)	1%	1%	Austin J. Ramme et al. [1].
Probability of Total Knee Arthroplasty (PTKA)	0–18%	2%	Mascarenhas et al. [22], Yanke et al. [18], McCormick et al. [17].
Probability of Reoperation (PR)	2–32%	15%	McCormick et al. [17].
Probability of 'No Issue' (PNI)	71–85%	82%	Nicholas Sgaglione et al. [13].
Probability of Success Repair (PSR)	70–90 %	80%	Nicholas Sgaglione et al. [13].
Probability of Success Reoperation (PSRO)	-	100%	Assumption
Probability of Success Total Knee Arthroplasty (PSTKA)	-	100%	Assumption
Probability of Repair to Reoperation (PRR)	-	20%	Assumption

Table 2: Input Parameters Definitions and Values for the Markov Model of Traditional Meniscus Transplantation Estimated Probability (Per Patient)

allograft transplantation procedure, which is $4750 in the data [1].

According to the probabilities after allograft transplantation listed in the chart above, the transition matrix of the Markov Model is determined. In the matrix, assumptions are made for lacking of exact statistics to refer: PSRO and PSTKA is set to be 100%, whereas PRR is set to be 20%. The transition matrix of the Markov Model is shown as below:

$$\text{Transition Matrix of the Markov Model} = \begin{bmatrix} 0.82 & 0.15 & 0.01 & 0.02 \\ 1.00 & 0.00 & 0.00 & 0.00 \\ 0.80 & 0.20 & 0.00 & 0.00 \\ 1.00 & 0.00 & 0.00 & 0.00 \end{bmatrix}$$

- Preliminary Estimated Cost of 3D Printing-based Meniscus (Per Meniscus Implant)

Because 3D printing technology in the biomedical area is still developing, there remains a gap between lab fabricated 3D printing prototype and clinical application. Risk analysis can be difficult to conduct due to lack of data in literature and online sources. So, for the 3D printing-based transplantation, the cost can only be roughly estimated. The cost of 3D printing-based soft tissue prototype prosthesis are usually analyzed by means of calculating the material cost, facility cost as well as labor cost per item in the lab scale [23]. Therefore, in this paper, the cost of 3D printing-based meniscus is also calculated in a similar way.

Item	Amount	Cost	Source
Human Collagen-II	22.5 ml	$805.5	Sigma Aldrich ($268.5 1KT)
Alginate	5 g	$0.7	Sigma Aldrich ($132 1kg)
Polycaprolactone (PCL)	1 g	$0.4	Sigma Aldrich ($211.5 500g)
TGF-β I	0.1 mg	$1,076.3	VWR ($538.15 0.05mg)
Cell obtained from patients	-	$0	obtained from patients themselves
ABS	63.5 g	$0.8	Yong He et al. [31]
Acetone	10 mL	$0.1	Yong He et al. [31]
Others (container, beaker, machine, electricity and labor cost etc.)	-	$27	Yong He et al. [31]
Total	-	$1,910.8	

Table 3: Input Parameters Definitions and Values for the Markov Model of 3D Printing-based Transplantation Cost

The ingredients included in the cost analysis are decided according to the bio-structure of human meniscus and the development of tissue engineering, especially in the scope of 3D bioprinting. Collagen-II serves as the main structure in cartilages, which takes up to 59% volume of cartilage structures [23,24]. A great amount of studies has been launched on biomaterials to fabricate biomimetic cartilage including meniscus using alginate-based bioinks. Polycaprolactone (PCL) is added to the material formula to mimic extracellular matrix (ECM) in meniscus. To solve the problem of low ECM formation, transforming growth factor-β I (TGF-β I) is used to form a cartilage-like ECM structure.

For 3D bioprinting, there are two types of printing techniques. One is direct printing using the inkjet or extrusion method to fabricate the desired structure. The other relates to molding method which prints the tissue casting mold for the cartilage first. Then, the cartilage is formed by casting the bioink into the mold in suitable environment [23]. Advantages of the molding technique include precise dimension, smooth surface and strong mechanical properties; therefore, the molding method is chosen here.

The cost of each 3D printed meniscal implant is calculated by adding every component needed in the printing material preparation, listed in Table 3.

Therefore, in this work, the Model for 3D printing-based treatment is similar to donor based treatment model except for the implant cost.

3. Results and Discussion

Table 4 is the result of cost and risk analysis using Markov model. The average total cost using 3D printing based implant is $1,610 less at $13,458, compared with $ 15,068 for the donor based transplantation. Our estimated costs are calculated using the following method: Consider a single patient after a meniscal transplantation, either using an allograft or a 3D printed implant. The states this patient can be, on a yearly basis, are NI, NR, NRO and NTKA; the transition probability between the states are illustrated in Table 2. When the patient enters one of the 4 states above, a cost will be associated according to Table 1. By simulating the states of this patient for 20 years, we can calculate the total cost this patient need over the 20-year period, for meniscal transplantation and costs induced by post-operative risks. To calculate the discounted cost over 20 years, a discount rate of 3% is added.

We note here that in addition to Table 2, we allow at most 3 times of NRO or NR before TKA; that means if the number of NRO and NR states reach 3, then the next state must be NTKA. This setup is enlightened by [1], and we decide to allow 3 times instead of other numbers here because in this setup, the survival rate of meniscus implant over 5 years is 91%, and 10 years 78%, which are close to what appears in the literature.

We simulate the states and costs of 10,000 patients, and take the average of their costs, for using allograft or 3D printed implant. The results are illustrated in Table 4. A 2-sample t-test between the discounted costs shows that over 20 years, the discounted cost using allograft and using 3D printed implant are significantly different, with a p-value of $7.2064e^{-81} \approx 0$.

		Traditional Transplantation	3D Printing-based Transplantation
Discounted	Cost	\$15,068	\$13,458
	Cost Differences	\$1,610	-
Undiscounted	Cost	\$21,996	\$19,104
	Cost Differences	\$2,892	-

Table 4: Cost Analysis and Risk Analysis Results from Markov Model including 3% discounted case and undiscounted case (discounted rate 0%)

For the therapy costs, we are also short of current data for precise cost analysis. Here we make several assumptions that the costs except for the implant cost, and transition probabilities for both donor based transplantation and 3D printing based transplantation are the same; however, the cost for 3D printing-based transplantation differs from traditional treatment due to the procedure disparities like operation of donor's meniscus. Besides, the probabilities of postoperative injury, reoperation and total knee arthroplasty may change too. These increase the difficulty of the estimation of 3D printing-based transplantation cost analysis. With the increasing development of 3D printing technology as well as the development of biomedical materials, tissue engineering, 3D printing technique will turn mature in the future. Meanwhile, more detailed and thorough investigation can be conducted to give an optimal estimation of the comparative cost using the model after more clinical studies are provided in the long run. This will help patient to do the decision making between the two methods in the future.

For the supply chain, the expense of allocation office, transportation, lab testing and fees that are induced in the upper stream of the supply chain can possibly be eliminated for 3D printing treatment compared to the allograft transplantation. This can further reduce the cost for the 3D printing method of the meniscal treatment.

4. Conclusion

A Markov model has been developed to evaluate the cost of meniscal treatment. Risk analysis is also considered and integrated in the model calculated as cost per patient. An estimation of 3D printing-based meniscal implant cost is conducted to compare the difference between the two mentioned methods. The results demonstrate the cost advantage for the incoming 3D printing method quantitatively, which display the potential of this technology. With the increasing development of 3D printing technology, more precise estimation of the costs can be made using our model after more clinical studies are provided. This will better help patients to do the decision making between the two methods.

Acknowledgements

Authors acknowledge the funding support from National Science Foundation and Texas A&M Engineer Experimental Station (TEES).

References

1. Ramme, Austin J., et al. "Cost effectiveness of meniscal allograft for torn discoid lateral meniscus in young women." The Physician and sportsmedicine just-accepted (2016).
2. Xu, J. (2014) The Praeger Handbook of Acupuncture for Pain Management: A Guide to How the "Magic Needles" Work, Praeger, Santa Barbara, CA.
3. Sgaglione, N. A., Steadman, J. R., Shaffer, B., Miller, M. D., and Fu, F. H. (2003) "Current Concepts in Meniscus Surgery: Reaction to Replacement", The Journal of Arthroscopic and Related surgery,19(10):161-188.

4. Noyes, F. R., Heckmann T. P., and Barber-Westin, S. D. (2012) “Meniscus Repair and Transplantation: A Comprehensive Update”, J. Orthop. Phys. Ther., 42(3):274-290.
5. Hutchinson, I. D., Moran, C. J., Warren, R. F., and Rodeo, S. A. (2014) “Restoration of the Meniscus:Form and Function”, American Journal of Sports Medicine, 42(4):987-998.
6. Guo, N., and Leu, M. C. (2013) “Additive Manufacturing: Technology, Applications and Research Needs”, Front. Mech. Eng., 8(3):215-243.
7. Huang, Y., and Leu, M. (2014) Frontiers of Additive Manufacturing Research and Education, University of Florida, Gainesville, FL.
8. Scott, J., Gupta, N., Weber, C., Newsome, S., Wohlers, T., and Caffrey, T. (2012) Additive Manufacturing: Status and Opportunities, Science and Technology Institute, Washington, DC.
9. Gardan, J. (2015) “Additive Manufacturing Technologies: State of the Art and Trends”, International Journal of Production Research, DOI: 10.1080/00207543.2015.1115909.
10. Petrovic, V., Gonzalez, J. V., H., Ferrando, O. J., Gordillo, J. D., Puchades, J. R. B., and Griñan, L. P. (2011) “Additive Layered Manufacturing: Sectors of Industrial Application Shown through Case Studies”, 49(4):1061-1079.
11. Vrancken, A. C. T., et al. "Variation in medial meniscus geometry: size or shape based." Transactions of the annual meeting of the Orthopaedic Research Society. Orthopaedic Research Society, 2012.
12. Noyes, Frank R., Timothy P. Heckmann, and Sue D. Barber-Westin. "Meniscus repair and transplantation: a comprehensive update." Journal of Orthopaedic & Sports Physical Therapy 42.3 (2012): 274-290.
13. Sgaglione, Nicholas A., et al. "Current concepts in meniscus surgery: resection to replacement." Arthroscopy: The Journal of Arthroscopic & Related Surgery 19.10 (2003): 161-188.
14. Lewis, Paul B., et al. "Multiple freeze-thaw cycled meniscal allograft tissue: A biomechanical, biochemical, and histologic analysis." Journal of Orthopaedic Research 26.1 (2008): 49-55.
15. Oro, Fernando Barrera, et al. "Autograft versus allograft: an economic cost comparison of anterior cruciate ligament reconstruction." Arthroscopy: The Journal of Arthroscopic & Related Surgery 27.9 (2011): 1219-1225.
16. Vangsness, C. Thomas, et al. "Soft tissue for allograft reconstruction of the human knee: a survey of the American Association of Tissue Banks." The American journal of sports medicine 24.2 (1996): 230-234.
17. McCormick, Frank, et al. "Survival and Reoperation Rates After Meniscal Allograft Transplantation Analysis of Failures for 172 Consecutive Transplants at a Minimum 2-Year Follow-up." The American journal of sports medicine (2014): 0363546513520115.
18. Yanke, Adam B., et al. "Clinical outcome of revision meniscal allograft transplantation: Minimum 2-year follow-up." Arthroscopy: The Journal of Arthroscopic & Related Surgery 30.12 (2014): 1602-1608.
19. Macario, Alex. "What does one minute of operating room time cost?" Journal of clinical anesthesia 22.4 (2010): 233-236.
20. Chia, Helena N., and Benjamin M. Wu. "Recent advances in 3D printing of biomaterials." Journal of biological engineering 9.1 (2015): 1.
21. Martelli, Nicolas, et al. "Advantages and disadvantages of 3-dimensional printing in surgery: A systematic review." Surgery 159.6 (2016): 1485-1500.
22. Mascarenhas, Randy, et al. "Meniscal allograft transplantation: preoperative assessment, surgical considerations, and clinical outcomes." Journal of Knee Surgery 27.06 (2014): 443-458.
23. He, Yong, Guang-huai Xue, and Jian-zhong Fu. "Fabrication of low cost soft tissue prostheses with the desktop 3D printer." Scientific reports 4 (2014).
24. Rhee, Stephanie, et al. "3D bioprinting of spatially heterogeneous collagen constructs for cartilage tissue engineering." ACS Biomaterials Science & Engineering 2.10 (2016): 1800-1805.